Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Ethyl 2-amino-4-isopropyl-1,3-thiazole-5-carboxylate

Alan R. Kennedy,[a]* Abedawn I. Khalaf,[a] Colin J. Suckling[a] and Roger D. Waigh[b]

[a]Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, Scotland, and [b]Department of Pharmaceutical Sciences, University of Strathclyde, Glasgow G4 0NR, Scotland

Correspondence e-mail: a.r.kennedy@strath.ac.uk

Key indicators

Single-crystal X-ray study
T = 295 K
Mean σ(C–C) = 0.003 Å
R factor = 0.038
wR factor = 0.109
Data-to-parameter ratio = 19.4

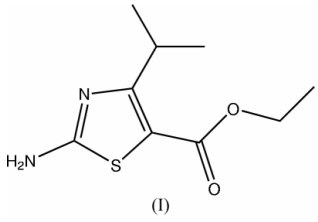
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 26 May 2004
Accepted 9 June 2004
Online 19 June 2004

Both the molecular and the crystal structures of the title compound, $C_9H_{14}N_2O_2S$, are similar to those of its 4-phenyl analogue. The supramolecular network is based upon N—H···N hydrogen-bonded centrosymmetric dimers linked by N—H···O contacts.

Comment

The quest for bioactive compounds led us to the synthesis of a variety of heterocylic compounds, among them the title compound, (I). There are many compounds in nature incorporating the thiazole moiety in their structure (Ikemoto *et al.*, 2003; Kumar *et al.*, 2002; El-Meligie & El-Awady, 2002), that have useful bioactivities. For example, Leucamide A was first extracted from the Australian marine sponge *Leucetta microraphis* and showed cytotoxicity toward several tumour cell lines (Wang & Nan, 2003). Thiazoles containing an isopropyl group were recently incorporated in the synthesis of minor-groove binders and this has led to a new class of potent antibacterial and antifungal compounds (Khalaf *et al.*, 2004; Antony *et al.*, 2004).



(I)

The molecular structure of (I) is unexceptional, with all ring bond lengths and angles (Table 1) close to the mean values obtained from 22 related fragments in the Cambridge Structural Database (Version 5.25, with updates to April 2004; Allen, 2002). Steric repulsion between the adjacent isopropyl and ester groups causes the main deviation from ideal geometry, widening the angles C2—C3—C4 and C3—C2—C7 to 133.90 (14) and 127.20 (14)°, respectively. However, all geometric parameters are in excellent agreement with those found for the 4-phenyl analogue of (I) (Lynch & McClenaghan, 2000). Indeed, the similarity of these two structures extends to their hydrogen-bonding motifs. Compound (I) mimics its analogue in forming hydrogen-bonded centrosymmetric dimers *via* near-linear N—H···N contacts (Table 2), the supramolecular network being completed by N—H···O contacts.

Experimental

Bromine (10.5 g, 65.3 mmol) was added to a stirred suspension of ethyl 4-methyl-3-oxopentanoate (10.0 g, 63.2 mmol) in water (50 ml)

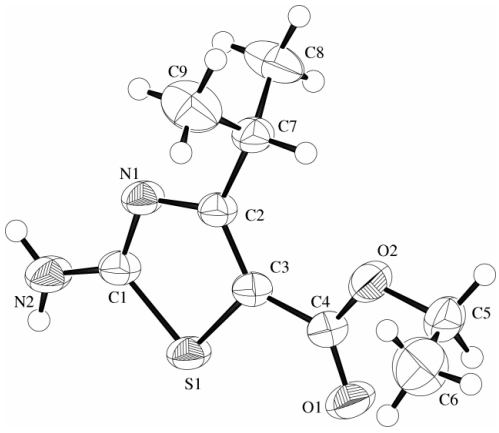


Figure 1
The molecular structure of (I), with 50% probability displacement ellipsoids.

at 273 K over a period of 45 min. After a further 30 min at 273 K, the reaction mixture was extracted with diethyl ether (150 ml). The organic layer was then dried over magnesium sulfate and filtered. The solvent was removed under reduced pressure to give ethyl 2-bromo-4-methyl-3-oxopentanoate as an oil (14.6 g, 61.1 mmol). This oil was added to a solution of thiourea (4.7 g, 61.1 mmol) in ethanol (50 ml). The reaction mixture was kept under reflux for 1 h. Ice-water (250 ml) was added and the mixture was basified with 18 *M* aqueous ammonia with vigorous stirring. The insoluble material was filtered off, washed with water and dried under reduced pressure at 303 K overnight. This gave the desired product as a pale-yellow crystalline material [6.7 g, 49% yield; m.p. 449–451 K, literature m.p. 449–451 K (Barton *et al.*, 1982)]. ^{1}H NMR ($CDCl_3$): 1.25 (6H, *d*, *J* = 8.0 Hz), 1.33 (3H, *t*, *J* = 7.1 Hz), 3.88 (1H, *hept*, *J* = 6.9 Hz), 4.27 (2H, *q*, *J* = 7.1 Hz), 5.41 (2H, *s*). IR (KBr): 3393, 3112, 1665, 1531, 1509, 1466, 1307, 1134, 1034 cm^{-1}.

