Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

N-[4-(Azetidin-1-ylsulfonyl)phenyl]-*N*-(2,4-difluorobenzyl)acetamide

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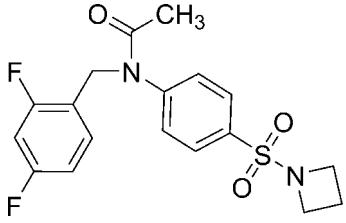
Received 30 August 2012; accepted 7 September 2012

Key indicators: single-crystal X-ray study; T = 293 K; mean σ(C–C) = 0.003 Å; R factor = 0.047; wR factor = 0.143; data-to-parameter ratio = 13.0.

In the title molecule, $C_{18}H_{18}F_2N_2O_3S$, the dihedral angle between the benzene rings is 79.40 (11)°. The 2,4-difluorobenzyl and azetidine fragments adopt a *trans* arrangement relative to the central benzene ring. In the crystal, weak C—H···O hydrogen bonds connect molecules into a two-dimensional network parallel to (001).

Related literature

For the pharmacological activity of sulfonamides, see: Song *et al.* (2007); Wang, Wang *et al.* (2010); Wang, Wan & Zhou (2010); Wang, Gan *et al.* (2010).



Experimental

Crystal data

$C_{18}H_{18}F_2N_2O_3S$
M_r = 380.40
Monoclinic, $P2_1/c$
a = 8.7793 (15) Å
b = 8.4442 (15) Å
c = 23.810 (4) Å
β = 97.312 (6)°
V = 1750.8 (5) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.23 mm^{-1}
T = 293 K
0.22 × 0.21 × 0.20 mm

Data collection

Bruker SMART CCD diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2001)
T_{min} = 0.000, T_{max} = 0.001
14668 measured reflections
3077 independent reflections
2684 reflections with $I > 2\sigma(I)$
R_{int} = 0.036

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.143
S = 1.04
3077 reflections
236 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.38 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
C5—H3···O3^{i}	0.93	2.44	3.336 (3)	162
C11—H9···O1^{ii}	0.93	2.51	3.406 (3)	162
C17—H18*B*···O1^{iii}	0.97	2.56	3.509 (4)	166

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

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: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL*.

This work was partially supported by the Specialized Research Fund for the Doctoral Program of Higher Education of China (SRFDP20110182110007), the Research Funds for the Central Universities (XDJK2012B026) and the National Innovative Training Program for College Students.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: LH5527).

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Wang, X.-L., Wan, K. & Zhou, C.-H. (2010). *Eur. J. Med. Chem.* **45**, 4631–4639.
Wang, X.-L., Wang, X.-L., Geng, R.-X. & Zhou, C.-H. (2010). *Chin. J. New Drugs*, **19**, 2050–2059.

supporting information

Acta Cryst. (2012). E**68**, o2929 [https://doi.org/10.1107/S1600536812038342]

N-[4-(Azetidin-1-ylsulfonyl)phenyl]-*N*-(2,4-difluorobenzyl)acetamide

Jian-Mei Lin, Jia-Wen Li and Jing-Song Lv

S1. Comment

Sulfonamides were extensively employed as effective antimicrobial agents for the prevention and cure of bacterial infections in humanbiological systems as early as 70 years ago, and recently have aroused considerable interest in biology and medicine for their diversified pharmacological activities including antibacterial, antifungal, antiviral, antitumor, anti-inflammatory and as carbonic anhydrase inhibitors (Song, *et al.*, 2007; Wang, Wang *et al.*, 2010). Our interest is to develop novel sulfonamide derivatives as antimicrobial agents and some structrally related sulfonamides have been reported as bioactive agents (Wang, Wan & Zhou, 2010; Wang & Gan *et al.*, 2010). Herein, we report the crystal structure of the title compound (I).

In the molecule of (I) (Fig. 1) the dihedral angle between the two benzene rings is 79.40 (11)°. The 2,4-difluorobenzyl and azetidine fragments adopt a trans arrangement relative to the central benzene ring. In the crystal, weak C—H···O hydrogen bonds connect molecules into a two-dimensional network (Fig. 2) parallel to (001).

