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# 5*H*-2,4-Dimethyl-6-phenyl-8,9-dihydropyrido[3′,2′:5,6][1,2]thiazino[3,2-*c*][1,4]oxazin-5-one 11,11-dioxide

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**Key indicators**

Single-crystal X-ray study
*T* = 293 K
Mean σ(C–C) = 0.003 Å
*R* factor = 0.035
*wR* factor = 0.091
Data-to-parameter ratio = 12.5

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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The structure of the title compound, $C_{18}H_{16}N_2O_4S$, with a new chiral pyrido[3′,2′:5,6][1,2]thiazino[3,2-*c*][1,4]oxazine ring system, is described. Both partially saturated thiazine and oxazine rings adopt diplanar conformations. The molecular packing is influenced by weak C—H···O and π–π interactions.

## Comment

In previous communications, we reported the synthesis and pharmacological evaluation of 2-substituted-3-benzoyl-4-hydroxypyrido[3,2-*e*]-1,2-thiazines of general structure (I). Some of these compounds, obtained in connection with various projects, exhibited, depending on the substituent *R*, antimycobacterial (Malinka *et al.*, 1998), psychopharmacological (Malinka *et al.*, 1994) or analgesic (Malinka *et al.*, 2002) activity under preliminary pharmacological screening. The pronounced biological activity of the pyridothiazines (I) stimulated us to continue our search and prepare analogues, modified at the β-dicarbonyl grouping partially incorporated into the 1,2-thiazine ring, in order to evaluate the influence of this structural change on biological activity. In this context, we reported the conversion of pyridothiazine (I*b*) (*R* = $CH_3$) into derivatives of type *E*-(II) and the synthesis of the model compound (IV) from (I*a*) (*R* = H) for a comparison of the spectroscopic data (Malinka *et al.*, 2004). X-ray investigation of pyridothiazines *E*-(II) (Malinka *et al.*, 2004) showed that the thiazine ring adopts a diplanar conformation, with the *N*-methyl substituent positioned axially with respect to the

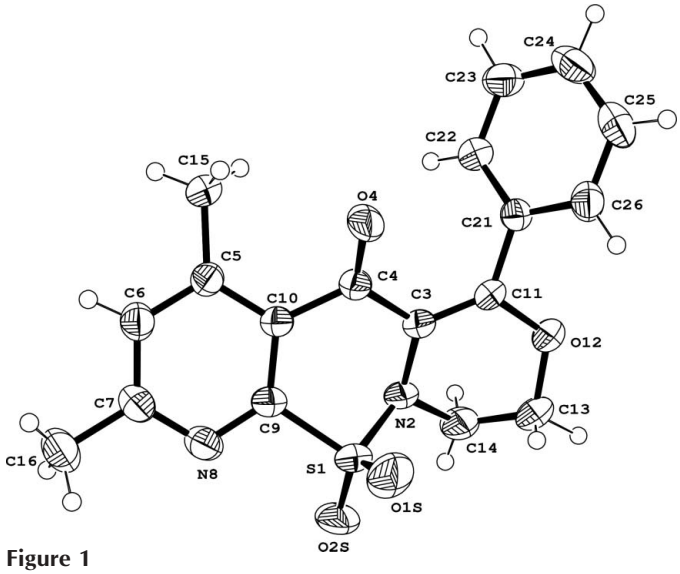
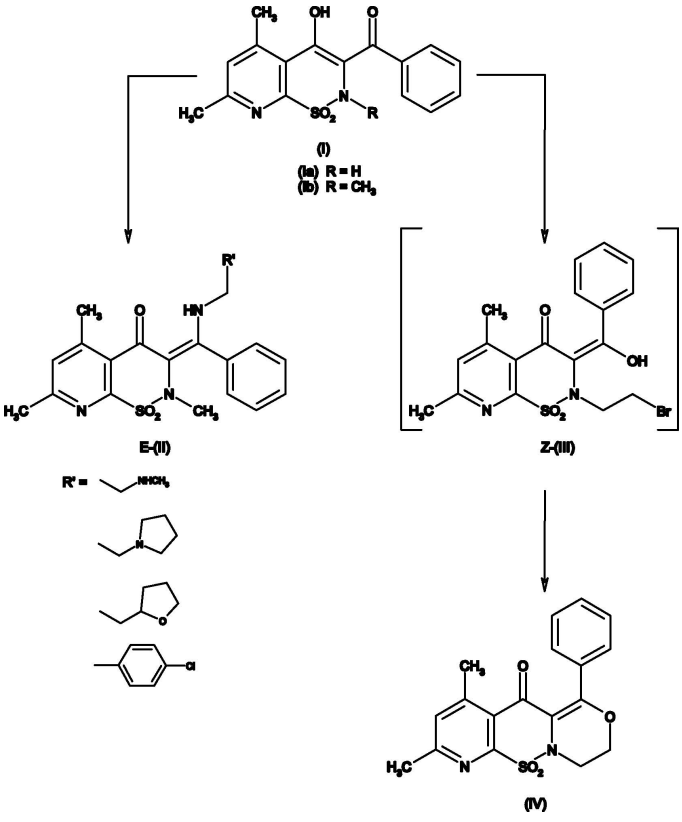



