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2-[7-Chloro-1,1-dioxo-2-(2,4,5-trifluorobenzyl)-3,4-dihydro-2*H*-1,2,4-benzothiadiazin-4-yl]acetic acid

Yanchun Yang,[a] Yuhua Guo[b] and Changjin Zhu[a]*

[a]Department of Applied Chemistry, Beijing Institute of Technology, Zhongguancun South Street, 100081 Beijing, People's Republic of China, and [b]Department of Chemistry and Environmental Engineering, Anyang Institute of Technology, Henan 455000, People's Republic of China
Correspondence e-mail: zcj@bit.edu.cn

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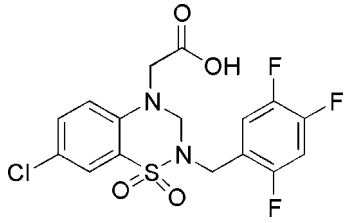
Key indicators: single-crystal X-ray study; T = 296 K; mean σ(C–C) = 0.003 Å; R factor = 0.047; wR factor = 0.131; data-to-parameter ratio = 17.5.

In the molecule of the title compound, $C_{16}H_{12}ClF_3N_2O_4S$, the thiadiazine ring adopts a half-chair conformation. The dihedral angle between the benzene ring of the benzothiadiazine ring system and trifluorophenyl group is 15.02 (7)°. In the crystal, centrosymmetrically related molecules are linked into dimers *via* pairs of O—H···O hydrogen bonds, generating $R_2^2(8)$ ring motifs. The dimers are further connected into a three-dimensional network by C—H···O hydrogen bonds.

Related literature

For the pharmacological properties of benzothiadiazine derivatives, see: Longman & Hamilton (1992); Buckheit *et al.* (1994); Yamada & Tang (1993); Phillips *et al.* (2002); Braghiroli *et al.* (2002); Pirotte *et al.* (1998); Francotte *et al.* (2007). For the biological properties and synthetic details of the title compound, see: Chen *et al.* (2010).



Experimental

Crystal data

$C_{16}H_{12}ClF_3N_2O_4S$
M_r = 420.79
Monoclinic, $P2_1/c$
a = 9.3628 (2) Å
b = 12.3134 (2) Å
c = 15.5597 (3) Å
β = 105.996 (1)°
V = 1724.39 (6) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.40 mm^{-1}
T = 296 K
0.20 × 0.20 × 0.20 mm

Data collection

Bruker APEXII CCD diffractometer
15140 measured reflections
4293 independent reflections
3302 reflections with $I > 2\sigma(I)$
R_{int} = 0.027

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.131
S = 1.04
4293 reflections
245 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.73 e Å^{-3}
$\Delta\rho_{min}$ = −0.82 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O4—H4···O3^{i}	0.82	1.86	2.676 (2)	171
C3—H3···O1^{ii}	0.93	2.47	3.391 (3)	169
C16—H16···O2^{iii}	0.93	2.46	3.387 (2)	172
C13—H13···O3^{iv}	0.93	2.51	3.307 (3)	144

Symmetry codes: (i) $-x+1, -y+2, -z+1$; (ii) $x, -y+\frac{3}{2}, z+\frac{1}{2}$; (iii) $-x+1, -y+2, -z$; (iv) $x+1, y, z$.

Data collection: *APEX2* (Bruker, 2005); cell refinement: *SAINT-Plus* (Bruker, 2001); data reduction: *SAINT-Plus*; 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*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: RZ2722).

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supplementary materials

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2-[7-Chloro-1,1-dioxo-2-(2,4,5-trifluorobenzyl)-3,4-dihydro-2*H*-1,2,4-benzothiadiazin-4-yl]acetic acid

Yanchun Yang, Yuhua Guo and Changjin Zhu

Comment

Benzothiadiazine derivatives have attracted considerable attention because they are endowed with a large spectrum of properties. Since the 1950's, various pharmacological investigations of newly synthesized benzothiadiazines demonstrated interesting pharmacological activities and showed great potential for the development of new medications for treating diseases (Longman & Hamilton, 1992; Buckheit *et al.*, 1994; Yamada & Tang, 1993; Phillips *et al.*, 2002; Braghiroli *et al.*, 2002; Pirotte *et al.*, 1998; Francotte *et al.*, 2007). The title compound, whose structure is reported herein, was synthesized and used as an aldose reductase inhibitor (Chen *et al.*, 2010).

