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Methyl 3-[3-(ethoxycarbonyl)thioureido]-1*H*-pyrazole-5-carboxylateBuwen Huang,^a Pei-Pei Kung,^a Arnold L. Rheingold,^b Antonio DiPasquale^b and Alex Yanovsky^{a*}^aPfizer Global Research and Development, La Jolla Labs, 10770 Science Center Drive, San Diego, CA 92121, USA, and ^bDepartment of Chemistry and Biochemistry, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093, USA
Correspondence e-mail: alex.yanovsky@pfizer.com

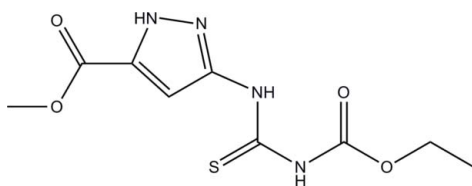
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Key indicators: single-crystal X-ray study; *T* = 208 K; mean $\sigma(\text{C}-\text{C}) = 0.003 \text{ \AA}$; *R* factor = 0.040; *wR* factor = 0.113; data-to-parameter ratio = 16.0.

The title compound, $\text{C}_9\text{H}_{12}\text{N}_4\text{O}_4\text{S}$, was proven to be the product of the reaction of methyl 5-amino-1*H*-pyrazole-3-carboxylate with ethyl isothiocyanatocarbonate. All non-H atoms of the molecule are planar, the mean deviation from the least squares plane being 0.048 \AA . The intramolecular N—H...O bond involving the NH-group, which links the thiourea and pyrazole fragments, closes a six-membered pseudo-heterocyclic ring, and two more hydrogen bonds (N—H...O with the participation of the pyrazole NH group and N—H...S involving the second thiourea NH group) link the molecules into infinite chains running along $[1\bar{2}0]$.

Related literature

For the structures of similar *N*-pyrazole-substituted thiourea derivatives, see: Pask *et al.* (2006); Wen *et al.* (2006).



Experimental

Crystal data

 $\text{C}_9\text{H}_{12}\text{N}_4\text{O}_4\text{S}$ $M_r = 272.29$ Triclinic, $P\bar{1}$ $a = 8.0855 (8) \text{ \AA}$ $b = 9.0035 (8) \text{ \AA}$ $c = 9.5959 (9) \text{ \AA}$ $\alpha = 64.510 (1)^\circ$ $\beta = 82.294 (1)^\circ$ $\gamma = 78.716 (1)^\circ$ $V = 617.39 (10) \text{ \AA}^3$ $Z = 2$ Mo $K\alpha$ radiation $\mu = 0.28 \text{ mm}^{-1}$ $T = 208 \text{ K}$ $0.20 \times 0.15 \times 0.10 \text{ mm}$

Data collection

Siemens P4 diffractometer with APEX CCD detector
Absorption correction: multi-scan (SADABS; Bruker, 2001)
 $T_{\min} = 0.947$, $T_{\max} = 0.973$ 5852 measured reflections
2653 independent reflections
2255 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.044$

Refinement

 $R[F^2 > 2\sigma(F^2)] = 0.040$ $wR(F^2) = 0.113$ $S = 1.04$

2653 reflections

166 parameters

H-atom parameters constrained

 $\Delta\rho_{\max} = 0.39 \text{ e \AA}^{-3}$ $\Delta\rho_{\min} = -0.28 \text{ e \AA}^{-3}$

Table 1

Hydrogen-bond geometry (\AA , $^\circ$).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$\text{N1}-\text{H1}\cdots\text{S1}^i$	0.87	2.51	3.347 (1)	161
$\text{N2}-\text{H2}\cdots\text{O2}$	0.87	1.92	2.657 (2)	141
$\text{N4}-\text{H4}\cdots\text{O3}^{ii}$	0.87	2.03	2.876 (2)	164

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

Data collection: SMART (Bruker, 1997); cell refinement: SAINT (Bruker, 1997); data reduction: SAINT; program(s) used to solve structure: SIR2004 (Burla *et al.*, 2005); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: ORTEP-32 (Farrugia, 1997); software used to prepare material for publication: WinGX (Farrugia, 1999).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: DN2451).

