# research papers

# Heterocyclic tautomerism: reassignment of two crystal structures of 2-amino-1,3-thiazolidin-4-one derivatives

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The structures of 5-(2-hydroxyethyl)-2-[(pyridin-2-yl)amino]-1,3-thiazolidin-4-one, $C_{10}H_{11}N_3O_2S$, (I), and ethyl 4-[(4-oxo-1,3-thiazolidin-2-yl)amino]benzoate, $C_{12}H_{12}N_2O_3S$, (II), which are identical to the entries with refcodes GACXOZ [Váňa et al. (2009). J. Heterocycl. Chem. **46**, 635–639] and HEGLUC [Behbehani & Ibrahim (2012). Molecules, **17**, 6362–6385], respectively, in the Cambridge Structural Database [Allen (2002). Acta Cryst. B**58**, 380–388], have been redetermined at 130 K. This structural study shows that both investigated compounds exist in their crystal structures as the tautomer with the carbonyl–imine group in the five-membered heterocyclic ring and an exocyclic amine N atom, rather than the previously reported tautomer with a secondary amide group and an exocyclic imine N atom. The physicochemical and spectroscopic data of the two investigated compounds are the same as those of GACXOZ and HEGLUC, respectively. In the thiazolidin-4-one system of (I), the S and chiral C atoms, along with the hydroxyethyl group, are disordered. The thiazolidin-4-one fragment takes up two alternative locations in the crystal structure, which allows the molecule to adopt R and S configurations. The occupancy factors of the disordered atoms are 0.883 (2) (for the R configuration) and 0.117 (2) (for the S configuration). In (I), the main factor that determines the crystal packing is a system of hydrogen bonds, involving both strong N—H···N and O—H···O and weak C—H···O hydrogen bonds, linking the molecules into a three-dimensional hydrogen-bond network. On the other hand, in (II), the molecules are linked via N—H···O hydrogen bonds into chains.

## 1. Introduction

1,3-Thiazolidin-4-one derivatives are a well known class of patented drugs, examples being hypoglycaemic thiazolidine-diones (pioglitazone and its analogues), aldose reductase inhibitors (epalrestat), anti-inflammatory agents (darbufe-lone) and new-generation diuretics (etozoline). In modern medicinal chemistry, the thiazolidinone core is a powerful biophore for the rational design of 'drug-like' molecules. Modern research into the pharmacological potential of 1,3-thiazolidin-4-ones has allowed the establishment of a wide spectrum of pharmacological activities, including anticancer, anti-inflammatory, antiviral, antiparasitic, antimicrobial and anti-oxidant (Lesyk & Zimenkovsky, 2004; Lesyk et al., 2011).
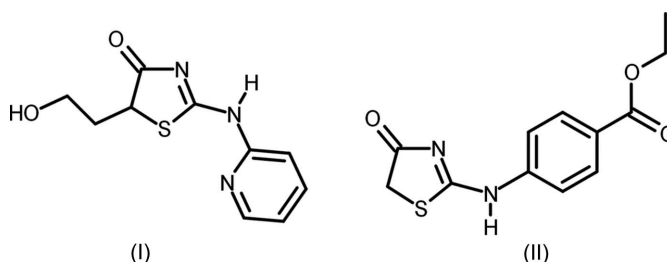


Scheme 1

It is worth noting that studies regarding amino–imino tautomerism in 2-amino(imino)-1,3-thiazolidin-4-one derivatives have been ongoing for almost 50 years. The investigations have been performed on crystalline and liquid phases using different spectroscopic techniques, e.g. IR, UV, and $^1$H and $^{13}$C NMR, or sometimes with quantum-chemical calculations. X-ray crystallography is not commonly used among the analytical methods applied to structural studies concerning



*A*1 (amine form)        *A*2 (imine form)
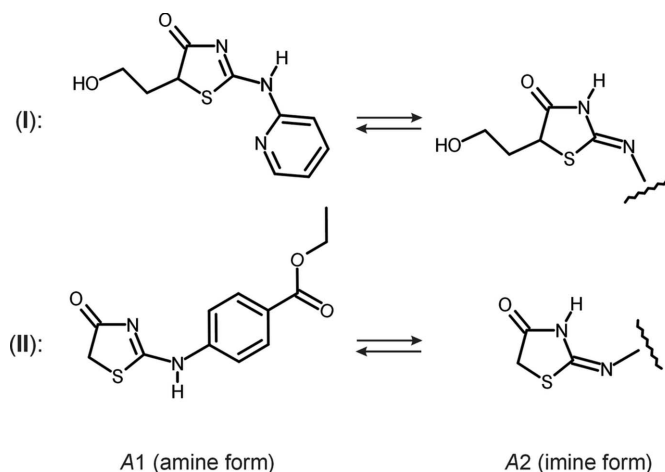
Scheme 2

tautomerism. In the Cambridge Structural Database (CSD, Version 5.35; Allen, 2002), we found only 21 structures with the amine form (refcodes EKELEL FIVPIJ, FOWQOY, IHUFAS, IMPTHA01, IMPTHA12, IMTAZO01, INMTZO, JOBGOW, KUKZUM, PACPIU, PATAZO, PTHAZO10, SALYOT, SINQOW, SINQUC, TEBDAH, ULACAM, VELBEU, WOSMAS and YUQCAP) and 16 with the imine form (refcodes EHITZO, GACXOZ, HEGLUC, HEGMAJ,

**Table 1**
Experimental details.

| | (I) | (II) |
|---|---|---|
| **Crystal data** | | |
| Chemical formula | $C_{10}H_{11}N_3O_2S$ | $C_{12}H_{12}N_2O_3S$ |
| $M_r$ | 237.28 | 264.30 |
| Crystal system, space group | Triclinic, $P\bar{1}$ | Triclinic, $P\bar{1}$ |
| Temperature (K) | 130 | 130 |
| $a$, $b$, $c$ (Å) | 5.78910 (15), 8.8045 (2), 10.9688 (3) | 3.9850 (2), 5.5113 (3), 26.8877 (14) |
| $\alpha$, $\beta$, $\gamma$ (°) | 90.638 (2), 95.794 (2), 107.990 (2) | 84.483 (5), 89.670 (5), 86.338 (5) |
| $V$ (Å$^3$) | 528.50 (3) | 586.58 (6) |
| $Z$ | 2 | 2 |
| Radiation type | Mo $K\alpha$ | Mo $K\alpha$ |
| $\mu$ (mm$^{-1}$) | 0.29 | 0.28 |
| Crystal size (mm) | $0.42 \times 0.22 \times 0.10$ | $0.40 \times 0.34 \times 0.05$ |
| | | |
| **Data collection** | | |
| Diffractometer | Agilent Xcalibur Atlas diffractometer | Agilent Xcalibur Atlas diffractometer |
| Absorption correction | Multi-scan (*CrysAlis PRO*; Agilent, 2012) | Multi-scan (*CrysAlis PRO*; Agilent, 2010) |
| $T_{min}$, $T_{max}$ | 0.939, 1.000 | 0.908, 1.000 |
| No. of measured, independent and observed $[I > 2\sigma(I)]$ reflections | 5332, 2501, 2338 | 7855, 2804, 2604 |
| $R_{int}$ | 0.016 | 0.017 |
| $(\sin\theta/\lambda)_{max}$ (Å$^{-1}$) | 0.684 | 0.684 |
| | | |
| **Refinement** | | |
| $R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, $S$ | 0.036, 0.088, 1.13 | 0.030, 0.078, 1.05 |
| No. of reflections | 2501 | 2804 |
| No. of parameters | 167 | 168 |
| No. of restraints | 4 | 0 |
| H-atom treatment | H atoms treated by a mixture of independent and constrained refinement | H atoms treated by a mixture of independent and constrained refinement |
| $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.34, −0.21 | 0.54, −0.23 |

Computer programs: *CrysAlis PRO* (Agilent, 2012), *SHELXS97* (Sheldrick, 2008), *SHELXL97* (Sheldrick, 2008), *ORTEP-3 for Windows* (Farrugia, 2012), *WinGX* (Farrugia, 2012), *OLEX2* (Dolomanov *et al.*, 2009) and *PLATON* (Spek, 2009).

