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5-HYDROXY-2-PYRAZOLINES AND SOME OF THEIR 1-SUBSTITUTED ANALOGS

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The use of 1,3-dicarbonyl compounds containing strong electron-withdrawing substituents (perfluoroalkyl, 4-nitrophenyl) at one of the carbonyl groups in reaction with hydrazine or its monosubstituted derivatives (4-nitro- and 2,4-dinitrophenylhydrazines) leads to the formation of stable intermediates for the synthesis of pyrazoles (5-hydroxy-2-pyrazolines) or their linear tautomers (hydrazones).

Keywords: 1,3-dicarbonyl compounds, hydrazines, hydrazones, 5-hydroxypyrazolines, pyrazoles.

The reaction of 1,3-dicarbonyl compounds with hydrazines is the most widely used method for the synthesis of pyrazoles [1]. It was considered that the cyclization to pyrazoles was realized through the intermediate formation of hydrazones, and in a number of cases they were isolated and were then converted into the pyrazoles [2-4]. At the same time this transformation presupposes the formation of 5-hydroxy-2-pyrazolines as an essential stage, and this was detected during investigations by special NMR spectroscopic methods [5-8]. Stable and isolable representatives of this type of compound have been described in the literature [9-13]. They were mostly obtained by the reaction of 1,3-diketones with derivatives of hydrazine in which there is a strong electron-withdrawing group (acyl, thioacyl, carbamoyl, thiocarbamoyl, etc.) [9-13]. 5-Hydroxy-2-pyrazolines are of interest as polydentate ligands [14, 15]; their copper and nickel chelates exhibit enhanced antimicrobial activity [16]. 5-Hydroxy-2-pyrazolines are also capable of exchange of their mobile semiaminal hydroxyl group in reactions with various nitrogen-containing reagents (amines, hydroxylamines, hydrazines) [17-19], opening up the way to the production of new derivatives of pyrazole functionalized at position 5. The results of investigations in the region of 5-hydroxy-2-pyrazolines were reviewed in [20].

Another possible way of stabilizing 5-hydroxy-2-pyrazolines in the reaction is to choose substituents in the 1,3-dicarbonyl component that according to their steric and/or electronic characteristics will prevent the elimination of water. This could in principle extend the range of accessible 5-hydroxy-2-pyrazolines.

In the present work we investigated the reaction of a wide range of 1,3-dicarbonyl compounds **1a-r** with hydrazine itself and some of its derivatives. In all the experiments we used ^{1}H NMR monitoring, tracing the variation of the ^{1}H NMR spectra of the reaction mixtures immediately after the reagents were mixed and at the end of any chemical transformations. This monitoring was based on the principal differences in the spectral characteristics of the initial reagents, the final pyrazoles, and also the hydrazones being expected and the targeted 5-hydroxy-2-pyrazolines. In particular, the hydrazones were easily identified by the methylene protons

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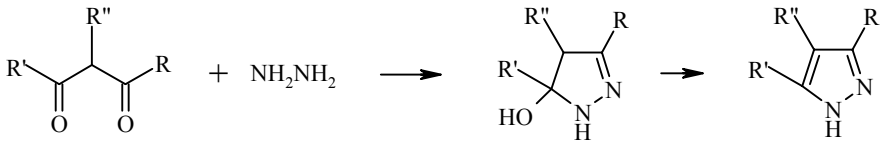
singlet signals in the region of 3.5-4.1 ppm, and the 5-hydroxy-2-pyrazolines were identified by the more upfield (2.4-2.8 ppm) absorption signals of the diastereotopic protons of the CH_2 group at position 4 of the ring, which as a rule form a typical AB system.



1, 2, 3*	R	R'		R	R'
a	Me	CF_3	**j**	Me	$C_6H_4NO_2$-4
b	Me	C_3F_7	**k**	C_6H_4OMe-4	H
c	*t*-Bu	CF_3	**l**	C_6H_4Me-4	H
d	*t*-Bu	C_3F_7	**m**	C_6H_4Cl-4	H
e	Ph	CF_3	**n**	Me	Me
f	Ph	C_3F_7	**o**	Me	Me
g	Me	C_6H_4OMe-4	**p**	Me	*t*-Bu
h	Me	Ph	**q**	*t*-Bu	*t*-Bu
i	Me	C_6H_4Cl-4			

*** 1-3 a-n**,**p**,**q** R" = H, **o** R" = Me.

The reaction of hydrazine with the 1,3-diketones **1a-f**, having a perfluoroalkyl group as one of the terminal substituents, results in the formation of the respective 5-hydroxy-2-pyrazolines **2a-f** (Tables 1 and 2), which in solution are transformed into pyrazoles after 1-2 months.