In the molecule of the title compound (Fig. 1), the thiadiazine ring (C7/N1/C4/C5/S1/N2) adopts a half-chair conformation, with puckering parameters Q_T = 0.5164 (19) Å, θ = 47.5 (2)° and φ = -25.9 (3)°. The deviation of the S1, N1 and N2 atoms from the plane of the benzene ring of the benzothiadiazin ring system are -0.0726 (6), 0.0305 (19) and 0.2655 (18) Å, respectively. The dihedral angle formed by the two six-membered aromatic rings C1–C6 and C11–C16 is 15.02 (7)°. In the crystal, centrosymmetrically related molecules interact to form dimers through pairs of O—H···O hydrogen bonds (Table 1) generating a $R^2_2(8)$ ring motif. The dimers are further linked into a three-dimensional network by intermolecular C—H···O hydrogen bonds (Table 1).

Experimental

A mixture of methyl 2-(7-chloro-1,1-dioxido-2-(2,4,5-trifluorobenzyl)-2*H*-benzo[*e*][1,2,4]thiadiazin-4(3*H*)-yl)acetate (1 mmol), 1,4-dioxane (5 ml) and saturated aqueous sodium hydroxide (5 ml) was stirred at room temperature for 2 h. The alkaline suspension was adjusted to be acidic with 0.1 molar HCl and extracted with ethyl acetate (3 × 20 ml). The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated to dryness under reduced pressure. Crystals suitable for X-ray diffraction were obtained by slow evaporation of a methanol solution of the compound (yield: 76%).

Refinement

H atoms were positioned geometrically and refined using a riding model, with C—H = 0.93–0.97 Å, O—H = 0.82 Å and with U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(O).

Computing details

Data collection: *APEX2* (Bruker, 2005); cell refinement: *SAINT-Plus* (Bruker, 2001); data reduction: *SAINT-Plus* (Bruker, 2001); 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* (Sheldrick, 2008).

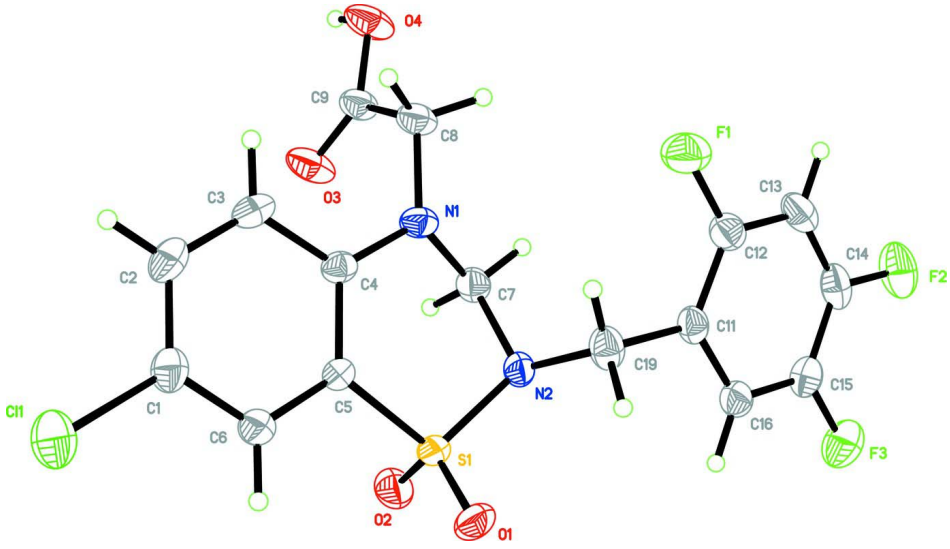

Figure 1

The molecular structure of the title compound, with 30% probability displacement ellipsoids.