HEGMEN, HEGMIR, HEGMOX, IMTAZO, IOTAGP, IXTAZD10, RIPMOT, ROMXUN, SOHHIH, ULACEQ, VAMPUW and YARLIN), the latter set including two structures, GACXOZ (Váňa *et al.*, 2009) and HEGLUC (Behbehani & Ibrahim, 2012), with an incorrectly specified tautomeric form, as will be demonstrated here.

As part of a programme aimed at the development of new biologically active compounds, we have prepared 5-(2-hydroxyethyl)-2-[(pyridin-2-yl)amino]-1,3-thiazolidin-4-one, (I) (*cf.* CSD refcode GACXOZ), and ethyl 4-[(4-oxo-1,3-thiazolidin-2-yl)amino]benzoate, (II) (*cf.* CSD refcode HEGLUC) (Scheme 1), and have made corrections to the interpretations of their previously published structures. According to the previous reports, the investigated compounds exist in tautomeric form *A*2, with a secondary amide group in the five-membered heterocyclic ring and an exocyclic imine N atom (see Scheme 2).

## 2. Experimental

### 2.1. Synthesis and crystallization

The title compounds were synthesized by methods used for obtaining 2-amino(imino)-1,3-thiazolidin-4-one derivatives (Subtel'na *et al.*, 2010; Geronikaki *et al.*, 2008; Ostapiuk *et al.*, 2012). Compound (I) was prepared by the [2+3]-cyclo-condensation reaction of 3-bromotetrahydrofuran-2-one (α-bromo-γ-butyrolactone) with 1-(pyridin-2-yl)thiourea in

the presence of fused sodium acetate in refluxing ethanol. Compound (II) was synthesized through cyclocondensation of ethyl 4-(2-chloroacetylamino)benzoate and ammonium thiocyanate in ethanol (Behbehani & Ibrahim, 2012). It is known that the above-mentioned reactions do not stop at the nucleophilic substitution stage (Geronikaki *et al.*, 2008; Ostapiuk *et al.*, 2012). The intermediate α-thiocyanatoamide undergoes spontaneous cyclization/rearrangement to give the thiazolidin-4-one derivative, (II).

The physicochemical and spectroscopic data of (I) and (II) (see *Supporting information*) are the same as for GACXOZ and HEGLUC, respectively. Crystals suitable for single-crystal X-ray diffraction analysis were grown by slow evaporation of solutions in methanol [for (I)] and dimethylformamide [for (II)].

### 2.2. Refinement

For both (I) and (II), N-bound H atoms were obtained from difference Fourier maps and refined freely and isotropically. The remaining H atoms were positioned geometrically and refined within the riding-model approximation, with methyl C—H = 0.98 Å, methylene C—H = 0.99 Å, methine C—H = 1.00 Å, C$sp^2$ C—H = 0.95 Å and O—H = 0.88 Å, and with $U_{iso}(H) = 1.5U_{eq}(C,O)$ for methyl and hydroxy H atoms, or $1.2U_{eq}(C)$ otherwise. The methyl groups were refined as rigid groups, which were allowed to rotate. Non-H atoms of the disordered part of the molecule of (I) were obtained from
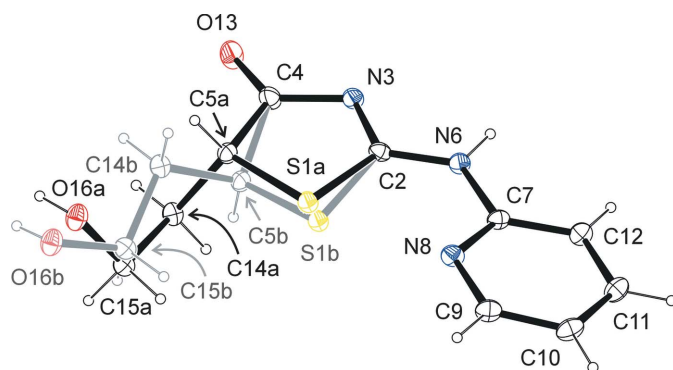
**Figure 1**
The molecular structure of (I), showing the atomic labelling scheme. Displacement ellipsoids are drawn at the 30% probability level. The disordered part *b* of the molecule is coloured grey, as distinct from the major component shown in black.
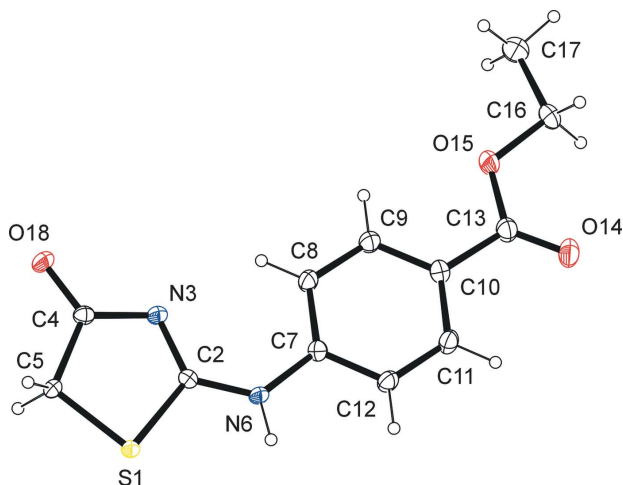


**Figure 2**
A view of the molecule of (II), showing the atomic labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

difference Fourier maps. During refinement, the atomic displacement ellipsoids of the corresponding atoms in the alternative conformations, *a* and *b*, were constrained to be identical. Corresponding bond distances within the two disordered components were restrained to be similar. The H atoms of the –OH groups of the hydroxyethyl residues in positions *a* and *b* were separated in an arbitrary manner by applying a H$\cdots$H distance restraint of 0.61 (2) Å.

## 3. Results and discussion
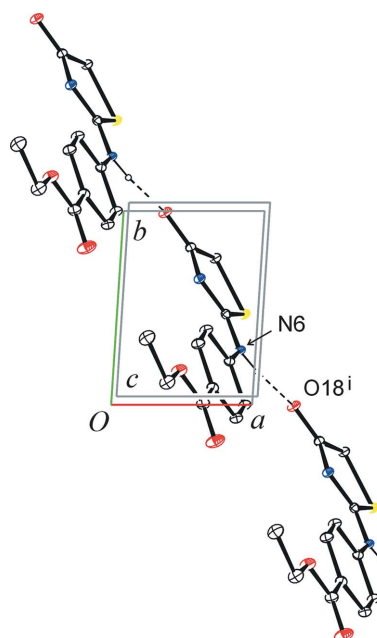
### 3.1. Tautomeric forms

Our revision of the X-ray studies has shown that, in their crystal structures, compounds (I) and (II) adopt tautomeric form *A1* rather than the previously suggested form *A2* (Scheme 2, and Figs. 1 and 2). In both structures, the H atom was located at the exocyclic N atom (N6). This observation for (II) is supported by the presence of an intermolecular N6—H6$\cdots$O18$^i$ hydrogen bond (Table 2 and Fig. 3), in which atom N6 acts as a proton donor and carbonyl atom O18 acts as a

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

| $D$—H$\cdots$$A$ | $D$—H | H$\cdots$$A$ | $D$$\cdots$$A$ | $D$—H$\cdots$$A$ |
|---|---|---|---|---|
| N6—H6$\cdots$O18$^i$ | 0.857 (17) | 1.954 (17) | 2.7882 (14) | 164.3 (17) |

Symmetry code: (i) $x + 1$, $y - 1$, $z$.



