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REACTION OF 1-ARYL-3-METHYL-PYRAZOL-5-ONES WITH 2-CYANOARYL-DIAZONIUM BISULFATES

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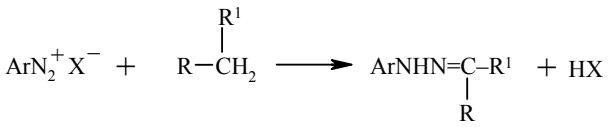
2-Cyanoaryldiazonium bisulfates, obtained by the action of nitrosyl sulfuric acid on isatin 3-hydrazone and its 5-bromo and 5-nitro derivatives, couple with 1-aryl-3-methylpyrazol-5-ones and form 4-arylhydrazones of 1-aryl-3-methylpyrazole-4,5-diones. It was established on the basis of data of IR, UV, and ^{1}H NMR spectra and of X-ray structural analysis that the coupling products exist in the hydrazone form stabilized by an intramolecular hydrogen bond.

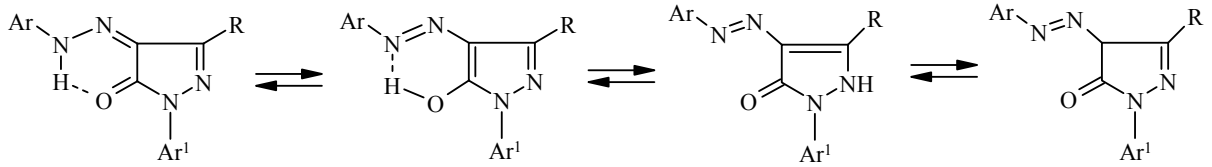
Keywords: 4-arylhydrazones of 1-aryl-3-methylpyrazole-4,5-diones, 1-aryl-3-methylpyrazol-5-ones, 2-cyanoaryldiazonium bisulfates, coupling reaction.

Aryldiazonium salts react readily with compounds containing an activated methylene group with the formation of arylhydrazones.



Of the heterocyclic compounds with an activated CH_2 group capable of a coupling reaction with aryldiazonium salts, some of the most studied are the 1-aryl-3-R-pyrazol-5-ones [1].

The products of coupling aryldiazonium salts with 1-aryl-3-R-pyrazol-5-ones may exist in four tautomeric forms **1a-d**. Preference must be given to structures **1a** and **1b**, stabilized by an intramolecular hydrogen bond.



1a **1b** **1c** **1d**

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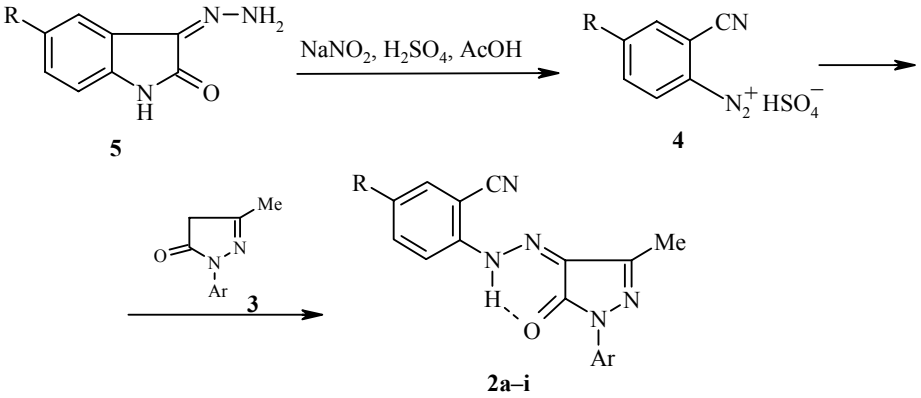
The use of physicochemical methods of investigation for establishing the structures of organic compounds has enabled strict and unequivocal determination of the tautomeric form in which the products of coupling aryldiazonium salts with 1-aryl-3-R-pyrazol-5-ones exist.

