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Dedicated to Full Member of the Russian Academy of Sciences N.S. Zefirov on His 70th Anniversary

Nitropyrazoles: XII.* Transformations of the 4-Methyl Group in 1,4-Dimethyl-3,5-dinitropyrazole and Cyclization of the Transformation Products

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Abstract—A preparative procedure for the synthesis of 1,4-dimethyl-3,5-dinitropyrazole by nitration of 1,4-dimethylpyrazole was developed. The reaction of 1,4-dimethyl-3,5-dinitropyrazole with dimethoxymethyl(dimethyl)amine (*N*,*N*-dimethylformamide dimethyl acetal) gave (*E*)-*N*,*N*-dimethyl-2-(1-methyl-3,5-dinitropyrazol-4-yl)ethenylamine. Acid hydrolysis of the latter afforded (1-methyl-3,5-dinitropyrazol-4-yl)acetaldehyde, and the reaction with sodium nitrite in hydrochloric acid led to formation of 2-hydroxymino-2-(1-methyl-3,5-dinitropyrazol-4-yl)acetaldehyde. The corresponding *O*-methyloxime and phenylhydrazone reacted with K_2CO_3 to give 6-methyl-4-nitropyrazolo[4,3-*d*]isoxazole-3-carbaldehyde *O*-methyloxime and 1-methyl-3-nitro-4-(2-phenyl-2*H*-1,2,3-triazol-4-yl)pyrazol-5-ol, respectively. Treatment of (1-methyl-3,5-dinitropyrazol-4-yl)-acetaldehyde with benzenediazonium chloride gave (1-methyl-3,5-dinitropyrazol-4-yl)acetaldehyde phenylhydrazone which underwent intramolecular cyclization with replacement of the 5-nitro group by the action of K_2CO_3 in acetonitrile; in the reaction with K_2CO_3 in ethanol, the 5-nitro group was replaced by ethoxy.

Pyrazole derivatives are very important from the practical viewpoint; the chemistry of pyrazoles has been well documented, and various convenient methods for the synthesis of these compounds have been developed [2]. On the other hand, there exists some deficiency in general synthetic approaches to bicyclic structures in which pyrazole ring is fused to other five-membered aromatic heterocycles. Known examples concerning preparation of such systems cannot be regarded as universal, and synthesis of each type of bicyclic compounds requires special selection of appropriate substituents and their introduction into pyrazole ring or the second heterocycle with subsequent cyclocondensation [3].

Our studies are aimed at developing universal synthetic approaches to bicyclic structures in which pyrazole ring is fused to various five-membered O-, S-, and N-heterocycles. We believe that such a general approach may involve the use as starting compounds only one type of substituted pyrazoles, namely 1-R-4-methyl-3,5-dinitropyrazoles. It includes preliminary modification of the 4-methyl group in 1-R-4-methyl-3,5-dinitropyrazoles via reactions with electrophiles or oxidants, followed by transformation of the modified compounds into the target bicyclic products through either intramolecular replacement of the nitro group or its substitution or reduction and subsequent cyclization.

The feasibility of the proposed scheme follows from specific chemical properties of nitropyrazoles, including their accessibility, high reactivity of the nitro group in nucleophilic substitution processes, strong activation of methyl group by the neighboring nitro groups in reactions with electrophiles, and the possibility for further functionalization of the bicyclic product via transformations of the remaining nitro group [4]. Moreover, we previously showed [1] that the nitro group in position *5* of 3(5)-nitropyrazoles is much more reactive toward nucleophiles than the 3-nitro group. Therefore, the 5-nitro group should be replaced with high selectivity both inter- and intramolecularly.

* For communication XI, see [1].

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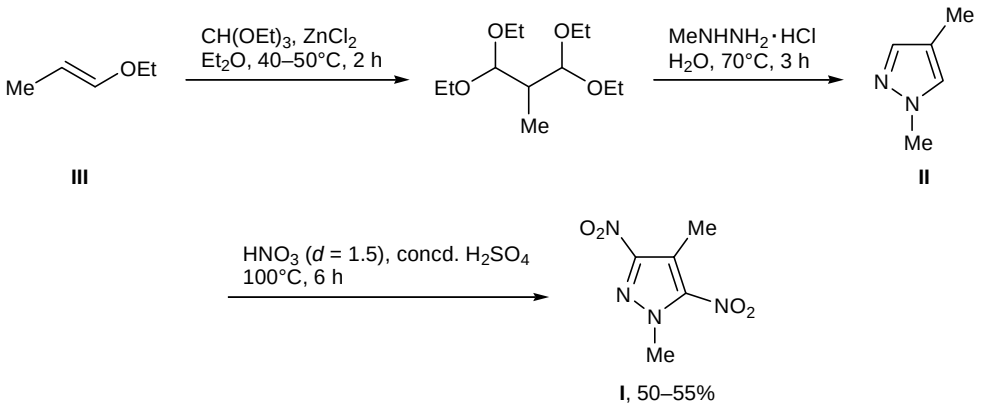
Scheme 1.

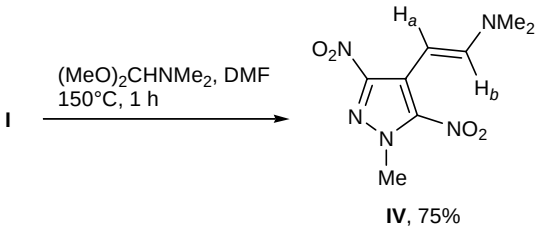


The present article reports on the development of a preparative procedure for the synthesis of 1,4-dimethyl-3,5-dinitropyrazole (**I**) as the simplest and convenient model of 1-R-4-methyl-3,5-dinitropyrazoles, purposeful transformation of the 4-methyl group in compound **I**, and cyclization of the products thus formed.

