SYNTHESIS AND PHYSICAL CHEMICAL PROPERTIES OF ISOMERS OF vic-ARYLAZONITRO-1-METHYLPYRAZOLES

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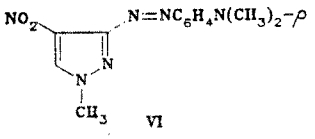
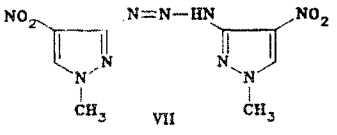
Taking account of special features of the diazotization of vic-aminonitro-1-methylpyrazoles, conditions have been found for synthesizing from them the isomers of arylazo-1-methylnitropyrazoles. The different behavior of these compounds under reducing conditions has been confirmed by polarographic data. The electronic absorption spectra of vic-arylazonitropyrazoles are interpreted.

Previously, we observed peculiarities in the diazotization of 4,5- and 5,4-aminonitro-1-methylpyrazoles compared to the 3,4-isomer, that give rise to certain difficulties in obtaining vic-arylazonitropyrazoles [1]. The purpose of the present work was to search for conditions for the synthesis of the isomers of arylazo-1-methylnitropyrazole from 3- and 5-nitropyrazoles (III, IV) and to study their physical chemical properties.

Aminonitropyrazole, I, and, analogously, 3-amino-1,5-dimethyl-4-nitropyrazole [1] are diazotized with sodium nitrite in hydrochloric acid without complications. This allows one to obtain, after coupling with N,N-dimethylaniline(V), 3-(4-N,N-dimethylaminophenylazo)-1-methyl-4-nitropyrazole (VI) in a high yield. When sulfuric or fluoboric acids are used, the diazotization reaction is complicated by the formation of 1,3-di(1-methyl-4-nitro-3-pyrazolyl)triazene (VII).



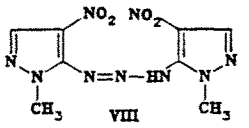
VI



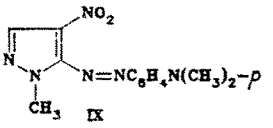
VII

The diazotization of 5-amino-1,3-dimethyl-4-nitropyrazole in hydrochloric or hydrobromic acid is accompanied by the replacement of an azo group by a halogen atom. In the presence of phenol, however, it is possible to obtain 5-(4-hydroxyphenylazo)-1,3-dimethyl-4-nitropyrazole in an 80% yield [1].

Taking this into account, we carried out the diazotization of 5-amino-4-nitropyrazole II in fluoboric acid. In this case, however, the reaction goes slowly and the principal product is dipyrazolyltriazene VIII. Compound VIII also is formed as an impurity in the diazotization of amine II with nitrosylsulfuric acid, but after coupling with azo-containing V it was possible to obtain 5-(4-N,N-dimethylaminophenylazo)-1-methyl-4-nitropyrazole IX in a 43% yield.



VIII



IX

On the diazotization of 4-amino-5-nitropyrazole IV in hydrochloric acid followed by coupling with phenol, 4-(4-hydroxyphenylazo)-1-methyl-5-chloropyrazole forms [1]. This is evidence of the rapid substitution of the nitro group in 1-methyl-5-nitropyrazole-4-diazonium chloride by a chlorine atom. Diazotization of aminonitropyrazole IV with nitrosylsulfuric acid goes to completion and is not complicated by the formation of triazene. But when conditions are created