2-[7-Chloro-1,1-dioxo-2-(2,4,5-trifluorobenzyl)-3,4-dihydro-2*H*- 1,2,4-benzothiadiazin-4-yl]acetic acid

Crystal data

$C_{16}H_{12}ClF_3N_2O_4S$
$M_r = 420.79$
Monoclinic, $P2_1/c$
Hall symbol: -P 2ybc
$a = 9.3628$ (2) Å
$b = 12.3134$ (2) Å
$c = 15.5597$ (3) Å
$\beta = 105.996$ (1)°
$V = 1724.39$ (6) Å^3
$Z = 4$
$F(000) = 856$
$D_x = 1.621$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 4599 reflections
$\theta = 2.8$–$28.3°$
$\mu = 0.40$ mm^{-1}
$T = 296$ K
Block, colourless
0.20 × 0.20 × 0.20 mm

Data collection

Bruker APEXII CCD diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
φ and ω scans
15140 measured reflections
4293 independent reflections
3302 reflections with $I > 2\sigma(I)$
$R_{int} = 0.027$
$\theta_{max} = 28.3°$, $\theta_{min} = 2.1°$
$h = -12 \rightarrow 12$
$k = -16 \rightarrow 15$
$l = -20 \rightarrow 20$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.047$
$wR(F^2) = 0.131$
$S = 1.04$
4293 reflections
245 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
$w = 1/[\sigma^2(F_o^2) + (0.0571P)^2 + 1.0199P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.73$ e Å^{-3}
$\Delta\rho_{min} = -0.82$ e Å^{-3}

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 (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.45256 (6)	0.88685 (5)	0.08722 (3)	0.04077 (16)
Cl1	−0.00328 (10)	0.62773 (8)	0.09172 (6)	0.0872 (3)
C11	0.8849 (2)	0.89923 (18)	0.16523 (14)	0.0394 (5)
C5	0.3729 (2)	0.79827 (17)	0.14930 (12)	0.0350 (4)
N2	0.62050 (19)	0.90503 (15)	0.15259 (11)	0.0387 (4)
F2	1.26561 (18)	1.08588 (15)	0.23239 (13)	0.0768 (5)
O1	0.46125 (19)	0.83390 (17)	0.00742 (10)	0.0607 (5)
F3	1.0586 (2)	1.12091 (14)	0.07690 (12)	0.0729 (5)
C12	0.9947 (3)	0.88393 (19)	0.24347 (15)	0.0458 (5)
C6	0.2388 (2)	0.75123 (19)	0.10327 (14)	0.0449 (5)
H6	0.1985	0.7648	0.0426	0.054*
N1	0.5746 (2)	0.82433 (15)	0.28393 (11)	0.0392 (4)
F1	0.97529 (19)	0.80656 (14)	0.30117 (11)	0.0714 (5)
O2	0.37472 (19)	0.98763 (15)	0.07985 (13)	0.0597 (5)
C4	0.4382 (2)	0.77835 (16)	0.24064 (12)	0.0341 (4)
C7	0.6157 (2)	0.92240 (18)	0.24459 (13)	0.0400 (5)
H7A	0.7126	0.9466	0.2802	0.048*
H7B	0.5445	0.9792	0.2456	0.048*
C3	0.3601 (3)	0.70893 (18)	0.28347 (14)	0.0435 (5)
H3	0.3996	0.6932	0.3438	0.052*
C2	0.2264 (3)	0.66393 (19)	0.23789 (16)	0.0484 (5)
H2	0.1761	0.6192	0.2679	0.058*
C1	0.1662 (3)	0.6843 (2)	0.14823 (16)	0.0489 (5)
C9	0.5751 (3)	0.8936 (2)	0.43292 (13)	0.0447 (5)
C8	0.6382 (3)	0.8131 (2)	0.37949 (13)	0.0462 (5)
H8A	0.7449	0.8232	0.3935	0.055*
H8B	0.6200	0.7400	0.3972	0.055*
C19	0.7430 (2)	0.8351 (2)	0.14144 (16)	0.0468 (5)
H19A	0.7213	0.8102	0.0800	0.056*
H19B	0.7531	0.7720	0.1800	0.056*
C16	0.9087 (2)	0.98074 (19)	0.10813 (15)	0.0442 (5)
H16	0.8376	0.9939	0.0542	0.053*
C15	1.0367 (3)	1.0414 (2)	0.13140 (16)	0.0482 (5)
C14	1.1431 (3)	1.0230 (2)	0.21047 (18)	0.0506 (6)
C13	1.1245 (3)	0.9440 (2)	0.26747 (17)	0.0527 (6)
H13	1.1968	0.9307	0.3209	0.063*
O4	0.6474 (2)	0.89659 (17)	0.51717 (10)	0.0651 (6)