S2. Experimental

A suspension of *N*-(4-(azetidin-1-ylsulfonyl)phenyl)acetamide (0.8 g, 3.0 mmol) and potassium carbonate (0.5 g, 3.6 mmol) was stirred in acetonitrile (30 mL) at 343 K. After half an hour, 1-(bromomethyl)-2,4-difluorobenzene (0.6 g, 3.0 mmol) was added, and the progress of the reaction was monitored by TLC. Upon completion, the reaction was extracted with chloroform (3 × 20 mL). The filtrate was concentrated and then directly purified by chromatographic column (petroleum ether/ethyl acetate) to afford the title compound (I). A crystal suitable for X-ray analysis was grown from a solution of (I) in a mixture of acetone and ethyl acetate by slow evaporation at room temperature.

S3. Refinement

H atoms were placed at calculated position with C—H = 0.93 Å (aromatic), 0.97Å (methylene) 0.96 Å (methyl). The U_{iso}(H) value was set equal to 1.2U_{eq}(C) or 1.5U_{eq}(C_{methyl}).

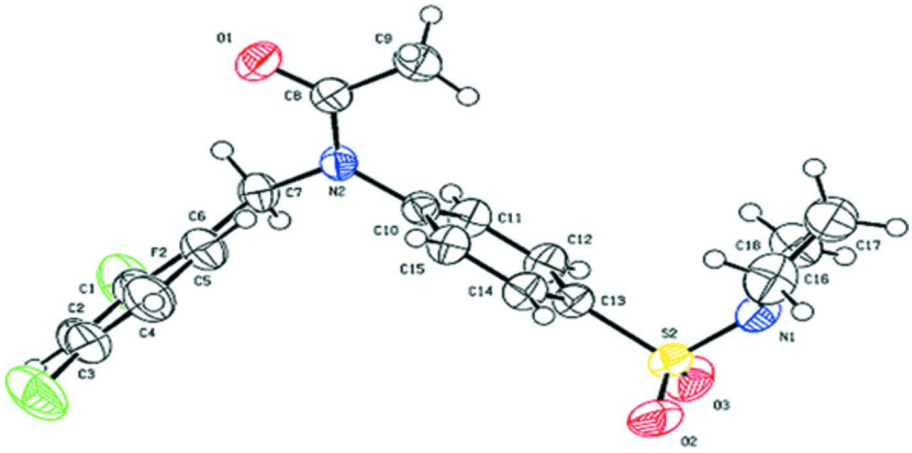

Figure 1

The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

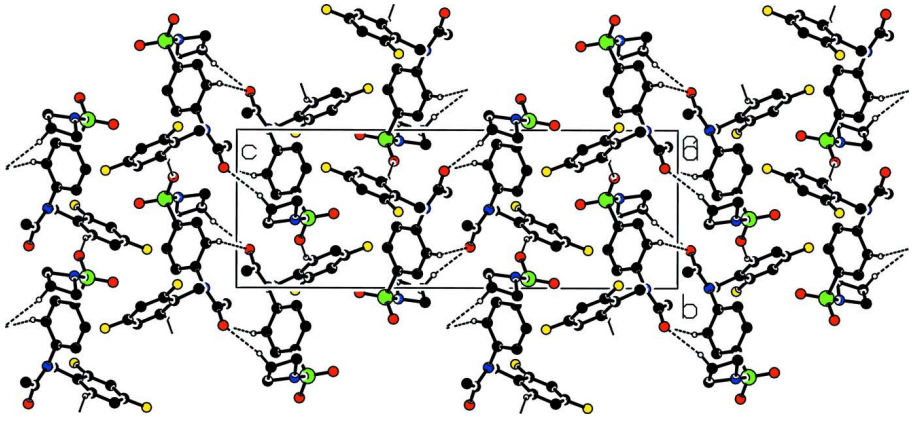

Figure 2

Part of the crystal structure with hydrogen bonds shown as dashed lines.

N-[4-(Azetidin-1-ylsulfonyl)phenyl]-*N*-(2,4-difluorobenzyl) acetamide

Crystal data

$C_{18}H_{18}F_2N_2O_3S$
$M_r = 380.40$
Monoclinic, $P2_1/c$
Hall symbol: -P 2ybc
$a = 8.7793\ (15)$ Å
$b = 8.4442\ (15)$ Å
$c = 23.810\ (4)$ Å
$\beta = 97.312\ (6)°$
$V = 1750.8\ (5)$ Å^3
$Z = 4$

$F(000) = 792$
$D_x = 1.443$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2005 reflections
$\theta = 1.3–25.0°$
$\mu = 0.23$ mm^{-1}
$T = 293$ K
Plate, colourless
0.22 × 0.21 × 0.20 mm