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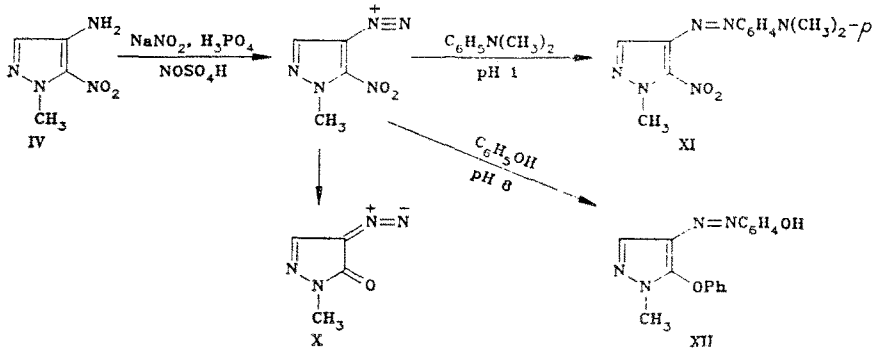
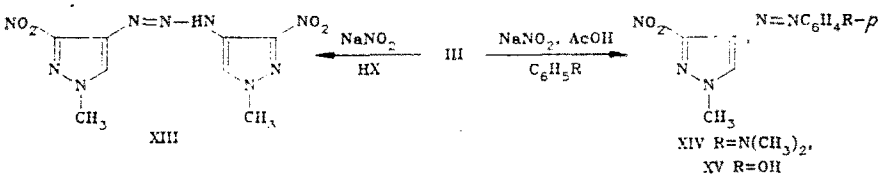
for coupling with compound V (dilution with water and bringing the diazo solution to a pH of 2–3), the nitro group in the 1-methyl-5-nitropyrazol-4-diazonium is replaced by a hydroxyl group to form quinonediazide (X). Diazotization of amine IV in phosphoric acid and coupling the diazonium salt with N,N-dimethylaniline at a pH of 1 leads to the formation of 4-(4-N,N-dimethylaminophenylazo)-1-methyl-5-nitropyrazole (XI) in a 15% yield. This yield is obviously due to the shift of the equilibrium to the side of the protonated form of dimethylaniline under the conditions for coupling. The 1-methyl-5-nitropyrazol-4-diazonium salt does not enter into a reaction with phenol in acid solution, but forms 4-(4-hydroxyphenylazo)-1-methyl-5-phenoxypyrazole (XII) in alkaline solution.



In the case of 4-amino-3-nitropyrazole III, regardless of the nature of the diazotization agent, mineral acid, and use of "direct" or "reverse" order of diazotization [2], di(1-methyl-3-nitro-4-pyrazole)triazene (XIII) is always present in the reaction mixture along with the diazo compound. The maximum yield of XIII (75%) is found with diazotization in 30% fluoboric acid. When one uses "reverse" order diazotization with compound III and sodium nitrite in acetic acid in the presence of an azo component (N,N-dimethylaniline, phenol) able to enter into the coupling reaction with a greater speed than that of triazene formation, it is possible to obtain azo dyes XIV and XV.



Previously it was shown that 5-(4-hydroxyphenylazo)-1,3-dimethyl-4-nitropyrazol is reduced by sodium hydrogen sulfide to 5-amino-1,3-dimethyl-4-nitropyrazole and p-aminophenol [1]. We have established that the reduction of 3-(4-hydroxyphenylazo)-1,5-dimethyl-4-nitropyrazole (XVI) takes place in analogous fashion.

Such a peculiarity in the behavior of 3- and 5-arylazo-4-nitropyrazoles is caused, obviously, by the distribution of electron density in the pyrazole ring. A nitro group in the π-electron-rich positions of the heterocycle is inert to the action of the reductant, whereas the relative π-deficiency of the 3 and 5 positions facilitates the reduction of the azo group. The formation of 3-amino-4-(4-hydroxyphenylazo)-1-methylpyrazole (XVII) on the reduction of 3-nitro-4-arylazopyrazole XV with sodium hydrogen sulfide and the results of the polarographic reduction of 3,4- and 4,3-arylazonitropyrazoles VI and XIV in DMF agree with this conclusion. Analysis of the polarographic waves by using the dependence of log $[i/i_g - i]$ on E [3] for compound VI showed that the first polarographic wave is a two-electron wave and reversible ($-E_{1/2}^{I}$ = 1.00 V, 2.3RT/nF = 29.8 mV) and the second, a one-electron wave and reversible ($-E_{1/2}^{II}$ = 1.25 V, 2.3RT/nF = 59.0 mV). According to the analysis of the polarogram of isomer XIV, the first wave corresponds to a reversible, one-electron process ($-E_{1/2}^{I}$ = 0.90 V) and the second to a reversible, two-electron process ($-E_{1/2}^{II}$ = 1.46 V). The data obtained are evidence of the sequential reduction of the arylazo and nitro groups in compound VI, which are reduced in reverse order in isomer XIV [3].