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supplementary materials

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Methyl 3-[3-(ethoxycarbonyl)thioureido]-1*H*-pyrazole-5-carboxylate

B. Huang, P.-P. Kung, A. L. Rheingold, A. DiPasquale and A. Yanovsky

Comment

The reaction of methyl 5-amino-1*H*-pyrazole-3-carboxylate with ethyl isothiocyanatocarbonate produces the pyrazole-thiourea derivative; its structure was established by the present X-ray study (Fig.1).

All non-H atoms of the molecule are planar (mean deviation from its least squares plane is 0.048 Å), in contrast to previously studied pyrazole-thiourea derivative (Wen *et al.*, 2006), where the pyrazole fragment has a nitrile substituent in position 4 and pyrazole/thiourea fragments form dihedral angle of 46.2°. Another similar compound, where pyrazole has no substituents in position 4 (Pask *et al.*, 2006), is also essentially planar, just like the title compound.

There are three NH-groups in the molecule which are responsible for the formation of three independent H-bonds in the crystal (Table 2). The intramolecular N2—H2···O2 bond closes the 6-membered pseudo-cycle, whereas two intermolecular H-bonds each produce typical centrosymmetric pairing motive, and their combination thus gives rise to infinite chains running along the [1,-2,0]. direction in the crystal (Fig. 2).

Experimental

A suspension of methyl 5-amino-1*H*-pyrazole-3-carboxylate (2.0 g, 14.2 mmol) in 10 ml of ethyl acetate and 40 ml of benzene was cooled to 0°C and stirred. To this solution, ethyl isothiocyanatocarbonate (2.04 g, 15.6 mmol) in 10 ml benzene was added dropwise. The resulting reaction mixture was allowed to warm up to room temperature, and stirring was continued for 5 h. The reaction mixture was filtered, and washed with plenty of ether to afford the desired product (3.32 g, 12.2 mmol, 86.0% yield). ¹H NMR (400 MHz, DMSO-d₆) δ p.p.m.: 13.99 (br. s., 1 H), 12.12 (br. s., 1 H), 11.48 (br. s., 1 H), 7.51 (s, 1 H), 4.22 (q, J=7.07 Hz, 2 H), 3.85 (s, 3 H), 1.26 (t, J=7.07 Hz, 3 H).

Refinement

All H atoms were placed in geometrically calculated positions (N—H 0.87 Å, C—H 0.94 Å, 0.97 Å, 0.98 Å, for aromatic, methyl and methylene H atoms respectively) and included in the refinement in riding motion approximation. The $U_{\text{iso}}(\text{H})$ were set to 1.2 U_{eq} of the carrying atom for aromatic, methylene, methyne and amine groups, and 1.5 U_{eq} for methyl H atoms.

Figures

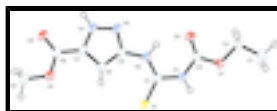


Fig. 1. Molecular structure of the title compound showing 50% probability displacement ellipsoids and atom numbering scheme; H atoms are drawn as circles with arbitrary small radius.

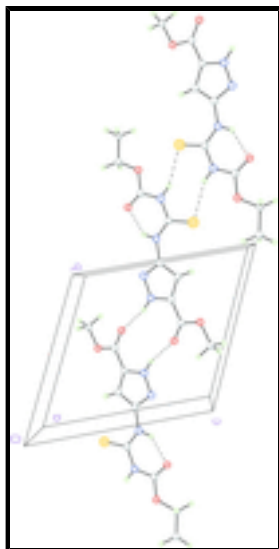


Fig. 2. Packing diagram for the title compound viewed approximately along the *a* axis; H-bonds are shown as dashed lines.

