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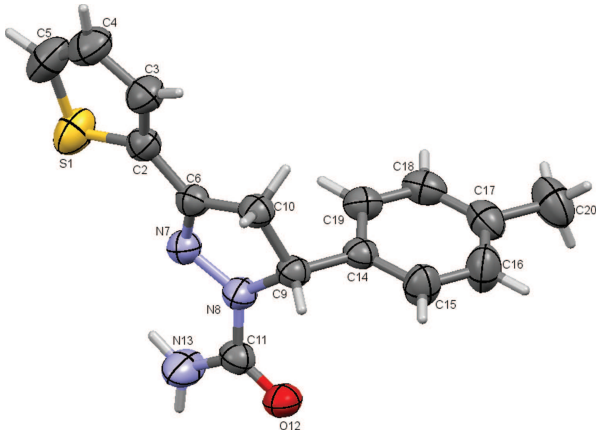
Crystal structure of 3-(thiophen-2-yl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazole-1-carboxamide



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Abstract

$C_{15}H_{15}N_3OS$, monoclinic, $P2_1/c$ (No. 14), $a = 10.2852(5)$ Å, $b = 10.1649(5)$ Å, $c = 14.7694(8)$ Å, $\beta = 107.442(2)°$, $V = 1473.12(13)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0449$, $wR_{ref}(F^2) = 0.1275$, $T = 293(2)$ K.

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The crystal structure is shown in the figure, Tables 1–3 contain details of the measurement method and a list of the atoms including atomic coordinates and displacement parameters.

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Table 1: Data collection and handling.

Crystal:	Yellow, rectangle, size 0.230×0.250×0.270 mm
Wavelength:	Cu K_α radiation (1.54178 Å)
μ:	19.42 cm^{-1}
Diffractometer, scan mode:	Bruker X8 Proteum, φ and ω scans
$2\theta_{max}$:	128.98°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	10384, 2414
$N(param)_{refined}$:	183
Programs:	Bruker data collection and reduction software [11], SHELX [12], Mercury [13]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	Site	x	y	z	U_{iso}
H(3)	4e	0.3322	0.9146	0.7028	0.074
H(4)	4e	0.1114	0.9251	0.7328	0.088
H(5)	4e	0.0918	0.7716	0.8485	0.097
H(9)	4e	0.8072	0.7724	0.7698	0.054
H(10A)	4e	0.6147	0.8848	0.7458	0.058
H(10B)	4e	0.5410	0.7824	0.6665	0.058
H(13A)	4e	0.8784	0.4812	1.0159	0.087
H(13B)	4e	0.7312	0.5160	0.9793	0.087
H(15)	4e	0.9065	0.7016	0.6544	0.076
H(16)	4e	0.9198	0.5647	0.5339	0.090
H(18)	4e	0.5876	0.3760	0.5458	0.071
H(19)	4e	0.5710	0.5139	0.6647	0.064
H(20A)	4e	0.7651	0.4121	0.3937	0.131
H(20B)	4e	0.6917	0.3017	0.4342	0.131
H(20C)	4e	0.8510	0.3137	0.4701	0.131

Source of material

A mixture of 3-(4-methylphenyl)-1-(thiophen-2-yl)prop-2-en-1-one (0.001 mol) and semicarbazine hydrochloride (0.01 mol) and potassium hydroxide (0.02 mol) in ethyl alcohol (20 mL) was refluxed on a water bath for 6–8 hrs. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into ice cold water and stirred. The solid separated was filtered and washed with ice cold water. The product was recrystallized from ethyl alcohol to get the title compound.

Table 3: Atomic displacement parameters (Å^2).