The 5-hydroxy-2-pyrazoline structure of these compounds was established on the basis of the ^{1}H NMR spectra (Table 2). Further evidence can be obtained from the ^{13}C NMR spectra. In the ^{13}C NMR spectra of compounds **2a-f** there are signals of the carbon atoms at position 5 of the ring in the region of 90-95 ppm (a quadruplet for compounds **1a**,**c**,**e** or a triplet for compounds **1b**,**d**,**f**), indicating conclusively a geminal arrangement of the perfluoroalkyl and hydroxyl groups.

The presence of the strong electron-withdrawing substituent at position 5 guarantees to some degree the stable existence of the 5-hydroxy-2-pyrazoline structure. The obtained results agree fully with authentic results on the structure of the products from the reactions of a series of fluoroalkyl-containing 1,3-diketones and conjugated acetylenic ketones with certain hydrazines [11].

The next subjects for investigation were the aroylacetones **1g-j**. In this case initial attack by the hydrazine is directed at the acetyl group, and this makes it possible to see the effect of the substituent in the aromatic ring on the stability of the 5-hydroxy-2-pyrazoline structure.

The reaction of the diketones **1g**,**h** with hydrazine leads to the formation of pyrazoles **3g**,**h**. In the case of 4-chlorobenzoylacetone (**1i**) it is possible by monitoring the ^{1}H NMR spectra to detect the intermediate accumulation of 5-hydroxy-2-pyrazoline **2i** (Table 2), but the final result is also the pyrazole **3i**.

In the transition to 4-nitrobenzoylacetone (**1j**) the reaction stops at the formation of 5-hydroxy-2-pyrazoline **2j**. Thus, it is possible to expect the appearance of stable 5-hydroxy-2-pyrazolines in the reactions of hydrazine with 1,3-aroyl ketones, if the substituent in the aromatic ring has electron-withdrawing characteristics comparable with the characteristics of the nitro group.

The reaction of hydrazine with aroylacetaldehydes **1k-m** leads to the pyrazoles **3k-m**. However, by monitoring the ^{1}H NMR spectra it is possible to detect the appearance of intermediate 5-hydroxy-2-pyrazoline structures **2k-m**, and the aromatic ring in them is at position 3, while the hydrogen atom is at position 5 of the ring. This follows from the upfield position of the signal for the absorption of the hydrogen atom in the ^{1}H NMR

TABLE 1. The Characteristics of Compounds **2**, **5**, **6**, **8**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
2a	$C_5H_7F_3N_2O$	35.77 / 35.71	4.12 / 4.20	16.71 / 16.67	85-86	55
2b	$C_7H_7F_7N_2O$	31.42 / 31.34	2.55 / 2.63	10.48 / 10.45	98-99	50
2c	$C_8H_{13}F_3N_2O$	45.65 / 45.69	6.25 / 6.24	13.41 / 13.33	134-135	53
2d	$C_{10}H_{13}F_7N_2O$	38.81 / 38.72	4.19 / 4.22	8.96 / 9.03	159-160	54
2e	$C_{10}H_{10}F_3N_2O$	52.03 / 52.16	4.97 / 3.94	12.15 / 12.17	89-90	51
2f	$C_{12}H_9F_7N_2O$	43.67 / 43.63	2.68 / 2.75	8.54 / 8.49	200-203	42
2j	$C_{10}H_{12}N_2O_2$	54.35 / 54.28	5.06 / 5.01	18.96 / 19.00	154-155	40
5c	$C_{16}H_{14}N_4O_5$	56.08 / 56.12	4.15 / 4.12	16.32 / 16.37	107-108	41
6c	$C_{16}H_{15}N_3O_3$	64.68 / 64.62	5.12 / 5.09	14.19 / 14.14	97-99	50
6d	$C_{16}H_{14}ClN_3O_2$	60.52 / 60.55	4.48 / 4.45	8.87 / 8.83	90-92	53
6e	$C_{16}H_{14}N_4O_5$	56.08 / 56.12	4.15 / 4.12	16.32 / 16.37		
8	$C_{17}H_{17}N_3O_3$	65.53 / 65.57	5.54 / 5.51	13.57 / 13.50		