It was established by data of ^{15}N and ^{13}C NMR spectroscopy [2] and by X-ray structural analysis [3-8] that these coupling products, as a rule, exist in the tautomeric form **1a**.

Until our work there was no information in the literature on the synthesis and structure determination of compounds **1** in which the group Ar might be phenyl containing the strong electron-withdrawing group CN in the position *ortho* to the –NH–N= grouping. However, the presence of such a group in conjugation with the remaining portion of the molecule may influence the tautomeric equilibrium.

In the present work we have synthesized 4-arylhydrazones of 1-aryl-3-methylpyrazole-4,5-diones **2** by the coupling reaction of 1-aryl-3-methylpyrazol-5-ones **3** with 2-cyanobenzenediazonium bisulfates **4**. The latter were obtained by treating 3-hydrazones of isatin and its 5-bromo and 5-nitro derivatives **5** with nitrosyl sulfuric acid by the procedure developed by us in [9].



5 **4** **2a–i**

2 a R = H, Ar = Ph; **b** R = H, Ar = 4-$HO_3SC_6H_4$; **c** R = Br, Ar = Ph; **d** R = H, Ar = 4-MeC_6H_4; **e** R = Br, Ar = 4-$HO_3SC_6H_4$; **f** R = NO_2, Ar = Ph; **g** R = NO_2, Ar = 4-MeC_6H_4; **h** R = NO_2, Ar = 4-$HO_3SC_6H_4$; **i** R = Br, Ar = 4-MeC_6H_4

The coupling of bisulfates **4** with 1-aryl-3-methylpyrazol-5-ones **3** takes place readily, the corresponding hydrazones **2** are formed in 43-94% yield at the usual temperature in aqueous alcoholic medium. Analysis of the ^1H NMR spectra of compounds **2a-c** confirmed that these compounds are in the hydrazone form in DMSO solution.

An X-ray structural investigation of hydrazones **2a** and **2b** was carried out to establish unequivocally the structure of the products of coupling aryldiazonium bisulfates **4** with 1-aryl-3-methylpyrazol-5-ones **3**. The results are shown in Figs. 1 and 2. Bond lengths and valence angles for compounds **2a** and **2b** are given in Tables 1 and 2.

Crystals of the molecules of the studied compounds **2** exist in the hydrazone tautomeric form. The pyrazole ring is planar (planarity is achieved with a precision of ±0.003 Å for compounds **2a** and **2b**), the substituents are practically coplanar with this plane. The dihedral angles between the plane of the pyrazolone and the planes of the benzene rings C(1)–C(2)–C(3)–C(5)–C(6)–C(7) and C(12)–C(13)–C(14)–C(15)–C(16)–C(17) were 167.3 and 173.9° for compound **2a** and 162.0 and 168.5° for compound **2b** respectively.

Intramolecular hydrogen bonds were detected in the molecules of the studied compounds at O(1)···H–N(4) with parameters O(1)···N(4) 2.768(2), O(1)···HN(4) 2.02(2), N(4)–H 0.96(2) Å, angle N(4)–H···O(1) 134(1)° for compound **2a** and O(1)···N(4) 2.757(2), O(1)···HN(4) 2.03(2), N(4)–H 0.93(2) Å, angle N(4)–H···O(1) 133(1)° for compound **2b**. We note that these hydrogen bonds close a practically planar six-membered ring in the molecules. The remaining geometric parameters in the molecules studied have the usual values [10].

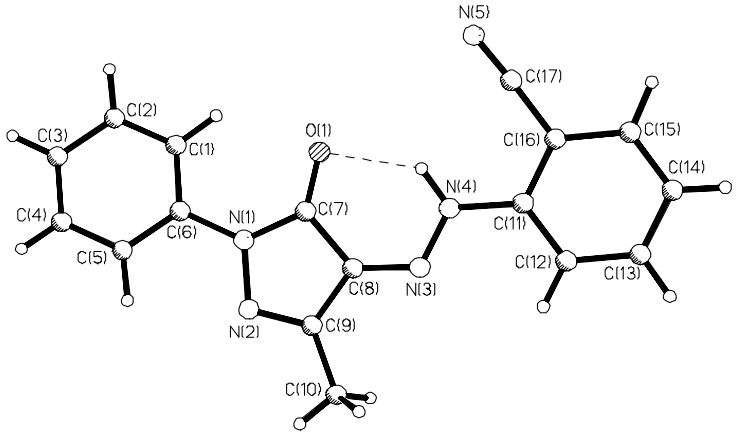


Fig. 1. General form of the **2a** molecule (the intramolecular hydrogen bond is shown dotted).