**Figure 3**
Part of the crystal structure of (II), showing the formation of the hydrogen-bonded chain along [110]. See Table 2 for symmetry code. H atoms not involved in hydrogen bonding (dashed lines) have been omitted for clarity.

proton acceptor. The formation of this N—H$\cdots$O hydrogen bond is promoted by the antiperiplanar conformation of the C2—N3 and N6—H6 bonds [torsion angle N3—C2—N6—H6 = 180 (2)°].

In (I), the presence of an intermolecular N6—H6$\cdots$N3$^i$ hydrogen bond between the amidine groups (Table 3 and Fig. 4*a*) may lead to ambiguity about the amine/imine character of atoms N3 and N6. It is known that the presence of N—H$\cdots$N hydrogen-bond contacts enhances the resonance effect, which is significant even for unassociated molecules. Therefore, one may be inclined to think that, for structure (I) forming hydrogen-bonded dimers, both tautomeric forms are possible, and that the C2—N3 and C2—N6 bond lengths do

**Table 3**
Hydrogen-bond geometry (Å, °) for (I).

| $D$—H$\cdots$$A$ | $D$—H | H$\cdots$$A$ | $D$$\cdots$$A$ | $D$—H$\cdots$$A$ |
|---|---|---|---|---|
| N6—H6$\cdots$N3$^i$ | 0.88 (2) | 2.10 (2) | 2.9733 (17) | 173 (2) |
| O16$a$—H16$A$$\cdots$O13$^{ii}$ | 0.84 | 2.00 | 2.7940 (19) | 158 |
| O16$b$—H16$B$$\cdots$O13$^{ii}$ | 0.84 | 1.86 | 2.692 (12) | 168 |
| C10—H10$\cdots$O16$a^{iii}$ | 0.95 | 2.52 | 3.442 (2) | 164 |
| C12—H12$\cdots$O13$^i$ | 0.95 | 2.31 | 3.199 (2) | 155 |
| C14$a$—H14$B$$\cdots$O16$a^{iv}$ | 0.99 | 2.54 | 3.448 (2) | 152 |

Symmetry codes: (i) $-x$, $-y + 1$, $-z + 1$; (ii) $-x + 1$, $-y$, $-z + 1$; (iii) $-x + 1$, $-y + 1$, $-z$; (iv) $x - 1$, $y$, $z$.
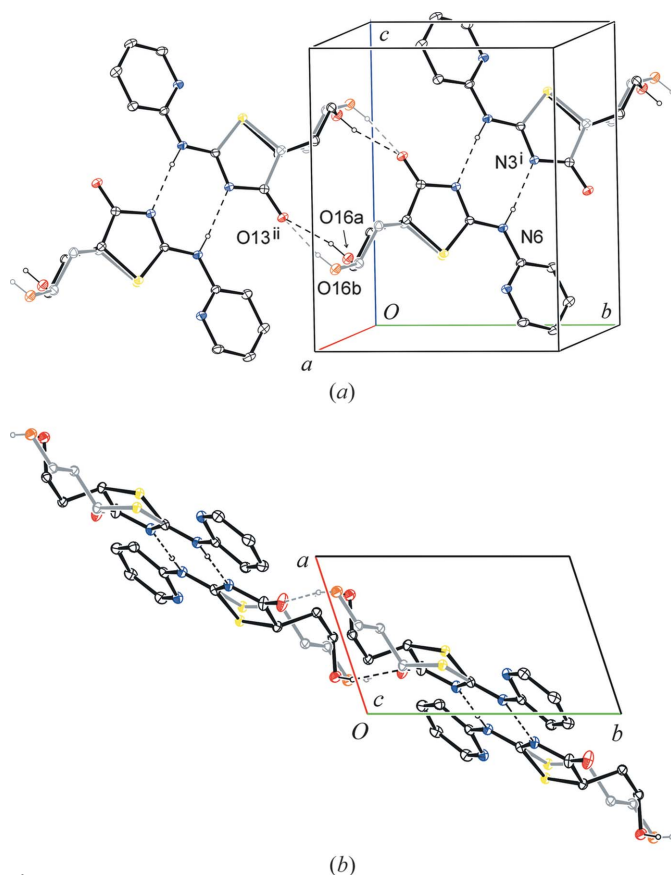
**Figure 4**
(a) The molecular tape in (I), generated by the centrosymmetric dimers. See Table 3 for symmetry codes. H atoms not involved in hydrogen bonding (dashed lines) have been omitted for clarity. (b) The molecular tape in (I), expanded along the [110] direction. Grey shading denotes the disordered part of the molecule.

not provide much useful information for solving this problem because of resonance interactions which render their lengths similar regardless of the tautomeric form. However, atom H6 was located and refined at this position and, in addition, analysis of the C2—N3 and C2—N6 bond lengths performed for tautomeric forms $A1$ and $A2$ did not confirm these suppositions.

The average C2—N3 and C2—N6 bond lengths in 20 2-amino-1,3-thiazolidin-4-one derivatives deposited in the CSD and exhibiting the $A1$ tautomeric form are similar and have values of 1.325 (1) and 1.315 (2) Å, respectively (refcodes EKELEL, FIVPIJ, FOBQOY, IHUFAS, IMPTHA12, IMTAZO01, INMTZO, JOBGOW, KUKZUM, PACPIU, PTHAZO10, SALYOT, SINQOW, SINQUC, TEBDAH, ULACAM, VELBEU, VEQFAA, WOSMAS and YUQCAP; $R < 0.07$). These mean C2—N3 and C2—N6 bond lengths are intermediate between the lengths of single and double C—N bonds. In comparison with the normal literature C=N double-bond value of 1.279 (1) Å (Allen *et al.*, 1987), they are lengthened by about $33\sigma$ and $16\sigma$, respectively. On the other hand, they are shortened by about $26\sigma$ and $24\sigma$, respectively, compared with the mean value for a $Csp^2$—N single-bond length of 1.383 (2) Å. This latter value was obtained from 117 structures of 2-imino-1,3-thiazolidin-4-one

derivatives substituted at N3 ($R < 0.07$). Based on six records revealing the $A2$ tautomeric form, the average C2—N3 and C2—N6 bond lengths were calculated as 1.374 (3) and 1.280 (2) Å, respectively (refcodes EHITZO, HEGMAJ, HEGMEN, HEGMIR, HEGMOX and VAMPUV; $R < 0.07$), which are clearly different from one another. The former is similar to the normal $Csp^2$—N single-bond length in heterocyclic rings, while the latter is close to a normal C=N double-bond length.

Our observations thus indicate an unequal resonance effect in tautomeric forms $A1$ and $A2$, which allows the use of the C—N bond lengths to distinguish the two forms. Crystal structure analysis of (I) and (II) shows that the interatomic lengths C2—N3 and C2—N6 [1.3256 (17) and 1.3385 (19) Å in (I), and 1.3182 (15) and 1.3282 (15) Å in (II), respectively] have comparable values, which is a typical feature of tautomeric form $A1$.

We thus submit that the original tautomeric assignments of GACXOZ and HEGLUC were incorrect, and propose they both be reassigned to the $A1$ form, supported by the evidence presented here. From the comparison of (I)/GACXOZ and (II)/HEGLUC it is clear that the molecules in pairs have the same geometry and, what is particularly important, very similar C2—N3 and C2—N6 bond lengths. In the first pair, the bond lengths are 1.326/1.322 and 1.338/1.337 Å, while in the second pair the values are 1.318/1.308 and 1.328/1.333 Å, respectively. The structural differences relate to the position of the mobile N—H hydrogen only. We think that incorrect localization of the H atom at the endocyclic and not at the exocyclic N atom in GACXOZ and HEGLUC is most likely a result of the fact that the H atoms bonded to N atoms were positioned geometrically and were treated using a riding model, with the $U_{iso}(H)$ parameter calculated and not refined. If the $U_{iso}(H)$ parameter had been refined in the earlier report, the mistake would have been noticed and corrected.