In interpreting the electronic absorption spectra of isomeric vic-(N,N-dimethylaminophenylazo)nitropyrazoles VI, IX, XI, and XIV, we used the rules established for (4-aminostyryl)pyrazoles [4]. In the spectra of the dyes synthesized there were intense, longwave bands, the energy of the S_0–S_1 transitions corresponding to them being obviously determined by the value of $|E_{HOMO} - E_{LUMO}|$. We estimated the energy of the HOMO of compounds VI, IX, and XIV from PE [photoelectron] spectra in which the first bands (first ionization potentials of 7.40, 7.45, and 7.41 eV, respectively) practically coincided. This means that with equality of the $|E_{HOMO}|$ of the isomers, 5-(4-dimethylphenylazo)-4-nitropyrazole IX must have the greatest

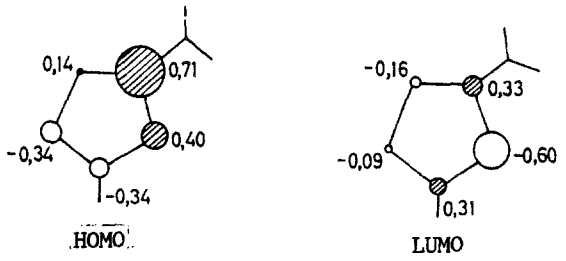


Fig. 1. The organization of the frontier MOs of 1-methyl-4-nitropyrazole (from calculation).

value of $|E_{LUMO}|$. According to a calculation for 1-methyl-4-nitropyrazole by the PPP-Configuration Interation method, the contribution of the atomic orbital (AO) of the $C_{(5)}$ atom to the LUMO considerably exceeds that of the AO of the $C_{(3)}$ atom [respectively, $(0.60)^2$ and $(0.16)^2$, Fig. 1]. For 1-methyl-3- and -5-nitropyrazoles, the contribution of the $C_{(4)}$ AO to the LUMO is equal, according to the calculation, to $(0.15)^2$ and $(0.40)^2$, respectively; introduction of the dimethylaminophenylazo group in the 5 position in 1-methyl-4-nitropyrazole lowers the energy of the LUMO to a greater degree than substitution in the 3 position. Such an approach allows one to interpret the position of the absorption bands in the spectra of isomers VI, IX, XI, and XIV.

EXPERIMENTAL

The electronic spectra were recorded on a Specord UV instrument in ethanol ($c \cdot 10^{-4}$ M), the IR spectra on a UR-20 instrument (KBr disks), the PMR spectra on a Tesla BS-467 (60 MHz, HMDS) instrument in DMSO-D_6. The TLC was done on Silufol UV-254 plates. The mass spectra were recorded on a Hewlett–Packard 5985 quadrupole chromato-mass spectrometer with direct introduction of the sample into the ionization region at an ionization potential of 70 eV and an admission temperature 10–15°C below the melting point of the sample. The PE spectra of compounds VI, IX, and XIV were measured on a Perkin–Elmer PS-18 spectrometer and calibrated relative to the $^2p_{1/2}$ and $^2p_{3/2}$ (Xe) lines at 12.13 and 13.43 eV. The polarographic reductions of arylazonitropyrazoles VI and XIV were carried out on a mercury drop electrode at room temperature in anhydrous DMF with tetrabutylammonium perchlorate (0.1 M) as supporting electrolyte and a $5 \cdot 10^{-4}$ M concentration of depolarizer. The values of $E_{1/2}$ were measured relative to a saturated calomel electrode. The quantum chemical calculations for the 1-methyl-3-, -4-, and -5-nitropyrazole molecules were carried out by the PPP method [5] in the approximation of varying "β" [6], taking account of configuration interaction and introducing the optimization of the internuclear distances of the ground state from the minimum energy of atomization by a program that realizes the Dewar algorithm [7].