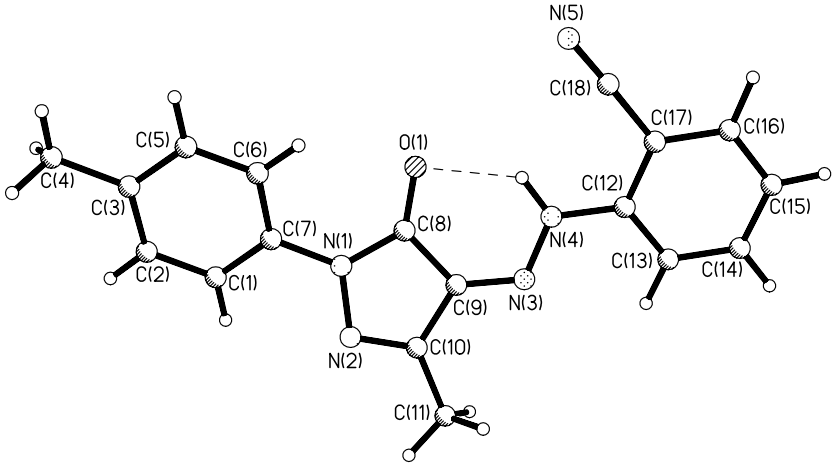


Fig. 2. General form of the **2b** molecule (the intramolecular hydrogen bond is shown dotted).

TABLE 1. Bond Lengths (*d*) in the Structures of Compounds **2a** and **2b**

Bond	*d*, Å		Bond	*d*, Å	
	2a	**2b**		**2a**	**2b**
O(1)–C(8)	1.239(2)	1.232(2)	C(3)–C(4)	—	1.499(2)
N(1)–C(8)	1.379(2)	1.370(2)	C(5)–C(6)	1.393(3)	1.386(2)
N(1)–C(7)	1.421(2)	1.418(2)	C(6)–C(7)	1.394(3)	1.389(2)
N(1)–N(2)	1.431(2)	1.411(2)	C(8)–C(9)	1.470(3)	1.464(2)
N(2)–C(10)	1.305(2)	1.296(2)	C(9)–C(10)	1.443(2)	1.439(2)
N(3)–C(9)	1.312(2)	1.303(2)	C(10)–C(11)	1.485(3)	1.483(2)
N(3)–N(4)	1.321(2)	1.315(2)	C(12)–C(13)	1.402(3)	1.394(2)
N(4)–C(12)	1.405(2)	1.396(2)	C(12)–C(17)	1.404(2)	1.395(2)
N(5)–C(18)	1.154(2)	1.146(2)	C(13)–C(14)	1.380(3)	1.377(2)
C(1)–C(2)	1.387(3)	1.383(2)	C(14)–C(15)	1.393(3)	1.387(2)
C(1)–C(7)	1.393(3)	1.389(2)	C(15)–C(16)	1.381(3)	1.384(2)
C(2)–C(3)	1.388(3)	1.394(2)	C(16)–C(17)	1.404(3)	1.395(2)
C(3)–C(5)	1.398(3)	1.389(2)	C(17)–C(18)	1.438(3)	1.442(2)

