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Synthesis and Crystal Structure of Ethyl-5-amino-1-(5-methyl-1-phenyl-4-pyrazolyl)carbonyl]-3-methylsulfanyl-1H-pyrazole-4-carboxylate

LI-RONG WEN, MING LI, SHU-WEN WANG, XUE-MEI LI, and SHU-SHENG ZHANG*

College of Chemistry and Molecular Engineering
Qingdao University of Science and Technology
Qingdao-266042, P.R. China
Fax: (86)(582)(4023927); Tel.: (86)(582)(4022750)
E-mail: zhangshush@public.qd.sd.cn

The title compound, ethyl-5-amino-1-phenyl-4-pyrazolyl)carbonyl]-3-methylsulfanyl-1H-pyrazole-4-carboxylate (**5**) ($C_{18}H_{19}N_5O_3S$) has been synthesized by the treatment of **4** with ethyl-2-cyano-3,3-dimethylthioacrylate in refluxed ethanol. The crystals of triclinic space group P1, with cell dimensions of $a = 11{,}482(9)$, $b = 12.460(9)$, $c = 15.024(11)$ Å, $\alpha = 71.392(12)$, $\beta = 89.557(12)$, $\gamma = 64.988(11)°$, $M_r = 385.44$, $V = 1826(2)$ Å^3, $\mu = 0.207$ mm^{-1}, $D_c = 1.402$ g cm^{-3} and $Z = 4$. The two pyrazole rings are almost coplanar, which is mainly due to the intramolecular interaction, while these two rings form angles with the benzene ring. The molecules are linked by N—H···O intermolecular hydrogen bonds into two-dimensional framework, and the packing is further stabilized by C—H···π and π···π interactions.

Key Words: Synthesis, Pyrazole, Crystal structure, Hydrogen bonds.

INTRODUCTION

Pyrazole and its derivatives represent one of the most active classes of compounds possessing a wide spectrum of biological activities. During the past years, considerable evidence has been accumulated to demonstrate the efficacy of pyrazole derivatives including antibacterial, antifungal, herbicidal, insecticidal and other biological activities[1–3]. Ketene dithioacetals are one of the most important and versatile reagents for the synthesis of pyrazole[4].

In view of the above mentioned reasons and as a continuation of our research for new and better biologically active agents, herein the synthesis of the novel compound, ethyl-5-amino-1-phenyl-4-pyrazolyl)carbonyl]-3-methylsulfanyl-1H-pyrazole-4-carboxylate (**5**) was described and characterized by ^{1}H NMR, IR, elemental analyses and X-ray diffraction.

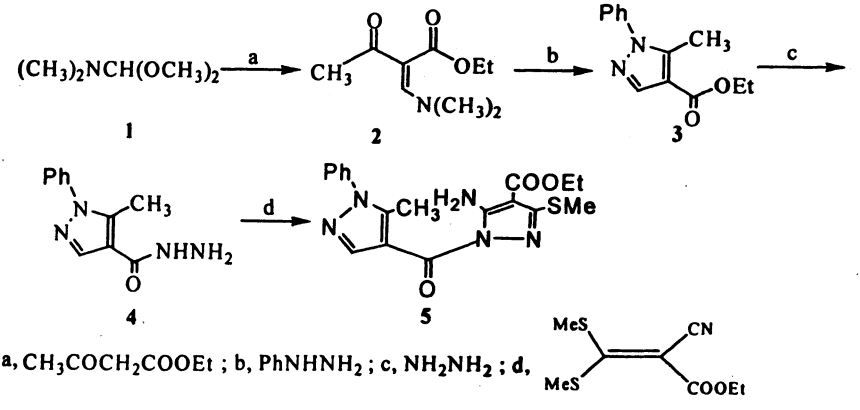
EXPERIMENTAL

All commercially available chemicals were of analytical reagent grade and used directly without further purification. ^{1}H NMR spectra ($CDCl_3$) were recorded on a Bruker AC-200 instrument with TMS as an internal standard and IR spectra were taken on a Nicolet 510P (KBr) spectrometer. The elemental analyses were performed on a Perkin-Elmer 240 analyzer. The melting point was determined on an X-4 microscopic melting apparatus and uncorrected.

The title compound **5** was synthesized by the reaction of **4** (1.236 g, 0.006 mol) with ethyl 2-cyano-3,3-dimethylthioacrylate (1.302 g, 0.006 mol) in refluxed ethanol. The intermediates of **1**, **2**, **3** were synthesized according to previously reported method[5]. Compound 5-methyl-1-phenyl-4-pyrazolylcarbohydrazide **4** was prepared by the reaction of hydrazine hydrate with **3**. The elemental and spectral of **5** are consistent with assigned structure.

