IUCrData

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4-[(3-Phenyl-4,5-dihydroisoxazol-5-yl)methyl]-2*H*-benzo[*b*][1,4]thiazin-3(4*H*)-one

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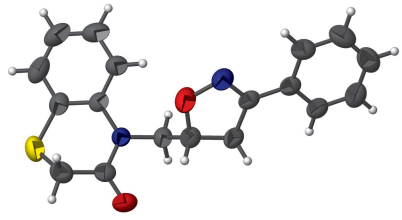
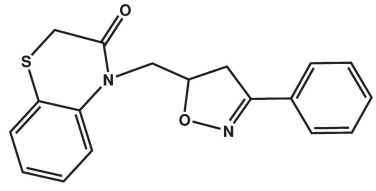
Structural data: full structural data are available from iucrdata.iucr.org

In the title compound, $C_{18}H_{16}N_2O_2S$, the 5-dihydroisoxazol-5-yl ring and its phenyl substituent are nearly coplanar, with the largest deviation from the mean plane being 0.0184 (16) Å. The thiomorpholin-3-one ring adopts a screw-boat conformation and the attached benzene ring makes a dihedral angle of 42.26 (7)° with the mean plane through the 3-phenyl-4,5-dihydroisoxazol-5-yl ring system. In the crystal, molecules are linked by pairs of C—H···N hydrogen bonds, forming inversion dimers. These dimers are linked *via* C—H···O hydrogen bonds, generating a three-dimensional network.

3D view



Chemical scheme



Structure description

1,4-Benzothiazines are a class of medicinally important heterocyclic compounds which are used extensively in drug design. It is well documented that 1,4-benzothiazin-3-one derivatives possess important pharmacological properties and play a vital role in the treatment of neurodegenerative disorders, such as Parkinson's disease and Alzheimer's disease (Shen *et al.*, 1996). They can also act as calcium channel blockers (Schwarz *et al.*, 1999), phosphodiesterase-7 inhibitors (Castro *et al.*, 2001) and anticataract agents (Kawashima *et al.*, 1994). Isoxazole derivatives represent a unique class of nitrogen- and oxygen-containing five-membered heterocycles. They are the components of a variety of natural products and medicinally useful compounds (Sperry *et al.*, 2005). Isoxazole derivatives with a variety of substituents are known to have various biological activities in both the pharmaceutical and agricultural areas (Lang & Lin, 1984; Boyd, 1991).

The present work is a continuation of our investigations of new derivatives of 2*H*-benzo[*b*][1,4]thiazin-3(4*H*)-one for their biological activities (Sebbar *et al.*, 2014*a*,*b*). The

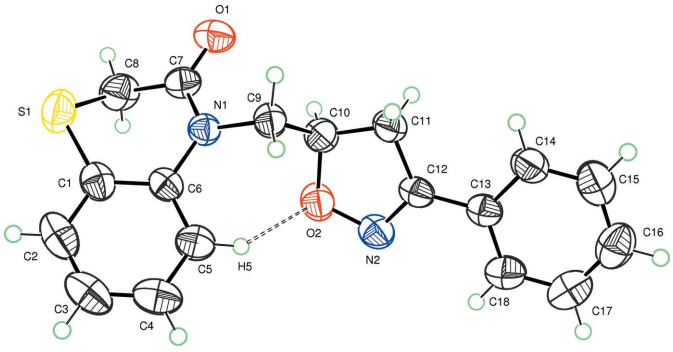


Figure 1
The molecular structure of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented as small circles of arbitrary radius.

nitrile oxide, formed *in situ* by chlorination of an oxime, reacts with 4-allyl-2*H*-benzo[*b*][1,4]thiazin-3(4*H*)-one in a biphasic medium (water–chloroform) at 0°C over 4 h to afford the unique cycloadduct 4-((3-phenyl-4,5-dihydroisoxazol-5-yl)-methyl)-2*H*-benzo[*b*] [1,4]thiazin-3(4*H*)-one.