TABLE 2. Valence Angles (ω) in the Structures of Compounds **2a** and **2b**

Angle	ω, deg.		Angle	ω, deg.	
	2a	**2b**		**2a**	**2b**
C(8)–N(1)–C(7)	130.4(2)	28.9(1)	N(1)–C(8)–C(9)	104.0(2)	103.8(1)
C(8)–N(1)–N(2)	111.5(1)	112.2(1)	N(3)–C(9)–C(10)	125.9(2)	126.0(2)
C(7)–N(1)–N(2)	118.1(1)	118.9(1)	N(3)–C(9)–C(8)	127.9(2)	128.2(1)
C(10)–N(2)–N(1)	107.5(1)	107.4(1)	C(10)–C(9)–C(8)	106.3(2)	105.8(1)
C(9)–N(3)–N(4)	117.1(2)	116.6(1)	N(2)–C(10)–C(9)	110.7(2)	110.9(1)
N(3)–N(4)–C(12)	119.8(2)	120.2(1)	N(2)–C(10)–C(11)	122.3(2)	122.5(1)
C(2)–C(1)–C(7)	119.1(2)	119.5(2)	C(9)–C(10)–C(11)	127.0(2)	126.6(2)
C(1)–C(2)–C(3)	121.2(2)	121.6(2)	C(13)–C(12)–C(17)	119.1(2)	119.5(2)
C(2)–C(3)–C(5)	119.3(2)	117.6(2)	C(13)–C(12)–N(4)	121.6(2)	121.5(2)
C(5)–C(3)–C(4)	—	120.8(2)	C(17)–C(12)–N(4)	119.3(2)	119.0(2)
C(2)–C(3)–C(4)	—	121.7(2)	C(14)–C(13)–C(12)	119.7(2)	119.5(1)
C(6)–C(5)–C(3)	120.3(2)	121.9(2)	C(13)–C(14)–C(15)	121.2(2)	121.2(2)
C(5)–C(6)–C(7)	119.5(2)	119.3(2)	C(16)–C(15)–C(14)	119.9(2)	119.9(2)
C(1)–C(7)–C(6)	120.7(2)	120.1(2)	C(15)–C(16)–C(17)	19.6(2)	119.3(2)
C(1)–C(7)–N(1)	119.4(2)	119.5(1)	C(12)–C(17)–C(16)	120.4(2)	120.5(2)
C(6)–C(7)–N(1)	119.9(2)	120.4(2)	C(12)–C(17)–C(18)	119.0(2)	119.4(1)
O(1)–C(8)–N(1)	128.6(2)	128.6(2)	C(16)–C(17)–C(18)	120.5(2)	120.0(1)
O(1)–C(8)–C(9)	127.4(2)	127.7(1)	N(5)–C(18)–C(17)	177.0(2)	178.2(2)

EXPERIMENTAL

The IR spectra were recorded on a Specord M 80 (KBr disks), and the UV spectra on a Uvidek 610 spectrophotometer in alcohol solution. The ^{1}H NMR spectra were obtained on a Bruker AM 300 (300 MHz) instrument in solutions of DMSO-d_6–CCl_4 as the internal standard.

X-ray Structural Investigations of Compounds 2a and 2b. Experiments were carried out at -163°C on a SMART 1000 CCD diffractometer (λMoKα = 0.71073 Å, graphite monochromator, ω-scanning with a step of 0.3°, exposure time 15 sec). Structures were solved by the direct method, revealing all the non-hydrogen atoms, and were refined by a full-matrix least squares method in an anisotropic approach for the non-hydrogen atoms. The hydrogen atoms were made apparent by Fourier difference syntheses and were refined isotropically. All calculations were carried out with SAINT [11] and SHELXTL-97 [12] (PC version) programs.

The crystals of compound **2a** were triclinic, at -163°C a = 7.372(3), b = 9.720(4), c = 11.193(4) Å; α = 108.44(1), β = 104.73(1), γ = 99.91(1)°; V = 708(1) Å^3; d_{calc} = 1.424 g/cm^3; Z = 2; space group P1. The final values of the reliability factors R_1 = 0.059 for 2236 reflections with $I > 2\sigma$ and R_w = 0.1692 for 4110 reflections.