### 3.2. Further details of the structural analysis

Some atoms in the crystal structure of (I) are disordered. This observation concerns the part of the molecule that includes atoms S1, C5, C14, C15 and O16 of the 2-hydroxyethyl-1,3-thiazolidin-4-one fragment. Each of these atoms takes up two alternative locations in the crystal structure, labelled $a$ and $b$. This arrangement results in two different enantiomers of the molecule, with atoms S1, C5, C14, C15 and O16 in position $a$ having an $R$ configuration and the atoms in position $b$ having an $S$ configuration (for the molecule shown in Fig. 1), and *vice versa* for a symmetry-related site. The occupancy factor for these five atoms in orientation $a$ is 0.883 (2), while in orientation $b$ the occupancy factor is 0.117 (2).

The thiazolidine ring with atoms S1 and C5 in arrangement $a$ is approximately planar (r.m.s. deviation = 0.0213 Å), while the ring with these atoms in arrangement $b$ is folded (r.m.s. deviation = 0.1130 Å) and adopts a half-chair conformation [Cremer & Pople (1975) puckering parameters $Q$ = 0.253 (8) Å and $\varphi$ = 130.0 (16)°].

The pairs of bonds S1—C2/N6—C7 and C2—N6/C7—N8 are in a synperiplanar conformation. The torsion angles S1$a$/S1$b$—C2—N6—C7 and C2—N6—C7—N8 are 4.2 (2)/−14.7 (3) and −10.6 (2)°, respectively. The arrangements of the two alternative hydroxyethyl residues are determined by torsion angles C5$a$—14$a$—C15$a$—O16$a$ = 55.8 (2)° and C5$b$—C14$b$—C15$b$—O16$b$ = 178.1 (14)°, from which the pairs of bonds C5$a$—C14$a$/C15$a$—O16$a$ and C5$b$—C14$b$/C15$b$—O16$b$ are synclinal and synperiplanar, respectively.

The heterocyclic and benzene rings in (II) are both flat and approximately coplanar. The dihedral angle between their mean planes is 6.59 (6)°. Atoms C13, O14, O15 and C16 form a flat system (r.m.s. deviation = 0.0015 Å) that is twisted out of the mean plane of the benzene ring by 2.23 (8)°. The remaining atom C17 is tilted from the planar system formed by atoms C13, O14, O15 and C16 and is 0.201 (3) Å from that plane. Atoms C13 and C17 are in an antiperiplanar conformation [torsion angle C13—O15—C16—C17 = 172.17 (12)°]. On the other hand, the C13==O14 carbonyl group is in a synperiplanar conformation relative to the S1—C2 bond of the heterocyclic ring [torsion angle S1—C2···C13—O14 = −1.83 (18)°].

The partial double-bond character of the C2—N6 bond in (I) and (II) accounts for the hindered rotation of the pyridin-2-ylamino [in (I)] or phenylamino [in (II)] residues in the analysed structures. The dihedral angles between the cyclic systems are 11.67 (11)/27.4 (4)° for (I) and 6.59 (6)° for (II). The two values given for (I) result from the previously described disorder concerning the arrangement of atoms S1 and C5 in the crystal structure.

The main factor that determines the crystal packing and the formation of the supramolecular structure of (I) is the system of hydrogen bonds, involving both strong N—H···N and O—H···O and weak C—H···O hydrogen bonds (Table 3). The N6—H6···N3[i] and C12—H12···O13[i] hydrogen bonds link (symmetry codes as in Table 3) the molecules into centrosymmetric dimers and generate centrosymmetric $R_2^2(8)$ (Bernstein *et al.*, 1995) ring motifs. Neighbouring dimers are linked through O16$a$—H16$A$···O13[ii] and O16$b$—H16$B$···

O13[ii] hydrogen bonds to form the next centrosymmetric ring motif of $R_2^2(14)$ type (Fig. 4$a$). These contacts link the molecules of (I) into tapes extending along the [110] direction (Table 3, and Figs. 4$a$ and 4$b$). Neighbouring molecular tapes are linked through nonclassical C10—H10···O16[iii] hydrogen bonds into layers parallel to the (111) plane, and these layers are connected by C14$a$—H14$B$···O16$a$[iv] hydrogen bonds, forming a three-dimensional hydrogen-bond network.

The molecules of (II) are linked in the crystal structure through N6—H6···O18[i] hydrogen bonds into chains extending along the [110] direction (Table 2 and Fig. 3).

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# supporting information

# Heterocyclic tautomerism: reassignment of two crystal structures of 2-amino-1,3-thiazolidin-4-one derivatives

**Andrzej K. Gzella, Marcin Kowiel, Aneta Suseł, Magdalena N. Wojtyra and Roman Lesyk**

### Computing details

For both compounds, data collection: *CrysAlis PRO* (Agilent, 2012); cell refinement: *CrysAlis PRO* (Agilent, 2012); data reduction: *CrysAlis PRO* (Agilent, 2012); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *WinGX* (Farrugia, 2012), OLEX2 (Dolomanov *et al.*, 2009) and *PLATON* (Spek, 2009).

### (I) 5-(2-Hydroxyethyl)-2-[(pyridin-2-yl)amino]-1,3-thiazolidin-4-one

*Crystal data*

| | |
|---|---|
| $C_{10}H_{11}N_3O_2S$ | $F(000) = 248$ |
| $M_r = 237.28$ | $D_x = 1.491$ Mg m$^{-3}$ |
| Triclinic, $P\bar{1}$ | Melting point = 459–461 K |
| $a = 5.78910 (15)$ Å | Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å |
| $b = 8.8045 (2)$ Å | Cell parameters from 3632 reflections |
| $c = 10.9688 (3)$ Å | $\theta = 3.0–29.1°$ |
| $\alpha = 90.638 (2)°$ | $\mu = 0.29$ mm$^{-1}$ |
| $\beta = 95.794 (2)°$ | $T = 130$ K |
| $\gamma = 107.990 (2)°$ | Lath, colourless |
| $V = 528.50 (3)$ Å$^3$ | $0.42 \times 0.22 \times 0.10$ mm |
| $Z = 2$ | |

*Data collection*

| | |
|---|---|
| Agilent Xcalibur Atlas diffractometer | 5332 measured reflections |
| Radiation source: Enhance (Mo) X-ray Source | 2501 independent reflections |
| Detector resolution: 10.3088 pixels mm$^{-1}$ | 2338 reflections with $I > 2\sigma(I)$ |
| $\omega$ scans | $R_{int} = 0.016$ |
| Absorption correction: multi-scan | $\theta_{max} = 29.1°$, $\theta_{min} = 2.4°$ |
| (*CrysAlis PRO*; Agilent, 2012) | $h = -6\rightarrow7$ |
| $T_{min} = 0.939$, $T_{max} = 1.000$ | $k = -11\rightarrow11$ |
| | $l = -14\rightarrow14$ |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | 167 parameters |
| Least-squares matrix: full | 4 restraints |
| $R[F^2 > 2\sigma(F^2)] = 0.036$ | Hydrogen site location: mixed |
| $wR(F^2) = 0.088$ | H atoms treated by a mixture of independent |
| $S = 1.13$ | and constrained refinement |
| 2501 reflections | |

$w = 1/[\sigma^2(F_o^2) + (0.0328P)^2 + 0.2306P]$
  where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max} = 0.34$ e Å$^{-3}$
$\Delta\rho_{min} = -0.21$ e Å$^{-3}$

