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Ethyl 2-amino-4-*tert*-butyl-1,3-thiazole-5-carboxylate and 6-methylimidazo[2,1-*b*]thiazole–2-amino-1,3-thiazole (1/1)

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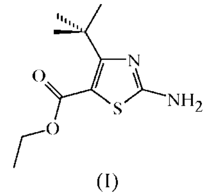
The structure of ethyl 2-amino-4-*tert*-butyl-1,3-thiazole-5-carboxylate, $C_{10}H_{16}N_2O_2S$, (I), and the structure of the 1:1 adduct 6-methylimidazo[2,1-*b*]thiazole–2-amino-1,3-thiazole (1/1), $C_6H_6N_2S\cdot C_3H_4N_2S$, (II), have been determined. The molecules in (I) associate *via* a hydrogen-bonded $R_2^2(8)$ dimer consisting of N—H···N interactions, with the hydrogen-bonding array additionally involving N—H···O interactions to one of the carboxylate O atoms. The 2-aminothiazole molecules in (II) also associate *via* an N—H···N hydrogen-bonded $R_2^2(8)$ dimer, with an additional N—H···N interaction to the Nsp^2 atom of the imidazothiazole moiety, creating hydrogen-bonded quartets.

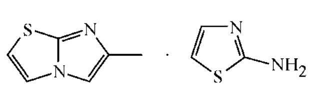
Comment

Aminothiazoles have been extensively studied for a range of biological and industrial applications (Lynch *et al.*, 1999; Toplak *et al.*, 2003). 2-Amino-1,3-thiazole, the structure of which was reported in 1982 (Caranoni & Reboul, 1982), is itself listed as a thyroid inhibitor (Merck, 2001). A search of the Cambridge Structural Database (CSD, Version 5.25 of April 2004; Allen, 2002) reveals that there are 73 crystal structures containing the 2-aminothiazole moiety, with 51 of those being pure organics. The present authors have recently published a paper on the packing modes of 2-amino-4-phenyl-1,3-thiazole derivatives (Lynch *et al.*, 2002) and have been investigating the structural aspects of 2-aminothiazole derivatives for the last six years. One such compound reported during this time was ethyl 4-*tert*-butyl-2-(3-phenylureido)-1,3-thiazole-5-carboxylate (Lynch & McClenaghan, 2002), which is currently the only structure of a 4-*tert*-butyl-5-ester derivative of an aminothiazole. However, we have recently determined the structure of ethyl 2-amino-4-*tert*-butyl-1,3-thiazole-5-carboxylate, (I), and report it here.

Another aminothiazole derivative is imidazo[2,1-*b*]thiazole, which has 11 analogues whose structures have previously been reported in the CSD. This bicyclic ring system can be prepared by refluxing a halomethyl ketone with 2-aminothiazole in ethanol. In an attempt to do so, using chloroacetone, an incomplete reaction yielded a mixture of the imidazo[2,1-*b*]thiazole derivative with the starting thiazole. The crystals that formed from the impure product were subsequently found to contain the 1:1 adduct of 6-methylimidazo[2,1-*b*]thiazole with 2-aminothiazole, (II), the structure of which is also reported here.



(I)



(II)

The structure of (I) consists of a single molecule (Fig. 1) which associates, *via* hydrogen-bonding interactions, to three symmetry-equivalent molecules (Fig. 2). One symmetry-

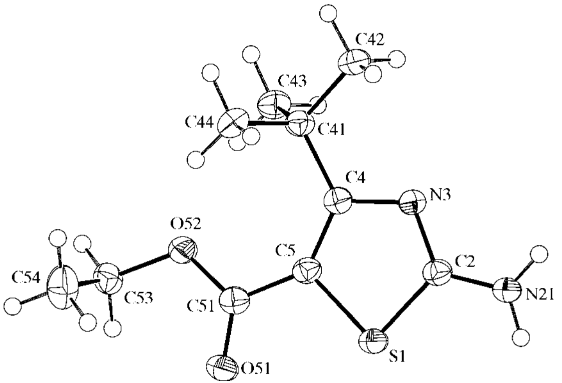


Figure 1
The molecular configuration and atom-numbering scheme for (I). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

