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Ethyl 5-amino-3-methylisoxazole-4-carboxylate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.063
wR factor = 0.151
Data-to-parameter ratio = 17.5

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

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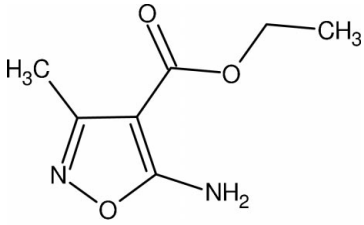
The title compound, $C_7H_{10}N_2O_3$, is planar and the structure is stabilized by an intramolecular N—H···O hydrogen bond. The molecules form dimers through N—H···O hydrogen bonds that are linked by N—H···N hydrogen bonds along the c axis.

Comment

Isoxazoles form part of many drugs used for antidepressant therapy (propionic acid derivative) (Skolnick, 2002), and act as antiviral compounds (methyltetrazole derivative; Giranda, 1995), as protein tyrosine phosphatase 1B inhibitors (carboxylic acid derivative; Zhao *et al.*, 2004) and as growth hormone secretagogue receptor (GHS-R) antagonists (carboxamides derivative; Liu *et al.*, 2004). In view of these important properties, the crystal structure of the title compound, (I), is presented here.



(I)

The isoxazole ring is planar and the ester group attached to it shows an extended conformation, which is observed from the torsion angles [C5—C4—C6—O8 = −178.73 (17)°, C4—C6—O8—C9 = 178.88 (17)° and C6—O8—C9—C10 = −179.55 (18)°]. The amine group is in an sp^2 hybridization state, as seen from the bond angles around it [C5—N11—H11A = 121.8 (16)°, C5—N11—H11B = 118.5 (17)° and H11A—N11—H11B = 120 (2)°]. The methyl, amine and ester substituent groups lie in the plane of the isoxazole ring (Fig. 1).

An intermolecular N—H···O hydrogen bond (Table 1) between amine atom N11 and carboxylate atom O7 stabilizes the structure and forms an S(6) pattern (Bernstein *et al.*, 1995). The molecules in the crystal structur are arranged such that interesting hydrogen-bond patterns are observed. A dimer is formed through N—H···O intermolecular hydrogen bonds between amine atom N11 and carboxylate atom O7($\frac{1}{2}-x$, $-\frac{1}{2}-y$, $1-z$), forming the ring pattern $R_2^2(12)$ (Fig. 2). These dimers are linked through an N—H···N hydrogen-bonded chain of type C(5) along the c axis, between atoms N11 and N2($\frac{1}{2}-x$, $-\frac{1}{2}+y$, $\frac{3}{2}-z$). Geometric details of the hydrogen bonds are in Table 1.

Experimental

The [3+2]-cycloaddition of a support-bound nitrile oxide with an alkyne or alkene is a useful synthetic route to isoxazoles or isoxazolines, respectively (Shankar *et al.*, 1998). Acetaldehyde (1 *M*) was treated with a solution of hydroxylamine hydrochloride (1 *M*, 0.6 ml) in anhydrous pyridine (50 ml) and kept at room temperature for 4 h. The reagent solution was decanted and washed with dimethylformamide (DMF) and dichloromethane (DCM), and then air dried. The resultant oxime was treated with *N*-chlorosuccinimide (NCS, 1.2 *M*) to obtain the chlorooxime, and treated with triethylamine (TEA, 5 ml) and DCM to form a nitrile oxide *in situ*. The nitrile oxide was then trapped by a dipolarophile (ethyl chloroaminocarboxylate, 1 *M*) afford the isoxazole derivative. The product was crystallized from DCM.