Katritzky *et al*. [5] described the synthesis of compound **I** by nitration of 1,4-dimethylpyrazole (**II**) with a mixture of sulfuric and nitric acids. However, the yield of dinitropyrazole **I** was poor (24%), and the reactant ratio did not allow the reaction to be performed on an enlarged scale under laboratory conditions. By varying the reactant ratio, we succeeded in selecting acceptable conditions for the nitration of 1,4-dimethylpyrazole (**II**), which (1) ensured preparation of dinitropyrazole **I** in a considerably larger yield (50–55%, Scheme 1) and (2) made it possible to obtain 40–50 g of the product in a single run. The optimal reactant ratio **II**–HNO_3 (d = 1.5)–H_2SO_4 was 1:2:20 by volume. As starting compound for the synthesis of 1,4-dimethylpyrazole (**II**) we used commercially available 1-ethoxypropene (**III**) [6, 7] (Scheme 1).

We believed it reasonable to build up an enamine fragment in position *4* of dinitropyrazole **I** by modification of the 4-methyl group and examine transformations of that fragment to obtain compounds capable of unergoing intramolecular cyclization (i.e., intramolecular substitution of the nitro group). Just the same approach turned out to be successful in the synthesis of benzo-fused heterocycles (benzisoxazoles and indazoles) from 2,4,6-trinitrotoluene [8]. We found conditions ensuring reaction of **I** with dimethoxymethyl(dimethyl)amine (*N*,*N*-dimethylformamide dimethyl acetal) to produce enamine **IV** (Scheme 2). The ^{1}H–^{1}H spin–spin coupling constant J_{ab} = 13.2 Hz in the ^{1}H NMR spectrum of **IV** indicates *trans* configuration of the exocyclic double bond. Iy should be noted that this reaction is the first example of direct modification of the methyl group in position *4* of pyrazole ring, leading to formation of a new carbon–carbon bond.

Scheme 2.

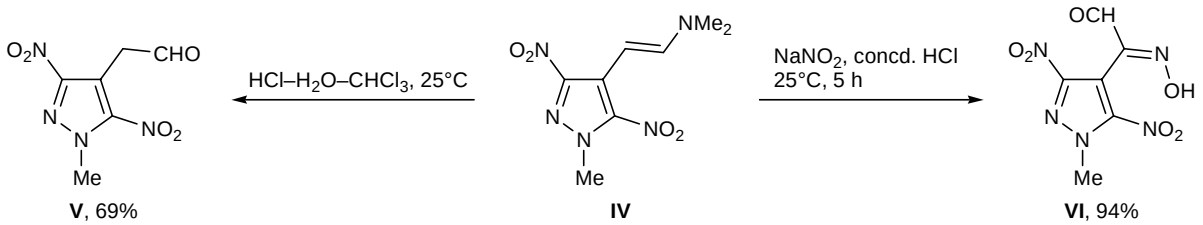


We compared the reactivity of compound **I** and some nitrotoluenes toward dimethylformamide dimethyl acetal (see table). The results showed that the activity of the 4-methyl group in pyrazole **I** is most similar to that of the methyl group in 2,4-dinitrotoluene [9].

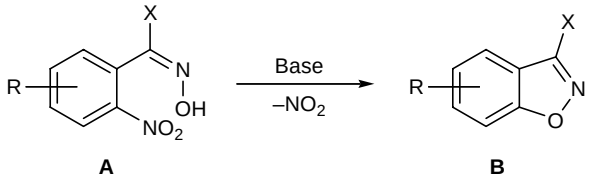
Hydrolysis of enamine **IV** with hydrochloric acid gave 1-methyl-3,5-dinitropyrazol-4-ylacetaldehyde (**V**). The reaction of **IV** with sodium nitrite in concentrated hydrochloric acid involved both hydrolysis and nitrosation; as a result, hydroxyimino(1-methyl-3,5-dinitropyrazol-4-yl)acetaldehyde (**VI**) was obtained (Scheme 3).

It is known [10] that compounds like **A** are capable of undergoing intramolecular nucleophilic substitution of the nitro group to give benz[*d*]isoxazoles **B** under basic conditions (Scheme 4). We anticipated that analogous cyclization should also occur with oximes of the pyrazole series, in which the hydroxyimino group is adjacent to nitro group. By treatment of oxime **VI** with potassium carbonate in ethanol we obtained hydroxypyrazolecarbonitrile **VIII** (Scheme 5). In keeping

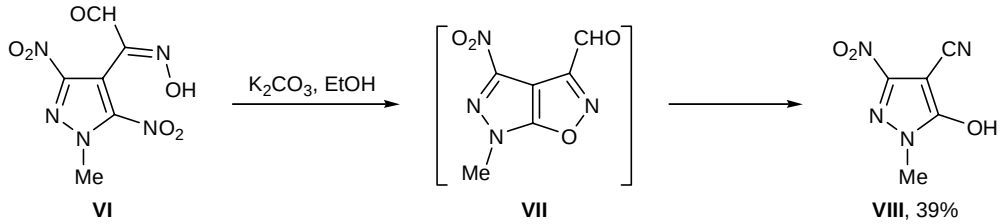
Scheme 3.