The synthetic pathway for title compound is outlined in **Scheme-1**.

Yield: 76.2%, m.p. 186–188°C. Anal. Calcd. (%) for $C_{18}H_{19}N_5O_3S$: C, 56.09; H, 4.97; N, 18.17; Found (%): C, 55.94; H, 5.03; N, 18.32. ^{1}H NMR: δ 8.64 (s, 1H), 7.59–7.60 (m, 5H), 4.21–4.24 (q, 2H), (s, 3H), 2.51 (s, 3H), 2.50 (m, 3H), 1.2–1.299 (t, 3H). IR (KBr, cm^{-1}): 3452, 3325 ν(N—H), 1682 ν(C=O), 1652 ν(C=O), 1616 ν(C=C, C=N).



Scheme-1. Procedure of preparing the title compound 5

Crystallographic Data and Structure Determination[6]

A suitable crystal of the title compound was mounted on a Bruker Smart 1000 CCD area diffractometer. Reflection data were measured at 20°C using Mo-Kα radiation (λ = 0.71073 Å) with a graphite monochromator[7]. The technique used was ω-scan with θ limits $1.45 < \theta < 25.00°$. Empirical absorption corrections were carried out by using the SADABS[8] program.

The structure of the title compound was solved by direct methods and refined by least squares on F^2 by using the SHELXTL[9] software package. All non-H atoms were anisotropically refined. All H atoms were fixed geometrically and treated as riding, with C—H distances = 0.93–0.97 Å and $U_{iso}(H) \doteq 1.2\ U_{eq}(C)$ [for the methyl H atoms $U_{iso}(H) = 1.5\ U_{eq}(C)$]. The final

conventional R = 0.0844 and wR = 0.2593 for $I > 2\sigma(I)$ with weighting scheme, $w = 1/[\sigma^2(F_0^2) + (0.1592P)^2 + 0.0000P]$, where $P = (F_0^2 + 2F_c^2)/3$. The molecular graphics were plotted using SHELXTL. Atomic scattering factors and anomalous dispersion corrections were taken from International Tables for X-ray Crystallography[10]. Softwares used to prepare material for publication were SHELXTL, PARST[11] and PLATON[12].

RESULTS AND DISCUSSION

The ketene dithioacetals are extensively used for the synthesis of polyfunctionalized heterocyles such as pyrazole and pyrimidine derivatives by the displacement of the methylthio group with substituted amine[13]. In spite of numerous reactions of ketene dithioacetals with nucleophiles such as amine or active methylene compounds, to our knowledge, the reaction with 5-methyl-1-phenyl-4-pyrazolyl carbohydrazide has been unknown for the purpose of synthesis of heterocycles. Thus, ethyl-5-amino-1-[(5-methyl-1-phenyl-4-pyrazolyl)-carbonyl]-3-methylsulfanyl-1H-pyrazole-4-carboxylate (**5**) has been synthesized and its crystal structure has been studied.

X-ray Crystal Structure of the Title Compound

A view of the title compound, showing the displacement ellipsoids and the atomic numbering, is given in Fig. 1. Packing diagram of the title compound is shown in Fig. 2. Table-1 contains atomic positions and equivalent temperature factors for nonhydrogen atoms. Selected bond lengths and angles are presented in Table-2. The hydrogen bonding interaction distances are listed in Table-3.

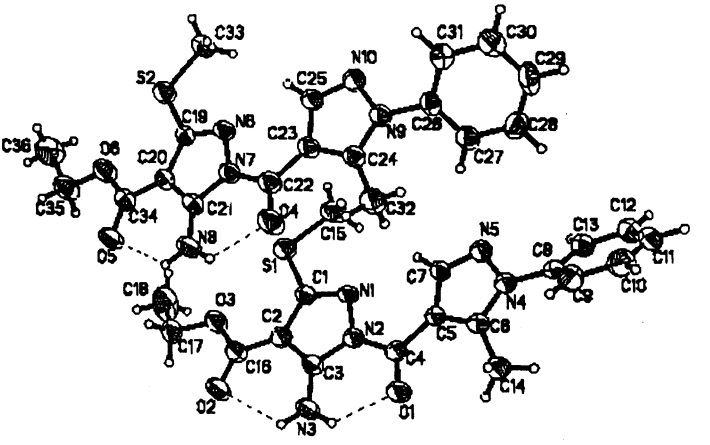


Fig. 1. The structure of compound (I) showing 50% probability displacement ellipsoids and the atom numbering scheme

In the crystal structure of **5**, the asymmetric unit contains two crystallographically independent molecules, **5A** and **5B**, respectively (Fig. 1). The bond lengths and angles in **5A** and **5B** are within normal ranges[14], and are comparable with

each other. The S1—C1 [1.736(3) Å] and S2—C19 [1.740(3) Å] bond lengths are shorter than that of S1—C15 [1.811(4) Å] and S2—C33 [1.804(3) Å] bond, which is due to the C—N double bonds in the pyrazole rings.