TABLE 2. The ^{1}H NMR Spectra of Compounds **2**

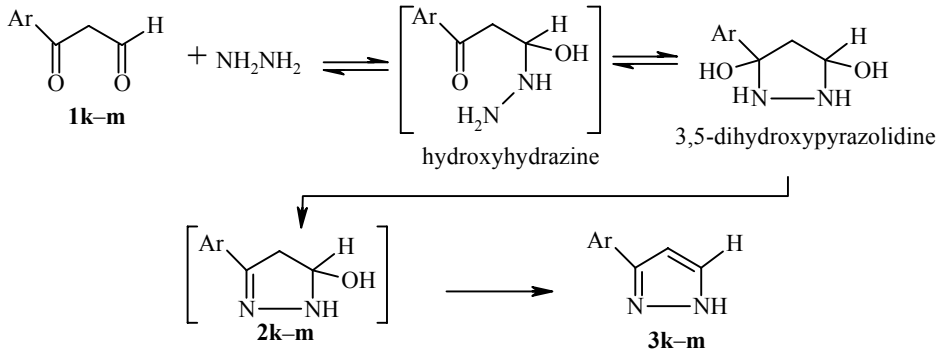
Compound	NMR spectrum, δ, ppm (*J*, Hz)*		
	R	R'	CH_2*[2]
2a	1.99 (3H, s, CH_3)	—	2.75; 3.07
2b	1.90 (3H, s, CH_3)	—	2.69; 2.97
2c	1.15 (9H, s, *t*-C_4H_9)	—	2.82; 2.97
2d	1.14 (9H, s, *t*-C_4H_9)	—	2.90; 3.18
2e	7.40-8.10 (m, 5H_{arom})	—	2.82; 2.97
2f	7.14-7.66 (m, 5H_{arom})	—	3.07; 3.16
2i	1.95 (3H, s, CH_3)	7.30-7.90 (m, 4H_{arom})	2.80 br. s
2j	1.95 (3H, s, CH_3)	7.80-8.15 (m, 4H_{arom})	2.78 br. s
2k	3.78 (3H, s, OCH_3); 6.63-7.94 (m, 4H_{arom})	5.25 (J_{AX}+J_{BX} = 8.0)	2.79; 2.96
2l	2.78 (3H, s, CH_3); 7.43-8.03 (m, 4H_{arom})	5.25 (J_{AB}+J_{BX} = 8.0)	3.28; 3.42
2m	7.57-8.20 (m, 4H_{arom})	5.71 (J_{AB}+J_{BX} = 8.0)	3.22; 3.39
2p	1.91 (3H, s, CH_3)	1.02 (9H, s, *t*-C_4H_9)	2.40; 2.83
2q	1.14 (9H, s, *t*-C_4H_9)	0.99 (9H, s, *t*-C_4H_9)	2.47; 2.83

* The NMR spectra were recorded in $CDCl_3$ (**2a-d**,**f**,**i**,**k-m**,**p**,**q**) and DMSO-d_6 (**2e**,**j**).

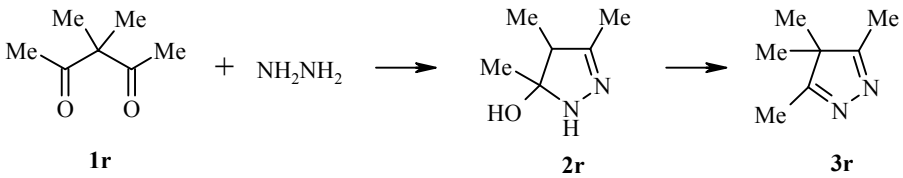
*[2] AB system, J_{AB} = 17.0-18.0 Hz.

spectra of the reaction mixture in the region of 5.25-5.70 ppm. In the alternative 5-hydroxy-2-pyrazoline structures with the aromatic ring at position 5 and the hydrogen atom at position 3 the signal of the latter must be in a substantially more downfield region of the spectrum [20]. Moreover, the signal represents the X part of an ABX system, the spin–spin coupling constants of which are characteristic of 3- and not 5-arylpyrazolines [21].

The obtained result means that, in the light of the substantial differences in the steric and electronic characteristics of the terminal substituents in the molecules of the aroylacetaldehydes, initial attack by the hydrazine is directed at the aldehyde carbonyl group. The intermediate, hydroxyhydrazine, formed in this way here undergoes cyclization to 3,5-dihydroxypyrazolidine by the addition of a second NH_2 function at the aroyl carbonyl group, while subsequent rapid elimination of a proton and hydroxyl group adjacent to the aryl substituent leads to the observed 3-aryl-5-hydroxy-2-pyrazolines **2k-m**, which then lose water relatively slowly with the formation of the final pyrazoles **3k-m**.



During the reaction of the aliphatic diketones **1n-r** with hydrazine only the pyrazoles **3n-r** were isolated. Nevertheless, in the case of acetylpinacoline **1p**, dipivaloylmethane **1q**, and α,α-dimethylacetylacetone the intermediate 5-hydroxy-2-pyrazolines **2p-r** were detected by monitoring the ^{1}H NMR spectra.