Scheme 4.



Scheme 5.



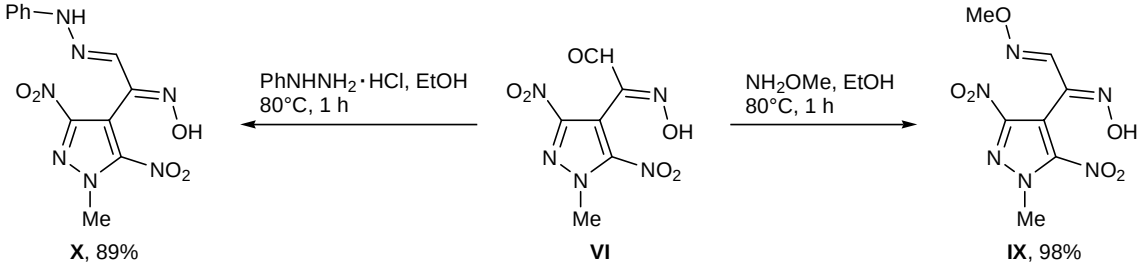
with published data [8], the reaction involves intermediate formation of pyrazolo[4,3-*d*]isoxazole **VII** which undergoes deformylation and opening of the isoxazole ring by the action of a base. The position of the hydroxy group in the pyrazole ring of **VIII** was determined by the HMBC two-dimensional correlation technique, on the basis of long-range $^{1}H–^{13}C$ coupling constants. In the HMBC spectrum of **VIII**, protons of the *N*-methyl group showed the only cross peak with a carbon atom whose signal is located at δ_C 159.27 ppm. According to published data [11], this signal belongs to the carbon atom attached to the hydroxy group (the CNO_2 carbon atom gives a broadened signal at δ_C 150.46 ppm). Thus the COH carbon atom is closer to the NCH_3 group than CNO_2, i.e., intramolecular substitution of nitro group in compound **VI** occurs just at position *5*.

To avoid opening of isoxazole ring like in **VII**, protection of the aldehyde group is commonly used. Many derivatives of such aldehydes are stable in basic medium, and they can be isolated and subjected to isoxazole ring closure [8]. We synthesized derivatives of hydroxyimino(pyrazolyl)acetaldehyde **VI** at the formyl group, *O*-methyloxime **IX** and phenylhydrazone **X**, by reactions with *O*-methylhydroxylamine and phenylhydrazine, respectively (Scheme 6). Treatment of compound **IX** with potassium carbonate in ethanol gave the corresponding 3-substituted 6-methyl-4-nitropyrazolo[4,3-*d*]isoxazole (**XI**) (Scheme 7). The structure of **XI** was established as follows. The data of

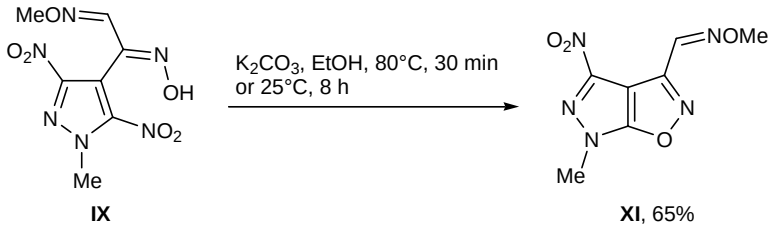
Reactivity of nitrotoluenes and 1,4-dimethyl-3,5-dinitropyrazole (**I**) toward dimethoxymethyl(dimethyl)amine

Compound	Solvent	Temperature, °C	Reaction time, h	Excess of dimethoxymethyl-(dimethyl)amine, mol %	Yield of enamine, %
2,4,6-Trinitrotoluene	Toluene	20	24	0	70
1,4-Dimethyl-3,5-dinitropyrazole	DMF	Reflux	1	150	75
2,4-Dinitrotoluene	DMF	Reflux	2	200	99
2,6-Dinitrotoluene	DMF	Reflux	9	100	91
2-Nitrotoluene	DMF	Reflux	26	0	86

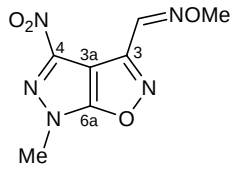
Scheme 6.



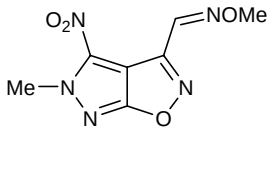
Scheme 7.



elemental analysis and mass spectrometry (*m*/*z* 225, M^+) were consistent with the formula $C_7H_7N_5O_4$. The ^{1}H NMR spectrum of compound **XI** contained only three signals at δ 8.23 (CH), 4.13 (NCH_3), and 4.05 ppm (OCH_3). On the basis of the HMBC spectrum (by long-range ^1H–^{13}C coupling constants) we identified all ^{13}C signals and proved that the nitro group in position *5* rather than *3* in compound **IX** was replaced, in keeping with our previous data [1]. In fact, the HMBC spectrum of **XI** revealed two cross peaks due to coupling between protons of the *N*-methyl group and carbon nuclei with chemical shifts δ_C of 142.60 and 168.25 ppm; the latter carbon atom gives a much stronger cross peak. The signal at δ_C 142.60 ppm belongs to the carbon atom linked to nitro group (a typical range of chemical shifts of pyrazole carbon atoms attached to a nitro group is 140–155 ppm [12]). In addition, this signal is strongly broadened, which is also typical of quaternary carbon atoms linked to a nitro group. Insofar as the correlation between the NCH_3 protons and the CNO_2 carbon atom is considerably weaker than that between NCH_3 and CO, the CNO_2 carbon atom is more distant from the *N*-methyl group than CO, and hence compound **XI** has structure **C** rather than **D**.