Data collection

Bruker SMART CCD diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2001)
T_{min} = 0.000, T_{max} = 0.001
14668 measured reflections
3077 independent reflections
2684 reflections with $I > 2\sigma(I)$
R_{int} = 0.036
θ_{max} = 25.0°, θ_{min} = 1.7°
h = −10→10
k = −9→10
l = −25→28

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.143
S = 1.04
3077 reflections
236 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
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0875P)^2 + 0.736P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.38 e Å^{-3}
Extinction correction: *SHELXL*, $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.017 (2)

Special details

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 (Å^2)

	x	y	z	U_{iso}*/U_{eq}
C1	0.6694 (2)	0.5645 (3)	0.33594 (10)	0.0447 (5)
C6	0.5341 (2)	0.5834 (2)	0.35904 (9)	0.0365 (5)
C5	0.4212 (3)	0.6715 (3)	0.32755 (10)	0.0490 (6)
H3	0.3291	0.6899	0.3419	0.059*
C4	0.4418 (3)	0.7332 (3)	0.27524 (11)	0.0597 (7)
H4	0.3647	0.7921	0.2544	0.072*
C3	0.5781 (3)	0.7056 (3)	0.25474 (11)	0.0585 (7)
C2	0.6955 (3)	0.6231 (3)	0.28413 (12)	0.0580 (7)
H6	0.7883	0.6073	0.2700	0.070*
C13	0.1006 (2)	0.1070 (3)	0.36580 (9)	0.0385 (5)
C12	0.2177 (3)	0.0895 (3)	0.41033 (10)	0.0432 (5)
H8	0.2401	−0.0099	0.4261	0.052*
C11	0.3003 (2)	0.2199 (3)	0.43111 (9)	0.0403 (5)
H9	0.3793	0.2088	0.4608	0.048*
C10	0.2657 (2)	0.3687 (2)	0.40761 (8)	0.0340 (5)

C14	0.0659 (2)	0.2550 (3)	0.34245 (9)	0.0416 (5)
H11	−0.0129	0.2661	0.3127	0.050*
C15	0.1482 (2)	0.3860 (3)	0.36341 (10)	0.0408 (5)
H12	0.1249	0.4855	0.3479	0.049*
C16	−0.2870 (3)	0.0478 (3)	0.36281 (14)	0.0658 (8)
H13A	−0.3687	0.0261	0.3324	0.079*
H13B	−0.2526	0.1567	0.3616	0.079*
C8	0.3049 (2)	0.6238 (2)	0.45767 (9)	0.0370 (5)
C9	0.1495 (3)	0.6048 (3)	0.47658 (11)	0.0512 (6)
H15A	0.1050	0.5065	0.4625	0.077*
H15B	0.0846	0.6909	0.4621	0.077*
H15C	0.1594	0.6050	0.5172	0.077*
C7	0.5160 (2)	0.5089 (3)	0.41508 (9)	0.0401 (5)
H7A	0.5562	0.4019	0.4155	0.048*
H7B	0.5774	0.5679	0.4448	0.048*
C18	−0.1690 (3)	−0.0912 (4)	0.42815 (12)	0.0616 (7)
H17A	−0.0888	−0.0364	0.4524	0.074*
H17B	−0.1762	−0.2011	0.4394	0.074*
C17	−0.3228 (3)	−0.0043 (4)	0.42063 (14)	0.0686 (8)
H18A	−0.4113	−0.0735	0.4195	0.082*
H18B	−0.3289	0.0821	0.4471	0.082*
N1	−0.1609 (2)	−0.0694 (2)	0.36736 (9)	0.0457 (5)
N2	0.35756 (18)	0.5030 (2)	0.42793 (7)	0.0351 (4)
O1	0.38424 (18)	0.74030 (19)	0.47069 (7)	0.0496 (4)
O2	−0.0512 (3)	−0.0306 (2)	0.27960 (8)	0.0689 (6)
O3	0.08117 (19)	−0.19746 (19)	0.35635 (9)	0.0595 (5)
F1	0.5958 (3)	0.7614 (3)	0.20283 (8)	0.0956 (7)
F2	0.78369 (17)	0.4820 (2)	0.36687 (8)	0.0728 (5)
S2	−0.00544 (6)	−0.05936 (7)	0.33804 (2)	0.0439 (2)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0383 (11)	0.0416 (13)	0.0557 (14)	−0.0018 (9)	0.0115 (10)	−0.0043 (10)
C6	0.0371 (10)	0.0311 (10)	0.0421 (11)	−0.0042 (8)	0.0083 (9)	−0.0032 (8)
C5	0.0438 (12)	0.0515 (14)	0.0535 (14)	0.0057 (10)	0.0137 (10)	0.0076 (11)
C4	0.0662 (16)	0.0605 (16)	0.0530 (14)	0.0034 (13)	0.0103 (12)	0.0172 (12)
C3	0.0729 (17)	0.0577 (16)	0.0481 (14)	−0.0133 (13)	0.0197 (12)	0.0055 (12)
C2	0.0581 (14)	0.0542 (15)	0.0678 (17)	−0.0120 (12)	0.0321 (13)	−0.0068 (13)
C13	0.0394 (11)	0.0356 (11)	0.0408 (11)	−0.0024 (9)	0.0056 (9)	−0.0033 (9)
C12	0.0475 (12)	0.0318 (11)	0.0494 (13)	0.0023 (9)	0.0024 (10)	0.0060 (9)
C11	0.0396 (10)	0.0384 (12)	0.0411 (11)	0.0002 (9)	−0.0021 (9)	0.0051 (9)
C10	0.0327 (10)	0.0326 (11)	0.0373 (10)	−0.0003 (8)	0.0074 (8)	0.0001 (8)
C14	0.0404 (11)	0.0413 (12)	0.0412 (11)	0.0013 (9)	−0.0021 (9)	0.0025 (9)
C15	0.0404 (11)	0.0346 (11)	0.0463 (12)	0.0024 (9)	0.0013 (9)	0.0055 (9)
C16	0.0453 (13)	0.0574 (17)	0.092 (2)	0.0090 (12)	0.0002 (14)	0.0004 (14)
C8	0.0399 (11)	0.0355 (12)	0.0352 (10)	0.0009 (9)	0.0029 (8)	0.0033 (9)
C9	0.0464 (12)	0.0544 (14)	0.0551 (14)	0.0036 (11)	0.0156 (11)	−0.0045 (11)

