organic compounds

Two thiazolino[2,3-a]isoquinolinone S-oxides

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The structures of two racemic thiazolino[2,3-a]isoquinolinone S-oxides, i.e. 8,9-dimethoxy-2,3,5,6-tetrahydro-10bH-thiazolo-[2,3-a]isoquinolin-3-one 1-oxide [$C_{13}H_{15}NO_4S$, (IIa)] and 8,9-dimethoxy-10b-methyl-2,3,5,6-tetrahydro-10bH-thiazolo-[2,3-a]isoquinolin-3-one 1-oxide [$C_{14}H_{17}NO_4S$, (IIb)], are described. The thiazolinone ring in (IIa) exists in an envelope conformation, while in (IIb), it assumes a half-chair conformation. In (IIa) and (IIb), the six-membered heterocyclic ring adopts an envelope conformation. The O atom at sulfur is oriented in a pseudo-axial position, whereas the H atom in (IIa) and the methyl group in (IIb), linked to the stereogenic C centre, occupy a bisectional position with respect to the partially saturated pyridine ring and a pseudo-axial position with respect to the thiazolinone ring. In both structures, the S=O group and the substituent at the stereogenic C centre are trans with respect to one another. Intermolecular C—H···O hydrogen bonds are observed in the crystal lattice of (IIa) and (IIb).

Comment

Our studies of the sulfur-mediated synthesis of isoquinoline alkaloids (Brózda, 1994; Chrzanowska et al., 1998) have stimulated our interest in partially reduced thiazolo[2,3-a]-isoquinoline-type heterocycles. We anticipated that the corresponding S-oxides with stereogenic sulfur may be attractive for the preparation of chiral non-racemic alkaloids. It turned out, however, that no systematic investigation had been carried out in this area. Thus, we have undertaken studies to learn more about this type of compound (Rozwa-dowska & Sulima, 2001). The relative configuration between the substituents at the stereogenic C-10b and S-1 centres was one of the most important problems to be solved. In order to solve the problem, the X-ray crystal structure analyses of two racemic thiazolino[2,3-a]isoquinolinone S-oxides, namely 8,9-dimethoxy-2,3,5,6-tetrahydro-10bH-thiazolo[2,3-a]iso-

quinolin-3-one 1-oxide, (IIa), and 8,9-dimethoxy-10b-methyl-2,3,5,6-tetrahydro-10bH-thiazolo[2,3-a]isoquinolin-3-one 1-oxide, (IIb), have been carried out.

$$\text{(Ia): } R = H \qquad \xrightarrow{H_2O_2/MeOH/H_2O} \qquad \text{(IIa): } R = H$$

(Ia): R = H
(Ib): R = Me

(IIa): R = H
(IIb): R = Me

The molecular structures of compounds (IIa) and (IIb) and the atom-labelling schemes are illustrated in Figs. 1 and 2, respectively. In both structures, the O atom at S1 is in a pseudo-axial position [the angles to the Cremer & Pople thiazolinone plane normals are 3.21 (11) and 3.56 (8)° for (IIa) and (IIb), respectively]. The H atom in (IIa) and the methyl group in (IIb) at C10b occupy a bisectional position with respect to the partially saturated pyridine ring [at 30.05 (7) and 37.66 (9)°, respectively] and a pseudo-axial position with respect to the five-membered thiazolinone ring [at 9.38 (8) and 7.24 (10)°, respectively]. The S1=O1 bond is trans with respect to C10b—H10B in (IIa) and C10b—C13 in (IIb) [the torsion angle H10B—C10b—S1—O1 is 170° in (IIa) and C13—C10b—S1—O1 is 170.36 (11)° in (IIb)].

Both methoxy groups on the fused aromatic ring in (IIa) are coplanar with the ring, whereas those in (IIb) are rotated by 12.65 (18) (C8—OCH₃) and 12.00 (7)° (C9—OCH₃) out of the plane of the ring.