Methyl 3-[3-(ethoxycarbonyl)thioureido]-1*H*-pyrazole-5-carboxylate

Crystal data

$C_9H_{12}N_4O_4S$

$M_r = 272.29$

Triclinic, $P\bar{1}$

Hall symbol: -P 1

$a = 8.0855$ (8) Å

$b = 9.0035$ (8) Å

$c = 9.5959$ (9) Å

$\alpha = 64.510$ (1)°

$\beta = 82.294$ (1)°

$\gamma = 78.716$ (1)°

$V = 617.39$ (10) Å³

$Z = 2$

$F_{000} = 284$

$D_x = 1.465$ Mg m⁻³

Mo $K\alpha$ radiation

$\lambda = 0.71073$ Å

Cell parameters from 3767 reflections

$\theta = 2.5$ – 27.8°

$\mu = 0.28$ mm⁻¹

$T = 208$ K

Block, colorless

$0.20 \times 0.15 \times 0.10$ mm

Data collection

Siemens P4
diffractometer with APEX CCD

Radiation source: fine-focus sealed tube

Monochromator: graphite

$T = 208$ K

φ and ω scans

Absorption correction: multi-scan
(SADABS; Bruker, 2001)

$T_{\min} = 0.947$, $T_{\max} = 0.973$

5852 measured reflections

2653 independent reflections

2255 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.044$

$\theta_{\text{max}} = 28.2^\circ$

$\theta_{\text{min}} = 2.4^\circ$

$h = -5 \rightarrow 10$

$k = -11 \rightarrow 11$

$l = -11 \rightarrow 12$

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.040$	$w = 1/[\sigma^2(F_o^2) + (0.0521P)^2 + 0.1805P]$
$wR(F^2) = 0.113$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.04$	$(\Delta/\sigma)_{\max} = 0.001$
2653 reflections	$\Delta\rho_{\max} = 0.39 \text{ e } \text{\AA}^{-3}$
166 parameters	$\Delta\rho_{\min} = -0.28 \text{ e } \text{\AA}^{-3}$
Primary atom site location: structure-invariant direct methods	Extinction correction: SHELXL (Sheldrick, 2008), $F_c^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Secondary atom site location: difference Fourier map	Extinction coefficient: 0.064 (8)

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.

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R -factors(gt) *etc.* and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.7861 (3)	0.9454 (2)	-0.0198 (2)	0.0539 (6)
H1A	0.6653	0.9725	-0.0320	0.081*
H1B	0.8446	1.0106	-0.1156	0.081*
H1C	0.8125	0.9706	0.0626	0.081*
C2	0.8414 (3)	0.7653 (2)	0.0194 (2)	0.0451 (5)
H2A	0.8135	0.7375	-0.0619	0.054*
H2B	0.9638	0.7366	0.0301	0.054*
C3	0.7832 (2)	0.5090 (2)	0.22047 (19)	0.0319 (4)
C4	0.6784 (2)	0.27556 (19)	0.44802 (18)	0.0285 (4)
C5	0.7965 (2)	-0.00499 (19)	0.46055 (19)	0.0300 (4)
C6	0.7316 (2)	-0.1229 (2)	0.5968 (2)	0.0310 (4)
H6	0.6562	-0.1048	0.6734	0.037*
C7	0.8050 (2)	-0.2725 (2)	0.59165 (19)	0.0312 (4)
C8	0.7909 (2)	-0.4462 (2)	0.6958 (2)	0.0328 (4)
C9	0.6497 (3)	-0.6292 (2)	0.9141 (2)	0.0435 (5)
H9A	0.6341	-0.6894	0.8550	0.065*