Atom	Site	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
S(1)	4*e*	0.31255(6)	0.68794(6)	0.87174(4)	0.0692(4)	0.0719(4)	0.0950(5)	0.0020(2)	0.0427(3)	0.0127(3)
O(12)	4*e*	0.9473(1)	0.5885(1)	0.88704(8)	0.0451(7)	0.0690(8)	0.0546(7)	0.0074(6)	0.0107(5)	0.0113(6)
N(7)	4*e*	0.6002(1)	0.6468(1)	0.85632(9)	0.0450(8)	0.0571(8)	0.0464(7)	0.0018(6)	0.0139(6)	0.0042(6)
N(8)	4*e*	0.7239(2)	0.6363(2)	0.8369(1)	0.0431(8)	0.0676(9)	0.0435(7)	0.0085(6)	0.0119(6)	0.0120(6)
N(13)	4*e*	0.8121(2)	0.5185(2)	0.9739(1)	0.0564(9)	0.095(1)	0.066(1)	0.0166(9)	0.0174(8)	0.0365(9)
C(2)	4*e*	0.3913(2)	0.7667(2)	0.7998(1)	0.0458(9)	0.0488(9)	0.0508(9)	−0.0022(7)	0.0131(7)	−0.0071(7)
C(3)	4*e*	0.3078(2)	0.8608(2)	0.7460(1)	0.053(1)	0.065(1)	0.066(1)	0.0097(9)	0.0179(9)	−0.0013(9)
C(4)	4*e*	0.1803(2)	0.8669(2)	0.7635(2)	0.053(1)	0.076(1)	0.091(2)	0.012(1)	0.020(1)	−0.005(1)
C(5)	4*e*	0.1691(2)	0.7804(3)	0.8288(2)	0.057(1)	0.082(2)	0.115(2)	−0.002(1)	0.043(1)	−0.009(1)
C(6)	4*e*	0.5272(2)	0.7318(2)	0.7985(1)	0.0439(9)	0.0459(9)	0.0431(8)	−0.0004(7)	0.0094(7)	−0.0022(7)
C(9)	4*e*	0.7288(2)	0.7127(2)	0.7526(1)	0.0421(9)	0.0501(9)	0.0418(8)	−0.0004(7)	0.0100(7)	0.0054(7)
C(10)	4*e*	0.5961(2)	0.7922(2)	0.7321(1)	0.0470(9)	0.0489(9)	0.0481(9)	0.0040(7)	0.0119(7)	0.0057(7)
C(11)	4*e*	0.8349(2)	0.5804(2)	0.9001(1)	0.050(1)	0.052(1)	0.0428(8)	0.0053(8)	0.0086(7)	0.0038(7)
C(14)	4*e*	0.7378(2)	0.6230(2)	0.6734(1)	0.0414(8)	0.0470(9)	0.0407(8)	0.0033(7)	0.0071(7)	0.0072(6)
C(15)	4*e*	0.8413(2)	0.6362(2)	0.6330(1)	0.064(1)	0.066(1)	0.067(1)	−0.0161(9)	0.029(1)	−0.0108(9)
C(16)	4*e*	0.8494(2)	0.5531(2)	0.5606(2)	0.082(2)	0.085(2)	0.073(1)	−0.011(1)	0.043(1)	−0.014(1)
C(17)	4*e*	0.7566(2)	0.4540(2)	0.5272(1)	0.075(1)	0.061(1)	0.0450(9)	0.008(1)	0.0106(9)	−0.0007(8)
C(18)	4*e*	0.6525(2)	0.4416(2)	0.5674(1)	0.057(1)	0.054(1)	0.056(1)	−0.0018(8)	0.0002(8)	−0.0011(8)
C(19)	4*e*	0.6426(2)	0.5244(2)	0.6391(1)	0.0455(9)	0.055(1)	0.0559(9)	−0.0019(8)	0.0098(8)	0.0023(8)
C(20)	4*e*	0.7671(3)	0.3620(3)	0.4492(2)	0.119(2)	0.082(2)	0.060(1)	0.008(1)	0.025(1)	−0.014(1)