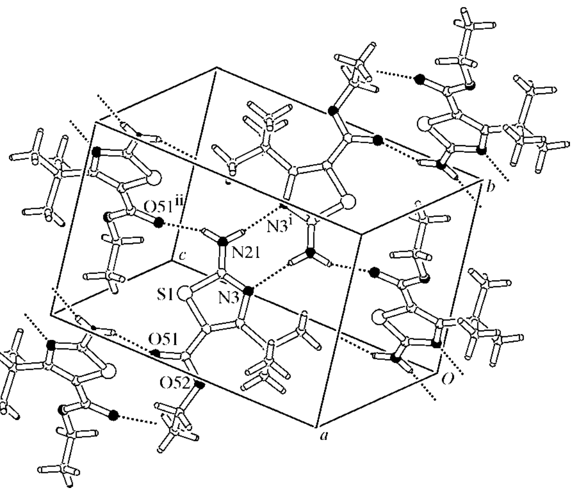


Figure 2
A packing diagram for (I). [Symmetry codes: (i) $1 - x, 1 - y, 1 - z$; (ii) $\frac{3}{2} - x, y + \frac{1}{2}, \frac{3}{2} - z$.]

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equivalent molecule forms a hydrogen-bonded $R_2^2(8)$ graph-set dimer (Etter, 1990) with (I) through an N—H···N interaction (Table 1), a feature common for 2-aminothiazole derivatives, while the other two associate to and from (I) through an N—H···O interaction. A similar packing mode has previously been observed in the structure of ethyl 2-amino-4-phenyl-1,3-thiazole-5-carboxylate (Lynch *et al.*, 2002), but is not observed in any other 5-ester-substituted 2-aminothiazole. This is probably due to the fact that, in each of these other structures, there are alternative exocyclic hydrogen-bonding acceptor atoms in addition to the two carboxylate O atoms. The ethyl chain twists out of the plane of the thiazole ring, with the C51—O52—C53—C54 torsion angle being 85.5 (2)°, compared with −168.5 (3)° in ethyl 4-*tert*-butyl-2-(3-phenylureido)-1,3-thiazole-5-carboxylate (Lynch & McClenaghan, 2002). One of the methyl groups in the *tert*-butyl moiety is aligned with the thiazole ring, with the N3—C4—C41—C42 torsion angle being −1.8 (2)°, similar to what was observed in ethyl 4-*tert*-butyl-2-(3-phenylureido)-1,3-thiazole-5-carboxylate [comparative torsion angle = 7.2 (5)°].

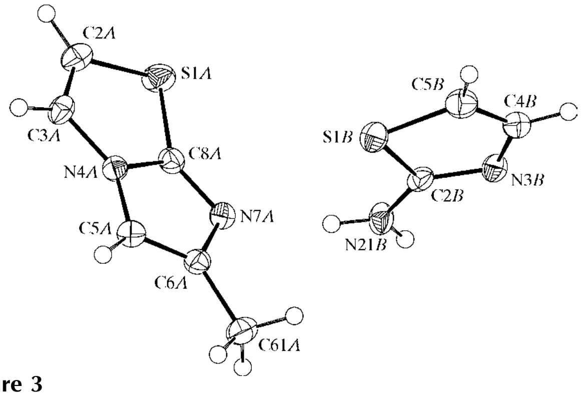

Figure 3
The molecular configuration and atom-numbering scheme for (II). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

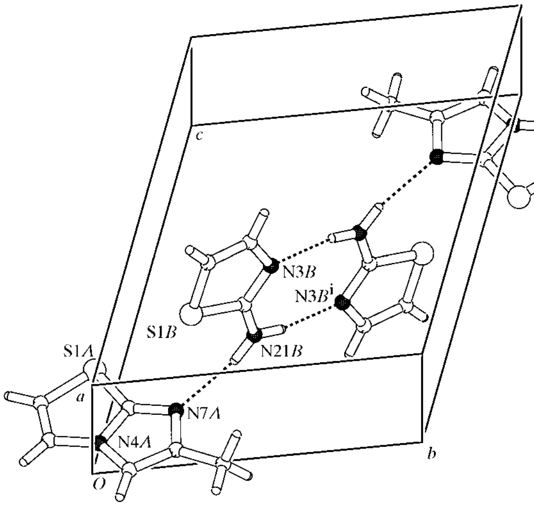

Figure 4
A packing diagram for (II). [Symmetry code: (i) $-x, 1-y, 1-z$.]

The structure of (II) comprises two adduct molecules associated by a single hydrogen-bonding interaction from one of the 2-amino H atoms to the Nsp^2 atom in the imidazothiazole system (Fig. 3). Although one of the present authors (DEL) has determined 16 co-crystal structures containing 2-aminothiazole derivatives, there are only two previously reported co-crystals containing 2-aminothiazole itself (Kuz'mina & Struchkov, 1984; Moers *et al.*, 2000), and both of these are organic salts. The structure of (II) is unique in that it is the first adduct (not an organic salt) of 2-aminothiazole. The molecules in (II) pack across an inversion centre to construct an associated quartet, with the 2-aminothiazoles forming a hydrogen-bonded $R_2^2(8)$ graph-set dimer (Fig. 4). Hydrogen-bonding associations are listed in Table 2. A C—H···N close contact is also observed between atom C2*A* and the 2-amino N atom. The distance between atoms N7*A* and S1*B* is 3.294 (3) Å.