The rather different behavior of the diketones **1n**,**o** and compounds **1p-r** can be explained in the following way. The elimination of the elements of water under the selected reaction conditions is clearly realized by an E2 mechanism. The bulky *tert*-butyl group at position 5 of the ring in compounds **2p**,**q** prevents the formation of a bond between one of the protons at position 4 of the ring and the external base, represented by the hydrazine, and also prevents solvation of the eliminated hydroxyl group. As a result of this the 5-hydroxy-2-pyrazolines accumulate and are detected by ^{1}H NMR spectroscopy.

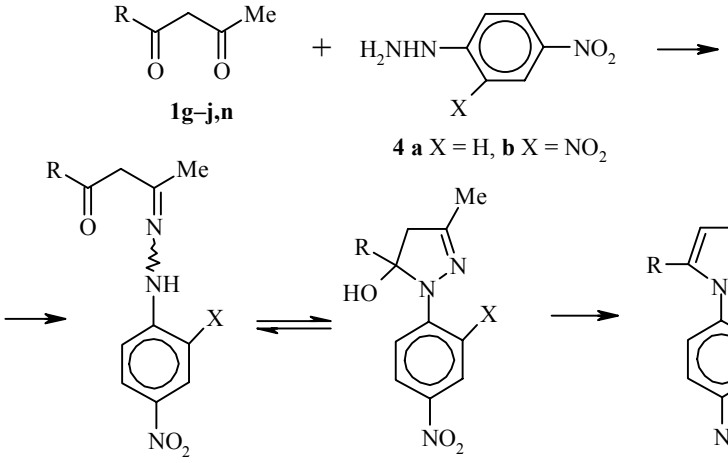
The slow elimination of water from 5-hydroxy-2-pyrazoline **2r**, formed during the reaction of hydrazine with α,α-dimethylacetylacetone **1r**, is most likely due to a different circumstance, i.e., the absence of the elements of aromaticity in the transition state on the path to the pyrazole **3r**, caused by structural factors.

However, all this is insufficient to stop the reaction at the stage of 5-hydroxy-2-pyrazolines. It is possible to state with a sufficient degree of certainty that the reaction of other aliphatic 1,3-diketones with hydrazine ends with the formation of the corresponding pyrazoles.

It was then necessary to determine to what degree the electron-withdrawing character of the substituent in the hydrazine molecule determines the stability of the 5-hydroxy-2-pyrazoline structure. For this purpose it was necessary to study the reaction of 1,3-diketones with monosubstituted hydrazines in which the withdrawing characteristics of the substituent are inferior to those of the acyl group. 4-Nitro- and 1,4-dinitrophenylhydrazines were used for this purpose.

The appearance of the intermediate hydrazone **5a** (but not the corresponding 5-hydroxy-2-pyrazoline) was observed by monitoring the ^{1}H NMR spectra during the reaction of 2,4-dinitrophenylhydrazine (**4b**) with acetylacetone **1n** (Table 3). The final product in this reaction was the pyrazole **7a**. The reaction of the benzoylacetone **1h** with the same substituted hydrazine stops at the hydrazone **5b**. It does not undergo cyclization even when kept in solution for several months. Thus, when 2,4-dinitrophenylhydrazine is used the cyclization process hydrazone → 5-hydroxy-2-pyrazoline becomes slow compared with the subsequent stage of aromatization to the corresponding pyrazole. This is most likely the result of steric hindrances to cyclization due to the *ortho*-substituent in the aromatic ring.

If this is so, the probability of observing the corresponding 5-hydroxypyrazoline structures should increase with 4-nitrophenylhydrazine (**4a**). In fact, in this case the presence of 5-hydroxy-2-pyrazolines **6a-c** can be detected by monitoring the ^{1}H NMR spectra before they are converted into the corresponding final products – the pyrazoles **7b-d**. It is noteworthy that in the case of the reaction with acetylacetone **1n**, where the probability of cyclization compared aroylacetones is higher for steric reasons, we did not observe the formation of the intermediate hydrazone in the reaction mixture. In the reaction with benzoylacetone **1h** and its 4-methoxy derivative **1g**, however, the monohydrazones **5c** and **5d** were detected as intermediates (Table 3).



