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# 2-Aminothiazole and 2-aminothiazolinone derivatives

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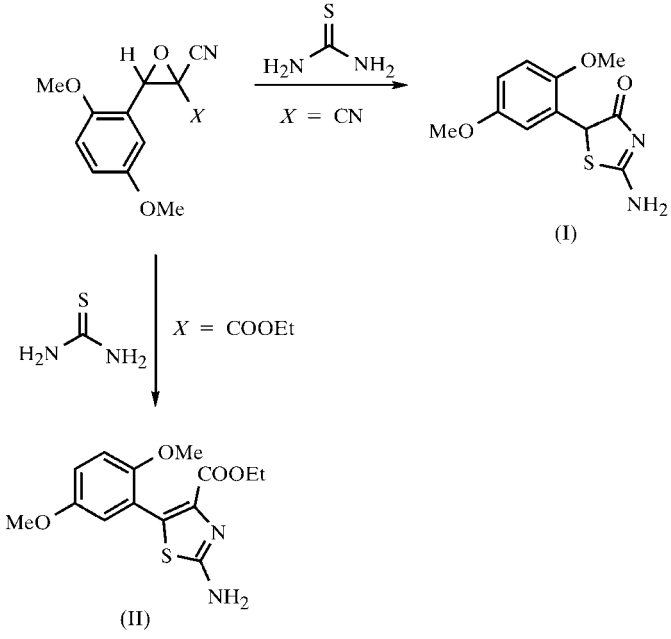
The reaction of different substituted $\alpha$-cyanooxiranes with thiourea resulted in the formation of the 2-aminothiazolinone derivative 2-amino-5-(2,5-dimethoxyphenyl)-1,3-thiazol-4(5*H*)-one, $C_{11}H_{12}N_2O_3S$, (I), and the 2-aminothiazole derivative ethyl 2-amino-5-(2,5-dimethoxyphenyl)-1,3-thiazole-4-carboxylate, $C_{14}H_{16}N_2O_4S$, (II). The geometries of the two crystallographically independent molecules in (II) are nearly identical but mirror related. The crystal structures of both compounds contain two types of intermolecular hydrogen bonds.

## Comment

Many naturally occurring and synthetic thiazole derivatives exhibit biological activities, such as antibiotic, anti-inflammatory, anthelmintic or fungicidal properties (Metzger, 1984; Crews *et al.*, 1988; Shinagawa *et al.*, 1997; Shivarama Holla *et al.*, 2003). The 1,3-thiazole ring can be prepared using several different methods (Metzger, 1984), although the most widely used approach relies on Hantzsch's synthesis (Hantzsch & Weber, 1887), which starts from $\alpha$-halocarbonyl derivatives. This method can be modified by replacement of the $\alpha$-halocarbonyl derivatives with 2-cyanooxiranes reacting as synthetic equivalents of the ketene dication (Robert *et al.*, 1995, and references therein). We focus our attention here on the synthesis of thiazole and thiazoline derivatives of 2,2-dicyanooxirane and 2-cyano-2-oxiranecarboxylate derivatives. On addition of thiourea, on the one hand, geminal dicyanooxirane derivatives were transformed into 2-aminothiazolinones, and on the other hand, ethyl 2-cyano-2-oxiranecarboxylate yielded 2-aminothiazoles. In this paper, we present the syntheses and structure determinations of 2-amino-5-(2,5-dimethoxyphenyl)-1,3-thiazol-4(5*H*)-one, (I), and ethyl 2-amino-5-(2,5-dimethoxyphenyl)-1,3-thiazole-4-carboxylate, (II). To the best of our knowledge, this is the first report of the crystal structure of the 2-aminothiazole derivative.

The molecular structure of (I) is shown in Fig. 1. The heterocyclic (thiazole) ring is close to being perfectly planar, and the angle between the least-squares planes of the phenyl and thiazole rings is 86.46 (4)°. Other geometric parameters are listed in Table 1. The two types of hydrogen-bonding interactions are illustrated in Fig. 2. The first involves N—H···N bonds between the amino group and the endocyclic thiazole N atom of two molecules symmetry-related by an inversion centre. These dimers are further connected into chains along the *a* axis *via* N—H···O interactions with adjacent dimeric units; see Table 2 for hydrogen-bonding details.