The aminonitropyrazoles were synthesized by the procedures in [8, 9].

The elementary analyses of compounds VI–XV and XVII corresponded to the calculated values.

3-(4-N,N-Dimethylaminophenylazo)-1-methyl-4-nitropyrazole (VI, $C_{12}H_{14}N_6O_2$). Diazotize 0.86 g (6 mmoles) of aminonitropyrazole I in 20 ml of 15% HCl at 0–5°C, add to half of the solution 0.67 g (5.5 mmoles) of N,N-dimethylaniline in 10 ml of 3% HCl and add sodium acetate to bring the pH to 3–4. At 10–15°C add the second half of the azo component and hold for 2 h before neutralizing with 25% aqueous ammonia. Wash and dry the precipitate. Yield 1.43 g (86%); T_{mp} 152–154°C (aqueous ethanol); λ_{max} 463 nm ($\log \varepsilon$ 4.27).

1,3-Di-(1-methyl-4-nitro-3-pyrazolyl)triazene (VII, $C_8H_9N_9O_4$). To 0.24 g (1.7 mmole) of amine I in 3 ml of 100% H_2SO_4 at 10–15°C add 0.5 ml of nitrosylsulfuric acid and hold for 2 h. According to TLC (chloroform:acetone, 5:1), a test sample neutralized with aqueous ammonia still contained, after extraction with ethyl acetate, starting compound (R_f 0.18). After neutralization with aqueous ammonia, separate the precipitate and dry it. Recrystallize from aqueous ethanol (1:1) to get 0.15 g (31%) of triazene VII; T_{mp} 206–208°C; M^+ 295; λ_{max} 368 nm (4.16).

1,3-Di(1-methyl-4-nitro-5-pyrazolyl)triazene (VIII, $C_8H_9N_9O_4$). The diazotization of 0.48 g (3.4 mmoles) of compound II in 10 ml of 30% fluoboric acid with a solution of 0.23 g (3.4 mmoles) of sodium nitrite in 2 ml of water does not go to completion in the course of several hours. Isolate the product as in the previous experiment. Yield 0.22 g (40%); T_{mp} 132–134°C (aqueous ethanol); λ_{max} 366 nm (3.95); M^+ 295.

5-(4-N,N-Dimethylaminophenylazo)-1-methyl-4-nitropyrazole (IX, $C_{12}H_{14}N_6O_2$). To 1.2 g (8.5 mmoles) of compound II in 15 ml 100% H_2SO_4 at 10–15°C add 2.5 ml nitrosylsulfuric acid. At the end of the diazotization (TLC of a neutralized test sample extracted with ethyl acetate shows starting amine II, R_f 0.78, to be absent) pour the solution onto 50 g of ice, add 1.0 g (8.5 mmoles) of compound V in 10 ml of acetic acid and sodium acetate to bring the pH

to 4–5. Hold the reaction mixture at 20°C for 1 h, neutralize with 10% aqueous ammonia, filter off the precipitate, wash it with water, and dry it. Chromatograph on a column with silica gel (100/250, ethyl acetate) to get 1.0 g (43%) compound IX; T_{mp} 171–173°C (aqueous ethanol); M^+ 274; λ_{max} 493 nm (4.00).

1-Methyl-4-diazo-5-pyrazolone (X, $C_4H_4N_4O$). Diazotize 1.20 g (8.5 mmoles) of aminonitropyrazole IV at 10–15°C with 2.5 ml of nitrosylsulfuric acid. Then pour it onto 50 g of ice, extract with ethyl acetate (5 × 20 ml), dry the extract with Na_2SO_4, and distill off the solvent. Yield 0.85 g (81%); T_{mp} 82–84°C (aqueous ethanol); λ_{max} 322 nm (3.51). IR spectrum: 1653 cm^{-1} (C=O). The mass spectrum shows M^+ 124 and the peak of the $[M - N_2]$ ion with m/z 96.