The molecule of the title compound contains the two fused six-membered rings of the 1,4-benzothiazine unit, linked, through a methylene group, to the 3-phenyl-4,5-dihydro-isoxazol-5-yl ring system, as shown in Fig. 1. The dihydro-isoxazole and phenyl rings are almost coplanar, as indicated by the dihedral angle of 1.33 (9)° between their planes. The six-membered heterocycle adopts a screw-boat conformation, as indicated by the total puckering amplitude Q_T = 0.6390 (2) Å, and a spherical polar angle θ = 65.02 (1)° with φ = 326.38 (2)°. The dihedral angle between the phenyl (C13–C18) and the benzene (C1–C6) rings is 42.42 (9)°. An intramolecular C5—H5···O2 interaction closes a seven-membered ring.

In the crystal, C10—H10···N2 hydrogen bonds form inversion dimers, generating $R_2^2(8)$ rings. These dimers are further connected by C2—H2···O1 hydrogen bonds, forming a three-dimensional network, Fig. 2 and Table 1.

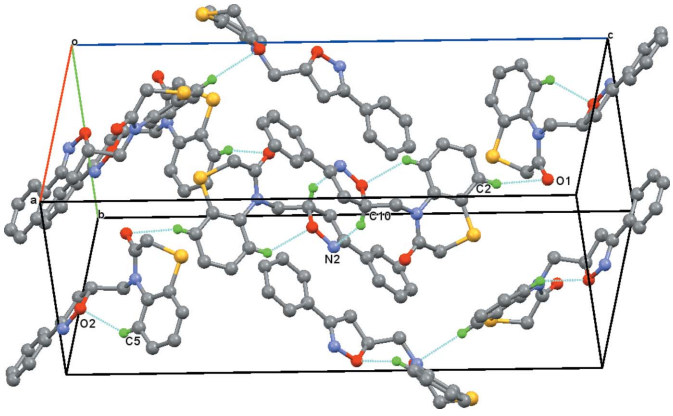


Figure 2
Molecules of the title compound linked by C—H···N and C—H···O hydrogen bonds forming a three-dimensional network. Hydrogen bonds are shown as blue dashed lines.

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

D—H···A	D—H	H···A	D···A	D—H···A
C10—H10···N2^{i}	0.98	2.64	3.405 (2)	136
C2—H2···O1^{ii}	0.93	2.64	3.538 (2)	161
C5—H5···O2	0.93	2.43	3.135 (2)	132

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

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{18}H_{16}N_2O_2S$
M_r	324.39
Crystal system, space group	Orthorhombic, *Pbca*
Temperature (K)	296
a, *b*, *c* (Å)	11.7526 (3), 10.4082 (3), 25.5656 (7)
V (Å^3)	3127.27 (15)
Z	8
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.22
Crystal size (mm)	0.35 × 0.31 × 0.22
Data collection	
Diffractometer	Bruker X8 APEX
Absorption correction	Multi-scan (*SADABS*; Bruker, 2009)
T_{min}, T_{max}	0.626, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	41764, 4391, 2776
R_{int}	0.049
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.694
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.042, 0.116, 1.02
No. of reflections	4391
No. of parameters	208
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.18, −0.23

Computer programs: *APEX2* and *SAINT* (Bruker, 2009), *SHELXT* (Sheldrick, 2015*a*), *SHELXL2014* (Sheldrick, 2015*b*), *ORTEPIII* (Burnett & Johnson, 1996), *ORTEP-3 for Windows* (Farrugia, 2012), *Mercury* (Macrae *et al.*, 2008), *PLATON* (Spek, 2009) and *publCIF* (Westrip, 2010).

Synthesis and crystallization

A 24% sodium hypochlorite solution (10 ml) was added dropwise to a solution of 4-allyl-2*H*-benzo[*b*][1,4]thiazin-3(4*H*)-one (0.5 g, 2.4 mmol) and benzaldoxime (0.52 ml, 4.8 mmol) in chloroform (30 ml) at 0°C. Stirring was continued for 4 h. The organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was then purified by column chromatography on silica gel using a mixture of hexane/ethyl acetate (*v*/*v* = 90/10) as eluent. Colourless crystals were isolated when the solvent was allowed to evaporate (yield = 38%, m.p. = 408 K).