1g–j,n

4 a X = H, **b** X = NO_2

5a–d

6a–e

7a–d

5 **a** X = NO_2, R = Me
b X = NO_2, R = Ph
c X = H, R = C_6H_4OMe-4
d X = H, R = Ph

6 **a** X = NO_2, R = Me
b X = H, R = C_6H_4OMe-4
c X = H, R = Ph
d X = H, R = C_6H_4Cl-4
e X = H, R = $C_6H_4NO_2$-4

7 **a** X = NO_2, R = Me
b X = H, R = Me
c X = H, R = C_6H_4OMe-4
d X = H, R = Ph

In addition, the reaction of 4-nitrophenylhydrazine with 4-chloro- (**1i**) and 4-nitrobenzoylacetones **1j** leads to the formation of stable 5-hydroxy-2-pyrazolines **6d** and **6e** respectively. Some increase in the electron-withdrawing characteristics of the aryl substituent at position 5 of the ring, due to the introduction of the chlorine atom or nitro group, was quite sufficient to prevent the formation of the pyrazoles.

Finally, in the reaction of 4-nitrobenzoylacetone with benzylhydrazine the corresponding 5-hydroxy-2-pyrazoline **8** was isolated.

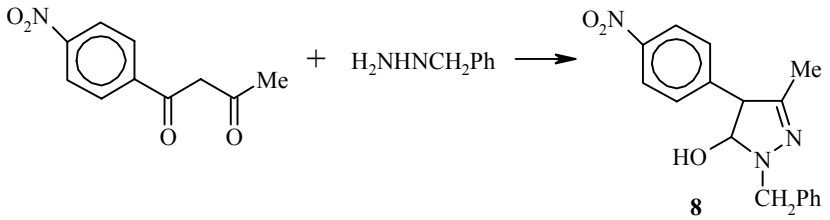


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TABLE 3. The ^{1}H NMR Spectra of Compounds **5a-e**, **6a**,**c-e**

Compound	^{1}H NMR spectrum, δ, ppm (*J*, Hz)*[2]		
	CH_3 (3H, s)	R	CH_2
5a	2.06	2.20 (3H, s, CH_3)	3.60 br. s
5b*[2]	2.13, 2.16	7.40-8.40 (m, $5H_{arom}$)	4.18 br. s 4.30 br. s
5c	2.07	3.77 (3H, s, OCH_3), 6.91-7.87 (m, $4H_{arom}$)	4.09 br. s
5d	2.01	6.70-8.00 (m, $5H_{arom}$)	4.02 br. s
6a	1.93	1.69 (3H, s, CH_3)	3.60 br. s
6c	2.09	7.00-8.00 (m, $5H_{arom}$)	3.12; 3.30*[3]
6d	2.05	6.98-7.83 (m, $4H_{arom}$)	3.08; 3.24*[3]
6e	2.14	6.70-8.20 (m, $5H_{arom}$)	3.13; 3.37*[3]

* The ^{1}H NMR spectra were recorded in $CDCl_3$–DMSO-d_6 1:1 (**5a-d**, **6a-d**) and $CDCl_3$ (**6e**).
*[2] Mixture of stereoisomers.
*[3] AB system, J_{AB} = 17.0-19.0 Hz.

Thus, it can be supposed that in the series of 1,3-aroyl ketones the introduction of such a strong electron-withdrawing substituent as the nitro group into the aromatic ring practically guarantees stabilization of the 5-hydroxy-2-pyrazoline structure.

In summary it is necessary to state that a full guarantee of the stable existence of 5-hydroxy-2-pyrazoline is provided by the presence of a substituent at position 1 of the ring, comparable in its withdrawing action with an acyl group, or the presence of a perfluoroalkyl substituent at position 5.

EXPERIMENTAL

The ^{1}H NMR spectra were obtained on a Tesla BS-497 spectrometer (100 MHz), and the ^{13}C NMR spectra were obtained on a Bruker AC-200 instrument (50.32 MHz). The melting points were determined in capillaries and were not corrected. The individuality of the products was monitored by TLC on Silufol UV-254 plates. The solvents were purified by standard procedures.

The characteristics and spectral data of compounds **2**, **5**, **6**, and **8** are given in Tables 1-3.

5-Hydroxy-3-methyl-5-trifluoromethyl-2-pyrazoline (2a). To 80% hydrazine hydrate (3.3 ml, 50 mmol) we added 1,1,1-trifluoro-2,4-pentanedione (7.7 g, 50 mmol) in chloroform (20 ml). After 1 h the chloroform layer was separated and dried with calcium chloride. The solvent was removed under vacuum, and the residue was washed with hexane and dried in air. Yield 4.62 g (55%); mp 85-86°C (85-86°C [10]).