C



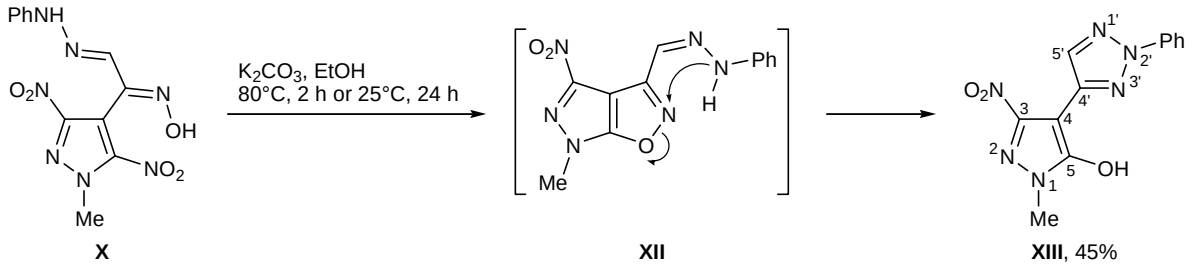
D

The structure of **XI** was also proved by X-ray analysis. These results will be reported elsewhere, but we can note that the N–O bond in pyrazoloisoxazole **XI** is appreciably longer than the corresponding bond in substituted benz[*d*]isoxazole [13]: 1.443 and 1.411 Å, respectively. This means that the N–O bond in **XI** is weaker than in the benzo-fused analog.

Under similar conditions, the cyclization of phenylhydrazone **X** afforded substituted 1,2,3-triazole **XIII** instead of expected pyrazoloisoxazole **XII** (Scheme 8). Obviously, compound **XIII** is formed via rearrangement of **XII**. An analogous recyclization was recently observed in the series of benz[*d*]isoxazoles [14]; however, in our case, it occurred much more readily, and (unlike benzo-fused analog) intermediate pyrazoloisoxazole **XII** could not be isolated or even detected. Obviously, the rate of its rearrangement is considerably higher than the rate of formation. As we noted above, the N–O bond in **XI** is weaker than the corresponding bond in the benzo-fused analog. Undoubtedly, the N–O bond in structurally related pyrazoloisoxazole **XII** is also weakened, which facilitates its cleavage via intramolecular nucleophilic substitution at the isoxazole nitrogen atom (Scheme 8).

According to the data of elemental analysis and mass spectrometry (the mass spectrum contained the molecular ion peak with *m*/*z* 286), compound **XIII** has the composition $C_{12}H_{10}N_6O_3$. In the ^{1}H NMR spectrum of **XIII**, signal from the *N*-methyl group appeared at δ 3.77 ppm (cf. δ 4.35 ppm for compound **X**; $\delta\Delta \approx$ 0.6 ppm). Protons in the *N*-methyl group of *O*-methyloxime **IX** give a signal at δ 4.33 ppm, while the corre-

Scheme 8.

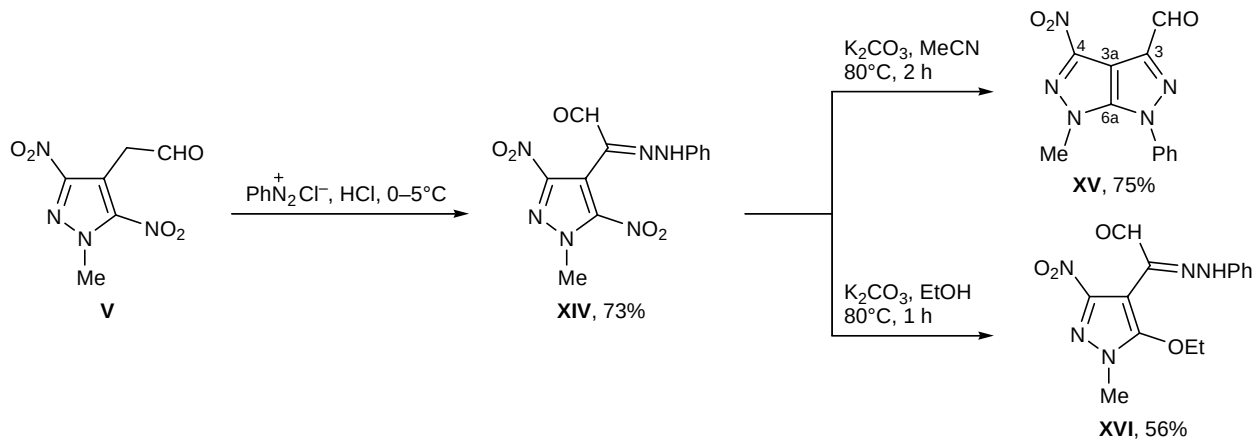


sponding signal of pyrazolo[4,3-*d*]isoxazole **XI** is located at δ 4.13 ppm, i.e., the upfield shift is only 0.2 ppm. Compound **VIII** possessing a hydroxy group in the pyrazole ring is characterized by a chemical shift of the *N*-methyl protons of δ 3.65 ppm, which is similar to that found for **XIII**. The ^{1}H NMR spectrum recorded from a solution of **XIII** in DMSO-d_6 lacked signal from NH proton, which is typical of phenylhydrazones (δ 10.70 ppm for compound **X**). In $CDCl_3$, the OH proton characteristically gives a broadened signal at δ 9.5–10 ppm.