X-ray analysis of (II) reveals that the crystals consist of two crystallographically independent molecules (*A* and *B*) related by a local pseudo-inversion centre. The atomic labelling schemes for these two molecules include the letter corre-

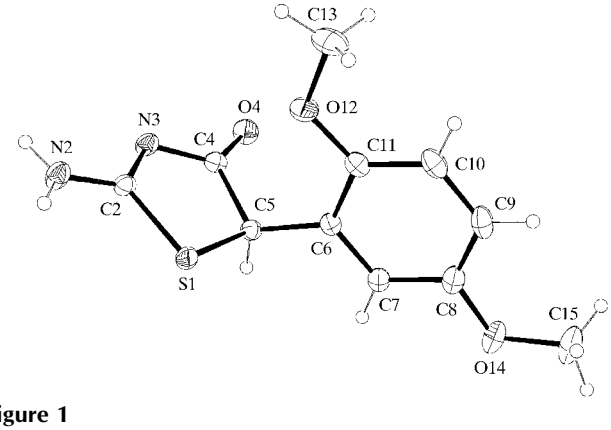



**Figure 1**
A view of the molecule of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

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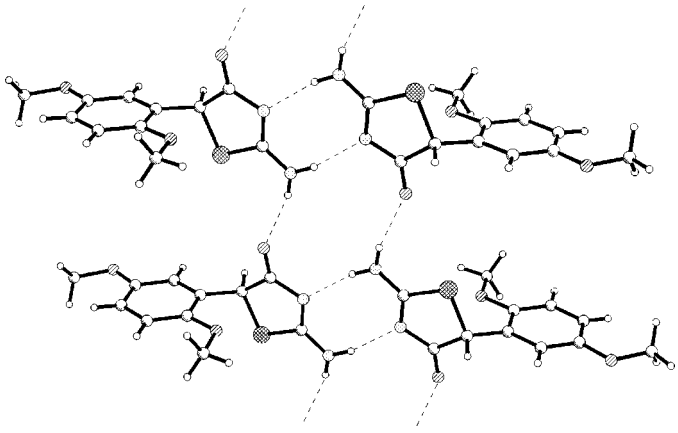

**Figure 2**
The intermolecular hydrogen bonding in (I), showing the formation of a chain of dimeric units that propagates along the *a* direction.

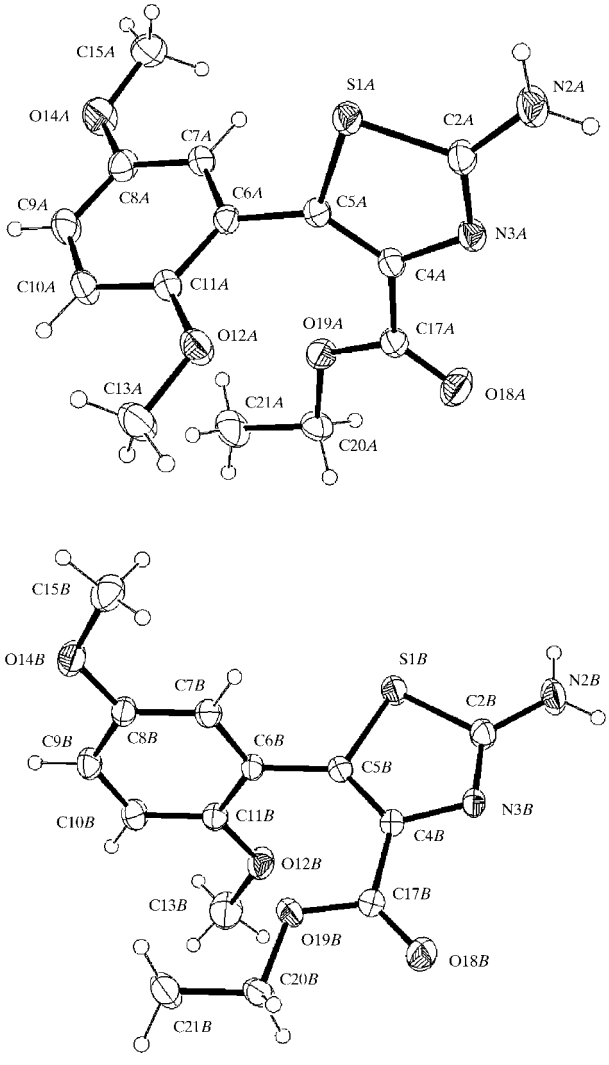


**Figure 3**
A view of the independent molecules, *A* and *B*, of (II), showing the atom-numbering schemes. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