The five-membered thiazolinone ring has an envelope conformation in (IIa) [Cremer & Pople (1975) puckering parameters: $Q = 0.415$ (2) Å and $\Phi = 358.2$ (3)°], with the S atom 0.730 (3) Å out of the plane defined by the remaining four atoms. For (IIb), the thiazolinone ring is found to be in a half-chair conformation twisted on S1—C10b [Cremer & Pople (1975) puckering parameters: $Q = 0.421$ (1) Å and $\Phi = 350.6$ (2)°]. In both compounds, the partially hydrogenated pyridine moiety has an envelope conformation [Cremer & Pople (1975) puckering parameters: for (IIa), $Q = 0.437$ (3) Å,
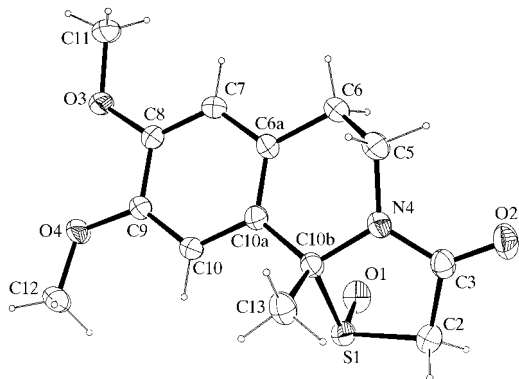

Figure 1
The molecular structure of (IIa) showing the atomic labelling scheme. Non-H atoms are drawn as 30% probability displacement ellipsoids and H atoms are shown as spheres of an arbitrary size.

$\Theta = 51.3\ (3)°$ and $\Phi = 56.4\ (4)°$; for (IIb), $Q = 0.451\ (2)$ Å, $\Theta = 52.6\ (3)°$ and $\Phi = 60.0\ (3)°$].

The dihedral angles between the best-fit planes of the central ring of the tricyclic skeleton and the outer six- and five-membered rings are 8.24 (14) and 36.82 (9)° in (IIa), and

Figure 2
The molecular structure of (IIb) showing the atomic labelling scheme. Non-H atoms are drawn as 30% probability displacement ellipsoids and H atoms are shown as spheres of an arbitrary size.

10.01 (7) and 41.05 (7)° in (IIb). The angles between the outer rings are 37.12 (10) and 41.37 (7)° in (IIa) and (IIb), respectively.

The bond lengths and angles in the partially reduced dimethoxyisoquinoline core of both compounds are similar to those observed in other structures (Pavkovic *et al.*, 1981; Chrzanowska *et al.*, 1987; Lee *et al.*, 1997; Warrener *et al.*, 1998; Maurin *et al.*, 1996; CSD, Version 5.20, Allen & Kennard, 1993). In the five-membered thiazolinone rings, the C3—N4 bond distances [1.342 (3) and 1.349 (2) Å in (IIa) and (IIb), respectively] are typical of a tertiary amide distance [1.346 (5) Å; Allen *et al.*, 1987]. The S1—O1 distances are similar [1.4836 (18) Å in (IIa) and 1.4817 (13) Å in (IIb)] and somewhat shorter than the C—S(=O)—C double bond [1.497 (1) Å; Allen *et al.*, 1987].

Apart from normal van der Waals interactions, the molecular packing in the solid state in both compounds is stabilized by possible C—H···O non-classical intermolecular hydrogen bonds (Tables 2 and 4).

Examination of the structures of (IIa) and (IIb) with *PLATON* (Spek, 1990) showed that there were no solvent-accessible voids in the crystal lattices.

Experimental

Compounds (IIa) and (IIb) were prepared from the corresponding thiazolino[2,3-a]isoquinolinones, (Ia) and (Ib), by oxidation with hydrogen peroxide in methanol/water (1:1) solutions (see Scheme). Sulfoxides (IIa) and (IIb) were isolated as single diastereomers in yields of 42 and 44%, respectively.

Compound (IIa)

Crystal data

$C_{13}H_{15}NO_4S$	$D_x = 1.388$ Mg m^{-3}
$M_r = 281.32$	Cu $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 49
$a = 19.967\ (2)$ Å	reflections
$b = 7.5484\ (9)$ Å	$\theta = 14.3–27.8°$
$c = 9.1666\ (13)$ Å	$\mu = 2.24$ mm^{-1}
$\beta = 102.967\ (11)°$	$T = 293\ (2)$ K
$V = 1346.3\ (3)$ Å^3	Plate, colourless
$Z = 4$	$0.50 \times 0.33 \times 0.22$ mm

Data collection

Kuma KM-4 diffractometer	$R_{int} = 0.044$
$\omega/2\theta$ scans	$\theta_{max} = 70.2°$
Absorption correction: ψ scan	$h = -24 \rightarrow 23$
(North *et al.*, 1968)	$k = -9 \rightarrow 0$
$T_{min} = 0.455$, $T_{max} = 0.611$	$l = 0 \rightarrow 11$
2735 measured reflections	2 standard reflections
2556 independent reflections	every 100 reflections
2119 reflections with $I > 2\sigma(I)$	intensity decay: 3.5%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.1120P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.050$	$+ 0.4410P]$
$wR(F^2) = 0.158$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.04$	$(\Delta/\sigma)_{max} = 0.001$
2556 reflections	$\Delta\rho_{max} = 0.86$ e Å^{-3}
174 parameters	$\Delta\rho_{min} = -0.33$ e Å^{-3}
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °) for (IIa).