H4	0.6053	0.9380	0.5435	0.098*
O3	0.4682 (2)	0.95079 (17)	0.39943 (11)	0.0645 (6)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0349 (3)	0.0559 (3)	0.0303 (2)	−0.0079 (2)	0.00703 (18)	0.0092 (2)
Cl1	0.0666 (5)	0.1026 (7)	0.0868 (6)	−0.0466 (5)	0.0117 (4)	0.0042 (5)
C11	0.0321 (10)	0.0454 (12)	0.0418 (11)	0.0012 (9)	0.0122 (8)	−0.0088 (9)
C5	0.0337 (10)	0.0405 (11)	0.0317 (9)	−0.0010 (8)	0.0107 (7)	0.0047 (8)
N2	0.0305 (8)	0.0499 (10)	0.0360 (8)	−0.0045 (7)	0.0095 (7)	−0.0032 (7)
F2	0.0449 (9)	0.0762 (11)	0.1085 (14)	−0.0195 (8)	0.0196 (9)	−0.0269 (10)
O1	0.0554 (10)	0.0992 (15)	0.0291 (7)	−0.0253 (10)	0.0143 (7)	−0.0050 (8)
F3	0.0804 (12)	0.0682 (11)	0.0810 (11)	−0.0100 (9)	0.0403 (10)	0.0087 (8)
C12	0.0422 (12)	0.0479 (13)	0.0464 (12)	0.0040 (10)	0.0108 (9)	0.0000 (10)
C6	0.0404 (12)	0.0546 (14)	0.0376 (10)	−0.0088 (10)	0.0072 (9)	0.0050 (9)
N1	0.0435 (10)	0.0441 (10)	0.0272 (8)	0.0020 (8)	0.0052 (7)	−0.0012 (7)
F1	0.0715 (11)	0.0740 (11)	0.0638 (10)	0.0000 (9)	0.0101 (8)	0.0207 (8)
O2	0.0453 (10)	0.0598 (11)	0.0706 (11)	0.0027 (8)	0.0101 (8)	0.0289 (9)
C4	0.0403 (11)	0.0337 (10)	0.0292 (9)	0.0057 (8)	0.0110 (8)	0.0000 (7)
C7	0.0384 (11)	0.0444 (12)	0.0362 (10)	−0.0029 (9)	0.0084 (8)	−0.0067 (8)
C3	0.0597 (14)	0.0408 (12)	0.0341 (10)	0.0057 (10)	0.0195 (9)	0.0073 (8)
C2	0.0582 (14)	0.0397 (12)	0.0555 (13)	−0.0028 (11)	0.0295 (11)	0.0075 (10)
C1	0.0440 (13)	0.0486 (13)	0.0552 (13)	−0.0125 (10)	0.0154 (10)	0.0009 (10)
C9	0.0438 (12)	0.0551 (14)	0.0305 (9)	0.0077 (10)	0.0025 (8)	−0.0027 (9)
C8	0.0468 (12)	0.0566 (14)	0.0310 (10)	0.0132 (11)	0.0036 (8)	−0.0007 (9)
C19	0.0383 (12)	0.0501 (13)	0.0527 (13)	−0.0044 (10)	0.0138 (9)	−0.0133 (10)
C16	0.0386 (11)	0.0549 (14)	0.0402 (11)	0.0035 (10)	0.0124 (9)	−0.0059 (9)
C15	0.0477 (13)	0.0486 (13)	0.0544 (13)	0.0009 (10)	0.0243 (11)	−0.0043 (10)
C14	0.0335 (11)	0.0531 (14)	0.0666 (15)	−0.0051 (10)	0.0160 (10)	−0.0196 (12)
C13	0.0352 (12)	0.0634 (16)	0.0525 (13)	0.0073 (11)	0.0005 (9)	−0.0104 (12)
O4	0.0648 (12)	0.0852 (14)	0.0333 (8)	0.0296 (10)	−0.0066 (8)	−0.0137 (8)
O3	0.0606 (11)	0.0843 (14)	0.0379 (8)	0.0325 (10)	−0.0042 (7)	−0.0133 (8)

Geometric parameters (Å, º)