sponding to the independent molecule (Fig. 3). The two independent mirror-related molecules have similar conformations (Fig. 4), and there are no significant differences in bond lengths and angles for molecules *A* and *B* (Table 3). The angles between the planes of the dimethoxyphenyl and thiazole rings are 69.32 (12) and 71.44 (12)° in molecules *A* and *B*,

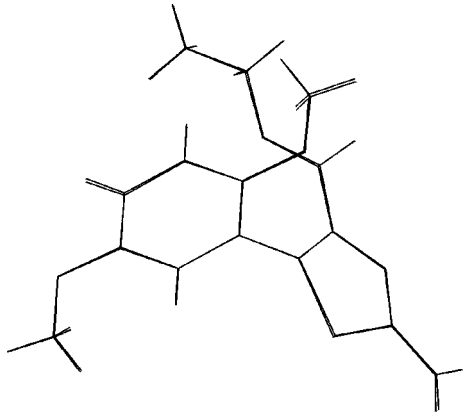

**Figure 4**
A superposition of the two independent molecules of (II).

respectively. As in (I), two types of intermolecular hydrogen bonds are present. The amino group of each molecule is involved both in an interaction with an endocyclic N atom and in the formation of an N—H···O bond with a neighbouring molecule. While in compound (I) the carbonyl O atom of the thiazolinone ring acts as a hydrogen-bond acceptor, in compound (II) one of the methoxy groups on each of the substituted phenyl rings serves as a hydrogen-bond acceptor; see Table 4 for hydrogen-bonding details.

## Experimental

For the preparation of (I), a mixture of 3-(2,5-dimethoxyphenyl)-2,2-oxiranedicarbonitrile (0.230 g, 1 mmol) and thiourea (0.076 g, 1 mmol) was dissolved in acetonitrile (5 ml) and stirred at room temperature for 24 h. The product precipitated from the reaction mixture in 68% yield (m.p. 469–471 K). $^1$H NMR (300 MHz, DMSO, p.p.m.): $\delta$ 3.68 (*s*, 3H), 3.70 (*s*, 3H), 5.34 (*s*, 1H), 6.73 (*d*, 1H), 6.87 (*dd*, 1H), 6.93 (*d*, 1H), 8.73 (*s*, 1H), 8.99 (*s*, 1H). Analysis found: C 52.08, H 4.36, N 10.96%; calculated for $C_{11}H_{12}N_2O_3S$: C 52.37, H 4.79, N 11.10%. Crystals suitable for X-ray diffraction were obtained by recrystallization from ethanol. For the preparation of (II), a mixture of ethyl 2-cyano-3-(2,5-dimethoxyphenyl)-2-oxiranecarboxylate (0.277 g, 1 mmol) and thiourea (0.076 g, 1 mmol) was dissolved in acetonitrile (5 ml) and refluxed for 6 h. Water (50 ml) was added to the reaction mixture and the solution was extracted with ether (3 × 50 ml). The organic layers were combined and dried over sodium sulfate(VI), and the solid residue was recrystallized from ethanol to give (II) in 49% yield (m.p. 404–405 K). $^1$H NMR (300 MHz, DMSO, p.p.m.): $\delta$ 1.03 (*t*, 3H), 3.66 (*s*, 3H), 3.71 (*s*, 3H), 4.01 (*q*, 2H), 6.79 (*d*, 1H), 6.89 (*dd*, 1H), 6.99 (*d*, 1H), 7.20 (*s*, 2H).