S1—O1	1.4836 (18)	C3—N4	1.342 (3)
S1—C2	1.809 (2)	N4—C10b	1.449 (3)
S1—C10b	1.851 (2)	N4—C5	1.454 (3)
C3—O2	1.231 (3)		
O1—S1—C2	106.37 (11)	C3—N4—C10b	117.02 (18)
O1—S1—C10b	107.90 (10)	C3—N4—C5	124.59 (19)
C2—S1—C10b	87.79 (11)	C10b—N4—C5	118.37 (18)

Table 2
Hydrogen-bonding geometry (Å, °) for (IIa).

D—H···A	D—H	H···A	D···A	D—H···A
C2—H2B···O2^i	0.97	2.37	3.332 (3)	169
C10—H10···O1^{ii}	0.93	2.41	3.116 (3)	132
C11—H11B···O4^{iii}	0.96	2.54	3.370 (4)	144

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

Compound (IIb)

Crystal data

$C_{14}H_{17}NO_4S$	Cu $K\alpha$ radiation
$M_r = 295.35$	Cell parameters from 47
Orthorhombic, $Pbca$	reflections
$a = 15.9407\ (15)$ Å	$\theta = 15.0–29.9°$
$b = 9.1737\ (10)$ Å	$\mu = 2.20$ mm^{-1}
$c = 19.015\ (2)$ Å	$T = 293\ (2)$ K
$V = 2780.7\ (5)$ Å^3	Prism, colourless
$Z = 8$	$0.33 \times 0.31 \times 0.20$ mm
$D_x = 1.411$ Mg m^{-3}	

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Kuma KM-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan
  (North *et al.*, 1968)
  $T_{min} = 0.509$, $T_{max} = 0.645$
2643 measured reflections
2643 independent reflections
2252 reflections with $I > 2\sigma(I)$

$\theta_{max} = 70.1°$
$h = 0 \rightarrow 19$
$k = 0 \rightarrow 11$
$l = -23 \rightarrow 0$
2 standard reflections
  every 100 reflections
  intensity decay: 7.1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.033$
$wR(F^2) = 0.098$
$S = 1.06$
2643 reflections
185 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0485P)^2 + 0.9585P]$
  where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.20$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.00190 (15)

In both compounds, all H atoms were located in difference Fourier maps and refined with a riding model (C—H = 0.93–0.97 Å) and with U_{iso} constrained to be 1.2 (1.5 for methyl groups) times U_{eq} of the parent atom. The methyl-H atoms were refined as rigid groups, which were allowed to rotate.

For both compounds, data collection: *KM*-4 *Software* (Kuma, 1991); cell refinement: *KM*-4 *Software*; data reduction: *KM*-4 *Software*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *WINGX* (Farrugia, 1999).

Table 3
Selected geometric parameters (Å, °) for (II*b*).

S1—O1	1.4817 (13)	C3—N4	1.349 (2)
S1—C2	1.8083 (18)	N4—C5	1.450 (2)
S1—C10b	1.8656 (16)	N4—C10b	1.4560 (19)
C3—O2	1.223 (2)		
O1—S1—C2	106.33 (8)	C3—N4—C5	123.49 (14)
O1—S1—C10b	108.47 (7)	C3—N4—C10b	116.68 (14)
C2—S1—C10b	87.97 (8)	C5—N4—C10b	119.78 (13)

Table 4
Hydrogen-bonding geometry (Å, °) for (II*b*).

D—H···A	D—H	H···A	D···A	D—H···A
C2—H2A···O4^i	0.97	2.56	3.410 (2)	147
C10—H10···O1^{ii}	0.93	2.56	3.482 (2)	170
C11—H11C···O2^{iii}	0.96	2.50	3.377 (3)	152
C13—H13B···O1^{ii}	0.96	2.46	3.386 (2)	161

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

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