S1—O1	1.4245 (17)	C4—C3	1.407 (3)
S1—O2	1.4277 (19)	C7—H7A	0.9700
S1—N2	1.6357 (18)	C7—H7B	0.9700
S1—C5	1.7540 (19)	C3—C2	1.374 (3)
Cl1—C1	1.734 (2)	C3—H3	0.9300
C11—C12	1.373 (3)	C2—C1	1.376 (3)
C11—C16	1.398 (3)	C2—H2	0.9300
C11—C19	1.502 (3)	C9—O3	1.217 (3)
C5—C6	1.389 (3)	C9—O4	1.300 (2)
C5—C4	1.405 (3)	C9—C8	1.514 (3)
N2—C7	1.460 (2)	C8—H8A	0.9700
N2—C19	1.482 (3)	C8—H8B	0.9700
F2—C14	1.347 (3)	C19—H19A	0.9700
F3—C15	1.347 (3)	C19—H19B	0.9700

C12—F1	1.355 (3)	C16—C15	1.374 (3)
C12—C13	1.383 (3)	C16—H16	0.9300
C6—C1	1.376 (3)	C15—C14	1.372 (4)
C6—H6	0.9300	C14—C13	1.360 (4)
N1—C4	1.389 (3)	C13—H13	0.9300
N1—C8	1.448 (2)	O4—H4	0.8200
N1—C7	1.453 (3)		

O1—S1—O2	118.58 (12)	C4—C3—H3	119.4
O1—S1—N2	109.19 (10)	C3—C2—C1	120.7 (2)
O2—S1—N2	108.23 (11)	C3—C2—H2	119.7
O1—S1—C5	109.30 (11)	C1—C2—H2	119.7
O2—S1—C5	107.43 (10)	C6—C1—C2	120.2 (2)
N2—S1—C5	102.98 (9)	C6—C1—Cl1	119.63 (19)
C12—C11—C16	116.8 (2)	C2—C1—Cl1	120.18 (18)
C12—C11—C19	122.8 (2)	O3—C9—O4	123.6 (2)
C16—C11—C19	120.4 (2)	O3—C9—C8	122.87 (19)
C6—C5—C4	121.91 (19)	O4—C9—C8	113.50 (19)
C6—C5—S1	115.88 (15)	N1—C8—C9	112.90 (18)
C4—C5—S1	122.18 (16)	N1—C8—H8A	109.0
C7—N2—C19	115.69 (18)	C9—C8—H8A	109.0
C7—N2—S1	110.23 (13)	N1—C8—H8B	109.0
C19—N2—S1	119.35 (14)	C9—C8—H8B	109.0
F1—C12—C11	118.7 (2)	H8A—C8—H8B	107.8
F1—C12—C13	117.7 (2)	N2—C19—C11	109.07 (18)
C11—C12—C13	123.6 (2)	N2—C19—H19A	109.9
C1—C6—C5	119.4 (2)	C11—C19—H19A	109.9
C1—C6—H6	120.3	N2—C19—H19B	109.9
C5—C6—H6	120.3	C11—C19—H19B	109.9
C4—N1—C8	121.46 (18)	H19A—C19—H19B	108.3
C4—N1—C7	116.70 (16)	C15—C16—C11	120.2 (2)
C8—N1—C7	115.48 (18)	C15—C16—H16	119.9
N1—C4—C5	120.34 (18)	C11—C16—H16	119.9
N1—C4—C3	123.12 (18)	F3—C15—C14	119.1 (2)
C5—C4—C3	116.53 (19)	F3—C15—C16	120.2 (2)
N1—C7—N2	112.00 (17)	C14—C15—C16	120.8 (2)
N1—C7—H7A	109.2	F2—C14—C13	120.0 (2)
N2—C7—H7A	109.2	F2—C14—C15	119.3 (2)
N1—C7—H7B	109.2	C13—C14—C15	120.7 (2)
N2—C7—H7B	109.2	C14—C13—C12	117.9 (2)
H7A—C7—H7B	107.9	C14—C13—H13	121.1
C2—C3—C4	121.29 (19)	C12—C13—H13	121.1
C2—C3—H3	119.4	C9—O4—H4	109.5

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O4—H4···O3^{i}	0.82	1.86	2.676 (2)	171
C3—H3···O1^{ii}	0.93	2.47	3.391 (3)	169

C16—H16···O2^{iii}	0.93	2.46	3.387 (2)	172
C13—H13···O3^{iv}	0.93	2.51	3.307 (3)	144

Symmetry codes: (i) −*x*+1, −*y*+2, −*z*+1; (ii) *x*, −*y*+3/2, *z*+1/2; (iii) −*x*+1, −*y*+2, −*z*; (iv) *x*+1, *y*, *z*.