## Compound (I)

*Crystal data*

$C_{11}H_{12}N_2O_3S$
$M_r = 252.29$
Triclinic, $P\overline{1}$
$a = 6.9572$ (5) Å
$b = 8.1499$ (7) Å
$c = 10.4564$ (10) Å
$\alpha = 99.800$ (2)°
$\beta = 101.050$ (2)°
$\gamma = 99.540$ (2)°
$V = 561.21$ (8) Å$^3$
$Z = 2$
$D_x = 1.493$ Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from all reflections
$\theta = 2.9$–27.5°
$\mu = 0.29$ mm$^{-1}$
$T = 293$ (2) K
Prism, colourless
0.40 × 0.35 × 0.30 mm

*Data collection*

Nonius KappaCCD diffractometer
$\varphi$ and $\omega$ scans
3846 measured reflections
2490 independent reflections
2349 reflections with $I > 2\sigma(I)$
$R_{int} = 0.014$
$\theta_{max} = 27.5°$
$h = -8 \rightarrow 9$
$k = -10 \rightarrow 10$
$l = -12 \rightarrow 13$

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.029$
$wR(F^2) = 0.078$
$S = 1.05$
2490 reflections
202 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0341P)^2 + 0.1774P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.27$ e Å$^{-3}$
$\Delta\rho_{min} = -0.22$ e Å$^{-3}$

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

| | | | |
|---|---|---|---|
| S1—C2 | 1.7488 (11) | C6—C11 | 1.4042 (16) |
| S1—C5 | 1.8185 (11) | C7—C8 | 1.3937 (17) |
| C2—N2 | 1.3134 (16) | C8—O14 | 1.3741 (16) |
| C2—N3 | 1.3270 (15) | C8—C9 | 1.379 (2) |
| N3—C4 | 1.3671 (15) | C9—C10 | 1.388 (2) |
| C4—O4 | 1.2211 (14) | C10—C11 | 1.3871 (17) |
| C4—C5 | 1.5462 (15) | C11—O12 | 1.3697 (16) |
| C5—C6 | 1.5051 (15) | O12—C13 | 1.4350 (16) |
| C6—C7 | 1.3863 (16) | O14—C15 | 1.4264 (18) |
| | | | |
| C2—S1—C5 | 90.41 (5) | C7—C6—C5 | 118.89 (10) |
| N2—C2—N3 | 123.15 (11) | C11—C6—C5 | 121.68 (10) |
| N2—C2—S1 | 119.43 (9) | C6—C7—C8 | 121.05 (11) |
| N3—C2—S1 | 117.41 (9) | O14—C8—C9 | 125.16 (12) |
| C2—N3—C4 | 112.25 (9) | O14—C8—C7 | 115.44 (12) |
| O4—C4—N3 | 124.39 (10) | C9—C8—C7 | 119.40 (12) |
| O4—C4—C5 | 120.63 (10) | C8—C9—C10 | 120.16 (12) |
| N3—C4—C5 | 114.90 (9) | C11—C10—C9 | 120.84 (12) |
| C6—C5—C4 | 117.84 (9) | O12—C11—C10 | 125.04 (11) |
| C6—C5—S1 | 112.49 (7) | O12—C11—C6 | 115.68 (10) |
| C4—C5—S1 | 104.59 (7) | C10—C11—C6 | 119.28 (12) |
| C7—C6—C11 | 119.27 (11) | C11—O12—C13 | 117.02 (12) |

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N2—H2$A$···N3$^{i}$ | 0.905 (19) | 2.04 (2) | 2.9281 (15) | 165.3 (17) |
| N2—H2$B$···O4$^{ii}$ | 0.860 (18) | 2.176 (19) | 3.0102 (15) | 163.1 (16) |

Symmetry codes: (i) $1-x, 1-y, 2-z$; (ii) $1+x, y, z$.

## Compound (II)

*Crystal data*

$C_{14}H_{16}N_2O_4S$
$M_r = 308.35$
Monoclinic, $P2_1$
$a = 8.1740$ (5) Å
$b = 22.8266$ (12) Å
$c = 9.0300$ (5) Å
$\beta = 116.444$ (1)°
$V = 1508.57$ (15) Å$^3$
$Z = 4$
$D_x = 1.358$ Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from all reflections
$\theta = 2.8$–27.5°
$\mu = 0.23$ mm$^{-1}$
$T = 293$ (2) K
Prism, colourless
0.40 × 0.40 × 0.30 mm

*Data collection*

Nonius KappaCCD diffractometer
$\varphi$ and $\omega$ scans
6339 measured reflections
6339 independent reflections
5468 reflections with $I > 2\sigma(I)$
$R_{int} = 0.031$
$\theta_{max} = 27.5°$
$h = -10 \rightarrow 10$
$k = -29 \rightarrow 23$
$l = -11 \rightarrow 11$

