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ORIGINAL PAPER

Synthesis, Spectroscopic Studies and X-ray Crystal Structures of New Pyrazoline and Pyrazole Derivatives

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Abstract The synthesis and characterization of some pyrazoline compounds of 1,3-diketones with hydrazine derivatives, namely, 1-(*S*-benzyldithiocarbazate)-3-methyl-5-phenyl-5-hydroxypyrazoline (**1**); 1-(2-thiophenecarboxylic)-3-methyl-5-phenyl-5-hydroxypyrazoline (**2**); 1-(2-thiophenecarboxylic)-3,5-dimethyl-5-hydroxypyrazoline (**3**); 1-(*S*-benzyldithiocarbazato)-3-methyl-5-phenylpyrazole (**4**); 1-(2-thiophenecarboxylic)-3-methyl-5-phenylpyrazole (**5**) and 1-(*S*-benzyldithiocarbazate)-3,5-dimethylpyrazole (**6**) are reported. Studies by IR, (^{1}H, ^{13}C)-NMR spectroscopies and single crystal X-ray diffraction revealed that compounds (**1**), (**2**) and (**3**) are formed as pyrazoline, whereas (**4**) and (**5**) are formed as pyrazole derivatives only under acidic conditions. Compound (**1**) crystallizes in orthorhombic $P2_12_12_1$, $a = 6.38960(10)$ Å, $b = 12.9176(3)$ Å, $c = 21.2552(5)$ Å, (**2**) crystallizes in monoclinic, $P2_1/n$, $a = 11.3617(2)$ Å, $b = 8.4988(2)$ Å, $c = 92.8900(10)$ Å and $\beta = 92.8900(5)°$, (**3**) crystallizes in monoclinic, $C2/c$, $a = 15.9500(5)$ Å, $b = 9.3766(3)$ Å, $c = 16.6910(5)$ Å and $\beta = 113.825(2)°$, (**4**) crystallizes in monoclinic, $P2_1/c$, $a = 15.228(4)$ Å, $b = 5.5714(13)$ Å, $c = 19.956(5)$ Å and $\beta = 91.575(7)°$ and (**6**) crystallizes in orthorhombic, $P2_12_12_1$, $a = 5.3920(2)$ Å, $b = 11.2074(5)$ Å, $c = 21.885(1)$ Å. The (**3**) derivative represents the first pyrazoline compound prepared from 2,4-pentanedione and characterized crystallographically.

Keywords 1,3-Diketones · Pyrazoline · Pyrazole derivatives · Crystal structures

Introduction

1,3-Diketones and related derivatives constitute an important class of organic compounds because they have the potential of binding to a great number of transition metal ions, as well as to main group metal centers. Furthermore, metal complexes containing pyrazole ligands have drawn considerable interest, owing to their unusual coordination chemistry and their biological and biochemical importance [1, 2].

Joshi and collaborators [3] have reported that benzoic acid hydrazide derivatives of 1,3-diketones can exist in several distinct isomeric forms. Some tautomeric possibilities for this class of compounds are shown ahead. According to the authors, literature data reveal conflicting reports about which tautomeric forms predominate in solution for such derivatives. Yakimovich et al. [4] from (^{1}H, ^{13}C) NMR spectral studies, proposed that acylhydrazones of 1,3-diketones can participate in the cycle-chain equilibrium between the hydrazonic (A, B), enhydrazinic (C), and/or 5-hydroxypyrazoline (D) forms and pyrazole (E) forms. Due to these observations, we decided to

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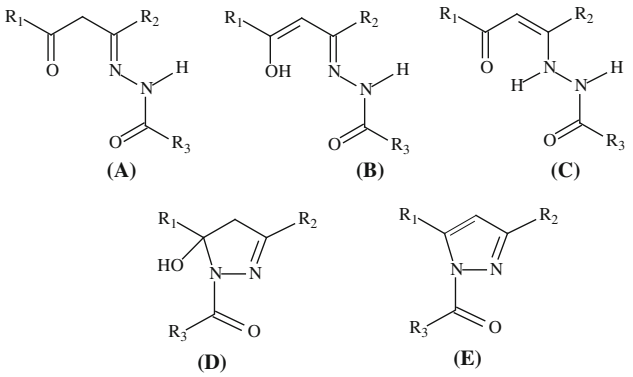


investigate, in detail, the preparation and the structural aspects of pyrazoline derivatives obtained from the cyclization of 1,3-diketones $RCOCH_2COCH_3$ (R = Me and Ph) with *S*-benzyldithiocarbazate and 2-thiophenecarboxylic hydrazine compounds. Moreover, this paper is an extension of research programs devoted to the investigation of the coordination modes of hydrazones and thiohydrazones with organotin(VI) compounds [5, 6]. Our studies demonstrated that the isomeric form is determined by the nature of the 1,3-diketone, by the structure of the hydrazine derivative, by the pH of the reaction medium and, to a certain extent, by the polarity of the solvent used in the condensation reactions.

Experimental

Materials and Methods

Solvents were purified and dried according to standard procedures. The reagents, 2,4-pentanedione, 4-phenyl-2, 4-butanedione, 2-thiophenecarboxylic hydrazide, were of the highest commercially available quality and the starting material, *S*-benzyldithiocarbazate, was prepared by a literature method [7]. IR spectra were recorded on a BOMEM MB100 FT-IR spectrophotometer in the 4000–400 cm^{-1} range using KBr pellets and microanalyses were performed using a FISSONS CHNS, mod. EA 108 microanalizer. NMR spectra were recorded on a VARIAN MERCURY PLUS spectrometer (7.05 T) operating at 300 MHz for ^1H and at 75.46 MHz for ^{13}C. The compound was dissolved in $CDCl_3$ or DMSO-d_6 containing TMS as internal reference (see Fig. 6 for atom numbering). Chemical shifts were expressed in δ (ppm) and coupling constants as *J* (Hz). The homonuclear and heteronuclear two-dimensional experiments (COSY, HMQC and HMBC) were completed using the field gradient mode.