5-Heptafluoropropyl-5-hydroxy-3-methyl-2-pyrazoline (2b), 3-*tert*-Butyl-5-hydroxy-5-trifluoromethyl-2-pyrazoline (2c), 3-*tert*-Butyl-5-heptafluoropropyl-5-hydroxy-2-pyrazoline (2d), 5-Hydroxy-3-phenyl-5-trifluoromethyl-2-pyrazoline (2e), 5-Heptafluoropropyl-5-hydroxy-3-phenyl-2-pyrazoline (2f), 5-Hydroxy-3-methyl-5-(4-nitrophenyl)-2-pyrazoline (2j). The compounds were obtained similarly to compound **2a** by the reaction of a solution of hydrazine hydrate with an equimolar amount of the respective ketones **1b-f**,**j** in chloroform. In the case of compounds **2b-f** the reaction products immediately separated as a precipitate, which was separated, washed with hexane, and dried in air.

3-*tert*-Butyl-5-hydroxy-5-trifluoromethyl-2-pyrazoline (2c). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 28.1 (CH_3); 33.3 [$C(CH_3)_3$]; 40.7 (CH_2); 91.1 ($C_{(5)}$, q, J_{CCF} = 30.0); 124.6 (CF_3); 158.5 (C=N).

5-Hydroxy-3-phenyl-5-trifluoromethyl-2-pyrazoline (2k). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 41.5 (CH_2); 91.4 ($C_{(5)}$, q, J_{CCF} = 31.9); 124.9 (CF_3); 125.8, 128.7, 128.8, 132.5 (C_{arom}); 147.8 (C=N).

5-Hydroxy-3,4,4,5-tetramethyl-2-pyrazoline (2r). ^{1}H NMR spectrum (deuterochloroform), δ, ppm: 0.80 (3H, s, CH_3); 1.01 (3H, s, CH_3); 1.46 (3H, s, CH_3); 1.80 (3H, s, CH_3).

3-Methyl-5-trifluoromethylpyrazole (3a). To 80% hydrazine hydrate (3.3 ml, 50 mmol) we added dropwise a solution of 1,1,1-trifluoro-2,4-pentanedione (7.7 g, 50 mmol) in chloroform (20 ml). The reaction mixture was kept for 2 months. Yield 3.75 g (50%); mp 89-90°C(89-90°C [21]).

3-*tert*-Butyl-5-trifluoromethylpyrazole (3c), 3-Phenyl-5-trifluoromethylpyrazole (3e), 5-(4-Methoxyphenyl)-3-methylpyrazole (3g), 3-Methyl-5-phenylpyrazole (3h), 5-(4-Chlorophenyl)-3-methylpyrazole (3i), 3-Methyl-5-(4-nitrophenyl)pyrazole (3j), 3-(4-Methoxyphenyl)pyrazole (3k), 3-(4-Methylphenyl)pyrazole (3l), 3-(4-Chlorophenyl)pyrazole (3m), 3,5-Dimethylpyrazole (3n), 3,4,5-Trimethylpyrazole (3o), 5-*tert*-Butyl-3-methylpyrazole (3p), 3,5-Di-*tert*-butylpyrazole (3q), 3,4,4,5-Tetramethyl-4H-pyrazole (3r). These compounds were obtained similarly to compound **3a** by the reaction of a solution of hydrazine hydrate with the respective 1,3-diketones **1a**,**c**,**e-r** in chloroform (**3c**,**g-i**,**k-q**) or DMSO (**3e**,**j**). In the case of compounds **3c**,**e** the reaction mixture was kept at room temperature for 1-2 months, and in the case of compounds **3g-q** for 3-7 days. Compound, mp, °C: **3c** – 180-182 (181-182 [10]); **3e** – 121-123 (121-123 [23]); **3g** – 233-234 (234-236 [10]); **3h** – 128-129 (128 [24]); **3i** – 142-144 (144-145 [10]); **3j** – 198-199 (196-196.5 [25]); **3k** – 126-127 (126 [26], 128 [27]); **3l** – 84-86 (82 [27], 87-88 [28]); **3m** – 96-98 (85 [27], 98 [29]); **3n** – 109 (107 [30]); **3o** – 135-136 (137-138 [31]); **3p** – 145-146 (150 [32]); **3q** – 190-192 (190-191 [10]); **3r** – 53-55 (50-55 [31]).