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Acknowledgements

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full crystallographic data

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Crystal data

$C_{18}H_{16}N_2O_2S$
M_r = 324.39
Orthorhombic, *Pbca*
a = 11.7526 (3) Å
b = 10.4082 (3) Å
c = 25.5656 (7) Å
V = 3127.27 (15) Å^3
Z = 8
F(000) = 1360
D_x = 1.378 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 4391 reflections
θ = 2.7–29.6°
μ = 0.22 mm^{-1}
T = 296 K
Block, colourless
0.35 × 0.31 × 0.22 mm

Data collection

Bruker X8 APEX diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
φ and ω scans
Absorption correction: multi-scan (SADABS; Bruker, 2009)
T_{min} = 0.626, T_{max} = 0.746
41764 measured reflections
4391 independent reflections
2776 reflections with $I > 2\sigma(I)$
R_{int} = 0.049
θ_{max} = 29.6°, θ_{min} = 2.7°
h = −16→16
k = −14→14
l = −35→35

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.116
S = 1.02
4391 reflections
208 parameters
0 restraints
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0471P)^2 + 0.5946P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.18 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.41617 (14)	0.54751 (16)	0.72451 (6)	0.0523 (4)
C2	0.31872 (17)	0.5156 (2)	0.75261 (7)	0.0697 (5)
H2	0.3001	0.5621	0.7825	0.084*
C3	0.25022 (17)	0.4171 (2)	0.73689 (9)	0.0753 (6)
H3	0.1870	0.3942	0.7567	0.090*
C4	0.27550 (15)	0.3520 (2)	0.69163 (9)	0.0702 (5)
H4	0.2286	0.2853	0.6806	0.084*
C5	0.37013 (13)	0.38471 (16)	0.66217 (7)	0.0542 (4)
H5	0.3846	0.3418	0.6309	0.065*
C6	0.44335 (11)	0.48065 (14)	0.67880 (6)	0.0435 (3)
C7	0.60226 (13)	0.62130 (15)	0.65330 (6)	0.0497 (4)
C8	0.54562 (16)	0.72680 (17)	0.68349 (8)	0.0663 (5)
H8A	0.4789	0.7563	0.6646	0.080*
H8B	0.5975	0.7987	0.6870	0.080*
C9	0.60129 (13)	0.40421 (14)	0.62058 (6)	0.0459 (3)
H9A	0.5695	0.3220	0.6309	0.055*
H9B	0.6818	0.4029	0.6288	0.055*
C10	0.58705 (13)	0.42034 (16)	0.56196 (6)	0.0521 (4)
H10	0.6170	0.5042	0.5512	0.062*
C11	0.64431 (13)	0.31506 (18)	0.53054 (6)	0.0569 (4)
H11A	0.7005	0.3499	0.5066	0.068*
H11B	0.6803	0.2522	0.5531	0.068*
C12	0.54543 (12)	0.25839 (15)	0.50168 (6)	0.0455 (3)
C13	0.55384 (12)	0.15192 (14)	0.46429 (6)	0.0459 (3)
C14	0.65787 (14)	0.09460 (18)	0.45405 (7)	0.0585 (4)
H14	0.7230	0.1232	0.4711	0.070*
C15	0.66500 (17)	−0.00510 (19)	0.41843 (8)	0.0702 (5)
H15	0.7351	−0.0431	0.4116	0.084*
C16	0.56970 (19)	−0.04828 (18)	0.39314 (8)	0.0720 (5)
H16	0.5754	−0.1147	0.3689	0.086*
C17	0.46626 (18)	0.00613 (19)	0.40342 (8)	0.0728 (5)
H17	0.4015	−0.0241	0.3866	0.087*
C18	0.45782 (14)	0.10545 (18)	0.43862 (7)	0.0601 (4)
H18	0.3871	0.1421	0.4454	0.072*
N1	0.54641 (10)	0.50614 (11)	0.65117 (5)	0.0430 (3)
N2	0.45035 (11)	0.31124 (14)	0.51224 (5)	0.0527 (3)
O1	0.69382 (10)	0.63712 (12)	0.63161 (5)	0.0650 (3)
O2	0.46655 (10)	0.41189 (12)	0.54839 (4)	0.0624 (3)
S1	0.50438 (4)	0.67123 (5)	0.74704 (2)	0.07191 (17)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0519 (9)	0.0552 (9)	0.0497 (9)	0.0146 (7)	0.0002 (7)	0.0048 (7)
C2	0.0669 (11)	0.0824 (13)	0.0598 (11)	0.0234 (11)	0.0166 (9)	0.0110 (10)