Single crystals of compounds (**1**), (**2**), (**3**), and (**6**), suitable for X-ray data collection, were grown by slowly evaporating the solvent from their MeOH solution at room temperature. Single crystals for (**4**) and (**5**) were obtained as reported in the synthesis section. The data collections were performed with Mo Kα radiation (λ = 71.073 pm) on a NONIUS KAPPA CCD instrument for (**1**), (**2**) and (**6**) and on a BRUKER KAPPA APEX II CCD diffractometer for (**3**), (**4**) and (**5**) applying standard procedures. X-ray crystal structures were solved by the heavy atom method with SHELXS-97 [8] and refined with the SHELXL-97 [9]. Hydrogen atom positions were calculated at idealized positions using the Riding model option of SHELXL-97 [9]. Additional crystal data and more information about the X-ray structural analyses are shown in Table 1. All of the structures of the pyrazoline and pyrazole derivatives are shown in Scheme 1 and their ORTEP plots are depicted in Figs. 1, 2, 3, 4, and 5. All relevant crystallographic information is presented in Table 1, and selected bond distances and angles in Table 2.

Synthesis

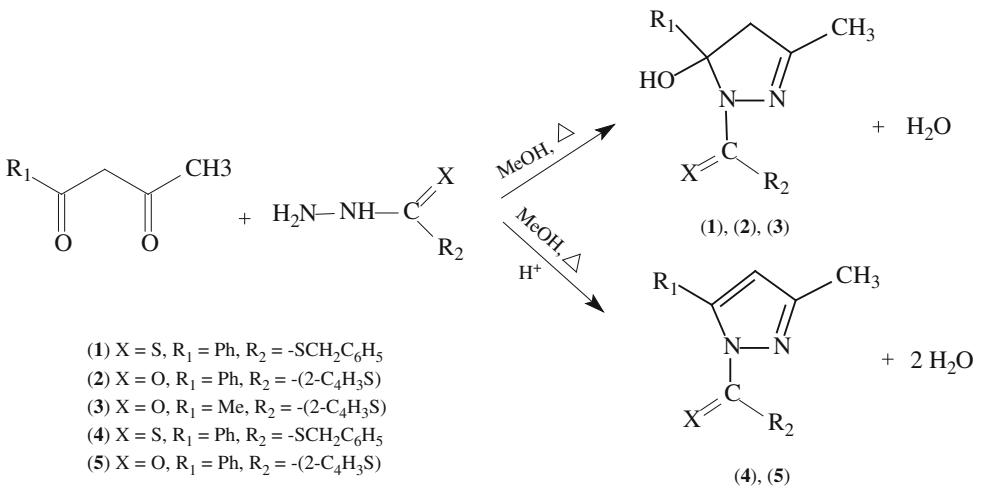
Compounds (**1**), (**2**), and (**3**) were prepared as follows: a solution of 1,3-diketone, $RCOCH_2COMe$ (4.0 mmol), where R is a methyl or a phenyl group, in 10 mL of MeOH was added to a solution of the appropriate hydrazide derivative (4.0 mmol) in 10 mL of MeOH. The mixture was refluxed for 1 h, obtaining yellow solutions for (**1**) and (**2**), and a colorless solution for (**3**). The clear solutions were slowly evaporated, leading appearance of colorless crystalline products, which were filtered, washed with hexane and dried in air. Compounds (**1**) and (**3**) pyrazoline derivatives can easily be obtained as single crystals by using CH_2Cl_2 as the reaction solvent.

Compounds (**4**), (**5**), and (**6**) were prepared as follows: pyrazole derivative compounds (**4**) and (**5**) were prepared employing an acid-catalyzed conversion by adding two drops of concentrated HCl in equimolar mixture of 4-phenyl-2,4-butanedione and the appropriate hydrazone in 20 mL of MeOH (Scheme 1). After about 2 h under reflux and slow evaporation of the solvent, deep yellow and colorless crystals precipitated from solutions of (**4**) and (**5**), respectively. Crystals suitable for X-ray diffraction studies for (**4**) were acquired by a slow evaporation technique from a hot hexane/CH_2Cl_2 (3:1, v/v) solution and (**5**) was obtained as a pure material. Equimolar mixture of 2,4-pentanedione and *S*-benzyldithiocarbazate in 20 mL of MeOH for 1 h, under the same conditions as described above, gave pyrazole (**6**) as yellow needles. However, similar treatment of 4-phenyl-2,4-butanedione with *S*-benzyldithiocarbazate afforded 5-hydroxy-4,5-dihydropyrazoline derivative (**1**) in excellent yield. It is noteworthy to mention that the presence of a strong electron-withdrawing substituent at 1- or 5-position of the 5-hydroxy-4,

Table 1 Crystallographic data for pyrazoline [(**1**), (**2**), (**3**)] and pyrazole [(**4**), (**6**)] derivatives