*Special details*

**Geometry**. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å$^2$)*

| | $x$ | $y$ | $z$ | $U_{iso}$*/$U_{eq}$ | Occ. (<1) |
|---|---|---|---|---|---|
| S1A | 0.40161 (15) | 0.38579 (7) | 0.27170 (4) | 0.01982 (15) | 0.883 (2) |
| C2 | 0.2062 (3) | 0.44461 (16) | 0.36246 (12) | 0.0199 (3) | |
| N3 | 0.1772 (2) | 0.38288 (14) | 0.47166 (10) | 0.0214 (3) | |
| C4 | 0.2935 (3) | 0.26908 (18) | 0.48923 (13) | 0.0267 (3) | |
| N6 | 0.0916 (2) | 0.55040 (14) | 0.32764 (11) | 0.0206 (3) | |
| H6 | 0.004 (4) | 0.572 (2) | 0.3822 (18) | 0.034 (5)* | |
| C7 | 0.0942 (3) | 0.62302 (16) | 0.21345 (12) | 0.0202 (3) | |
| N8 | 0.2530 (2) | 0.60269 (15) | 0.14094 (11) | 0.0230 (3) | |
| C9 | 0.2538 (3) | 0.66848 (18) | 0.03061 (13) | 0.0259 (3) | |
| H9 | 0.3640 | 0.6533 | −0.0234 | 0.031* | |
| C10 | 0.1021 (3) | 0.75713 (19) | −0.00803 (13) | 0.0274 (3) | |
| H10 | 0.1087 | 0.8026 | −0.0862 | 0.033* | |
| C11 | −0.0599 (3) | 0.77766 (19) | 0.07079 (14) | 0.0274 (3) | |
| H11 | −0.1652 | 0.8388 | 0.0472 | 0.033* | |
| C12 | −0.0682 (3) | 0.70917 (18) | 0.18365 (13) | 0.0233 (3) | |
| H12 | −0.1794 | 0.7202 | 0.2386 | 0.028* | |
| O13 | 0.2882 (3) | 0.19347 (15) | 0.58229 (10) | 0.0383 (3) | |
| C15A | 0.5049 (3) | 0.0412 (2) | 0.2396 (2) | 0.0218 (4) | 0.883 (2) |
| H15A | 0.4441 | −0.0734 | 0.2128 | 0.026* | 0.883 (2) |
| H15B | 0.4880 | 0.1044 | 0.1670 | 0.026* | 0.883 (2) |
| C5A | 0.4400 (3) | 0.2454 (2) | 0.38628 (14) | 0.0206 (3) | 0.883 (2) |
| H5A | 0.6166 | 0.2736 | 0.4186 | 0.025* | 0.883 (2) |
| C14A | 0.3496 (3) | 0.07226 (19) | 0.33477 (15) | 0.0219 (3) | 0.883 (2) |
| H14A | 0.3511 | −0.0003 | 0.4030 | 0.026* | 0.883 (2) |
| H14B | 0.1786 | 0.0475 | 0.2970 | 0.026* | 0.883 (2) |
| O16A | 0.7567 (2) | 0.08204 (17) | 0.28591 (13) | 0.0269 (3) | 0.883 (2) |
| H16A | 0.7756 | 0.0159 | 0.3375 | 0.040* | 0.883 (2) |
| S1B | 0.3118 (10) | 0.3571 (5) | 0.2556 (4) | 0.01982 (15) | 0.117 (2) |
| C5B | 0.312 (3) | 0.2013 (16) | 0.3623 (11) | 0.0206 (3) | 0.117 (2) |
| H5B | 0.1685 | 0.1039 | 0.3387 | 0.025* | 0.117 (2) |
| C14B | 0.547 (2) | 0.1577 (14) | 0.3752 (11) | 0.0219 (3) | 0.117 (2) |
| H14C | 0.5457 | 0.0840 | 0.4428 | 0.026* | 0.117 (2) |
| H14D | 0.6892 | 0.2551 | 0.3939 | 0.026* | 0.117 (2) |
| C15B | 0.564 (3) | 0.077 (2) | 0.2534 (17) | 0.0218 (4) | 0.117 (2) |
| H15C | 0.4218 | −0.0207 | 0.2370 | 0.026* | 0.117 (2) |
| H15D | 0.5559 | 0.1502 | 0.1864 | 0.026* | 0.117 (2) |

| | | | | | |
|---|---|---|---|---|---|
| O16B | 0.778 (2) | 0.0357 (15) | 0.2525 (11) | 0.0269 (3) | 0.117 (2) |
| H16B | 0.7745 | −0.0389 | 0.3001 | 0.040* | 0.117 (2) |

*Atomic displacement parameters (Å$^2$)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| S1A | 0.0243 (3) | 0.0197 (2) | 0.0173 (2) | 0.0081 (2) | 0.0067 (2) | 0.00383 (16) |
| C2 | 0.0251 (7) | 0.0173 (6) | 0.0162 (6) | 0.0040 (5) | 0.0048 (5) | 0.0009 (5) |
| N3 | 0.0285 (7) | 0.0208 (6) | 0.0167 (5) | 0.0093 (5) | 0.0056 (5) | 0.0035 (4) |
| C4 | 0.0405 (9) | 0.0245 (7) | 0.0194 (7) | 0.0151 (7) | 0.0078 (6) | 0.0030 (6) |
| N6 | 0.0242 (6) | 0.0225 (6) | 0.0167 (5) | 0.0082 (5) | 0.0065 (5) | 0.0046 (5) |
| C7 | 0.0233 (7) | 0.0186 (6) | 0.0163 (6) | 0.0028 (5) | 0.0025 (5) | 0.0034 (5) |
| N8 | 0.0280 (7) | 0.0226 (6) | 0.0186 (6) | 0.0067 (5) | 0.0065 (5) | 0.0041 (5) |
| C9 | 0.0286 (8) | 0.0287 (8) | 0.0189 (7) | 0.0052 (6) | 0.0073 (6) | 0.0045 (6) |
| C10 | 0.0291 (8) | 0.0307 (8) | 0.0190 (7) | 0.0039 (6) | 0.0032 (6) | 0.0095 (6) |
| C11 | 0.0259 (8) | 0.0294 (8) | 0.0256 (7) | 0.0072 (6) | 0.0011 (6) | 0.0089 (6) |
| C12 | 0.0228 (7) | 0.0247 (7) | 0.0221 (7) | 0.0061 (6) | 0.0045 (5) | 0.0045 (6) |
| O13 | 0.0691 (9) | 0.0381 (7) | 0.0218 (5) | 0.0333 (6) | 0.0163 (5) | 0.0136 (5) |
| C15A | 0.0223 (11) | 0.0206 (11) | 0.0222 (8) | 0.0058 (8) | 0.0040 (8) | 0.0014 (7) |
| C5A | 0.0244 (9) | 0.0209 (8) | 0.0184 (7) | 0.0095 (7) | 0.0032 (6) | 0.0034 (6) |
| C14A | 0.0216 (8) | 0.0198 (8) | 0.0248 (8) | 0.0064 (6) | 0.0052 (6) | 0.0025 (6) |
| O16A | 0.0254 (7) | 0.0284 (8) | 0.0295 (8) | 0.0108 (5) | 0.0069 (5) | 0.0088 (6) |
| S1B | 0.0243 (3) | 0.0197 (2) | 0.0173 (2) | 0.0081 (2) | 0.0067 (2) | 0.00383 (16) |
| C5B | 0.0244 (9) | 0.0209 (8) | 0.0184 (7) | 0.0095 (7) | 0.0032 (6) | 0.0034 (6) |
| C14B | 0.0216 (8) | 0.0198 (8) | 0.0248 (8) | 0.0064 (6) | 0.0052 (6) | 0.0025 (6) |
| C15B | 0.0223 (11) | 0.0206 (11) | 0.0222 (8) | 0.0058 (8) | 0.0040 (8) | 0.0014 (7) |
| O16B | 0.0254 (7) | 0.0284 (8) | 0.0295 (8) | 0.0108 (5) | 0.0069 (5) | 0.0088 (6) |