**Figure 1**
A view of the molecule of (IV), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented as small spheres of arbitrary radii.

thiazine ring. This configuration avoids steric hindrance between this group and the neighbouring double-bonded 3-aromatic substituent. However, inspection of a Dreiding model showed that such a conformation should prevent cyclization of the oxazine ring in (IV) and suggested, in contrast with (II), an equatorially positioned 2-N—C bond and *Z* stereochemistry around the exocyclic double bond in the hypothetical intermediate *Z*-(III), and therefore also in (IV). To verify our assumption, we report here the structure of (IV), which is of particular interest as this heterocycle contains the pyrido[3′2′:5,6][1,2]thiazino[3,2-*c*][1,4]oxazine ring system, the structural characteristics of which have not been reported previously.




A search of the Cambridge Structural Database (CSD; version of November 2004; Allen, 2002; Bruno *et al.*, 2002) did not reveal any crystal structures of compounds containing the pyrido–thiazine–oxazine system, showing only two organic structures with a pyrido[4,3-*c*]-1,2-thiazine unit (Fanghänel *et al.*, 1996) and 35 organic structures with a benzo[3,2-*e*]-1,2-thiazine fragment, *e.g.* meloxicam, the non-steroidal anti-inflammatory and analgesic agent (Luger *et al.*, 1996). Moreover, (IV) is currently being tested pharmacologically and the structural data should be helpful in understanding structure–activity relationships within this series of heterocycles, (I)–(IV).

The three-ring fused system of the title compound, (IV), comprises an aromatic pyridine ring and partially saturated thiazine and oxazine rings. The pyridine ring is planar to within 0.017 (2) Å. The thiazine and oxazine rings both adopt diplanar conformations, with asymmetry parameters $\Delta C_2^{S1,N2}$ = 8.8 (2)° and $\Delta C_2^{C13,C14}$ = 0.6 (3)°, respectively (Duax & Norton, 1975), and two torsion angles close to 0° [S1—C9—C10—C4 = −4.3 (2)° and N2—C3—C4—C10 = −1.7 (2)° in the thiazine ring, and C14—N2—C3—C11 = −8.1 (2)° and C13—O12—C11—C3 = −7.3 (3)° in the oxazine ring]. According to our assumption, atom O2*S* and the N2—C14 bond occupy equatorial positions, and the second O1*S* atom and the lone pair on atom N2 occupy axial positions with respect to the plane of the thiazine ring. This spatial arrangement on the thiazine ring favours the observed cyclization of the third oxazine ring. The S atom (Table 1) exhibits a distorted tetrahedral configuration, with the largest deviations in the O═S═O and N—S—C angles. The bond lengths S═O, S—N and S—C are comparable with those in similar substructures (Allen *et al.*, 1995). Atom N2 has a flattened pyramidal configuration, the sum of the angles around N2 being 348.1°, a value intermediate between $sp^3$ and $sp^2$ hybridization. This pyramidal configuration causes the chirality of the molecule, with the *R*-enantiomeric form observed in the crystal structure. The presence of bulky oxo and phenyl substituents on adjacent positions of the thiazine and oxazine rings is apparently the cause of significant asymmetry in the exocyclic bond angles at C11 [127.92 (16) and 108.87 (16)°], C11—C21 bond stretching [1.487 (2) Å] and the distortion of the C10, C4, O4, C3, C11 and C21 $\pi$-electron system from planarity [deviations of 0.153 (1) and −0.130 (1) Å for C21 and O4, respectively].

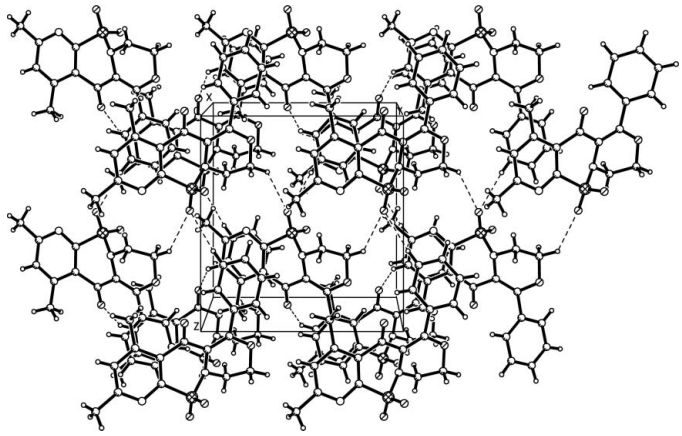


**Figure 2**
The molecular packing of (IV), viewed down the *a* axis. Dashed lines indicate weak C—H···O interactions.

In the crystal structure, molecules form a three-dimensional network *via* weak intermolecular C—H···O interactions (Table 2; Spek, 2003). The pyridine and phenyl rings belonging to the molecules related by a $2_1$ axis overlap each other; the shortest intermolecular contacts are C5···C26$^{i}$ = 3.435 (3) Å and C5···C21$^{ii}$ = 3.404 (3) Å, characteristic of $\pi$-stacking. The angle between the overlapping planes of these rings is 10.9 (1)°, forming molecular stacks in the [100] direction;