	(**1**)	(**2**)	(**3**)	(**4**)	(**6**)
Formula	$C_{18}H_{18}N_2OS_2$	$C_{15}H_{14}N_2O_2S$	$C_{10}H_{12}N_2O_2S$	$C_{18}H_{16}N_2S_2$	$C_{13}H_{14}N_2S_2$
Formula weight	342.46	286.34	224.28	324.45	262.38
Crystal system	Orthorhombic	Monoclinic	Monoclinic	Monoclinic	Orthorhombic
Space group	$P2_12_12_1$	$P2_1/n$	$C2/c$	$P2_1/c$	$P2_12_12_1$
Crystal color	Colorless	Colorless	Colorless	Yellow	Yellow
Z	4	4	8	4	4
T (K)	293(2)	293(2)	293(2)	293(2)	293(2)
a (Å)	6.38960(10)	11.3617(2)	15.9500(5)	15.228(4)	5.3920(2)
b (Å)	12.9176(3)	8.4988(2)	9.3766(3)	5.5714(13)	11.2074(5)
c (Å)	21.2552(5)	14.8959(3)	16.6910(5)	19.956(5)	21.885(1)
β (°)	90	92.8900(10)	113.825(2)	91.575(7)	90
V (Å^3)	1754.37(6)	1436.53(5)	2283.53	1692.5(7)	1322.5(1)
ρ_{calcd} (g cm^{-3})	1.297	1.324	1.305	1.273	1.318
Index ranges	$-7 \le h \le 7$	$-14 \le h \le 14$	$-16 \le h \le 11$	$-21 \le h \le 21$	$-6 \le h \le 6$
	$-15 \le k \le 15$	$-11 \le k \le 11$	$-9 \le k \le 9$	$-4 \le k \le 7$	$-13 \le k \le 13$
	$-25 \le l \le 25$	$-19 \le l \le 19$	$-16 \le l \le 17$	$-25 \le l \le 28$	$-25 \le l \le 26$
F(000)	720	600	944	680	552
μ (mm^{-1})	0.309	0.228	0.266	0.312	0.382
Refinement method	i	i	i	i	i
Reflections collected	23496	10533	5488	16132	11233
Data/parameters	3090/211	3278/182	1317/136	4940/199	2594/157
GOF on F^2	1.234	1.086	1.098	0.763	1.075
R_1 $[I > 2\sigma(I)]$[ii]	0.0590	0.0546	0.0548	0.0459	0.0482
wR_2 $[I > 2\sigma(I)]$[iii]	0.1809	0.1699	0.1670	0.1036	0.1156

(i) Full-matrix least-squares on F^2, (ii) $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$, (iii) $wR_2 = [\sum_w(|F_o|^2 - |F_c|^2)^2/\sum_w|F_o^2|^2]^{1/2}$



Scheme 1 Condensation reactions on preparation of pyrazoline [(**1**), (**2**), (**3**)] and pyrazole [(**4**), (**5**)] derivatives

5-dihydropyrazoline ring is a necessary condition of their stability.

(1). Anal. Calcd for $C_{18}H_{18}N_2OS_2$: (342.47 g mol^{-1}): C, 63.13; H, 5.30; N, 8.18; S, 18.72. Found: C, 62.99; H, 5.61; N, 8.27; S, 19.67%; color: colorless; yield: 81%; m.p.: 125–127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.09 (d, 3H, $-CH_3$); 3.21 (dd, J 18.8 Hz, 2H, $-CH_2-$); 4.35 (dd, J 13.2 Hz, 2H, $-CH_2-$); 6.47 (s, 1H, –OH). ^{13}C NMR (300 MHz, $CDCl_3$): δ 16.0 (^{1}C), 158.4 (^{2}C), 54.6(^{3}C), 97.3(^{4}C); 142.3 (^{5}C); 191.2 (^{9}C); 39.2 (^{10}C). IR (KBr):

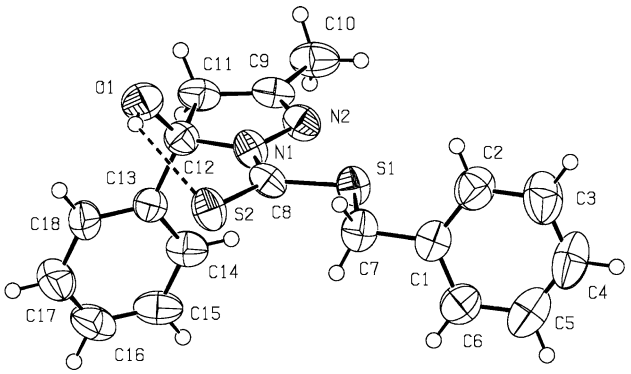


Fig. 1 ORTEP plot of (**1**) with the displacement parameters drawn at the 30% probability level. The *dashed line* indicates an intramolecular hydrogen bonding

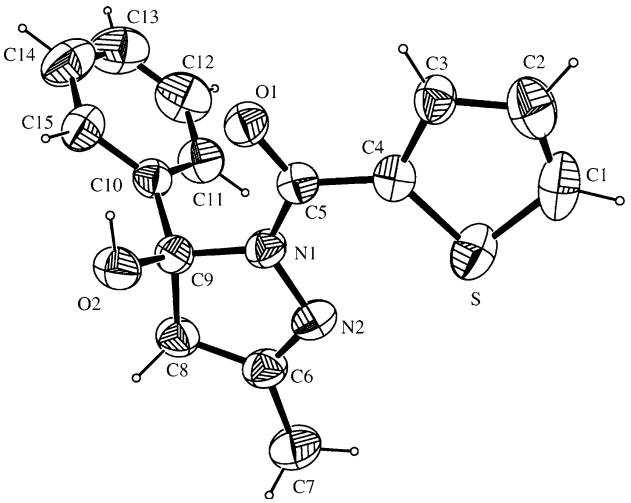


Fig. 2 ORTEP plot of (**2**) with the displacement parameters drawn at the 30% probability level

$\nu_{max.}/cm^{-1}$: 3356 (O–H), 1629 (C=N), 1494, 1461 (C=C), 1377 (C–N), 1320 (C–O), 1252, 854 (C = S), 981 (C–S–S).