C3	0.0579 (11)	0.0884 (15)	0.0797 (13)	0.0079 (10)	0.0217 (10)	0.0245 (12)
C4	0.0530 (10)	0.0714 (12)	0.0863 (14)	−0.0099 (9)	0.0019 (9)	0.0188 (11)
C5	0.0497 (8)	0.0538 (9)	0.0592 (10)	−0.0013 (7)	0.0002 (7)	0.0063 (8)
C6	0.0402 (7)	0.0454 (8)	0.0450 (8)	0.0074 (6)	−0.0005 (6)	0.0080 (6)
C7	0.0438 (8)	0.0533 (9)	0.0522 (9)	−0.0016 (7)	−0.0074 (7)	0.0031 (7)
C8	0.0650 (11)	0.0482 (9)	0.0858 (13)	−0.0028 (8)	−0.0004 (10)	−0.0060 (9)
C9	0.0453 (8)	0.0498 (8)	0.0425 (8)	0.0068 (6)	−0.0022 (6)	0.0007 (6)
C10	0.0485 (8)	0.0642 (10)	0.0436 (8)	0.0027 (7)	−0.0028 (7)	0.0009 (7)
C11	0.0413 (8)	0.0835 (12)	0.0459 (8)	0.0013 (8)	−0.0003 (6)	−0.0087 (8)
C12	0.0370 (7)	0.0612 (9)	0.0383 (7)	0.0002 (7)	0.0002 (6)	0.0100 (7)
C13	0.0440 (8)	0.0540 (9)	0.0399 (7)	−0.0026 (7)	0.0017 (6)	0.0103 (7)
C14	0.0474 (9)	0.0698 (11)	0.0583 (10)	−0.0009 (8)	0.0052 (7)	−0.0011 (9)
C15	0.0731 (12)	0.0669 (12)	0.0707 (12)	0.0076 (10)	0.0157 (10)	0.0000 (10)
C16	0.0975 (16)	0.0535 (10)	0.0648 (12)	−0.0091 (10)	0.0013 (11)	−0.0019 (9)
C17	0.0792 (13)	0.0665 (12)	0.0727 (13)	−0.0157 (10)	−0.0147 (10)	0.0011 (10)
C18	0.0491 (9)	0.0676 (11)	0.0637 (11)	−0.0041 (8)	−0.0055 (8)	0.0050 (9)
N1	0.0405 (6)	0.0449 (7)	0.0437 (7)	0.0028 (5)	−0.0012 (5)	0.0003 (5)
N2	0.0446 (7)	0.0686 (9)	0.0450 (7)	0.0067 (6)	−0.0046 (6)	0.0051 (6)
O1	0.0485 (6)	0.0717 (8)	0.0748 (8)	−0.0112 (6)	0.0023 (6)	0.0029 (6)
O2	0.0507 (6)	0.0866 (9)	0.0500 (6)	0.0193 (6)	−0.0083 (5)	−0.0092 (6)
S1	0.0788 (3)	0.0722 (3)	0.0647 (3)	0.0081 (2)	−0.0025 (2)	−0.0221 (2)

Geometric parameters (Å, º)