*Geometric parameters (Å, º)*

| | | | |
|---|---|---|---|
| S1A—C2 | 1.7655 (15) | C12—H12 | 0.9500 |
| S1A—C5A | 1.8178 (16) | C15A—O16A | 1.427 (2) |
| C2—N3 | 1.3256 (17) | C15A—C14A | 1.520 (3) |
| C2—N6 | 1.3385 (19) | C15A—H15A | 0.9900 |
| C2—S1B | 1.660 (5) | C15A—H15B | 0.9900 |
| N3—C4 | 1.3744 (19) | C5A—C14A | 1.532 (2) |
| C4—O13 | 1.2227 (18) | C5A—H5A | 1.0000 |
| C4—C5A | 1.528 (2) | C14A—H14A | 0.9900 |
| C4—C5B | 1.535 (13) | C14A—H14B | 0.9900 |
| N6—C7 | 1.4119 (17) | O16A—H16A | 0.8400 |
| N6—H6 | 0.88 (2) | S1B—C5B | 1.813 (13) |
| C7—N8 | 1.3251 (19) | C5B—C14B | 1.520 (14) |
| C7—C12 | 1.396 (2) | C5B—H5B | 1.0000 |
| N8—C9 | 1.3473 (18) | C14B—C15B | 1.533 (15) |
| C9—C10 | 1.384 (2) | C14B—H14C | 0.9900 |
| C9—H9 | 0.9500 | C14B—H14D | 0.9900 |
| C10—C11 | 1.387 (2) | C15B—O16B | 1.397 (16) |
| C10—H10 | 0.9500 | C15B—H15C | 0.9900 |

| | | | |
|---|---|---|---|
| C11—C12 | 1.382 (2) | C15B—H15D | 0.9900 |
| C11—H11 | 0.9500 | O16B—H16B | 0.8400 |
| | | | |
| C2—S1A—C5A | 89.64 (7) | C14A—C15A—H15B | 109.2 |
| N3—C2—N6 | 118.87 (13) | H15A—C15A—H15B | 107.9 |
| N3—C2—S1B | 120.45 (18) | C4—C5A—C14A | 111.18 (14) |
| N6—C2—S1B | 118.35 (18) | C4—C5A—S1A | 105.24 (11) |
| N3—C2—S1A | 117.77 (11) | C14A—C5A—S1A | 112.27 (11) |
| N6—C2—S1A | 123.35 (10) | C4—C5A—H5A | 109.3 |
| C2—N3—C4 | 111.24 (12) | C14A—C5A—H5A | 109.3 |
| O13—C4—N3 | 123.02 (14) | S1A—C5A—H5A | 109.3 |
| O13—C4—C5A | 121.08 (14) | C15A—C14A—C5A | 112.54 (14) |
| N3—C4—C5A | 115.86 (12) | C15A—C14A—H14A | 109.1 |
| O13—C4—C5B | 123.3 (5) | C5A—C14A—H14A | 109.1 |
| N3—C4—C5B | 107.5 (4) | C15A—C14A—H14B | 109.1 |
| C2—N6—C7 | 126.46 (13) | C5A—C14A—H14B | 109.1 |
| C2—N6—H6 | 114.2 (13) | H14A—C14A—H14B | 107.8 |
| C7—N6—H6 | 119.3 (13) | C15A—O16A—H16A | 109.5 |
| N8—C7—C12 | 124.43 (13) | C2—S1B—C5B | 87.4 (4) |
| N8—C7—N6 | 116.53 (12) | C14B—C5B—C4 | 105.5 (9) |
| C12—C7—N6 | 119.04 (13) | C14B—C5B—S1B | 113.8 (9) |
| C7—N8—C9 | 117.15 (13) | C4—C5B—S1B | 106.5 (7) |
| N8—C9—C10 | 123.26 (14) | C14B—C5B—H5B | 110.3 |
| N8—C9—H9 | 118.4 | C4—C5B—H5B | 110.3 |
| C10—C9—H9 | 118.4 | S1B—C5B—H5B | 110.3 |
| C9—C10—C11 | 118.06 (13) | C5B—C14B—C15B | 107.7 (11) |
| C9—C10—H10 | 121.0 | C5B—C14B—H14C | 110.2 |
| C11—C10—H10 | 121.0 | C15B—C14B—H14C | 110.2 |
| C12—C11—C10 | 120.01 (14) | C5B—C14B—H14D | 110.2 |
| C12—C11—H11 | 120.0 | C15B—C14B—H14D | 110.2 |
| C10—C11—H11 | 120.0 | H14C—C14B—H14D | 108.5 |
| C11—C12—C7 | 117.06 (14) | O16B—C15B—C14B | 113.1 (13) |
| C11—C12—H12 | 121.5 | O16B—C15B—H15C | 109.0 |
| C7—C12—H12 | 121.5 | C14B—C15B—H15C | 109.0 |
| O16A—C15A—C14A | 112.19 (16) | O16B—C15B—H15D | 109.0 |
| O16A—C15A—H15A | 109.2 | C14B—C15B—H15D | 109.0 |
| C14A—C15A—H15A | 109.2 | H15C—C15B—H15D | 107.8 |
| O16A—C15A—H15B | 109.2 | C15B—O16B—H16B | 109.5 |
| | | | |
| C5A_a—S1A_a—C2—N3 | 4.74 (12) | C5B—C4—C5A—C14A | −43.3 (9) |
| C5A—S1A—C2—N6 | −176.87 (13) | O13—C4—C5A—S1A | −178.17 (14) |
| C5A—S1A—C2—S1B | −99.0 (5) | N3—C4—C5A—S1A | −0.17 (18) |
| N6—C2—N3—C4 | 175.93 (13) | C5B—C4—C5A—S1A | 78.4 (10) |
| S1B—C2—N3—C4 | 13.5 (3) | C2—S1A—C5A—C4 | −2.25 (12) |
| S1A—C2—N3—C4 | −5.60 (17) | C2—S1A—C5A—C14A | 118.83 (13) |
| C2—N3—C4—O13 | −178.53 (15) | O16A—C15A—C14A—C5A | 55.8 (2) |
| C2—N3—C4—C5A | 3.5 (2) | C4—C5A—C14A—C15A | −175.19 (15) |
| C2—N3—C4—C5B | −25.5 (6) | S1A—C5A—C14A—C15A | 67.21 (17) |

| | | | | |
|---|---|---|---|---|
| N3—C2—N6—C7 | −177.41 (13) | N3—C2—S1B—C5B | 3.1 (5) | |
| S1B—C2—N6—C7 | −14.7 (3) | N6—C2—S1B—C5B | −159.4 (5) | |
| S1A—C2—N6—C7 | 4.2 (2) | S1A—C2—S1B—C5B | 88.8 (7) | |
| C2—N6—C7—N8 | −10.6 (2) | O13—C4—C5B—C14B | −59.0 (11) | |
| C2—N6—C7—C12 | 168.97 (14) | N3—C4—C5B—C14B | 148.0 (7) | |
| C12—C7—N8—C9 | −0.9 (2) | C5A—C4—C5B—C14B | 35.7 (7) | |
| N6—C7—N8—C9 | 178.62 (12) | O13—C4—C5B—S1B | 179.7 (3) | |
| C7—N8—C9—C10 | 1.3 (2) | N3—C4—C5B—S1B | 26.7 (8) | |
| N8—C9—C10—C11 | −0.6 (2) | C5A—C4—C5B—S1B | −85.6 (11) | |
| C9—C10—C11—C12 | −0.6 (2) | C2—S1B—C5B—C14B | −132.4 (10) | |
| C10—C11—C12—C7 | 1.0 (2) | C2—S1B—C5B—C4 | −16.6 (7) | |
| N8—C7—C12—C11 | −0.3 (2) | C4—C5B—C14B—C15B | 175.6 (11) | |
| N6—C7—C12—C11 | −179.74 (13) | S1B—C5B—C14B—C15B | −67.9 (14) | |
| O13—C4—C5A—C14A | 60.0 (2) | C5B—C14B—C15B—O16B | 178.1 (14) | |
| N3—C4—C5A—C14A | −121.96 (15) | | | |