(2). Anal. Calcd for $C_{15}H_{14}N_2SO_2$: (286.35 g mol^{-1}): C, 62.92; H, 4.93; N, 9.78; S, 11.20. Found: C, 61.99; H, 4.85; N, 9.75; S, 12.27%; color: colorless; yield: 75%; m.p.: 161–163 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.15 (d, 3H, $–CH_3$); 3.23 (dd, J 18.0 Hz, 2H, $–CH_2–$); 5.29 (s, 1H, –OH). ^{13}C NMR (300 MHz, $CDCl_3$): δ 16.1 (^{1}C), 155.0 (^{2}C), 53.5 (^{3}C), 94.5 (^{4}C); 143.5 (^{5}C); 160.2 (^{9}C); 135.0 (^{10}C). IR (KBr): $\nu_{max.}/cm^{-1}$: 3411 (O–H), 1610 (C=O), 1630 (C=N), 1513, 1445 (C=C), 1313 (C–O), 1378 (C–N).

(3). Anal. Calcd for $C_{10}H_{12}N_2OS_2$: (224.28 g mol^{-1}): C, 53.55; H, 5.39; N, 12.49; S, 14.29. Found: C, 53.04; H, 5.62; N, 12.40; S, 15.94%; color: colorless; yield: 65%; m.p.: 102–105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.85 (s, 3H, $–CH_3$); 2.99 (dd, J 18.0 Hz, 2H, $–CH_2–$); 2.04 (s, 3H, $–CH_3$); 5.06 (s, 1H, –OH). ^{13}C NMR (300 MHz, $CDCl_3$): δ 16.2 (^{1}C), 155.4 (^{2}C), 50.8 (^{3}C), 92.7 (^{4}C); 26.9 (^{5}C); 160.4 (^{9}C); 135.4 (^{10}C). IR (KBr): $\nu_{max.}/cm^{-1}$: 3414

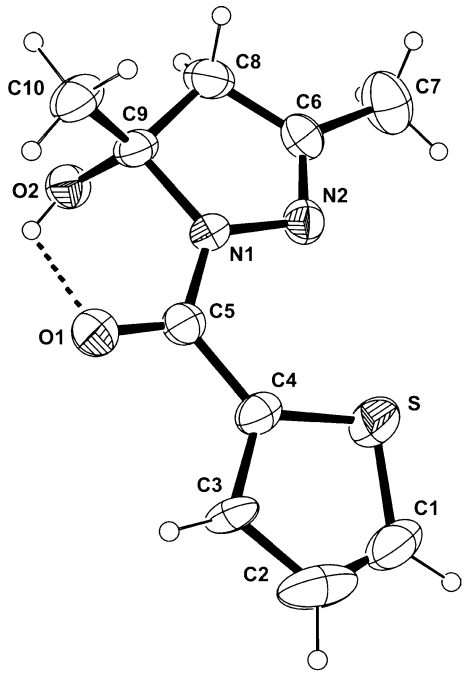


Fig. 3 ORTEP plot of (**3**) with the displacement parameters drawn at the 30% probability level. The *dashed line* indicates an intramolecular hydrogen bonding

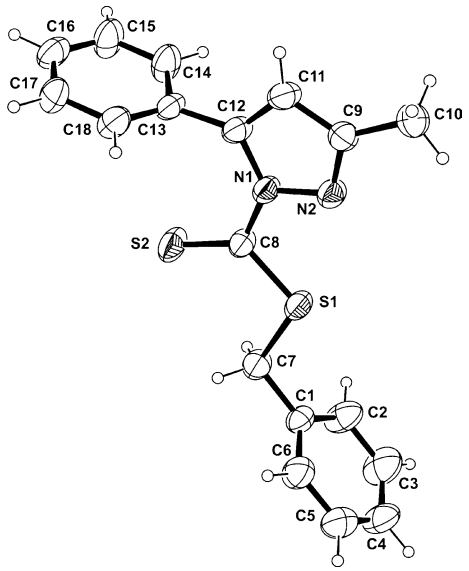


Fig. 4 ORTEP plot of (**4**) with the displacement parameters drawn at the 30% probability level

(O–H), 1600 (C=O), 1638 (C=N), 1512, 1445 (C=C), 1378 (C–N), 1322 (C–O).

