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trans-(3*R*,2a*S*)-(−)-3-Phenyl-2,3,5,6,7,8-hexahydro-oxazolo[3,2-*a*]pyridine-5-thione

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.006 Å
R factor = 0.058
wR factor = 0.167
Data-to-parameter ratio = 22.2

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

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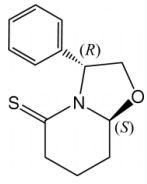
The crystal structure of the title compound, $C_{13}H_{15}NOS$, is very similar to that of the corresponding oxazolopyridin-5-one. However, a significant participation of a tautomeric thio–enolic form is observed, as reflected by the short N—C(=S) bond length of 1.328 (4) Å.

Comment

Chiral, non-racemic hexahydrooxazolo[3,2-*a*]pyridin-5-ones are strategic starting materials for the asymmetric synthesis of alkaloids and piperidine derivatives, *via* the stereoselective C—C bond formation at the position α to the N atom (Micouin *et al.*, 1994; Husson & Royer, 1999; Amat *et al.*, 2003, and references therein). The stereoselectivity of this key step is mainly driven by the geometry of the fused rings of the oxazolopyridine moiety and by the functionalization of atom C5. The synthesis and X-ray structure of *trans*-(3*R*,2a*S*)-(−)-3-phenyl-2,3,5,6,7,8-hexahydro-oxazolo[3,2-*a*]pyridin-5-one have been recently reported (Amat *et al.*, 2003; Roa *et al.*, 2003). The carbonyl group at C5 can be easily substituted by a thiocarbonyl group (see *Experimental*), providing (I), for which we report here the X-ray characterization.



(I)

The core of (I) consists of *trans*-fused rings (Fig. 1). As expected, the synthesis does not modify the absolute configuration of the chiral centers, which are retained as 2a*S* and 3*R*. The five-membered oxazole ring (O1/C2/C3/N4/C2a) approximates an envelope conformation on O1, as described by the puckering descriptor $\varphi = 173.7\ (6)^\circ$ (Cremer & Pople, 1975; Spek, 2003). A similar puckering analysis describes the six-membered N4/C2a/C8/C7/C6/C5 ring as an envelope on C8, with angles $\theta = 59.9\ (5)$ and $\varphi = 123.6\ (6)^\circ$ (Boeyens, 1978; Spek, 2003). For the six-membered ring, the mean deviation from the N4/C2a/C7/C6/C5 least-squares plane is 0.018 Å and atom C8 deviates from this plane by −0.627(3) Å; in the case of the oxazole ring, the mean deviation from the C2/C3/N4/C2a plane is 0.023 Å and atom O1 deviates by −0.527(3) Å. The resulting *trans*-fused bicyclic system is almost planar, with a dihedral angle between the rings of 14.7 (3)°. The phenyl ring at C3 makes a dihedral angle of 78.86 (9)° with the mean plane of the bicyclic system (excluding H atoms), minimizing steric hindrance for the overall molecule.

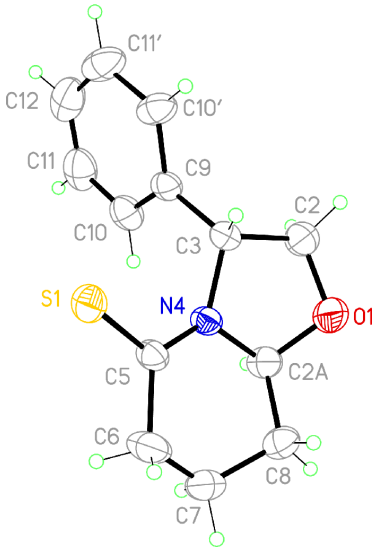


Figure 1
The structure of (I), with displacement ellipsoids at the 20% probability level for non-H atoms. H atoms are shown as small spheres of arbitrary radii.

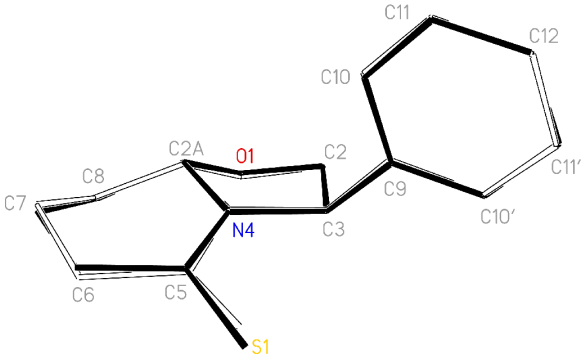


Figure 2
The superimposed fit for the molecules of (I) (solid lines) and the starting material (open lines). The atom-numbering scheme is given for (I). For clarity, H atoms have been omitted for both molecules.