^{1}H NMR ($CDCl_3$): δ 2.297 (s, 3H, CH_3), 3.089–3.146 (dd, 1H, $C_{4\text{-H}}$b; J = 18.0, 8.5 Hz), 3.708–3.781 (dd, 1H, $C_{4\text{-H}}$a; J = 19.0, 10 Hz), 5.460–5.490 (dd, 1H, $C_{5\text{-H}}$c; J = 18.5, 9.5 Hz), 5.503 (s, 2H, -NH_2), 7.017–7.382 (m, 7H, Ar—H and thiophene ring-H). ^{13}C NMR ($CDCl_3$): δ 21.08 (1C, CH_3), 43.72 (1C, C-4), 60.01 (1C, C-5), 125.39 (2C, Ar—C), 127.55 (1C, 5m ring-C), 128.24 (1C, Ar—C), 129.54 (2C, Ar—C), 135.07 (1C, 5m ring-C), 137.24 (1C, 5m ring-C), 139.39 (1C, 5m ring-C), 147.39 (1C, C-3), 150.24 (1C, Ar—C), 155.10 (1C, C=O). MS (m/z): 286 (M+1, 39), 285 (M+, 32), 268 (8), 241 (10), 240 (100) Anal. Calcd. for $C_{15}H_{15}N_3$ OS: C, 63.13; H, 5.30; N, 14.73% Found: C, 63.03; H, 5.20; N, 14.66%. M. P. 168–171° C.

Experimental details

All hydrogen atoms were identified in difference Fourier syntheses. The H atom were fixed geometrically and allowed to ride on their parent atoms: C—H = 0.93–0.98 Å with $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl H atoms and $1.2U_{eq}$(C) for other H atoms.

Discussion

The five-membered heterocyclic pyrazole analogues have been extensively used as building blocks in organic synthesis. They have been efficiently transformed into a potential medicinally and pharmaceutically important molecule. Pyrazole derivatives have known to exhibit diverse biological applications such as antidiabetic [1], anaesthetic [2], antimicrobial and antioxidant [3]. In addition, they have also shown potential anticancer [4], antiamoebic [5], potent and selective inhibitors of tissue-nonspecific alkaline phosphatase. Earlier we have synthesized α and β-unsaturated compounds which served as useful intermediates for the synthesis of pyrazolines [6] and thiazepines [7]. As a part of our ongoing research on pyrazoles [8], the synthesis, characterization and the structural structure determination was undertaken.

The molecular structure of the title compound is twisted. The study of torsion angles, assymmetric parameters and least squares plane reveals that the central pyrazole ring adopts a flattened envelope conformation with C9 atom deviating by 0.0588(18) Å from the Cremer and Pople plane [9]. This is confirmed by the puckering amplitude $Q = 0.0934(18)$ Å and $\varphi = 77.2(10)$ °. The carboxamide group is slightly twisted from the pyrazole ring as indicated by the torsions angles N13—C11—N8—N7 = 10.1(2)° and O12—C11—N8—N7 = −170.01(15)°. The pyrazole ring is nearly coplanar with the thiophene ring as indicated by the dihedral angle value of 6.51° whereas the pyrazole ring is almost orthogonal to the methylphenyl ring as indicated by the dihedral angle value of 86.13(9)°. The thiophene and the methylphenyl ring are inclined at an angle of 83.1(1)° with each other.

The title compound is chiral. In the arbitrarily chosen asymmetric molecule, the compound possess a chiral center at C9 with *R* conformation. Since the compound crystallizes in a centrosymmetric space group, we can surmise that the compound is a racemic mixture. The molecular conformation is stabilized by a strong intramolecular N–H···N hydrogen bond between the nitrogen of the pyrazole ring and the nitrogen of the amide moiety which form *S(6)* ring motif. In the crystal, the N–H···O hydrogen bond links pairs of molecules related by inversion ($R^2_2(8)$ ring motif [10]). The packing of the molecules when viewed down along the *a* axis indicate that the molecules exhibit layered stacking to form a two dimensional structure.

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