The crystals of **2b** were triclinic, at -163°C a = 7.490(2), b = 10.574(3), c = 10.657(3) Å; α = 109.04(1), β = 102.97(1), γ = 101.46(1)°; V = 743(1) Å^3; d_{calc} = 1.419 g/cm^3; Z = 2, space group P1. The final values of the reliability factors were R_1 = 0.058 for 2455 reflections with $I > 2\sigma$ and R_w = 0.2203 for 4326 reflections.

4-(2-Cyanophenyl)hydrazone of 3-Methyl-1-phenylpyrazole-4,5-dione (2a). Finely powdered sodium nitrite (1.4 g, 0.02 mol) was added gradually with stirring during 30 min to conc. H_2SO_4 cooled to 0-5°C. Isatin 3-hydrazone (**5**, R = H) (1 g, 0.0062 mol) was then added gradually during 15 min to the resulting nitrosyl sulfuric acid, periodically adding glacial acetic acid (8 ml). The resulting mixture was stirred at 5-10°C for 30 min, and poured into a mixture of water (50 ml) and ice (50 g). A solution of 3-methyl-1-phenylpyrazol-5-one (1.1 g, 0.0063 mol) in alcohol (10 ml) cooled to 5°C was added gradually with stirring to the obtained suspension at room temperature. The reaction mixture was stirred for 1 h at 20°C. The precipitated solid was

filtered off, washed three times on the filter with water, and recrystallized from alcohol–DMF. Arylhydrazone **2a** (0.8 g, 42.6%) was obtained; mp 225-226°C. IR spectrum, ν, cm^{-1}: 2220 (CN), 1720 (CO), 1610 (N–N=C). UV spectrum, λ_{max}, nm (log ε): 205.6 (1.92), 247.6 (1.94), 380.8 (1.91). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.35 (3H, s, CH_3); 7.18-7.46 (5H, m, C_6H_5); 7.72-7.85 (4H, m, C_6H_4); 13.58 (1H, s, NH). Found, %: C 67.14; H 4.21; N 22.71. $C_{17}H_{13}N_5O$. Calculated, %: C 67.31; H 4.32; N 23.09.

The other arylhydrazones **2** were obtained analogously from the appropriate salts **4** and 1-aryl-3-methylpyrazol-5-ones **3**.

4-(2-Cyanophenyl)hydrazone of 3-Methyl-1-(*p*-sulfophenyl)pyrazole-4,5-dione (2b). Yield 63%; mp 331°C (water). IR spectrum, ν, cm^{-1}: 2230 (CN), 1665 (CO), 1605 (N–N=C), 1345, 1120 (SO_2OH). UV spectrum, λ_{max}, nm (log ε): 205.2 (1.84), 250.0 (1.55), 385.6 (1.62). ^{1}H NMR (DMSO-d_6), δ, ppm: 2.35 (3H, s, CH_3); 7.30-7.53 (4H, C_6H_4-*o*); 7.72-7.92 (4H, C_6H_4-*p*); 8.22 (1H, s, SO_3H); 13.60 (1H, s, NH). Found, %: C 53.12; H 3.42; N 18.01. $C_{17}H_{13}N_5O_4S$. Calculated, %: C 53.25; H 3.42; N 18.36.

4-(4-Bromo-2-cyanophenyl)hydrazone of 3-Methyl-1-phenylpyrazole-4,5-dione (2c). Yield 51%; mp 232°C (alcohol–DMF). IR spectrum, ν, cm^{-1}: 2224 (CN), 1720 (CO), 1625 (N–N=C). UV spectrum, λ_{max}, nm (log ε): 206 (1.78), 246.8 (1.72), 385.6 (1.73). Found, %: C 53.12; H 3.16; N 18.32. $C_{17}H_{12}BrN_5O$. Calculated, %: C 53.42; H 3.16; N 18.32.