Crystal data

$C_9H_{14}N_2O_2S$
M_r = 214.28
Monoclinic, $P2_1/n$
a = 7.8757 (10) Å
b = 9.1080 (11) Å
c = 15.8434 (12) Å
β = 100.853 (9)°
V = 1116.1 (2) Å^3
Z = 4
D_x = 1.275 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 24 reflections
θ = 18.7–19.8°
μ = 0.27 mm^{-1}
T = 295 (2) K
Plate, colourless
0.65 × 0.40 × 0.18 mm

Data collection

Rigaku AFC-7*S* diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.760, T_{max} = 0.950
2849 measured reflections
2674 independent reflections
2119 reflections with $I > 2\sigma(I)$
R_{int} = 0.023
θ_{max} = 28.0°
$h = 0 \rightarrow 10$
$k = 0 \rightarrow 11$
$l = -20 \rightarrow 19$
3 standard reflections
every 150 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.109
S = 1.03
2674 reflections
138 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0493P)^2 + 0.2832P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

S1—C1	1.7350 (15)	N1—C1	1.3226 (18)
S1—C3	1.7468 (15)	N1—C2	1.371 (2)
O1—C4	1.2149 (19)	N2—C1	1.331 (2)
O2—C4	1.3357 (19)	C2—C3	1.3707 (19)
C1—S1—C3	88.68 (7)	C3—C2—C7	127.20 (14)
C1—N1—C2	111.26 (12)	N1—C2—C7	117.60 (12)
N1—C1—N2	123.58 (14)	C2—C3—C4	133.90 (14)
N1—C1—S1	114.78 (12)	C2—C3—S1	110.09 (12)
N2—C1—S1	121.64 (12)	C4—C3—S1	116.01 (11)
C3—C2—N1	115.18 (13)		
C2—N1—C1—S1	−1.08 (18)	N1—C2—C3—S1	0.45 (18)
C3—S1—C1—N1	1.13 (13)	C1—S1—C3—C2	−0.85 (12)
C1—N1—C2—C3	0.4 (2)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H1···O1^{i}	0.85 (2)	2.08 (2)	2.902 (2)	163 (2)
N2—H2···N1^{ii}	0.86 (2)	2.15 (2)	3.006 (2)	177 (2)

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

The amine H atoms were located in a difference map and refined isotropically; all other H atoms were constrained to idealized geometry with a riding model, with U_{iso}(H) = 1.5U_{eq}(C). C—H distances: CH_3 = 0.96 Å, CH_2 = 0.97 Å and CH = 0.98 Å.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1992); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

References

Allen, F. A. (2002). *Acta Cryst.* B**58**, 380–388.
Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.
Antony, N. G., Fox, K. R., Johnston, B. F., Khalaf, A. I., Mackay, S. P., McGroarty, I. S., Parkinson, J. A., Skellern, G. G., Suckling, C. J. & Waigh, R. D. (2004). *Bioorg. Med. Chem. Lett.* **14**, 1353–1356.
Barton, A., Breukelman, S. P., Kaye, P. T., Meakins, G. D. & Morgan, D. J. (1982). *J. Chem. Soc. Perkin Trans.* 1, pp. 159–164.
El-Meligie, S. & El-Awady, R. A. (2002). *J. Heterocycl. Chem.* **39**, 1133–1138.
Ikemoto, N., Liu, J., Brands, K. M. J., McNamara, J. M. & Reider, P. (2003). *Tetrahedron*, **59**, 1317–1325.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Khalaf, A. I., Waigh, R. D., Drummond, A. J., Pringle, B., McGroarty, I., Skellern, G. G. & Suckling, C. J. (2004). *J. Med. Chem.* **47**, 2133–2156.
Kumar, R., Rai, D., Ko, S. C. C. & Lown, J. W. (2002). *Heterocycl. Commun.* **8**, 521–530.
Lynch, D. E. & McClenaghan, I. (2000). *Acta Cryst.* C**56**, e586.
Molecular Structure Corporation (1988). *MSC/AFC Diffractometer Control Software.* MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Molecular Structure Corporation (1992). *TEXSAN.* MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.

Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.

Wang, W. L. & Nan, F. (2003). *J. Org. Chem.* **68**, 1636–1639.