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

## Experimental

The title compound was prepared by heating 3-benzoyl-4-hydroxypyrido-1,2-thiazine in dimethylformamide containing an excess of 1,2-dibromoethane/NaOEt, according to the method of Malinka *et al.* (2004). The reaction gave a mixture of the enantiomers, which probably separated during the process of crystallization. Crystals suitable for X-ray diffraction analysis were grown by slow evaporation of a propan-1-ol solution.

*Crystal data*

$C_{18}H_{16}N_2O_4S$
$M_r = 356.39$
Monoclinic, $P2_1$
$a = 7.618$ (1) Å
$b = 10.280$ (2) Å
$c = 10.936$ (1) Å
$\beta = 99.55$ (1)°
$V = 844.6$ (2) Å$^3$
$Z = 2$
$D_x = 1.401$ Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 4038 reflections
$\theta = 1.9$–24.5°
$\mu = 0.22$ mm$^{-1}$
$T = 293$ (2) K
Prism, yellow
0.80 × 0.51 × 0.13 mm

*Data collection*

Kuma KM-4 diffractometer
$\omega$ scans
Absorption correction: numerical (*X-RED*; Stoe & Cie, 1999)
$T_{min} = 0.890$, $T_{max} = 0.975$
10 762 measured reflections
3439 independent reflections
2962 reflections with $I > 2\sigma(I)$
$R_{int} = 0.095$
$\theta_{max} = 28.7°$
$h = -10 \rightarrow 10$
$k = -9 \rightarrow 13$
$l = -14 \rightarrow 14$

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.035$
$wR(F^2) = 0.091$
$S = 0.96$
3439 reflections
275 parameters
Only H-atom coordinates refined
$w = 1/[\sigma^2(F_o^2) + (0.048P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.22$ e Å$^{-3}$
$\Delta\rho_{min} = -0.31$ e Å$^{-3}$
Extinction correction: *SHELXL97*
Extinction coefficient: 0.028 (4)
Absolute structure: Flack (1983), with 1315 Friedel pairs
Flack parameter: −0.05 (6)

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| S1—O2S | 1.4244 (15) | O12—C13 | 1.437 (3) |
| S1—O1S | 1.429 (2) | N2—C3 | 1.438 (2) |
| S1—N2 | 1.6450 (17) | N2—C14 | 1.471 (3) |
| S1—C9 | 1.777 (2) | C3—C11 | 1.350 (3) |
| O4—C4 | 1.2236 (19) | C3—C4 | 1.480 (2) |
| O12—C11 | 1.361 (2) | C4—C10 | 1.491 (3) |
| | | | |
| O2S—S1—O1*S* | 119.00 (11) | C3—N2—C14 | 114.06 (16) |
| O2S—S1—N2 | 106.43 (9) | C3—N2—S1 | 116.23 (12) |
| O1*S*—S1—N2 | 112.11 (10) | C14—N2—S1 | 117.82 (13) |
| O2S—S1—C9 | 111.00 (11) | C3—C11—O12 | 123.16 (16) |
| O1S—S1—C9 | 107.91 (11) | C3—C11—C21 | 127.92 (16) |
| N2—S1—C9 | 98.50 (8) | O12—C11—C21 | 108.87 (16) |

**Table 2**
Hydrogen-bond geometry (Å, °).

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| C6—H61···O4 | 0.86 (3) | 2.52 (3) | 3.136 (3) | 129 (2) |
| C13—H132···O2*S* | 1.11 (4) | 2.42 (3) | 3.207 (3) | 126 (2) |
| C23—H231···O2*S* | 0.94 (3) | 2.49 (3) | 3.426 (3) | 171 (3) |

The assumed absolute stereochemistry of the title compound was confirmed by refinement of the Flack (1983) parameter. All H atoms were located in a difference Fourier map and their coordinates were refined with isotropic displacement parameters $U_{iso}(H) = 1.5U_{eq}(C)$. Refined C—H distances were in the range 0.79 (3)–1.11 (4) Å.

Data collection: *CrysAlisCCD* (Kuma Diffraction, 2001); cell refinement: *CrysAlisRED* (Kuma Diffraction, 2001); data reduction: *CrysAlisRED*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *XP* (Sheldrick, 1989); software used to prepare material for publication: *SHELXL97* and *WinGX* (Farrugia, 1999).

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