C7	0.0310 (10)	0.0428 (12)	0.0466 (12)	0.0017 (8)	0.0056 (9)	0.0045 (9)
C18	0.0587 (15)	0.0660 (17)	0.0618 (16)	0.0032 (13)	0.0146 (13)	0.0028 (13)
C17	0.0558 (15)	0.0649 (18)	0.088 (2)	0.0014 (13)	0.0218 (15)	−0.0165 (16)
N1	0.0413 (10)	0.0402 (11)	0.0541 (12)	−0.0020 (8)	0.0009 (9)	−0.0068 (8)
N2	0.0316 (8)	0.0346 (9)	0.0395 (9)	−0.0028 (7)	0.0068 (7)	0.0008 (7)
O1	0.0548 (9)	0.0397 (9)	0.0534 (10)	−0.0071 (7)	0.0036 (8)	−0.0062 (7)
O2	0.0911 (14)	0.0710 (13)	0.0438 (10)	−0.0216 (11)	0.0058 (9)	−0.0158 (9)
O3	0.0549 (10)	0.0342 (9)	0.0909 (14)	0.0033 (7)	0.0156 (9)	−0.0119 (9)
F1	0.1171 (15)	0.1121 (16)	0.0652 (11)	−0.0096 (12)	0.0409 (11)	0.0288 (10)
F2	0.0422 (8)	0.0833 (12)	0.0961 (13)	0.0171 (8)	0.0213 (8)	0.0172 (9)
S2	0.0484 (4)	0.0368 (4)	0.0468 (4)	−0.0036 (2)	0.0076 (3)	−0.0109 (2)

Geometric parameters (Å, º)