TABLE-1
ATOMIC COORDINATES ($\times 10^4$) AND THERMAL PARAMETERS ($Å^2 \times 10^3$)

Atom	x	y	z	U_{eq}	Atom	x	y	z	U_{eq}
S(1)	1157(1)	1449(1)	3846(1)	59(1)	C(10)	10182(4)	18(4)	1362(3)	56(1)
S(2)	-3541(1)	3882(1)	1071(1)	53(1)	C(11)	10615(4)	-1123(4)	1260(3)	54(1)
N(1)	3522(2)	1320(3)	3982(2)	38(1)	C(12)	10024(3)	-1885(4)	1658(3)	57(1)
N(2)	4218(2)	1741(3)	4422(2)	37(1)	C(13)	9023(3)	-1497(3)	2152(3)	48(1)
N(3)	3896(3)	2935(3)	5444(2)	50(1)	C(14)	8279(3)	1027(4)	3715(3)	49(1)
N(4)	7533(2)	46(3)	2777(2)	39(1)	C(15)	2038(4)	530(4)	3130(3)	60(1)
N(5)	6540(3)	-243(3)	2635(2)	48(1)	C(16)	1205(3)	3029(3)	5320(2)	38(1)
N(6)	-1191(3)	3816(3)	1129(2)	38(1)	C(17)	-964(3)	3404(4)	5563(3)	50(1)
N(7)	-447(2)	4157(3)	1617(2)	38(1)	C(18)	-1745(4)	2714(5)	5605(4)	89(2)
N(8)	-642(3)	5041(3)	2837(2)	51(1)	C(19)	-2275(3)	4100(3)	1483(2)	36(1)
N(9)	2909(2)	2480(3)	-9(2)	38(1)	C(20)	-2291(3)	4590(3)	2218(2)	36(1)
N(10)	1909(2)	2474(3)	-351(2)	48(1)	C(21)	-1104(3)	4633(3)	2284(2)	37(1)
O(1)	6038(2)	1924(2)	4691(2)	53(1)	C(22)	804(3)	3973(3)	1454(3)	42(1)
O(2)	1227(2)	3648(2)	5794(2)	52(1)	C(23)	1409(3)	3355(3)	791(2)	37(1)
O(3)	189(2)	2810(3)	5179(2)	50(1)	C(24)	2711(3)	3002(3)	671(2)	37(1)
O(4)	1355(2)	4340(3)	1899(2)	63(1)	C(25)	926(3)	2991(3)	127(2)	44(1)
O(5)	-3129(2)	5396(2)	3424(2)	52(1)	C(26)	4061(3)	1949(3)	-406(2)	37(1)
O(6)	-4320(2)	4872(3)	2624(2)	54(1)	C(27)	5259(3)	1213(3)	160(3)	44(1)
C(1)	2369(3)	1746(3)	.4241(2)	35(8)	C(28)	6339(3)	715(3)	-249(3)	54(1)
C(2)	2260(3)	2444(3)	4851(2)	37(1)	C(29)	6239(4)	904(4)	-1200(3)	60(1)
C(3)	3464(3)	2431(3)	4949(2)	37(1)	C(30)	5043(4)	1612(4)	-1759(3)	54(1)
C(4)	5492(3)	1516(3)	4281(2)	37(1)	C(31)	3958(3)	2140(3)	-1357(3)	45(1)
C(5)	6103(3)	841(3)	3640(2)	34(1)	C(32)	3715(4)	3209(4)	1113(3)	55(1)
C(6)	7303(3)	686(3)	3389(2)	36(1)	C(33)	-2916(4)	3376(4)	95(3)	59(1)
C(7)	5691(3)	240(3)	3145(2)	42(1)	C(34)	-3251(3)	4988(3)	2818(3)	41(1)
C(8)	8606(3)	-347(3)	2272(2)	37(1)	C(35)	-5336(4)	5243(4)	3196(3)	63(1)
C(9)	9156(3)	439(3)	1855(2)	47(1)	C(36)	-6431(4)	5086(5)	2838(3)	83(1)

In the crystal structure of **5**, the asymmetric unit contains two crystallographically independent molecules, **5A** and **5B**, respectively (Fig. 1). The bond lengths and angles in **5A** and **5B** are within normal ranges[14], and are comparable with each other. The S1—C1 [1.736(3) Å] and S2—C19 [1.740(3) Å] bond lengths are shorter than that of S1—C15 [1.811(4) Å] and S2—C33 [1.804(3) Å] bond, which is due to the C—N double bonds in the pyrazole rings.