*Hydrogen-bond geometry (Å, º)*

| $D$—H⋯$A$ | $D$—H | H⋯$A$ | $D$⋯$A$ | $D$—H⋯$A$ |
|---|---|---|---|---|
| N6—H6⋯N3[i] | 0.88 (2) | 2.10 (2) | 2.9733 (17) | 173 (2) |
| O16a—H16$A$⋯O13[ii] | 0.84 | 2.00 | 2.7940 (19) | 158 |
| O16b—H16$B$⋯O13[ii] | 0.84 | 1.86 | 2.692 (12) | 168 |
| C10—H10⋯O16a[iii] | 0.95 | 2.52 | 3.442 (2) | 164 |
| C12—H12⋯O13[i] | 0.95 | 2.31 | 3.199 (2) | 155 |
| C14a—H14$B$⋯O16a[iv] | 0.99 | 2.54 | 3.448 (2) | 152 |

Symmetry codes: (i) −x, −y+1, −z+1; (ii) −x+1, −y, −z+1; (iii) −x+1, −y+1, −z; (iv) x−1, y, z.

## (II) Ethyl 4-[(4-oxothiazolidin-2-yl)amino]benzoate

*Crystal data*

| | |
|---|---|
| $C_{12}H_{12}N_2O_3S$ | $F(000) = 276$ |
| $M_r = 264.30$ | $D_x = 1.496$ Mg m$^{-3}$ |
| Triclinic, $P\overline{1}$ | Melting point = 461–462 K |
| $a = 3.9850$ (2) Å | Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å |
| $b = 5.5113$ (3) Å | Cell parameters from 5612 reflections |
| $c = 26.8877$ (14) Å | $\theta = 2.3$–29.0° |
| $\alpha = 84.483$ (5)° | $\mu = 0.28$ mm$^{-1}$ |
| $\beta = 89.670$ (5)° | $T = 130$ K |
| $\gamma = 86.338$ (5)° | Lath, colourless |
| $V = 586.58$ (6) Å$^3$ | 0.40 × 0.34 × 0.05 mm |
| $Z = 2$ | |

*Data collection*

| | |
|---|---|
| Agilent Xcalibur Atlas diffractometer | 7855 measured reflections |
| | 2804 independent reflections |
| Radiation source: Enhance (Mo) X-ray Source | 2604 reflections with $I > 2\sigma(I)$ |
| Detector resolution: 10.3088 pixels mm$^{-1}$ | $R_{int} = 0.017$ |
| $\omega$ scans | $\theta_{max} = 29.1°$, $\theta_{min} = 2.3°$ |
| Absorption correction: multi-scan (*CrysAlis PRO*; Agilent, 2010) | $h = -5 \rightarrow 5$ |
| | $k = -7 \rightarrow 7$ |
| $T_{min} = 0.908$, $T_{max} = 1.000$ | $l = -35 \rightarrow 35$ |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | Hydrogen site location: mixed |
| Least-squares matrix: full | H atoms treated by a mixture of independent |
| $R[F^2 > 2\sigma(F^2)] = 0.030$ | and constrained refinement |
| $wR(F^2) = 0.078$ | $w = 1/[\sigma^2(F_o^2) + (0.0367P)^2 + 0.3017P]$ |
| $S = 1.05$ | where $P = (F_o^2 + 2F_c^2)/3$ |
| 2804 reflections | $(\Delta/\sigma)_{max} < 0.001$ |
| 168 parameters | $\Delta\rho_{max} = 0.54$ e Å$^{-3}$ |
| 0 restraints | $\Delta\rho_{min} = -0.23$ e Å$^{-3}$ |

*Special details*

**Geometry**. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å$^2$)*

| | *x* | *y* | *z* | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| S1 | 0.90166 (7) | 0.46485 (5) | 0.05976 (2) | 0.01454 (9) |
| C2 | 0.7690 (3) | 0.4621 (2) | 0.12301 (4) | 0.0130 (2) |
| N3 | 0.5653 (3) | 0.64554 (18) | 0.13492 (4) | 0.0152 (2) |
| C4 | 0.4898 (3) | 0.8077 (2) | 0.09439 (4) | 0.0145 (2) |
| C5 | 0.6724 (3) | 0.7546 (2) | 0.04612 (4) | 0.0151 (2) |
| H5A | 0.8277 | 0.8836 | 0.0360 | 0.018* |
| H5B | 0.5092 | 0.7468 | 0.0188 | 0.018* |
| N6 | 0.8822 (3) | 0.27244 (18) | 0.15391 (4) | 0.0148 (2) |
| H6 | 1.014 (4) | 0.167 (3) | 0.1409 (7) | 0.028 (4)* |
| C7 | 0.8121 (3) | 0.2168 (2) | 0.20533 (4) | 0.0142 (2) |
| C8 | 0.6325 (3) | 0.3760 (2) | 0.23453 (5) | 0.0177 (2) |
| H8 | 0.5475 | 0.5321 | 0.2203 | 0.021* |
| C9 | 0.5797 (3) | 0.3034 (2) | 0.28469 (5) | 0.0188 (3) |
| H9 | 0.4585 | 0.4111 | 0.3049 | 0.023* |
| C10 | 0.7019 (3) | 0.0748 (2) | 0.30575 (4) | 0.0168 (2) |
| C11 | 0.8843 (3) | −0.0814 (2) | 0.27639 (5) | 0.0185 (2) |
| H11 | 0.9711 | −0.2368 | 0.2908 | 0.022* |
| C12 | 0.9398 (3) | −0.0119 (2) | 0.22645 (5) | 0.0174 (2) |
| H12 | 1.0643 | −0.1191 | 0.2065 | 0.021* |
| C13 | 0.6394 (3) | −0.0095 (2) | 0.35919 (5) | 0.0198 (3) |
| O14 | 0.7419 (3) | −0.20429 (19) | 0.37957 (4) | 0.0322 (3) |
| O15 | 0.4537 (3) | 0.15882 (17) | 0.38186 (3) | 0.0237 (2) |
| C16 | 0.3732 (4) | 0.0971 (3) | 0.43390 (5) | 0.0244 (3) |
| H16A | 0.5800 | 0.0440 | 0.4532 | 0.029* |
| H16B | 0.2180 | −0.0367 | 0.4374 | 0.029* |
| C17 | 0.2087 (4) | 0.3256 (3) | 0.45242 (5) | 0.0288 (3) |
| H17A | 0.0085 | 0.3785 | 0.4323 | 0.043* |
| H17B | 0.3674 | 0.4549 | 0.4496 | 0.043* |
| H17C | 0.1435 | 0.2917 | 0.4875 | 0.043* |
| O18 | 0.2933 (2) | 0.98859 (16) | 0.09484 (3) | 0.01938 (19) |