The geometry of (I) is very similar (Table 1) to that of the starting material; a fit between both structures, excluding S1 and H atoms, gives an r.m.s. deviation of 0.083 Å (Fig. 2). Hence, the substitution of the carbonyl group at C5 by a thiocarbonyl group does not significantly affect the geometry of the oxazolopyridine core. However, a structural feature observed in (I) points out its potential utility as a synthon for alkaloid synthesis; the short bond length N4—C5 of 1.328 (4) Å indicates a significant participation of a tautomeric thio–enolic form in the solid state and, probably, in solution. This distance is even shorter than that observed for the starting material, 1.3513 (1) Å (Roa *et al.*, 2003). This behavior should facilitate the functionalization at C5. On the other hand, due to the large radius of the S atom, a good stereoselectivity can be expected for this synthetic step.

Experimental

0.300 g of *trans*-(3*R*,2a*S*)-(−)-3-phenyl-2,3,5,6,7,8-hexahydrooxazolo-[3,2-*a*]pyridine-5-one was dissolved in anhydrous benzene (30 ml) and 0.335 g of Lawesson's reagent [2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane 2,4-disulfide] was added to the solution. The reaction was refluxed until all starting material had been consumed, *ca* 1 h [TLC monitoring, SiO_2, hexane–AcOEt (7:3)]. Solvent was then removed under vacuum and the crude product purified by column chromatography [SiO_2, petroleum ether–AcOEt (9:1)], yielding (I) as a pale yellow solid (yield: 81%; m.p. 372 K). Single crystals were obtained by slow evaporation of an AcOEt solution at 298 K. The successful substitution of the carbonyl group by a thiocarbonyl fragment was confirmed by IR data [starting material: ν(C=O) = 1649 cm^{-1}; (I): ν(C=S) = 1594 cm^{-1}], as well as ^{13}C NMR data [$CDCl_3$, displacement for C5; starting material: δ = 168 p.p.m.; (I): δ = 203 p.p.m.].

Crystal data

$C_{13}H_{15}NOS$
M_r = 233.32
Orthorhombic, $P2_12_12_1$
a = 7.7811 (7) Å
b = 10.4190 (9) Å
c = 15.3834 (12) Å
V = 1247.15 (18) Å^3
Z = 4
D_x = 1.243 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 68 reflections
θ = 4.7–13.7°
μ = 0.24 mm^{-1}
T = 296 (1) K
Plate, pale yellow
0.65 × 0.60 × 0.18 mm

Data collection

Bruker *P*4 diffractometer
ω scans
Absorption correction: ψ scan (*XSCANS*; Siemens, 1996)
T_{min} = 0.858, T_{max} = 0.960
4962 measured reflections
3247 independent reflections
1958 reflections with $I > 2\sigma(I)$
R_{int} = 0.019
θ_{max} = 28.7°
$h = -10 \rightarrow 10$
$k = -14 \rightarrow 14$
$l = -20 \rightarrow 20$
3 standard reflections
every 97 reflections
intensity decay: 0.5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.058
$wR(F^2)$ = 0.167
S = 1.03
3247 reflections
146 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0716P)^2 + 0.236P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.29 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.023 (4)
Absolute structure: Flack (1983), 1374 Friedel pairs
Flack parameter = −0.03 (15)

Table 1
Selected geometric parameters (Å, °).

S1—C5	1.652 (3)	C3—N4	1.477 (4)
O1—C2a	1.409 (5)	C3—C9	1.489 (5)
O1—C2	1.412 (5)	N4—C5	1.328 (4)
C2—C3	1.540 (5)	C5—C6	1.520 (5)
C2a—C8	1.476 (5)	C6—C7	1.415 (5)
C2a—N4	1.483 (4)	C7—C8	1.490 (5)
C2a—O1—C2	105.2 (3)	C5—N4—C2a	125.5 (2)
O1—C2—C3	107.1 (3)	C3—N4—C2a	109.2 (2)
O1—C2a—C8	111.2 (3)	N4—C5—C6	115.5 (3)
O1—C2a—N4	103.0 (3)	N4—C5—S1	123.9 (2)
C8—C2a—N4	112.1 (3)	C6—C5—S1	120.5 (2)
N4—C3—C9	115.6 (3)	C7—C6—C5	119.0 (3)
N4—C3—C2	100.1 (3)	C6—C7—C8	115.3 (3)
C9—C3—C2	113.0 (3)	C2a—C8—C7	109.4 (3)
C5—N4—C3	124.0 (3)		

All H atoms were placed at idealized positions and treated as riding atoms, with C—H distances constrained to 0.93 (aromatic CH), 0.97 (CH_2) or 0.98 Å (CH), and U_{iso}(H) = 1.2 U_{eq}(parent).

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1998); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXL*97.

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