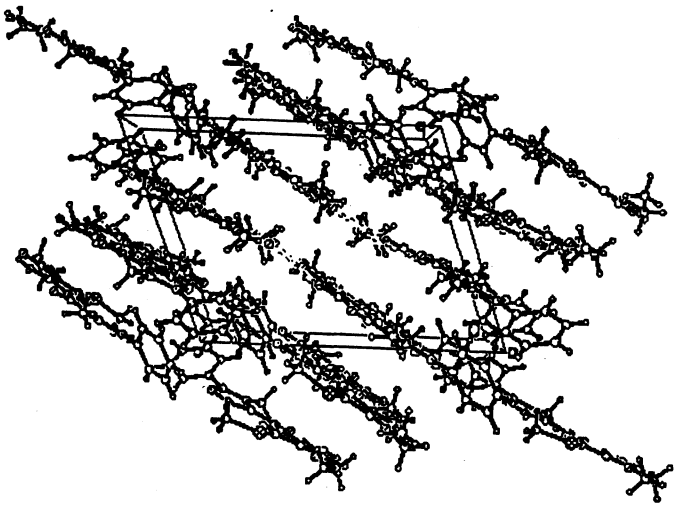


Fig. 2. Packing diagram of the title compound, showing the two-dimensional framework

TABLE-2
SELECTED GEOMETRIC PARAMETERS (Å, °)

Bond	Distance	Bond	Distance
S(1)—C(1)	1.736(3)	S(2)—C(33)	1.804(3)
S(1)—C(15)	1.811(4)	N(3)—C(3)	1.326(4)
S(2)—C(19)	1.740(3)	N(8)—C(21)	1.316(4)
Angle	(°)	Angle	(°)
C(1)—S(1)–C(15)	99.59(16)	N(2)—C(4)—C(5)	119.1(3)
C(19)—S(2)–C(33)	101.10(16)	N(7)—C(22)—C(23)	119.9(3)
C(1)—S(1)–C(33)	0.4(3)	C(33)—S(2)—C(19)—N(6)	–4.7(3)
C(1)—S(1)–C(33)	–179.9(3)	C(33)—S(2)—C(19)—C(20)	175.2(3)

TABLE-3
HYDROGEN-BONDING GEOMETRY (Å, °)

D—H···A	D–H···A	H···A	D···A	D—H···A
N(3)—H(3A)···O(1)	0.86	2.08	2.677(5)	126
N(3)—H(3B)···O(2)	0.86	2.35	2.901(5)	122
N(3)—H(3A)···O(5)^{i}	0.86	2.19	2.947(5)	146
N(8)—H(8A)···O(4)	0.86	2.06	2.655(5)	126
N(8)—H(3B)···O(5)	0.86	2.32	2.876(5)	123
N(8)—H(8B)···O(2)^{i}	0.86	2.19	2.924(5)	144

Symmetry codes: (i) –x, 1 – y, 1 – z

There are three rings in both **5A** and **5B**, respectively, each forming a plane. The mean planes of the two pyrazole rings are almost coplanar with dihedral angles of 8.2(2) and 8.7(2)° with respect to one another, in **5A** and **5B**, respectively. This is

mainly due to the intramolecular interactions, N3—H3A···O1 and N3—H3B···O2 in **5A** and N8—H8A···O4 and N8—H8B···O5 in **5B**. While the dihedral angles between these two pyrazole rings and the benzene ring are 44.5(2) and 39.8(2)°, respectively, in molecule **5A**, and 43.9(2) and 38.7(2)° in molecule **5B**. So the whole compound is not a plane molecule. In both molecules **5A** and **5B**, the ester moieties are nearly planar with the largest deviation of atom C18 twisting –0.741(1) Å from the plane of O2/O3/C16/C17 in **5A**, while atom C36 twisting 0.055(1) Å from the plane of O5/O6/C34/C35 in **5B**. These two fragments distort 4.75(14) and 1.64(12)° from their attached pyrazole rings, respectively.

In the crystal structure of **5**, the molecules are linked by N3—H3B···O5 and N8—H8B···O2 interactions into dimers (Fig. 2). The packing is further stabilized by the C28—H28···Cg5 and C32—H32A···Cg2 interactions (see Table-3; Cg5 and Cg2 denote to the centroids of the C8—C13 and N4/N5/C5—C7 rings, respectively).

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