4-(2-Cyanophenyl)hydrazone of 3-Methyl-1-(*p*-tolyl)pyrazole-4,5-dione (2d). Yield 86%; mp 234°C (alcohol–DMF). IR spectrum, ν, cm^{-1}: 2230 (CN), 1670 (CO), 1605 (N–N=C). UV spectrum, λ_{max} (log ε): 205.6 (1.84), 246.8 (1.76), 381.2 (1.69). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.33 and 2.34 (3H, s, CH_3 and 3H, s, CH_3); 7.20-7.88 (8H, m, C_6H_4-*p* and C_6H_4-*o*); 13.64 (1H, s, NH). Found, %: C 69.38; H 4.48; N 22.34. $C_{18}H_{15}N_5O$. Calculated, %: C 68.12; H 4.78; N 22.07.

4-(4-Bromo-2-cyanophenyl)hydrazone of 3-Methyl-1-(*p*-sulfophenyl)pyrazole-4,5-dione (2e). Yield 74%; mp 341°C (alcohol–water). IR spectrum, ν, cm^{-1}: 2240 (CN), 1665 (CO), 1615 (N–N=C), 1335, 1115 (SO_2OH). UV spectrum, λ_{max}, nm (log ε): 206.8 (1.67), 250.4 (1.28), 394.0 (1.39). Found, %: C 44.37; H 2.42; N 15.48. $C_{17}H_{12}BrN_5O_4S$. Calculated, %: C 44.16; H 2.61; N 15.15.

4-(2-Cyano-4-nitrophenyl)hydrazone of 3-Methyl-1-phenylpyrazole-4,5-dione (2f). Yield 69%; mp 275°C (alcohol–DMF). IR spectrum, ν, cm^{-1}: 2228 (CN), 1735 (CO), 1615 (N–N=C), 1540, 1365 (NO_2). UV spectrum, λ_{max}, nm (log ε): 204.4 (1.59), 246.4 (1.58), 393.6 (1.59). Found, %: C 59.03; H 3.15; N 23.78. $C_{17}H_{12}N_6O_3$. Calculated, %: C 58.62; H 3.47; N 24.13.

4-(2-Cyano-4-nitrophenyl)hydrazone of 3-Methyl-1-(*p*-tolyl)pyrazole-4,5-dione (2g). Yield 83%; mp 280°C (alcohol–DMF). IR spectrum, ν, cm^{-1}: 2234 (CN), 1705 (CO), 1620 (N–N=C), 1515(NO_2), 1340. UV spectrum, λ_{max}, nm (log ε): 206.0 (1.73), 244.4 (1.68), 394.2 (1.28). Found, %: C 59.54; H 4.25; N 23.47. $C_{18}H_{14}N_6O_3$. Calculated, %: C 59.66; H 3.89; N 23.19.

4-(2-Cyano-4-nitrophenyl)hydrazone of 3-Methyl-1-(*p*-sulfophenyl)pyrazole-4,5-dione (2h). Yield 72%; mp 369°C (alcohol–water). IR spectrum, ν, cm^{-1}: 2235 (CN), 1660 (CO), 1625 (N–N=C), 1520(NO_2), 1370, 1330, 1125 (SO_2OH). UV spectrum, λ_{max}, nm (log ε): 205.2 (1.76), 301.2 (1.41), 400.0 (0.91). Found, %: C 47.28; H 2.98; N 19.09. $C_{17}H_{12}N_6O_6S$. Calculated, %: C 47.66; H 2.82; N 19.61.

4-(4-Bromo-2-cyanophenyl)hydrazone of 3-Methyl-1-(*p*-tolyl)pyrazole-4,5-dione (2i). Yield 94%; mp 243°C (alcohol–DMF). IR spectrum, ν, cm^{-1}: 2232 (CN), 1660 (CO), 1620 (N–N=C). UV spectrum, λ_{max} (log ε): 208.8 (1.84), 247.2 (1.78), 385.2 (1.64). Found, %: C 54.18; H 3.42; N 17.18. $C_{18}H_{14}N_5O$. Calculated, %: C 54.46; H 3.56; N 17.67.

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