3-*tert*-Butyl-5-heptafluoropropylpyrazole (3d). This compound was obtained similarly to compound **3a** by the reaction of 80% hydrazine hydrate (3.3 ml, 50 mmol) with a solution of 2,2-dimethyl-6,6,7,7,8,8,8-heptafluoro-3,5-octanedione (14.8 g, 50 mmol) in chloroform (50 ml). Yield 9.19 g (63%); mp 104-105°C. ^{1}H NMR spectrum (deuterochloroform), δ, ppm: 1.32 (9H, s, *tert*-C_4H_9); 6.31 (1H, s, CH). Found %: C 41.12; H 3.81. $C_{10}H_{11}F_7N_2$. Calculated %: C 41.09; H 3.76.

4-Methylbenzoylacetone 2,4-Dinitrophenylhydrazone (5b). To a solution of 2,4-dinitrophenylhydrazine (1.98 g, 10 mmol) in chloroform (20 ml) we added benzoylacetone **1** (1.65 g, 10 mmol). After 24 h the reaction mixture was diluted with water, and the chloroform layer was separated and dried over calcium chloride. The solvent was evaporated under vacuum, and the residue was washed with hexane and dried in air. Yield 1.37 g (40%); mp 154-155°C (154-155°C [10]).

5-Hydroxy-3-methyl-1-(4-nitrophenyl)-5-phenyl-2-pyrazoline (6c). Benzoylacetone **1h** (1.65 g, 10 mmol) was added to a solution of 4-nitrophenylhydrazine **4a** (1.53 g, 10 mmol) in a mixture of chloroform and DMSO (3:1, 20 ml). After 24 h the reaction mixture was diluted with water, and the chloroform layer was separated and dried over calcium chloride. The solvent was evaporated under vacuum, and the residue was washed with hexane and dried in air. Yield 1.12 g (38%); mp 124-125°C (124-125°C [10]).

5-(4-Chlorophenyl)-5-hydroxy-3-methyl-1-(4-nitrophenyl)-3-pyrazoline (6d) and 5-Hydroxy-3-methyl-5-(4-nitrophenyl)-2-pyrazoline (6e). This compound was obtained similarly to compound **6c** by the reaction of compounds **1i** and **1j** with 4-nitrophenylhydrazine **4a**.

1-(2,4-Dinitrophenyl)-3,5-dimethylpyrazole (7a). To 2,4-dinitrophenylhydrazine (1.98 g, 10 mmol) we added 2,4-pentanedione (1.00 g, 10 mmol). The reaction mixture was kept for 5 days in chloroform–DMSO solution (1:1, 20 ml). The mixture was then diluted with water, and the chloroform layer was separated and dried with calcium chloride. The solvent was removed under vacuum, and the residue was washed with hexane and dried in air. Yield 1.11 g (42%); mp 148-150°C (122°C [32]).

3,5-Dimethyl-1-(4-nitrophenyl)pyrazole (7b), 5-(4-Methoxyphenyl)-3-methyl-1-(4-nitrophenyl)-pyrazole (7c), 3-Methyl-1-(4-nitrophenyl)-5-phenylpyrazole (7c). The compounds were obtained similarly to compound **7a** by holding the reaction mixture of 4-nitrophenylhydrazine (1.53 g, 10 mmol) and the diketones

1h,**i**,**k** (10 mmol) for 3-7 days in chloroform–DMSO solution (1:1, 20 ml). Compound, mp, °C: **7b** – 154-156 (101-102.5 [34]); **7c** – 147-149 (147-149 [10]); **7d** – 102-103 (100-101 [35]).

1-Benzyl-5-hydroxy-3-methyl-5-(4-nitrophenyl)-2-pyrazoline (8). The compound was obtained similarly to compound **6c** by the reaction of 4-nitrobenzoylacetone **1j** with benzylhydrazine in chloroform (20 ml). ^{1}H NMR spectrum (deuterochloroform), δ, ppm, *J* (Hz): 1.94 (3H, s, CH_3); 2.89 (2H, br. s, CH_2); 3.92 and 4.08 (2H, AB system, J_{AB} = 18, CH_2); 7.00-8.30 (9H, m, H_{arom}).