The determination of the structure of (II) and examination of the packing associations may now lead to a series of adducts containing 2-aminothiazole and heterocyclic bases, as opposed to continuing to try to obtain co-crystals (either adducts or organic salts) with organic acids.

Experimental

Compound (I) was obtained from Key Organics Ltd and was crystallized from ethanol. Compound (II) was prepared by refluxing equimolar amounts of 2-amino-1,3-thiazole and chloroacetone in ethanol for 16 h. Upon removal of the reaction solvent, the product was washed with aqueous NaOH and then extracted into dichloromethane. Crystals of (II) grew from the resultant liquid after removal of the extraction solvent.

Compound (I)

Crystal data

$C_{10}H_{16}N_2O_2S$
$M_r = 228.31$
Monoclinic, $P2_1/n$
$a = 10.6248\ (8)$ Å
$b = 8.6055\ (5)$ Å
$c = 13.0135\ (9)$ Å
$\beta = 92.977\ (4)°$
$V = 1188.24\ (14)$ Å^3
$Z = 4$
$D_x = 1.276$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3289 reflections
$\theta = 2.9$–$27.5°$
$\mu = 0.26$ mm^{-1}
$T = 120\ (2)$ K
Prism, colourless
0.42 × 0.32 × 0.08 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995)
$T_{\min} = 0.913$, $T_{\max} = 0.977$
9227 measured reflections
2093 independent reflections
1668 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.082$
$\theta_{\max} = 25.0°$
$h = -12 \rightarrow 12$
$k = -10 \rightarrow 10$
$l = -15 \rightarrow 15$

Table 1
Hydrogen-bonding geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
N21—H21···N3$^{\rm i}$	0.88	2.14	3.016 (2)	173
N21—H22···O51$^{\rm ii}$	0.88	2.02	2.858 (2)	158

Symmetry codes: (i) $1-x, 1-y, 1-z$; (ii) $\frac{3}{2}-x, \frac{1}{2}+y, \frac{3}{2}-z$.

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.106$
$S = 1.08$
2093 reflections
140 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0601P)^2 + 0.0328P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.20$ e Å^{-3}
$\Delta\rho_{\min} = -0.34$ e Å^{-3}

Compound (II)

Crystal data

$C_6H_6N_2S{\cdot}C_3H_4N_2S$
$M_r = 238.33$
Triclinic, $P\overline{1}$
$a = 6.9195$ (2) Å
$b = 9.1860$ (2) Å
$c = 9.6953$ (3) Å
$\alpha = 69.5204$ (17)°
$\beta = 71.4823$ (16)°
$\gamma = 74.2770$ (17)°
$V = 538.48$ (3) Å^3

$Z = 2$
$D_x = 1.470$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 9410 reflections
$\theta = 2.9$–27.5°
$\mu = 0.47$ mm^{-1}
$T = 120$ (2) K
Plate, colourless
0.26 × 0.08 × 0.04 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995)
$T_{\min} = 0.885$, $T_{\max} = 0.982$
12 593 measured reflections

2472 independent reflections
2224 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.072$
$\theta_{\max} = 27.6$°
$h = -8 \rightarrow 9$
$k = -11 \rightarrow 11$
$l = -12 \rightarrow 12$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.105$
$S = 1.05$
2472 reflections
137 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0468P)^2 + 0.3904P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.26$ e Å^{-3}
$\Delta\rho_{\min} = -0.44$ e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N21B—H21B···N3$B^{\rm i}$	0.88	2.14	3.010 (2)	170
N21B—H22B···N7A	0.88	2.10	2.933 (2)	159
C2A—H2A···N21$B^{\rm ii}$	0.95	2.59	3.531 (2)	174

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

All H atoms were included in the refinement at calculated positions in the riding-model approximation, with N—H distances of 0.88 Å, and C—H distances of 0.95 (aromatic H atoms), 0.98 (CH_3 H atoms) and 0.99 Å (CH_2 H atoms), and with $U_{\rm iso}({\rm H}) = 1.25U_{\rm eq}({\rm C,N})$.

For both compounds, data collection: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT* (Nonius, 1998); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO*, *SCALEPACK* (Otwinowski & Minor, 1997) and *COLLECT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLUTON*94 (Spek, 1994) and *PLATON*97 (Spek, 1997); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1738). Services for accessing these data are described at the back of the journal.

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