4-(4-N,N-Dimethylaminophenylazo)-1-methyl-5-nitropyrazole (XI, $C_{12}H_{14}N_6O_2$). To 0.72 g (5 mmoles) of amine IV in 10 ml of 70% phosphoric acid add 0.34 g (5 mmoles) of sodium nitrite in 2 ml of water. Gradually add to the diazo solution a solution of 0.6 g (5 mmoles) of compound V in 10 ml of acetic acid. At the end of the coupling, neutralize the solution, filter off the precipitate, wash it with water, and dry it. Yield 0.2 g (15%), T_{mp} 148–150°C (aqueous ethanol); M^+ 274; λ_{max} 472 nm (4.22). IR spectrum: 1370, 1525 cm^{-1} (NO_2).

4-(4-Hydroxyphenylazo)-1-methyl-5-phenoxypyrazole (XII, $C_{16}H_{14}N_4O_2$). To 2.0 g (14 mmoles) of amine IV in 20 ml of 96% H_2SO_4 and 60 ml of water add a solution of 1.0 g (14 mmoles) of sodium nitrite in 10 ml of water. The diazo solution at 0–5°C is gradually added to 1.3 g (14 mmoles) of phenol in 50 ml of 10% sodium carbonate solution, maintaining a pH of 8–10. At the end of the coupling, bring the pH to 6–7, filter off the precipitate, wash it with water and dry it. Yield 2.0 g (49%); T_{mp} 214-216°C (aqueous ethanol); M^+ 294; λ_{max} 361 nm (4.36). Nitro group bands are absent in the IR spectrum.

1,3-Di(1-methyl-3-nitro-4-pyrazolyl)triazene (XIII, $C_8H_9N_9O_4$). Diazotize 0.72 g (5 mmoles) of aminonitropyrazole III in 10 ml of 100% H_2SO_4 at 10–15°C with 1.4 ml of nitrosylsulfuric acid. After 1 h, pour the mixture onto 30 g of ice and add 10% aqueous ammonia until precipitation begins. Separate the product, wash it with water and dry it. Yield 0.60 g (41%); T_{mp} 205–207°C (ethanol); M^+ 295; λ_{max} 400 nm (4.07). IR spectrum: 1347, 1360, 1544, 1563 cm^{-1} (NO_2).

Diazotization in 30% HBF_4 gives a yield of 1.29 g (87%).

4-(4-N,N-Dimethylaminophenylazo)-1-methyl-3-nitropyrazole (XIV, $C_{12}H_{14}N_6O_2$). Dissolve 0.72 g (5 mmoles) of compound III in 20 ml of water with heating. Add 0.36 g (5.2 mmoles) of sodium nitrite, cool quickly to obtain a finely dispersed suspension, and add this in portions to 0.60 g (5 mmoles) of dimethylaniline at 10–15°C. Hold this for 0.5 h, neutralize with dilute, aqueous ammonia, separate the precipitate, and wash it with water and dry it. Yield 1.06 g (77%); T_{mp} 197–199°C (AcOH); λ_{max} 459 nm (4.37). IR spectrum: 1360, 1535 cm^{-1} (NO_2).

4-(4-Hydroxyphenylazo)-1-methyl-3-nitropyrazole (XV, $C_{10}H_9N_5O_3$). Prepare this in the same way as compound XIV using phenol instead of dimethylaniline. Yield 0.41 g (33%); T_{mp} 201–202°C (ethanol); λ_{max} 369 nm (4.28). PMR spectrum: 3.98 (3H, s, 1-CH_3), 6.96 and 7.67 (4H, 2d, C_6H_4, J = 8.5 Hz), 8.20 ppm (1H, s, 5-H).