In the ^{13}C spectrum of compound **XIII** in DMSO-d_6, the C^5 (COH) signal appears at δ_C 151.8 ppm, which is consistent with published data [15]. The chemical shift of C^5 in pyrazolo[4,3-*d*]isoxazole **XI** (see above) is 168.25 ppm. The ^{15}N NMR spectrum of **XIII** contains only two signals from the triazole ring, at δ_N –69.44 ($N^{1'}$) and –133.36 ppm ($N^{2'}$) (relative to CH_3NO_2); the signals were assigned on the basis of the HSQC two-dimensional correlation spectrum using long-range ^{1}H–^{15}N coupling constants (cf. [16]). No signal from $N^{3'}$ was detected. An analogous pattern was observed in [14] for a benzo-fused analog. We also recorded the HMBC spectrum of compound **XIII**, which showed a correlation between the methyl protons and carbon atom bearing the hydroxy group; no cross peak between the methyl protons and carbon atom linked to the nitro group was present (a broadened signal from that carbon atom was located at δ_C 149.6 ppm). These data indicate that, like in compound **IX**, just the nitro group in position *5* of pyrazole **X** is replaced via intramolecular nucleophilic attack.

By reaction of pyrazolylacetaldehyde **V** with benzenediazonium chloride we obtained 2-(1-methyl-3,5-dinitropyrazol-4-yl)-2-phenylhydrazonoacetaldehyde (**XIV**) (Scheme 9) as a result of azo coupling at the activated methylene group. Like oximes derived from aromatic ketones having a nitro group in the *ortho* position (structure **A** in Scheme 4), the corresponding arylhydrazones are also capable of undergoing intramolecular substitution of the *ortho*-nitro group by the action of bases to produce *N*-arylindazoles [17]. An analogous intramolecular cyclization might be expected for hydrazone **XIV** with formation of pyrazolo[3,4-*c*]pyrazole **XV**. However, heating of hydrazone **XIV** with potassium carbonate in ethanol resulted in replacement of the 5-nitro group by ethoxy to give compound **XVI** (Scheme 9). Obviously, the system EtOH–K_2CO_3 is a stronger nucleophile than the terminal hydrazone fragment (PhNH) in the presence of K_2CO_3 as deprotonating agent. In the latter case, nucleophilic substitution also occurs at the 5-position

Scheme 9.



of the pyrazole ring. This follows, e.g., from the fact that the ^1H–^{13}C HMBC spectrum contains cross peaks due to correlation of the NCH_3 and OCH_2 protons with the same carbon nuclei while no other cross peaks for the NCH_3 protons are observed. In addition, the NOESY spectrum revealed coupling between the NCH_3 and OCH_2 protons, which is possible only when the ethoxy group is located at position *5* of the pyrazole ring. We succeeded in effecting intramolecular cyclization of hydrazone **XIV** to expected 6-methyl-4-nitro-1-phenylpyrazolo[3,4-*c*]pyrazole (**XV**) by carrying out the reaction with K_2CO_3 in acetonitrile instead of ethanol (Scheme 9). In the NOESY spectrum of **XV** we observed correlation between the NCH_3 protons and *ortho*-protons in the benzene ring on N^1; this means that the nitro group in position *5* was replaced via nucleophilic attack by the PhNH group. The structure of compound **XV** was also proved by X-ray analysis (the crystallographic data will be reported elsewhere).

Thus transformation of the 4-methyl group in 1,4-dimethyl-3,5-dinitropyrazole (**I**) with the use of dimethylformamide dimethyl acetal leads to compounds capable of undergoing intramolecular cyclization (intramolecular substitution of the nitro group) to afford bicyclic systems consisting of two five-membered aromatic heterocycles or products of their subsequent transformations. In all cases, only the 5-nitro group is replaced. In the subsequent communications we will report on other ways of transformation of the 4-methyl group in compound **I** with a view to obtain systems containing a pyrazole ring fused to five-membered aromatic heterocycles.

EXPERIMENTAL

The IR spectra were recorded on a Specord M-82 spectrometer from samples prepared as KBr pellets or solutions in $CHCl_3$ (c = 0.01 mol/l, d = 3 mm). The ^1H and ^{13}C NMR spectra were recorded on Bruker WM-250, Bruker AC-300, and Bruker AC-500 instruments. The chemical shifts were measured relative to tetramethylsilane. The mass spectra (electron impact, 70 eV) were obtained on a Kratos MS-30 mass spectrometer. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates.

1,4-Dimethyl-3,5-dinitropyrazole (I). 1,4-Dimethylpyrazole [6, 7], 25.0 ml (d = 0.96 g/cm^3, 0.250 mol), was added dropwise under stirring to 500 ml of concentrated sulfuric acid, maintaining the temperature below 35°C. Nitric acid (d = 1.5 g/cm^3), 50 ml, was added to the mixture under vigorous stirring at 30–40°C. The mixture was vigorously stirred for 6 h at 90–100°C, cooled, and poured into 1 kg of ice water. Air was bubbled through the resulting suspension on slight heating to remove nitrogen oxide, the mixture was extracted with ethyl acetate (3×400 ml), the extract was washed with aqueous ammonia until neutral reaction and dried over Na_2SO_4, the solvent was distilled under reduced pressure, and the solid residue was recrystallized from ethanol. Yield 25.6 g (55.1%), colorless crystals, mp 107–108°C (from EtOH); published data [5]: mp 101–102°C. IR spectrum, ν, cm^{-1}: 1532, 1524, 1328, 1316 (NO_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 4.23 s (3H, NCH_3), 2.57 s (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 150.38 (C^3), 144.02 (C^5), 114.30 (C^4), 42.52 (CH_3), 9.64 (NCH_3). Mass spectrum: m/z 186 $[M]^+$. Found, %: C 32.34; H 3.20; N 29.92. $C_5H_6N_4O_4$. Calculated, %: C 32.27; H 3.25; N 30.10.