(4). Anal. Calcd for $C_{18}H_{16}N_2S_2$: (324.46 g mol^{-1}): C, 66.63; H, 4.97; N, 8.63; S, 19.76. Found: C, 64.47; H, 5.14; N, 8.65; S, 21.16%; color: deep yellow; yield: 76%; m.p.: 101–103 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.34 (d, 3H, $–CH_3$); 6.27 (s, 1H, = CH–); 4.35 (s, 2H, $–CH_2–$). ^{13}C

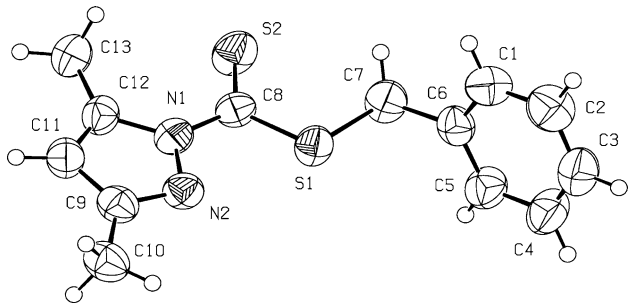


Fig. 5 ORTEP plot of (**6**) with the displacement parameters drawn at the 30% probability level

NMR (300 MHz, $CDCl_3$): δ 13.7 (^{1}C), 147.0 (^{2}C), 114.4 (^{3}C), 151.7 (^{4}C); 131.9 (^{5}C); 199.1 (^{9}C); 41.7 (^{10}C). IR (KBr): $\nu_{max.}/cm^{-1}$: 1573 (C=N), 1490, 1453 (C=C), 1377 (C–N), 1275, 853 (C=S), 969 (C–S–S).

(5). Anal. Calcd for $C_{15}H_{12}N_2OS$: (268.33 g mol^{-1}): C, 67.14; H, 4.51; N, 10.44; S, 11.95. Found: C, 65.74; H, 4.72; N, 10.34; S, 13.27%; color: colorless; yield: 55%; m.p.: 122–123 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.73 (s, 3H, $-CH_3$); 6.58 (d, 1H, = CH–). ^{13}C NMR (300 MHz, $CDCl_3$): δ 14.7 (^{1}C), 155.3 (^{2}C), 108.1 (^{3}C), 138.0 (^{4}C); 145.5 (^{5}C); 160.6 (^{9}C); 137.5 (^{10}C). IR (KBr): $\nu_{max.}/cm^{-1}$: 1681 (C=O), 1574 (C=N), 1502, 1468 (C=C), 1355 (C–N).

(6). Anal. Calcd for $C_{13}H_{14}N_2S$: (262.39 g mol^{-1}): C, 59.51; H, 5.38; N, 10.68; S, 24.44. Found: C, 57.83; H, 5.44; N, 10.46; S, 25.56%; color: deep yellow; yield: 75%; m.p.: 90–92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.08 (s, 3H, $-CH_3$); 5.90 (q, 3H, $-CH_3$); 2.55 (d, 3H, $-CH_3$); 4.23 (s, 2H, $-CH_2-$). ^{13}C NMR (300 MHz, $CDCl_3$): δ 13.6 (^{1}C), 145.5 (^{2}C), 113.2 (^{3}C), 151.7 (^{4}C); 17.3 (^{5}C); 200.3 (^{9}C); 41.3 (^{10}C). IR (KBr): $\nu_{max.}/cm^{-1}$: 1580 (C=N), 1489, 1454 (C=C), 1367 (C–N), 1274, 863 (C=S), 963 (C–S–S).

Results and Discussion

Crystal Structure of (**1**)

The ORTEP plot of (**1**) is shown in Fig. 1 along with the atom numbering scheme. Selected bond lengths and angles with their estimated standard deviations are compiled in Table 2. The structure obtained confirms the cyclization reaction and formation of the 5-hydroxy-4,5-dihydropyrazoline derivative. The compound crystallizes into an

Table 2 Selected bond distances (Å) and angles for pyrazoline [(**1**), (**2**), (**3**)] and pyrazole [(**4**), (**6**)] derivatives

	(**1**)	(**4**)	(**6**)		(**2**)	(**3**)
S1–C7	1.810(5)	1.806(2)	1.812(3)	S–C4	1.704(2)	1.684(4)
S1–C8	1.727(5)	1.736(2)	1.745(3)	C4–C5	1.475(2)	1.478(5)
S2–C8	1.679(5)	1.622(2)	1.630(3)	O1–C5	1.233(2)	1.231(4)
O1–C12	1.393(6)			O2– 9	1.404(2)	1.407(4)
N1–C8	1.353(6)	1.393(3)	1.394(4)	N1–C5	1.355(2)	1.354(4)
N1–C12	1.501(6)	1.386(3)	1.403(4)	N1–C9	1.487(2)	1.494(4)
N1–N2	1.407(6)	1.384(2)	1.386(4)	N1–N2	1.397(2)	1.390(4)
N2–C9	1.284(7)	1.311(3)	1.315(4)	N2–C6	1.282(3)	1.273(5)
C9–C10	1.487(2)	1.488(3)	1.485(5)	C6–C7	1.484(3)	1.490(6)
C9–C11	1.482(7)	1.409(3)	1.422(5)	C6–C8	1.494(3)	1.462(6)
C11–C12	1.540(7)	1.344(3)	1.349(5)	C8–C9	1.542(2)	1.509(5)
C12–C13	1.534(7)	1.484(3)	1.483(5)	C9–C10	1.524(3)	1.502(5)
C7–S1–C8	102.6(2)	102.47(11)	102.21(15)	S–C4–C5	128.06(14)	129.5(3)
S1–C8–S2	125.7(3)	125.12(15)	125.26(19)	O1–C5–C4	120.59(15)	120.2(3)
S2–C8–N1	120.6(4)	124.46(16)	124.8(2)	O1–C5–N1	118.85(16)	119.3(3)
S1–C8–N1	113.6(3)	110.43(15)	109.99(19)	C4–C5–N1	120.52(15)	120.5(3)
C8–N1–N2	118.4(4)	117.44(17)	117.5(2)	C5–N1–N2	122.84(15)	121.0(3)
N1–N2–C9	107.2(4)	105.57(18)	105.1(2)	N1–N2–C6	107.73(16)	107.8(3)
C8–N1–C12	128.2(4)	131.97(19)	131.3(3)	C5–N1–C9	123.00(14)	125.1(3)
N2–C9–C11	114.9(5)	110.4(2)	111.0(3)	N2–C6–C8	114.43(16)	114.0(5)
C9–C11–C12	104.5(4)	107.8(2)	107.6(3)	C6–C8–C9	103.72(15)	105.1(3)
N1–C12–C13	110.4(4)	127.0(2)	125.7(3)	N1–C9–C10	109.64(14)	113.7(3)
C11–C12–C13	111.7(4)	127.4(2)	129.1(3)	C8–C9–C10	114.26(15)	114.7(3)
O1–C12–C13	113.5(4)			O2–C9–C10	113.64(15)	111.1(3)
N1–C12–C11	99.7(4)	105.6(2)	105.2(2)	N1–C9–C8	100.26(14)	99.5(3)