*Atomic displacement parameters (Å²)*

|  | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| S1 | 0.01742 (16) | 0.01331 (14) | 0.01236 (14) | 0.00285 (11) | 0.00282 (10) | −0.00122 (10) |
| C2 | 0.0132 (5) | 0.0136 (5) | 0.0126 (5) | −0.0021 (4) | 0.0011 (4) | −0.0021 (4) |
| N3 | 0.0167 (5) | 0.0141 (5) | 0.0145 (5) | 0.0019 (4) | 0.0017 (4) | −0.0020 (4) |
| C4 | 0.0147 (5) | 0.0137 (5) | 0.0153 (5) | −0.0005 (4) | 0.0011 (4) | −0.0033 (4) |
| C5 | 0.0167 (6) | 0.0129 (5) | 0.0149 (5) | 0.0025 (4) | 0.0020 (4) | 0.0000 (4) |
| N6 | 0.0170 (5) | 0.0129 (5) | 0.0141 (5) | 0.0028 (4) | 0.0021 (4) | −0.0023 (4) |
| C7 | 0.0155 (5) | 0.0136 (5) | 0.0136 (5) | −0.0012 (4) | −0.0004 (4) | −0.0015 (4) |
| C8 | 0.0233 (6) | 0.0133 (5) | 0.0161 (6) | 0.0023 (5) | 0.0015 (5) | −0.0007 (4) |
| C9 | 0.0238 (6) | 0.0157 (6) | 0.0166 (6) | 0.0020 (5) | 0.0023 (5) | −0.0020 (4) |
| C10 | 0.0190 (6) | 0.0162 (6) | 0.0150 (6) | −0.0019 (5) | −0.0004 (4) | −0.0002 (4) |
| C11 | 0.0224 (6) | 0.0136 (5) | 0.0187 (6) | 0.0015 (5) | −0.0010 (5) | 0.0002 (4) |
| C12 | 0.0205 (6) | 0.0133 (5) | 0.0182 (6) | 0.0025 (5) | 0.0005 (5) | −0.0019 (4) |
| C13 | 0.0238 (6) | 0.0185 (6) | 0.0166 (6) | −0.0004 (5) | 0.0008 (5) | 0.0003 (5) |
| O14 | 0.0480 (7) | 0.0236 (5) | 0.0217 (5) | 0.0104 (5) | 0.0064 (4) | 0.0063 (4) |
| O15 | 0.0336 (5) | 0.0215 (5) | 0.0143 (4) | 0.0049 (4) | 0.0051 (4) | 0.0020 (3) |
| C16 | 0.0315 (7) | 0.0260 (7) | 0.0142 (6) | 0.0027 (6) | 0.0048 (5) | 0.0024 (5) |
| C17 | 0.0338 (8) | 0.0298 (7) | 0.0214 (7) | 0.0054 (6) | 0.0058 (6) | −0.0011 (5) |
| O18 | 0.0223 (5) | 0.0150 (4) | 0.0201 (4) | 0.0060 (3) | 0.0021 (3) | −0.0024 (3) |

*Geometric parameters (Å, º)*

| | | | |
|---|---|---|---|
| S1—C2 | 1.7770 (12) | C9—H9 | 0.9500 |
| S1—C5 | 1.7957 (12) | C10—C11 | 1.3918 (18) |
| C2—N3 | 1.3182 (15) | C10—C13 | 1.4915 (17) |
| C2—N6 | 1.3282 (15) | C11—C12 | 1.3811 (17) |
| N3—C4 | 1.3634 (15) | C11—H11 | 0.9500 |
| C4—O18 | 1.2287 (15) | C12—H12 | 0.9500 |
| C4—C5 | 1.5279 (16) | C13—O14 | 1.2054 (16) |
| C5—H5A | 0.9900 | C13—O15 | 1.3400 (16) |
| C5—H5B | 0.9900 | O15—C16 | 1.4470 (15) |
| N6—C7 | 1.4171 (15) | C16—C17 | 1.5081 (19) |
| N6—H6 | 0.859 (19) | C16—H16A | 0.9900 |
| C7—C8 | 1.3946 (17) | C16—H16B | 0.9900 |
| C7—C12 | 1.3977 (16) | C17—H17A | 0.9800 |
| C8—C9 | 1.3881 (17) | C17—H17B | 0.9800 |
| C8—H8 | 0.9500 | C17—H17C | 0.9800 |
| C9—C10 | 1.3902 (17) | | |
| | | | |
| C2—S1—C5 | 89.35 (5) | C9—C10—C11 | 119.57 (11) |
| N3—C2—N6 | 125.95 (11) | C9—C10—C13 | 121.63 (12) |
| N3—C2—S1 | 117.49 (9) | C11—C10—C13 | 118.79 (11) |
| N6—C2—S1 | 116.55 (9) | C12—C11—C10 | 120.38 (11) |
| C2—N3—C4 | 111.51 (10) | C12—C11—H11 | 119.8 |
| O18—C4—N3 | 124.59 (11) | C10—C11—H11 | 119.8 |
| O18—C4—C5 | 119.87 (10) | C11—C12—C7 | 119.75 (11) |

| | | | |
|---|---|---|---|
| N3—C4—C5 | 115.53 (10) | C11—C12—H12 | 120.1 |
| C4—C5—S1 | 105.83 (8) | C7—C12—H12 | 120.1 |
| C4—C5—H5A | 110.6 | O14—C13—O15 | 124.04 (12) |
| S1—C5—H5A | 110.6 | O14—C13—C10 | 124.54 (12) |
| C4—C5—H5B | 110.6 | O15—C13—C10 | 111.42 (11) |
| S1—C5—H5B | 110.6 | C13—O15—C16 | 116.64 (10) |
| H5A—C5—H5B | 108.7 | O15—C16—C17 | 106.36 (11) |
| C2—N6—C7 | 129.30 (10) | O15—C16—H16A | 110.5 |
| C2—N6—H6 | 115.7 (12) | C17—C16—H16A | 110.5 |
| C7—N6—H6 | 115.0 (12) | O15—C16—H16B | 110.5 |
| C8—C7—C12 | 120.37 (11) | C17—C16—H16B | 110.5 |
| C8—C7—N6 | 123.86 (11) | H16A—C16—H16B | 108.6 |
| C12—C7—N6 | 115.76 (11) | C16—C17—H17A | 109.5 |
| C9—C8—C7 | 119.11 (11) | C16—C17—H17B | 109.5 |
| C9—C8—H8 | 120.4 | H17A—C17—H17B | 109.5 |
| C7—C8—H8 | 120.4 | C16—C17—H17C | 109.5 |
| C8—C9—C10 | 120.81 (12) | H17A—C17—H17C | 109.5 |
| C8—C9—H9 | 119.6 | H17B—C17—H17C | 109.5 |
| C10—C9—H9 | 119.6 | | |
| | | | |
| C5—S1—C2—N3 | 2.42 (10) | C7—C8—C9—C10 | −0.3 (2) |
| C5—S1—C2—N6 | −178.37 (10) | C8—C9—C10—C11 | 1.1 (2) |
| N6—C2—N3—C4 | −178.45 (11) | C8—C9—C10—C13 | −178.21 (12) |
| S1—C2—N3—C4 | 0.67 (14) | C9—C10—C11—C12 | −0.94 (19) |
| C2—N3—C4—O18 | 176.49 (11) | C13—C10—C11—C12 | 178.37 (12) |
| C2—N3—C4—C5 | −4.32 (15) | C10—C11—C12—C7 | 0.04 (19) |
| O18—C4—C5—S1 | −174.96 (9) | C8—C7—C12—C11 | 0.75 (19) |
| N3—C4—C5—S1 | 5.82 (13) | N6—C7—C12—C11 | 179.87 (11) |
| C2—S1—C5—C4 | −4.21 (8) | C9—C10—C13—O14 | −179.18 (13) |
| N3—C2—N6—C7 | 1.3 (2) | C11—C10—C13—O14 | 1.5 (2) |
| S1—C2—N6—C7 | −177.79 (10) | C9—C10—C13—O15 | 0.89 (18) |
| C2—N6—C7—C8 | −8.0 (2) | C11—C10—C13—O15 | −178.41 (11) |
| C2—N6—C7—C12 | 172.90 (12) | O14—C13—O15—C16 | −0.5 (2) |
| C12—C7—C8—C9 | −0.62 (19) | C10—C13—O15—C16 | 179.45 (11) |
| N6—C7—C8—C9 | −179.66 (11) | C13—O15—C16—C17 | 172.17 (12) |

*Hydrogen-bond geometry (Å, º)*

| D—H···A | D—H | H···A | D···A | D—H···A |
|---|---|---|---|---|
| N6—H6···O18[i] | 0.857 (17) | 1.954 (17) | 2.7882 (14) | 164.3 (17) |

Symmetry code: (i) *x*+1, *y*−1, *z*.