(*E*)-*N*,*N*-Dimethyl-2-(1-methyl-3,5-dinitropyrazol-4-yl)ethenylamine (IV). 1,4-Dimethyl-3,5-dinitropyrazole (**I**), 30.0 g (0.161 mol), was dissolved in 250 ml of DMF, 55 ml (0.414 mol) of dimethoxymethyl(dimethyl)amine was added, and the mixture was heated to the boiling point and kept for 1 h at that temperature. The mixture was cooled, the solvent was distilled off under reduced pressure, and the solid residue was recrystallized from ethanol. Yield 29.1 g (74.8%), dark green crystals, mp 114–115°C (from EtOH). IR spectrum, ν, cm^{-1}: 1552, 1380 (NO_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 7.93 d (1H, H_b, J = 13.2 Hz), 5.62 d (1H, H_a, J = 13.2 Hz), 4.19 s (3H, NCH_3), 2.99 s [6H, $N(CH_3)_2$]. ^{13}C NMR spectrum, δ_C, ppm: in DMSO-d_6: 151.62 (CH_b), 146.90 (C^3), 139.43 (C^5), 120.19 (C^4), 80.00 (CH_a), 43.28 (NCH_3); in $CDCl_3$: 151.71 (CH_b), 147.70 (C^3), 139.56 (C^5), 120.71 (C^4), 81.04 (CH_a), 43.42 (NCH_3), 40.78 br [$N(CH_3)_2$]. Mass spectrum: m/z 241 $[M]^+$. Found, %: C 39.60; H 4.53; N 28.43. $C_8H_{11}N_5O_4$. Calculated, %: C 39.84; H 4.60; N 29.04.

(1-Methyl-3,5-dinitropyrazol-4-yl)acetaldehyde (V). Compound **IV**, 20.0 g (0.083 mol), was dissolved in 200 ml of chloroform, 300 ml of 2 M hydrochloric acid was added, the mixture was stirred for 1 h, and the aqueous phase was separated and extracted with ethyl acetate (3×100 ml). The extracts were combined with the organic phase and dried over Na_2SO_4, and the solvent was distilled off under reduced pressure. The oily residue was crystallized from carbon tetrachloride. Yield 12.3 (69.3%), light brown solid substance,

mp 89–90°C (from CCl_4). IR spectrum, ν, cm^{-1}: 1724 (C=O); 1528, 1344 (NO_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 9.69 s (1H, CHO), 4.33 s (2H, CH_2), 4.28 s (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 196.84 (CHO), 150.60 (C^3), 144.39 (C^5), 109.57 (C^4), 42.59 (CH_3), 38.31 (CH_2). Mass spectrum: *m*/*z* 186 $[M - CO]^+$. Found, %: C 33.73; H 2.80; N 25.96. $C_6H_6N_4O_5$. Calculated, %: C 33.65; H 2.82; N 26.16.

2-Hydroxyimino-2-(1-methyl-3,5-dinitropyrazol-4-yl)acetaldehyde (VI). A solution of 17.5 g (0.254 mol) of sodium nitrite in 100 ml of water was added dropwise over a period of 1.5–2 h at room temperature to a solution of 30.0 g (0.124 mol) of compound **IV** in 300 ml of concentrated hydrochloric acid. The mixture was stirred for 3 h and was left overnight. It was then diluted with 1000 ml of water and stirred for 30 min. The precipitate was filtered off, washed with cold water (3×100 ml), and dried. Yield 28.3 g (93.6%), light yellow crystals, mp 163–167°C (decomp.). IR spectrum, ν, cm^{-1}: 3265 br (OH); 1704 (C=O); 1536, 1336 (NO_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 14.00 s (1H, OH), 9.73 s (1H, CH), 4.33 s (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 188.76 (CHO), 149.03 (C^3), 146.29 (C=NOH), 143.44 (C^5), 102.14 (C^4), 42.52 (CH_3). Mass spectrum: *m*/*z* 243 $[M]^+$. Found, %: C 29.61; H 2.04; N 28.62. $C_6H_5N_5O_6$. Calculated, %: C 29.64; H 2.07; N 28.80.

5-Hydroxy-1-methyl-3-nitropyrazole-4-carbonitrile monohydrate (VIII). Compound **VI**, 1.00 g (4.1 mmol), was dissolved in 20 ml of ethanol, 0.57 g (4.1 mmol) of potassium carbonate was added, and the mixture was stirred for 15 h at room temperature. The mixture was poured into 100 ml of water, hydrochloric acid was added to a weakly acidic reaction, and the precipitate was filtered off, washed with cold water (2×20 ml), and dried. Yield 0.27 g (39.0%), light yellow substance, mp 70–80°C (loss of H_2O), 215–220°C (decomp.). IR spectrum, ν, cm^{-1}: 3460 br (OH); 2248 (C≡N); 1540, 1352 (NO_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.64 s (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 159.28 (C^5), 150.48 (C^3), 112.32 (CN), 69.52 (C^4), 34.36 (CH_3). Mass spectrum: *m*/*z* 168 $[M]^+$. Found, %: C 32.34; H 3.27; N 28.90. $C_5H_6N_4O_4$. Calculated, %: C 32.27; H 3.25; N 30.10.