Table 3 Intramolecular hydrogen-bond parameters (Å, °) for compounds (**1**) and (**3**)

	D–H···A	*d* (D–H)	*d* (H···A)	*d* (D···A)	∠(DHA)
(**1**)	O1–H1···S2	0.82	2.55	3.145	130.8
(**3**)	O2–H2···O1	0.82	2.65	3.129	119.8
	O2–H2···O1^{i}	0.82	1.97	2.754	158.9

Symmetry code: (i) −x + 3/2, −y +1/2, –z

orthorhombic crystal system and exhibits an intramolecular hydrogen bonding O1–H1···S2 = 2.55 Å (Table 3), which helps in stabilizing the crystal structure. The N2–C9 = 1.284(7) Å double bond length and the C9–C11 = 1.482(7), C11–C12 = 1.540(7), N1–C12 = 1.501(6) and N1–N2 = 1.407(6) Å single bond lengths are very close to those found in pyrazoline derivatives [(**2**), (**3**)] (Table 2). The S2–C8 = 1.727(5) and S1–C8 = 1.679(5) Å bond lengths indicate, respectively, single and double-bond nature. As expected, the bond angles of O1–C12–C13 = 113.5(4)°, C11–C12–N1 = 99.7(4)°, O1–C12–C11 = 109.8(4)° and C13–C12–N1 = 110.4(4)° indicate that the C12 asymmetric center is sp^3 hybridized. The structure of (**1**) shows that each ring is nearly planar, with the mean deviations from planarity being 0.0227 and 0.0075 Å for the pyrazoline and 5-phenyl rings, respectively. The rings, however, are twisted with respect to each other. The angle between the mean planes of the rings is 87.6(2)°.

Crystal Structures of (**2**) and (**3**)

The ORTEP plots of (**2**) and (**3**) are illustrated in Figs. 2 and 3, respectively, and all relevant crystallographic information is given in Table 1, while bond lengths and angles are summarized in Table 2. The crystallographic data showed that both compounds crystallize into a monoclinic lattice and the molecules are formed as five-membered diazo ring corresponding to non-aromatic 5-hydroxy-4,5-dihydropyrazoline derivatives. In (**3**), an intramolecular hydrogen bond O2–H2···O1 = 2.65 Å (Table 3) stabilizes the conformation of the molecule about the C9–N1, N1–C5 and C5–C4 single bonds. The five cyclic N1–N2 = 1.397(2), N2–C6 = 1.282(3), C6–C8 = 1.494(3), C8–C9 = 1.542(2) and C9–N1 = 1.487(2) Å bond lengths found in 4-phenyl-2,4-butanedione derivative (**2**) are slightly longer than the compared distances observed in 2,4-pentanedione derivative (**3**) (Table 2). This observation may be attributed to the fact that the phenyl group is a more electron-withdrawing group than the methyl group. A similar effect was also observed in the structures of (**4**) and (**6**) pirazole derivatives (Table 2). In both compounds (**2**) and (**3**), the angles around the C9 asymmetric center are in the range of 99.5(3)°–113.64(15)°, indicating a sp^3 hybridization. The structures of (**2**) and (**3**) show that the angles between the mean planes of the two five-membered rings are 7.7(1)° for (**2**) and 9.45(1)° for (**3**). The means derivations from planarity for the pyrazoline and thiophene rings are 0.0225 and 0.0055 Å for (**2**) and 0.0512 and 0.0074 Å for (**3**), respectively.

Crystal Structures of (**4**) and (**6**)

The ORTEP plots of (**4**) and (**6**) are shown in Figs. 4 and 5 and all relevant crystallographic information is given in Table 1, while bond lengths and angles are summarized in Table 2. The crystallographic data showed that (**4**) crystallizes into a monoclinic lattice and (**6**) into an orthorhombic one. The substitution of the methyl group in (**6**) by the phenyl group in (**4**) leads to modifications in the crystal packing of the molecules in each case (see Table 1). As observed in 5-hydroxy-4,5-dihydropyrazoline derivatives [(**1**), (**2**)], the pyrazole ring bond lengths of C9–C11 = 1.409(3), C11–C12 = 1.344(3), C12–N1 = 1.386(3), N1–N2 = 1.384(2) and N2–C9 = 1.311(3) Å, found in 4-phenyl-2,4-butanedione derivative (**4**), are slightly longer than the compared lengths observed in 2,4-pentanedione derivative (**6**) (Table 2). However, these bond lengths are shorter than the equivalent bond lengths found in pyrazoline (**1**), due to its aromatization, with water elimination, forming (**4**). The bond lengths of N1–C8 = 1.393(3) Å observed in (**4**) is longer than the similar bond lengths of N1–C8 = 1.353(3) Å found in (**1**) indicating some degree of overlap between the N1 lone pair of electrons and the π-system of C=S bond, as expected. The bond angles of C11–C12–C13 = 127.4(2)° and N1–C12–C13 = 127.0(2)° observed in (**4**) are considerably larger than the equivalent bond angles of C11–C12–C13 = 111.7(4)° and N1–C12–C13 = 110.4(4)° found in (**1**), indicating rehybridization of C11 and C12 atoms from sp^3 to sp^2 with water elimination from (**1**). The bond lengths and the angles observed for (**6**) are very close to those found for (**4**), so it is unnecessary to compare one with the other (Table 2).