C1—F2	1.359 (3)	C15—H12	0.9300
C1—C2	1.375 (4)	C16—N1	1.479 (3)
C1—C6	1.381 (3)	C16—C17	1.516 (5)
C6—C5	1.382 (3)	C16—H13A	0.9700
C6—C7	1.502 (3)	C16—H13B	0.9700
C5—C4	1.383 (4)	C8—O1	1.223 (3)
C5—H3	0.9300	C8—N2	1.356 (3)
C4—C3	1.369 (4)	C8—C9	1.499 (3)
C4—H4	0.9300	C9—H15A	0.9600
C3—F1	1.350 (3)	C9—H15B	0.9600
C3—C2	1.362 (4)	C9—H15C	0.9600
C2—H6	0.9300	C7—N2	1.463 (3)
C13—C14	1.386 (3)	C7—H7A	0.9700
C13—C12	1.388 (3)	C7—H7B	0.9700
C13—S2	1.766 (2)	C18—N1	1.470 (3)
C12—C11	1.376 (3)	C18—C17	1.527 (4)
C12—H8	0.9300	C18—H17A	0.9700
C11—C10	1.393 (3)	C18—H17B	0.9700
C11—H9	0.9300	C17—H18A	0.9700
C10—C15	1.384 (3)	C17—H18B	0.9700
C10—N2	1.439 (3)	N1—S2	1.612 (2)
C14—C15	1.380 (3)	O2—S2	1.419 (2)
C14—H11	0.9300	O3—S2	1.4296 (18)
F2—C1—C2	118.4 (2)	H13A—C16—H13B	111.1
F2—C1—C6	117.2 (2)	O1—C8—N2	121.09 (19)
C2—C1—C6	124.5 (2)	O1—C8—C9	121.4 (2)
C1—C6—C5	116.1 (2)	N2—C8—C9	117.43 (19)
C1—C6—C7	119.94 (19)	C8—C9—H15A	109.5
C5—C6—C7	123.92 (19)	C8—C9—H15B	109.5
C6—C5—C4	121.6 (2)	H15A—C9—H15B	109.5
C6—C5—H3	119.2	C8—C9—H15C	109.5
C4—C5—H3	119.2	H15A—C9—H15C	109.5
C3—C4—C5	118.5 (2)	H15B—C9—H15C	109.5

C3—C4—H4	120.7	N2—C7—C6	114.27 (17)
C5—C4—H4	120.7	N2—C7—H7A	108.7
F1—C3—C2	118.8 (2)	C6—C7—H7A	108.7
F1—C3—C4	118.3 (3)	N2—C7—H7B	108.7
C2—C3—C4	122.9 (2)	C6—C7—H7B	108.7
C3—C2—C1	116.3 (2)	H7A—C7—H7B	107.6
C3—C2—H6	121.8	N1—C18—C17	88.7 (2)
C1—C2—H6	121.8	N1—C18—H17A	113.9
C14—C13—C12	120.43 (19)	C17—C18—H17A	113.9
C14—C13—S2	119.25 (16)	N1—C18—H17B	113.9
C12—C13—S2	120.32 (17)	C17—C18—H17B	113.9
C11—C12—C13	119.6 (2)	H17A—C18—H17B	111.1
C11—C12—H8	120.2	C16—C17—C18	87.9 (2)
C13—C12—H8	120.2	C16—C17—H18A	114.0
C12—C11—C10	119.96 (19)	C18—C17—H18A	114.0
C12—C11—H9	120.0	C16—C17—H18B	114.0
C10—C11—H9	120.0	C18—C17—H18B	114.0
C15—C10—C11	120.28 (19)	H18A—C17—H18B	111.2
C15—C10—N2	120.25 (18)	C18—N1—C16	91.5 (2)
C11—C10—N2	119.41 (17)	C18—N1—S2	125.64 (16)
C15—C14—C13	119.97 (19)	C16—N1—S2	126.87 (18)
C15—C14—H11	120.0	C8—N2—C10	123.67 (16)
C13—C14—H11	120.0	C8—N2—C7	118.69 (17)
C14—C15—C10	119.72 (19)	C10—N2—C7	117.64 (17)
C14—C15—H12	120.1	O2—S2—O3	120.79 (12)
C10—C15—H12	120.1	O2—S2—N1	106.48 (12)
N1—C16—C17	88.8 (2)	O3—S2—N1	105.75 (11)
N1—C16—H13A	113.8	O2—S2—C13	107.50 (11)
C17—C16—H13A	113.8	O3—S2—C13	107.47 (10)
N1—C16—H13B	113.8	N1—S2—C13	108.35 (10)
C17—C16—H13B	113.8		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C5—H3···O3^{i}	0.93	2.44	3.336 (3)	162
C11—H9···O1^{ii}	0.93	2.51	3.406 (3)	162
C17—H18*B*···O1^{iii}	0.97	2.56	3.509 (4)	166

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