supplementary materials

H9B	0.5509	-0.6267	0.9831	0.065*
H9C	0.7486	-0.6844	0.9741	0.065*
N1	0.69023 (19)	0.44206 (16)	0.35749 (16)	0.0322 (3)
H1	0.6316	0.5127	0.3917	0.039*
N2	0.77543 (19)	0.16936 (16)	0.39615 (16)	0.0327 (3)
H2	0.8340	0.2152	0.3099	0.039*
N3	0.9003 (2)	-0.07384 (17)	0.37579 (17)	0.0360 (4)
N4	0.9033 (2)	-0.23814 (17)	0.46052 (17)	0.0344 (3)
H4	0.9626	-0.3141	0.4333	0.041*
O1	0.75193 (17)	0.67399 (14)	0.16595 (14)	0.0374 (3)
O2	0.87813 (18)	0.43041 (15)	0.15826 (15)	0.0425 (3)
O3	0.87755 (18)	-0.56425 (14)	0.67884 (15)	0.0407 (3)
O4	0.67259 (17)	-0.46002 (15)	0.80911 (15)	0.0397 (3)
S1	0.54880 (6)	0.22717 (5)	0.60563 (5)	0.03395 (17)

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0681 (15)	0.0334 (10)	0.0449 (11)	-0.0077 (10)	0.0106 (10)	-0.0060 (8)
C2	0.0512 (12)	0.0338 (9)	0.0352 (9)	-0.0029 (8)	0.0133 (8)	-0.0061 (8)
C3	0.0347 (9)	0.0267 (8)	0.0311 (8)	0.0000 (7)	0.0010 (7)	-0.0119 (6)
C4	0.0312 (9)	0.0247 (7)	0.0300 (8)	0.0008 (6)	-0.0025 (7)	-0.0137 (6)
C5	0.0340 (9)	0.0240 (8)	0.0333 (8)	0.0005 (6)	-0.0013 (7)	-0.0154 (7)
C6	0.0343 (9)	0.0257 (8)	0.0346 (8)	0.0005 (6)	0.0007 (7)	-0.0171 (7)
C7	0.0346 (9)	0.0259 (8)	0.0359 (9)	-0.0010 (7)	-0.0003 (7)	-0.0174 (7)
C8	0.0356 (9)	0.0295 (8)	0.0373 (9)	-0.0036 (7)	0.0003 (7)	-0.0189 (7)
C9	0.0499 (12)	0.0310 (9)	0.0460 (11)	-0.0095 (8)	0.0089 (9)	-0.0147 (8)
N1	0.0393 (8)	0.0234 (7)	0.0306 (7)	-0.0001 (6)	0.0074 (6)	-0.0127 (6)
N2	0.0405 (8)	0.0234 (7)	0.0313 (7)	-0.0012 (6)	0.0061 (6)	-0.0124 (6)
N3	0.0436 (9)	0.0251 (7)	0.0383 (8)	-0.0008 (6)	0.0038 (7)	-0.0160 (6)
N4	0.0403 (9)	0.0256 (7)	0.0396 (8)	-0.0003 (6)	0.0042 (7)	-0.0195 (6)
O1	0.0432 (7)	0.0254 (6)	0.0341 (6)	-0.0013 (5)	0.0113 (5)	-0.0091 (5)
O2	0.0514 (8)	0.0321 (7)	0.0377 (7)	0.0001 (6)	0.0138 (6)	-0.0160 (6)
O3	0.0490 (8)	0.0263 (6)	0.0472 (7)	-0.0015 (6)	0.0073 (6)	-0.0204 (6)
O4	0.0455 (8)	0.0274 (6)	0.0448 (7)	-0.0050 (5)	0.0098 (6)	-0.0174 (5)
S1	0.0400 (3)	0.0257 (2)	0.0328 (2)	-0.00173 (17)	0.00760 (18)	-0.01324 (18)

Geometric parameters (\AA , $^\circ$)

C1—C2	1.486 (3)	C5—N2	1.401 (2)
C1—H1A	0.9700	C6—C7	1.380 (2)
C1—H1B	0.9700	C6—H6	0.9400
C1—H1C	0.9700	C7—N4	1.343 (2)
C2—O1	1.463 (2)	C7—C8	1.466 (2)
C2—H2A	0.9800	C8—O3	1.214 (2)
C2—H2B	0.9800	C8—O4	1.329 (2)
C3—O2	1.214 (2)	C9—O4	1.452 (2)
C3—O1	1.3278 (19)	C9—H9A	0.9700
C3—N1	1.374 (2)	C9—H9B	0.9700