Infrared Spectroscopy

The IR spectra of the pyrazoline [(**2**), (**3**)] and pyrazole [(**4**), (**5**), (**6**)] derivatives are consistent with the formation of hydrazones but are not useful for distinguishing the tautomers (A), (B), (C), and (D) [3]. However, this technique is important to distinguish between pyrazoline and pyrazole derivatives. The IR spectra of (**1**), (**2**) and (**3**) show broad bands in the 3411–3356 cm^{-1} range, attributed to *ν*(O–H) stretching vibrations. Strong bands at 1610, 1600 and 1681 cm^{-1} found in the spectra of (**2**), (**3**) and (**5**), respectively, are assigned to acyl *ν*(C=O) absorptions. The highest absorption, at 1681 cm^{-1}, observed in (**5**), is

consistent with overlap reduction between the N1 lone pair of electrons and the π-system of C=O bond due to the aromatic nature of the pyrazole ring. On the other hand, the intramolecular hydrogen bonding (C=O···H–O), observed in (**3**) contributes to lengthen the C=O bond and consequently shifts the *ν*(C=O) absorption to lower frequencies. The azomethine *ν*(C=N) stretching mode overlapping with other possible absorptions appears as a strong band in the region around 1630 cm^{-1} in the spectra of (**1**), (**2**) and (**3**), whereas this same stretching mode appears at about 1575 cm^{-1} in the spectra of (**4**), (**5**) and (**6**), indicating that these compounds are aromatic. The *ν*(C=S) absorptions observed for (**4**) and (**6**) appear at higher frequencies compared to (**1**) and corroborate with the reduction of overlap between the N1 lone pair of electrons after aromatization takes place.

(^{1}H, ^{13}C) NMR Spectroscopy

The ^{1}H NMR spectra (Fig. 6 for atom numbering) of the pyrazoline derivatives (**1**), (**2**) and (**3**) measured in $CDCl_3$ show that they exist exclusively in the cyclic tautomeric form (D). The signal of the terminal $^1CH_3$ appears at 2.09 ppm for (**1**), at 2.15 ppm for (**2**) and at 1.85 ppm for (**3**), whereas the magnetically and chemically nonequivalent $^3CH_2$ methylene hydrogens appear as two doublets at 3.21 ppm ($^2J_{HH}$ = 18.8 Hz) for (**1**), 3.23 ppm ($^2J_{HH}$ = 18.0 Hz) for (**2**) and at 2.99 ppm ($^2J_{HH}$ = 18.0 Hz) for (**3**). The spectrum of (**1**) also showed $^{10}CH_2$ methylene signal at 4.35 ppm as two doublets due to geminal coupling ($^2J_{HH}$ = 13.2 Hz). The signal of the –OH group appear as a broad singlet at 6.47, 5.29 and at 6.51 ppm in (**1**), (**2**) and (**3**), respectively. The dissolution of compound (**1**) in DMSO-d_6, which is a basic dipolar solvent, results in the appearing of a yellow solution, indicating that its pyrazoline (form D) may be transformed into possible linear tautomers (A), (B), (C) or pyrazole form (E). Concerning this, only signals of pyrazoline, form (D), are observed in the spectrum of (**1**), obtained from $CDCl_3$, showing that the proportion of its linear tautomer (A or C) [10], in DMSO-d_6 solution, is less than 3%. Indeed, this is observed for other molecules [10, 11]. The ^{1}H NMR spectrum in $CDCl_3$ solution at room temperature shows that the 5-hydroxypyrazoline (**3**) derivative quickly suffers aromaticity, implying in water elimination, forming the condensation product 1-(2-thyophenecarboxylic)-3,5-dimethylpyrazole. In the ^{1}H NMR spectrum of (**3**) there are signals of non-equivalent $^3CH_2$ methylene hydrogens at 2.99 ppm and ^{3}CH aromatic hydrogen at 6.06 ppm due to the presence of 5-hydroxypyrazoline (D form) and pyrazole (E form), respectively. The (D)/(E) ratio is approximately equal to 3:1. On the other hand, this same compound in DMSO-d_6 solution exists exclusively as in the solid state, i.e., 5-hydroxypyrazoline (form D). The D form is probably stabilized by the formation of an intramolecular hydrogen bond between OH group and molecules of the solvent.