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.053$
$wR(F^2) = 0.139$
$S = 1.04$
6339 reflections
385 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0772P)^2 + 0.6156P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.83$ e Å$^{-3}$
$\Delta\rho_{min} = -0.23$ e Å$^{-3}$
Absolute structure: Flack (1983), 2796 Friedel pairs
Flack parameter = 0.02 (8)

**Table 3**
Selected interatomic distances (Å) for (II).

| | | | |
|---|---|---|---|
| S1$A$—C5$A$ | 1.739 (3) | S1$B$—C5$B$ | 1.742 (3) |
| S1$A$—C2$A$ | 1.753 (3) | S1$B$—C2$B$ | 1.753 (3) |
| C2$A$—N3$A$ | 1.307 (4) | C2$B$—N3$B$ | 1.298 (4) |
| C2$A$—N2$A$ | 1.332 (4) | C2$B$—N2$B$ | 1.347 (4) |
| N3$A$—C4$A$ | 1.381 (4) | N3$B$—C4$B$ | 1.386 (4) |
| C4$A$—C5$A$ | 1.370 (4) | C4$B$—C5$B$ | 1.351 (4) |
| C4$A$—C17$A$ | 1.484 (4) | C4$B$—C17$B$ | 1.482 (4) |
| C5$A$—C6$A$ | 1.478 (4) | C5$B$—C6$B$ | 1.487 (4) |
| C6$A$—C7$A$ | 1.388 (4) | C6$B$—C7$B$ | 1.382 (4) |
| C6$A$—C11$A$ | 1.394 (4) | C6$B$—C11$B$ | 1.393 (4) |
| C7$A$—C8$A$ | 1.390 (4) | C7$B$—C8$B$ | 1.401 (4) |
| C8$A$—C9$A$ | 1.377 (5) | C8$B$—O14$B$ | 1.373 (4) |
| C8$A$—O14$A$ | 1.382 (4) | C8$B$—C9$B$ | 1.381 (5) |
| C9$A$—C10$A$ | 1.382 (5) | C9$B$—C10$B$ | 1.376 (5) |
| C10$A$—C11$A$ | 1.398 (4) | C10$B$—C11$B$ | 1.395 (4) |
| C11$A$—O12$A$ | 1.376 (4) | C11$B$—O12$B$ | 1.366 (4) |
| O12$A$—C13$A$ | 1.414 (4) | O12$B$—C13$B$ | 1.405 (5) |
| O14$A$—C15$A$ | 1.413 (5) | O14$B$—C15$B$ | 1.428 (5) |
| C17$A$—O18$A$ | 1.198 (4) | C17$B$—O18$B$ | 1.196 (4) |
| C17$A$—O19$A$ | 1.328 (4) | C17$B$—O19$B$ | 1.332 (4) |
| O19$A$—C20$A$ | 1.447 (4) | O19$B$—C20$B$ | 1.441 (4) |
| C20$A$—C21$A$ | 1.498 (5) | C20$B$—C21$B$ | 1.499 (5) |

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N2$A$—H2$A$···N3$B^{iii}$ | 0.86 | 2.13 | 2.980 (4) | 168 |
| N2$A$—H2$B$···O14$A^{iii}$ | 0.86 | 2.45 | 3.248 (4) | 156 |
| N2$B$—H2$C$···N3$A^{iv}$ | 0.86 | 2.12 | 2.971 (4) | 168 |
| N2$B$—H2$D$···O14$B^{iv}$ | 0.86 | 2.37 | 3.178 (4) | 158 |

Symmetry codes: (iii) $x, y, z-1$; (iv) $x, y, 1+z$.

For (I), all H atoms were located in difference Fourier syntheses and were included in the refinement [C—H = 0.928 (18)–0.99 (2) Å]. For (II), H atoms were placed at calculated positions (C—H = 0.93–0.97 Å) and treated as riding.

For both compounds, data collection: *COLLECT* (Nonius, 1998); cell refinement and data reduction: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); structure solution: *SHELXS*97 (Sheldrick, 1997); structure refinement: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97 and *PLATON* (Spek, 2003).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1642). Services for accessing these data are described at the back of the journal.

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