C4—N2	1.338 (2)	C9—H9C	0.9700
C4—N1	1.387 (2)	N1—H1	0.8700
C4—S1	1.6617 (16)	N2—H2	0.8700
C5—N3	1.340 (2)	N3—N4	1.344 (2)
C5—C6	1.397 (2)	N4—H4	0.8700
C2—C1—H1A	109.5	N4—C7—C6	107.60 (14)
C2—C1—H1B	109.5	N4—C7—C8	119.72 (14)
H1A—C1—H1B	109.5	C6—C7—C8	132.67 (16)
C2—C1—H1C	109.5	O3—C8—O4	123.84 (16)
H1A—C1—H1C	109.5	O3—C8—C7	123.32 (16)
H1B—C1—H1C	109.5	O4—C8—C7	112.84 (14)
O1—C2—C1	106.83 (15)	O4—C9—H9A	109.5
O1—C2—H2A	110.4	O4—C9—H9B	109.5
C1—C2—H2A	110.4	H9A—C9—H9B	109.5
O1—C2—H2B	110.4	O4—C9—H9C	109.5
C1—C2—H2B	110.4	H9A—C9—H9C	109.5
H2A—C2—H2B	108.6	H9B—C9—H9C	109.5
O2—C3—O1	125.25 (16)	C3—N1—C4	127.95 (13)
O2—C3—N1	125.62 (15)	C3—N1—H1	116.0
O1—C3—N1	109.13 (13)	C4—N1—H1	116.0
N2—C4—N1	114.69 (14)	C4—N2—C5	129.41 (14)
N2—C4—S1	126.73 (12)	C4—N2—H2	115.3
N1—C4—S1	118.59 (11)	C5—N2—H2	115.3
N3—C5—C6	112.89 (14)	C5—N3—N4	103.49 (14)
N3—C5—N2	114.22 (15)	C7—N4—N3	112.76 (13)
C6—C5—N2	132.89 (15)	C7—N4—H4	123.6
C7—C6—C5	103.26 (14)	N3—N4—H4	123.6
C7—C6—H6	128.4	C3—O1—C2	116.14 (14)
C5—C6—H6	128.4	C8—O4—C9	115.46 (13)

Hydrogen-bond geometry (\AA , $^\circ$)

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N1—H1 \cdots S1 ⁱ	0.87	2.51	3.347 (1)	161
N2—H2 \cdots O2	0.87	1.92	2.657 (2)	141
N4—H4 \cdots O3 ⁱⁱ	0.87	2.03	2.876 (2)	164

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

Fig. 1

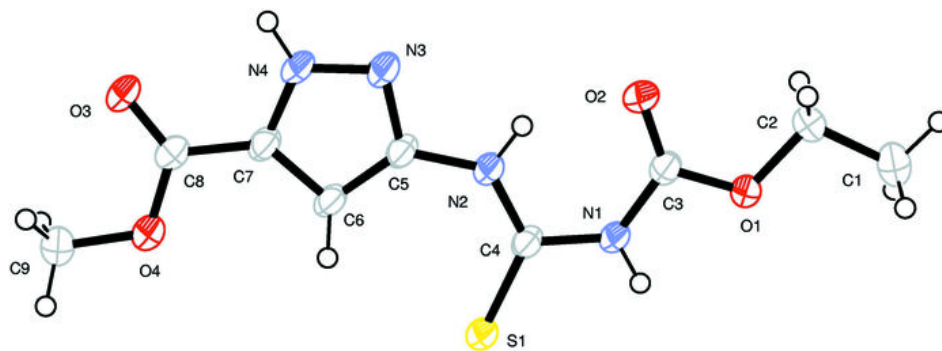


Fig. 2