2-Hydroxyimino-2-(1-methyl-3,5-dinitropyrazol-4-yl)acetaldehyde *O*-methyloxime (IX). *O*-Methylhydroxylamine hydrochloride, 1.89 g (0.023 mol), and sodium hydroxide, 0.82 g (0.021 mol), were added to 75 ml of ethanol, the mixture was stirred for 30 min, and 5.00 g (0.021 mol) of compound **VI** was added. The mixture was heated for 1 h under reflux and cooled, the solvent was distilled off under reduced pressure, the solid residue was treated with water, and the undissolved material was filtered off, washed with cold water, and dried. Yield 5.48 g (97.9%), light yellow crystalline substance, mp 85–86°C (from $CHCl_3$–CCl_4, 1:1). IR spectrum, ν, cm^{-1}: 3360 br (OH); 1704 (C=O); 1536, 1336 (NO_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 12.75 s (1H, OH), 8.13 s (1H, CH), 4.32 s (3H, NCH_3), 3.74 s (3H, OCH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 149.00 (C^3), 145.80 (C=NOH), 143.18 (C^5), 140.90 (C=NOMe), 104.31 (C^4), 62.27 (OCH_3), 42.31 (NCH_3). Mass spectrum: *m*/*z* 272 $[M]^+$. Found, %: C 31.96; H 2.77; N 28.01. $C_7H_8N_6O_6$. Calculated, %: C 30.89; H 2.96; N 30.88.

2-Hydroxyimino-2-(1-methyl-3,5-dinitropyrazol-4-yl)acetaldehyde phenylhydrazone (X). Compound **VI**, 2.00 g (8.2 mmol), was dissolved in 30 ml of ethanol, 1.19 g (8.2 mmol) of phenylhydrazine hydrochloride was added, and the mixture was heated for 1 h under reflux. It was then cooled and poured into 300 ml of water, and the precipitate was filtered off, washed with water, and dried. Yield 2.44 g (89.0%), orange solid substance, mp 178–179°C. IR spectrum, ν, cm^{-1}: 3320 br (NH, OH); 1528, 1336 (NO_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 12.00 s (1H, OH), 10.58 s (1H, NH), 7.75 s (1H, CH), 7.15 br.m (2H, *m*-H), 6.72 br.m (3H, *o*-H, *p*-H), 4.32 s (3H, CH_3). Mass spectrum: *m*/*z* 333 $[M]^+$. Found, %: C 42.70; H 3.40; N 28.70. $C_{12}H_{11}N_7O_5$. Calculated, %: C 43.25; H 3.33; N 29.42.

6-Methyl-4-nitropyrazolo[4,3-*d*]isoxazole-3-carbaldehyde *O*-methyloxime (XI). Compound **IX**, 2.00 g (7.3 mmol), was dissolved in 30 ml of ethanol, 1.01 g (7.3 mmol) of potassium carbonate was added, and the mixture was heated for 30 min under reflux. It was then cooled, the solvent was distilled off under reduced pressure, and the solid residue was treated with 150 ml of water. The undissolved material was filtered off, dried, and recrystallized from ethanol. Yield 1.08 g (65.3%), yellow crystalline substance, mp 138–140°C (from EtOH). IR spectrum, ν, cm^{-1}: 1544, 1336 (NO_2). ^1H NMR spectrum (acetone-d_6), δ, ppm: 8.23 s (1H, CH), 4.13 s (3H, NCH_3), 4.05 s (3H, OCH_3). ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: 168.25 (C^{6a}), 150.42 (C^3), 142.60 (C^4), 138.02 (C=NOMe), 103.33 (C^{3a}), 63.72 (OCH_3), 37.50 (NCH_3). IR spectrum, ν, cm^{-1}: 1544, 1336 (NO_2). Mass spectrum, *m*/*z*: 225 $[M]^+$, 227 $[M + 2H]^+$. Found,

%: C 37.54; H 3.24; N 30.72. $C_7H_7N_5O_4$. Calculated, %: C 37.34; H 3.13; N 31.10.

1-Methyl-3-nitro-4-(2-phenyl-2*H*-1,2,3-triazol-4-yl)pyrazol-5-ol (XIII). Compound **X**, 1.00 (3.0 mmol), was dissolved in 15 ml of ethanol, 0.41 g (3.0 mmol) of potassium carbonate was added, and the mixture was heated for 2 h under reflux. It was then cooled, poured into 150 ml of water, hydrochloric acid was added to a weakly acidic reaction, and the precipitate was filtered off, washed with water, dried, and recrystallized from methanol. Yield 0.39 (45.4%), yellow crystalline substance, mp 193–194°C (from MeOH). IR spectrum ($CHCl_3$), ν, cm^{-1}: 3220 br (OH); 1528, 1352 (NO_2). ^1H NMR spectrum, δ, ppm: in DMSO-d_6: 8.22 s (1H, CH), 8.08 d (2H, *o*-H), 7.57 t (1H, *p*-H), 7.45 t (2H, *m*-H), 3.75 s (3H, CH_3); in $CDCl_3$: 9.70 br.s (1H, OH), 8.50 s (1H, CH), 7.98 d (2H, *o*-H), 7.52 t (1H, *p*-H), 7.42 t (2H, *m*-H), 3.87 s (3H, NCH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 151.76 (C^5), 149.57 (C^3), 139.20 (C^i), 138.57 ($C^{4'}$), 136.81 ($C^{5'}$), 129.70 (C^m), 127.72 (C^p), 118.45 (C^o), 88.72 (C^4), 34.73 (CH_3). ^{15}N NMR spectrum (DMSO-d_6, $MeNO_2$), δ_N, ppm: –69.44 ($N^{1'}$), –111.40 (N^2), –133.36 ($N^{2'}$), –204.95 (N^1). Mass spectrum: *m*/*z* 286 $[M]^+$. Found, %: C 49.69; H 3.48; N 28.79. $C_{12}H_{10}N_6O_3$. Calculated, %: C 50.35; H 3.52; N 29.36.