Crystal data

$C_7H_{10}N_2O_3$
$M_r = 170.17$
Monoclinic, $C2/c$
$a = 12.642\ (2)$ Å
$b = 8.5036\ (14)$ Å
$c = 16.934\ (3)$ Å
$\beta = 98.488\ (3)^\circ$
$V = 1800.5\ (5)$ Å^3
$Z = 8$
$D_x = 1.256$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 7495 reflections
$\theta = 2.4$–28.0°
$\mu = 0.10$ mm^{-1}
$T = 293\ (2)$ K
Rectangular block, colourless
$0.27 \times 0.25 \times 0.22$ mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
Absorption correction: none
7495 measured reflections
2070 independent reflections
1494 reflections with $I > 2\sigma(I)$
$R_{int} = 0.027$
$\theta_{max} = 28.0^\circ$
$h = -16 \rightarrow 16$
$k = -11 \rightarrow 11$
$l = -18 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.063$
$wR(F^2) = 0.151$
$S = 1.14$
2070 reflections
118 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0647P)^2 + 0.5335P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.002$
$\Delta\rho_{max} = 0.17$ e Å^{-3}
$\Delta\rho_{min} = -0.13$ e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.024 (2)

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N11—H11A···N2^{i}	0.85 (3)	2.14 (3)	2.981 (3)	172 (2)
N11—H11B···O7^{ii}	0.85 (3)	2.16 (3)	2.915 (2)	148 (2)
N11—H11B···O7^{iii}	0.85 (3)	2.39 (3)	2.921 (3)	122 (2)

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

All C-bound H atoms were positioned geometrically (C—H = 0.96 and 0.97 Å) and allowed to ride on their parent atoms, with U_{iso}(H) values of 1.2 or 1.5 times U_{eq}(parent atom). All other H atoms were identified from a difference Fourier map and refined isotropically.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003), *ORTEP-3* (Farrugia, 1997) and *ZORTEP* (Zsolnai, 1998); software used to prepare material for publication: *PLATON*).

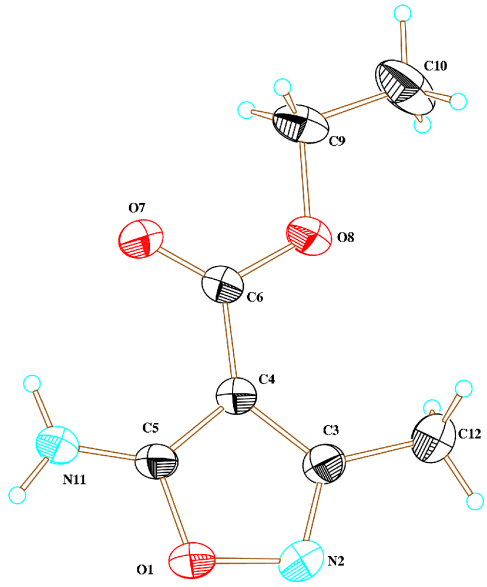


Figure 1
ZORTEP (Zsolnai, 1998) plot of the molecule, with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

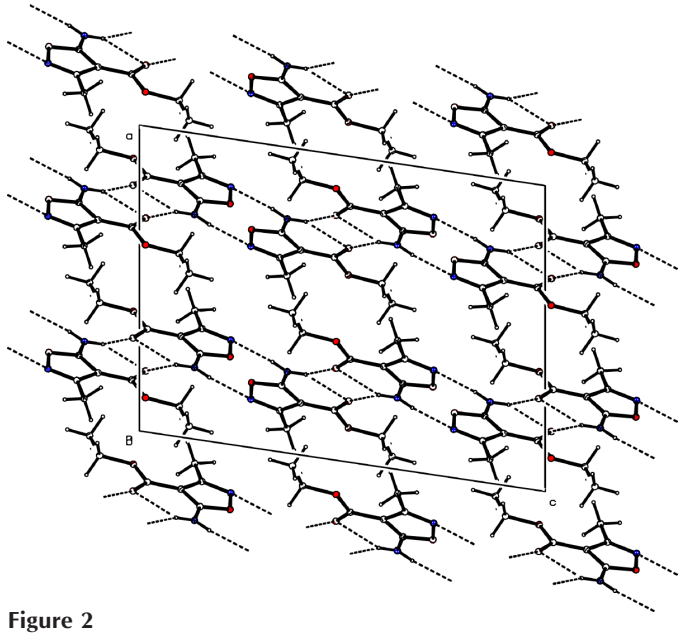


Figure 2
A packing diagram of the crystal structure, viewed down the *b* axis. Dashed lines represent hydrogen bonds.

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