C1—C2	1.392 (2)	C9—H9B	0.9700
C1—C6	1.397 (2)	C10—O2	1.4607 (19)
C1—S1	1.7506 (18)	C10—C11	1.516 (2)
C2—C3	1.364 (3)	C10—H10	0.9800
C2—H2	0.9300	C11—C12	1.498 (2)
C3—C4	1.373 (3)	C11—H11A	0.9700
C3—H3	0.9300	C11—H11B	0.9700
C4—C5	1.386 (2)	C12—N2	1.2744 (19)
C4—H4	0.9300	C12—C13	1.467 (2)
C5—C6	1.385 (2)	C13—C14	1.385 (2)
C5—H5	0.9300	C13—C18	1.392 (2)
C6—N1	1.4271 (18)	C14—C15	1.383 (3)
C7—O1	1.2217 (19)	C14—H14	0.9300
C7—N1	1.3677 (19)	C15—C16	1.369 (3)
C7—C8	1.498 (2)	C15—H15	0.9300
C8—S1	1.792 (2)	C16—C17	1.367 (3)
C8—H8A	0.9700	C16—H16	0.9300
C8—H8B	0.9700	C17—C18	1.374 (3)
C9—N1	1.4673 (18)	C17—H17	0.9300
C9—C10	1.517 (2)	C18—H18	0.9300
C9—H9A	0.9700	N2—O2	1.4098 (18)
C2—C1—C6	120.06 (17)	O2—C10—H10	109.6
C2—C1—S1	119.53 (14)	C11—C10—H10	109.6

C6—C1—S1	120.41 (13)	C9—C10—H10	109.6
C3—C2—C1	120.86 (19)	C12—C11—C10	101.61 (12)
C3—C2—H2	119.6	C12—C11—H11A	111.4
C1—C2—H2	119.6	C10—C11—H11A	111.4
C2—C3—C4	119.42 (18)	C12—C11—H11B	111.4
C2—C3—H3	120.3	C10—C11—H11B	111.4
C4—C3—H3	120.3	H11A—C11—H11B	109.3
C3—C4—C5	120.71 (19)	N2—C12—C13	121.56 (14)
C3—C4—H4	119.6	N2—C12—C11	113.95 (14)
C5—C4—H4	119.6	C13—C12—C11	124.49 (13)
C6—C5—C4	120.58 (17)	C14—C13—C18	118.47 (16)
C6—C5—H5	119.7	C14—C13—C12	120.53 (14)
C4—C5—H5	119.7	C18—C13—C12	121.00 (14)
C5—C6—C1	118.28 (14)	C15—C14—C13	120.06 (17)
C5—C6—N1	120.62 (14)	C15—C14—H14	120.0
C1—C6—N1	121.03 (14)	C13—C14—H14	120.0
O1—C7—N1	121.51 (15)	C16—C15—C14	120.51 (18)
O1—C7—C8	121.76 (15)	C16—C15—H15	119.7
N1—C7—C8	116.73 (14)	C14—C15—H15	119.7
C7—C8—S1	110.53 (12)	C17—C16—C15	120.05 (19)
C7—C8—H8A	109.5	C17—C16—H16	120.0
S1—C8—H8A	109.5	C15—C16—H16	120.0
C7—C8—H8B	109.5	C16—C17—C18	120.13 (18)
S1—C8—H8B	109.5	C16—C17—H17	119.9
H8A—C8—H8B	108.1	C18—C17—H17	119.9
N1—C9—C10	113.45 (12)	C17—C18—C13	120.77 (17)
N1—C9—H9A	108.9	C17—C18—H18	119.6
C10—C9—H9A	108.9	C13—C18—H18	119.6
N1—C9—H9B	108.9	C7—N1—C6	123.40 (12)
C10—C9—H9B	108.9	C7—N1—C9	116.36 (12)
H9A—C9—H9B	107.7	C6—N1—C9	120.16 (12)
O2—C10—C11	105.13 (12)	C12—N2—O2	109.95 (12)
O2—C10—C9	109.56 (13)	N2—O2—C10	109.35 (11)
C11—C10—C9	113.23 (13)	C1—S1—C8	95.70 (8)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C10—H10···N2^{i}	0.98	2.64	3.405 (2)	136
C2—H2···O1^{ii}	0.93	2.64	3.538 (2)	161
C5—H5···O2	0.93	2.43	3.135 (2)	132

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