REFERENCES

1. A. N. Kost, and I. I. Grandberg, *Adv. Heterocycl. Chem.*, **6**, 347 (1966).
2. J. Elguero and G. I. Iranzo, *J. Chem. Res. (S)*, 120 (1990).
3. P. P. Kondrat'ev, Z. E. Skryabina, V. I. Saloutin, and L. M. Khalilov, *Zh. Org. Khim.*, **28**, 1380 (1992).
4. K. N. Zelenin, M. Yu. Malov, S. I. Yakimovich, P. B. Terent'ev, and A. G. Kalandarishvili, *Zh. Org. Khim.*, **24**, 426 (1988).
5. S. I. Selivanov, R. A. Bogatkin, and B. A. Ershov, *Zh. Org. Khim.*, **17**, 886 (1981).
6. S. I. Selivanov, R. A. Bogatkin, and B. A. Ershov, *Zh. Org. Khim.*, **18**, 909 (1982).
7. S. I. Selivanov, K. G. Golodova, Ya. A. Abbasov, and B. A. Ershov, *Zh. Org. Khim.*, **20**, 1494 (1984).
8. S. I. Selivanov, K. G. Golodova, and B. A. Ershov, *Zh. Org. Khim.*, **22**, 2073 (1986).
9. S. I. Yakimovich and K. N. Zelenin, *Zh. Obshch. Khim.*, **65**, 705 (1995).
10. K. N. Zelenin, V. V. Alekseev, and A. R. Tygysheva, *Tetrahedron*, **51**, 11251 (1995).
11. S. I. Yakimovich, I. V. Zerova, K. N. Zelenin, V. V. Alekseev, and A. R. Tugusheva, *Zh. Obshch. Khim.*, **66**, 418 (1996).
12. K. N. Zelenin, V. V. Alekseev, O. B. Kuznetsova, A. G. Saminskaya, S. I. Yakimovich, and I. V. Zerova, *Zh. Org. Khim.*, **35**, 383 (1999).
13. K. N. Zelenin, V. V. Alekseev, V. A. Khrustalev, S. I. Yakimovich, V. N. Nikolaev, and N. V. Koshmina, *Zh. Org. Khim.*, **20**, 180 (1984).
14. A. B. Khudoyarov, Kh. T. Sharipov, V. G. Yusupov, and N. A. Parpiev, *Koordinats. Khim.*, **13**, 1113 (1987).
15. K. N. Zelenin, L. A. Khorseeva, V. V. Alekseev, O. V. Arapov, Z. M. Matveeva, V. G. Yusupov, M. M. Karimov, and N. A. Parpiev, *Zh. Obshch. Khim.*, **59**, 1191 (1989).
16. K. N. Zelenin, L. A. Khorseeva, and V. V. Alekseev, *Khim.-Farm. Zh.*, **26**, No. 5, 30 (1992).
17. K. N. Zelenin, M. Yu. Malov, I. P. Bezhan, V. A. Khrustalev, and S. I. Yakimovich, *Khim. Geterotsikl. Soedin.*, 854 (1985).
18. K. N. Zelenin, M. Yu. Malov, I. P. Bezhan, V. A. Khrustalev, and S. I. Yakimovich, *Khim. Geterotsikl. Soedin.*, 1000 (1985).
19. K. N. Zelenin, A. Yu. Ershov, M. Yu. Malov, and S. I. Yakimovich, *Dokl. Akad. Nauk*, **289**, 1132 (1986).
20. K. N. Zelenin and S. I. Yakimovich (Yakimovitch), *Targets Heterocycl. Syst.*, **2**, 207 (1998); *Chem. Abs.*, **131**, 73578 (1999).
21. M. Yu. Malov, *Thesis for Candidate of Chemical Sciences* [in Russian], Leningrad (1988).
22. T. Nishiwaki, *J. Chem. Soc., B*, 885 (1967).
23. T. Nishiwaki, *Bull. Chem. Soc. Japan*, **42**, 3024 (1969).
24. B. Sjollema, *Liebigs Ann. Chem.*, **279**, 249 (1894).
25. P. Yates and D. W. Farnum, *Tetrahedron*, **18**, 881 (1962).
26. I. I. Grandberg, Vei-py Din, and A. N. Kost, *Zh. Obshch. Khim.*, **30**, 1373 (1960).
27. M. R. Grimmett, K. H. R. Lim, and R. T. Weaveas, *Aust. J. Chem.*, **32**, 2203 (1979).
28. C. Barat, *J. Indian. Chem. Soc.*, **8**, 801 (1931).

29. N. K. Kochketkov, E. D. Khomutova, O. B. Mikhailova, and A. N. Nesmeyanov, *Izv. Akad. Nauk. Ser. Khim.*, 1181 (1957).
30. L. Knorr and G. Rosengarten, *Liebigs Ann. Chem.*, **279**, 237 (1894).
31. L. Knorr and B. Oettiger, *Liebigs Ann. Chem.*, **279**, 244 (1894).
32. L. Knorr and G. Rosengarten, *Liebigs Ann. Chem.*, **279**, 231 (1894).
33. O. L. Brady, *J. Chem. Soc.*, 759 (1931).
34. D. M. Burness, *J. Org. Chem.*, **21**, 97 (1956).
35. K. Auwers and H. Stuhlmann, *Berichte*, **59**, 1054 (1926).