2-(1-Methyl-3,5-dinitropyrazol-4-yl)acetaldehyde phenylhydrazone (XIV). A solution of 0.70 g (10.1 mmol) of sodium nitrite in 3 ml of water was added under stirring to a mixture of 1.22 g (9.4 mmol) of aniline hydrochloride, 4 ml of concentrated hydrochloric acid, and 4 ml of water, maintaining the temperature at 0–5°C. The mixture was stirred for 5 min, and sodium acetate was added to pH 5, and a solution of 2.00 g (9.3 mmol) of compound **V** in 45 ml of ethanol was added at 5°C. The mixture was stirred for 1.5 h and poured into 400 ml of water, and the precipitate was filtered off, washed with cold water, and dried. Yield 0.74 g (73.0%), dark orange solid, mp 173–175°C. IR spectrum, ν, cm^{-1}: 3244 (NH); 1660 (C=N); 1548, 1528, 1348, 1332 (NO_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 10.88 s (1H, NH), 9.56 s (1H, CH), 7.35 m (4H, *o*-H, *m*-H), 7.08 t (1H, *p*-H), 4.42 s (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 187.71 (CHO), 150.03 (C^3), 144.16 (C^5), 142.53 (**C**=NNHPh), 129.55 (C^i), 129.36 (C^m), 123.55 (C^p), 115.09 (C^o), 103.90 (C^4), 42.82 (CH_3). Mass spectrum: *m*/*z* 318 $[M]^+$. Found, %: C 45.50; H 3.21; N 26.14. $C_{12}H_{10}N_6O_5$. Calculated, %: C 45.29; H 3.17; N 26.41.

6-Methyl-4-nitro-1-phenylpyrazolo[3,4-*c*]pyrazole-3-carbaldehyde (XV). Compound **XIV**, 0.50 g (1.57 mmol), was dissolved in 20 ml of acetonitrile, 0.22 g (1.57 mmol) of potassium carbonate was added, and the mixture was heated for 2 h under reflux. The mixture was cooled, poured into 150 ml of water, and neutralized with hydrochloric acid, and the precipitate was filtered off, washed with water, dried and purified by column chromatography. Yield 0.32 g (75.1%), light brown substance, mp 241–243°C. IR spectrum, ν, cm^{-1}: 1704 (C=O); 1532, 1364 (NO_2). ^1H NMR spectrum (DMSO-d_6, 80°C), δ, ppm: 10.16 s (1H, CHO), 7.79 d (2H, *o*-H), 7.63 t (2H, *m*-H), 7.60 t (1H, *p*-H), 3.91 s (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6, 80°C), δ_C, ppm: 183.52 (CHO), 149.55 (C^{6a}), 140.96 (C^4), 136.84 (C^3), 135.99 (C^i), 129.33 (C^m, C^p), 124.49 (C^o), 108.04 (C^{3a}), 38.30 (CH_3). Mass spectrum: *m*/*z* 271 $[M]^+$. Found, %: C 52.43; H 3.47; N 25.33. $C_{12}H_9N_5O_3$. Calculated, %: C 53.14; H 3.34; N 25.82.

2-(5-Ethoxy-1-methyl-3-nitropyrazol-4-yl)acetaldehyde phenylhydrazone (XVI). Compound **XIV**, 0.50 g (1.57 mmol), was dissolved in 20 ml of ethanol, 0.22 g (1.57 mmol) of potassium carbonate was added, and the mixture was heated for 1 h under reflux. The mixture was cooled, poured into 150 ml of water, and neutralized with hydrochloric acid. The precipitate was filtered off, washed with water, and dried. Yield 0.28 g (56.2%), bright yellow substance, mp 198–200°C. IR spectrum, ν, cm^{-1}: 3256 (NH); 1684 (C=O); 1540, 1344 (NO_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 10.75 s (1H, NH), 9.61 s (1H, CH), 7.39 d (2H, *o*-H), 7.32 t (2H, *m*-H), 7.05 t (1H, *p*-H), 4.05 q (2H, CH_2), 3.81 s (3H, NCH_3), 1.28 t (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 189.03 (CHO), 152.05 (C^5), 150.32 (C^3), 142.89 (C=NNHPh), 132.68 (C^i), 129.16 (C^m), 122.82 (C^p), 114.71 (C^o), 88.30 (C^4), 68.92 (CH_2), 35.11 (NCH_3), 14.33 (CH_3). Mass spectrum: *m*/*z* 317 $[M]^+$. Found, %: C 52.67; H 4.79; N 21.77. $C_{14}H_{15}N_5O_4$. Calculated, %: C 52.99; H 4.76; N 22.07.

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