According to the ^{13}C NMR spectroscopy, compounds (**1**), (**2**) (prepared from 4-phenyl-2,4-butanedione) and (**3**) (synthesized from 2,4-pentanedione) have structures

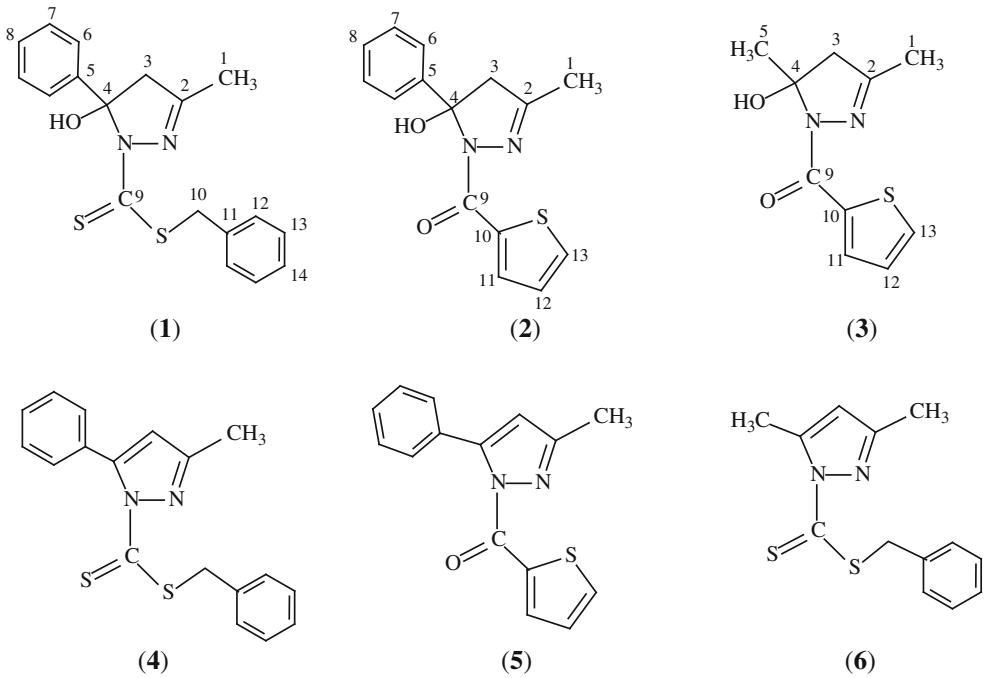


Fig. 6 Structural formulas of the 5-hydroxypyrazoline [(**1**), (**2**), (**3**)] forms and pyrazole [(**4**), (**5**), (**6**)] derivatives synthesized in this work and numbering scheme for NMR assignments

corresponding the 5-hydroxypyrazoline (D form). Their spectra showed singlet arising from ^{3}C atoms at 54.6, 53.5 and 50.8 ppm, whereas the asymmetrical ^{4}C atom signals were observed at 97.3, 94.5 and 92.7 ppm for (**1**), (**2**) and (**3**), respectively. The X-ray diffraction study of compound (**3**) showed conclusively that this derivative has the 5-hydroxypyrazoline structure in the solid state. It is noteworthy to mention that the reactions of carbonylhydrazides with 2,4-pentanedione can be used as routes for the synthesis of the corresponding 5-hydroxypyrazoline form.

Some authors [5] have postulated, however, that it is difficult to isolate stable compounds like this from 2,4-pentanedione. The ^{13}C NMR spectra of (**4**), (**5**) and (**6**) showed peaks of ^{3}C and ^{4}C atoms in the aromatic region (108–152 ppm), obviously due to the formation of pyrazole derivatives with water elimination from the 5-hydroxypyrazoline form.

Conclusions

According to the reported results in this field, the presence of a strong electron-withdrawing substituent at the 1- or 5-positions of the pyrazole ring is a very important condition for preparing stable (5-hydroxypyrazoline) derivatives. However, the preparation of the 5-hydroxypyrazoline derivative (**3**) from 2,4-pentanedione contrasts with that. Pyrazole instead of pyrazoline are obtained as main product only under acidic conditions and it is noteworthy to mention that the (**3**) pyrazoline derivative is the first compound prepared from 2,4-pentanodione, which was crystallographically characterized.

Supporting Information Available

Crystallographic data for the structural analysis of the compounds have been deposited at the Cambridge Crystallographic Data Center (CCDC). The CCDC numbers are 697461 (**1**), 697618 (**2**), 697462 (**3**), 697619 (**4**), 697463 (**6**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, United Kingdom; Fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.

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References

1. Evans IR, Howard JAK, Szécsényi KM, Leovac VM, Jacimovic ZK (2004) J Coord Chem 57:469
2. Bienvenue E, Choua S, Loborecio MA, Marzin C, Pacheco P, Seta P, Tarrago GJ (1995) Inorg Biochem 57:157
3. Joshi KC, Bohra R, Joshi BS (1992) Inorg Chem 31:598
4. Yakimovich SI, Zerova IV, Zelenin KN, Alekseev VV, Tugusheva AR (1997) Russ J Org Chem 33:370
5. De Sousa GF, Deflon VM, Gambardella MTP, Francisco RHP, Ardison JD, Niquet E (2006) Inorg Chem 45:4518
6. De Sousa GF, Deflon V, Manso LCC, Ellena J, Mascarenhas YP, Lang ES, Gatto CC, Mahieu B (2007) Trans Met Chem 32:649
7. Tarafder MTH, Ali AM, Elias MS, Crouse KA, Silong S (2000) Trans Met Chem 25:706
8. Sheldrich GM (1997) SHELXS97, program for automatic solution of crystal structures. University of Göttingen, Germany
9. Sheldrich GM (1997) SHELXL97, program for crystal structure refinement. University of Göttingen, Germany
10. Zelenin KN, Alekseyev VV, Kuzneysova OB, Saminskaya AG, Yakimovich SI, Zerova LV (1999) Russ J Org Chem 35:357
11. Zelenin KN, Alekseyev VV, Tygysheva AR (1995) Tetrahedron 51:11256