Reduction of 3-(Hydroxyphenylazo)-1,5-dimethyl-4-nitropyrazole (XVI). Prepare an aqueous solution of sodium hydrosulfide by passing hydrogen sulfide through a suspension of 3.9 g (5 mmoles) of crystalline sodium sulfide hydrate in 15 ml of water. Mix 0.5 g (2 mmoles) of compound XVI [1] and 0.02 g magnesium sulfate in 4 ml of water, heat to 75–80°C, and add the prepared sodium hydrogen sulfide solution. The reaction goes to completion only when 4 mmoles of sodium hydrogen sulfide is used. Hold for 1 h at 75–80°C and for 1 h at 20°C; then filter off the precipitate, wash it with water and dry it, to obtain 0.26 g (75%) of 3-amino-1,5-dimethyl-4-nitropyrazole, T_{mp} 206–208°C (according to [8], T_{mp} 209–210°C). After acidification of the filtrate to pH 5–6, p-aminophenol was identified in the filtrate by means of TLC with a standard.

3-Amino-4-(4-hydroxyphenylazo)-1-methylpyrazole (XVII, $C_{10}H_{11}N_5O$). To 0.49 g (2 mmoles) of azo dye XVI and 0.02 g of magnesium sulfate in 10 ml of water at 75–80°C, add a solution of sodium hydrogen sulfide, hold for 1 h, cool to 20°C, and acidify with 5% HCl to a pH of 5–6. Filter off the precipitate, wash it with a small amount of water and dry it. Yield 0.21 (49%); T_{mp} 203–204°C (aqueous ethanol); M^+ 217; λ_{max} 370 nm (4.26). PMR spectrum: 3.70 (3H, s, 1-CH_3); 5.78 (2H, s, NH_2), 6.84 and 7.66 (4H, 2d, C_6H_4, J = 8.5 Hz), 8.07 ppm (1H, s, 5-H).

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SYNTHESIS OF β-HYDROXYALKYLPYRAZOLES BY REACTION OF β-ARYLACRYLOYLOXIRANES WITH HYDRAZINE

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Reaction of β-arylacryloyloxiranes with hydrazine hydrate takes place via intermediate α,β-epoxyalkylpyrazoles which then undergo intramolecular oxidative-reductive disproportionation to yield β-hydroxyalkylpyrazoles.

α,β-Unsaturated ketones and α,β-epoxyketones react with hydrazine hydrate to form pyrazolines, hydroxypyrazolines, and allyl alcohols [1–3]. Use of conjugated α,β-epoxyketones in the reaction with hydrazine permits a comparative analysis of the reactivity of the epoxyketone and enone fragments of the molecules and to bring about the synthesis of novel substituted pyrazoles. With this aim we have studied the reaction of β-arylacryloyloxiranes Ia-*l* with hydrazine hydrate.

Reaction of Ia-*l* with hydrazine hydrate in organic solvent in the range 20–100°C leads to the formation of 5(3)-aryl-3(5)-(2-hydroxyalkyl)pyrazoles IIa-*l* in 53–82% yield independently of the degree of substitution of the α- and β-carbon atoms in the epoxy ring.

The structure of IIa-*l* was shown by their chemical reactions and by IR and PMR spectra and, for compound IIc, ^{13}C NMR and mass spectral data. The IR spectra of IIa-*l* show the absence of bands in the region 1600–1800 cm^{-1}, characteristic of double bonds and carbonyl groups in the starting epoxy ketones, and the presence of NH and OH stretching bands near 3450 and 3620 cm^{-1}, respectively, together with pyrazole and aromatic ring absorptions in the region 1300–1600 cm^{-1}.

The PMR spectra of the β-hydroxyalkylpyrazoles IIa-*l* (Table 1) differ according to the nature of their R^1, R^2, R^3, and Ar substitution but they all show a characteristic singlet for the 4-H pyrazole proton at 6.30–6.40 ppm.

Acetylation of compounds IIa, e, g, j–*l* with acetic anhydride gives the corresponding N-acetyl-β-acetoxyalkylpyrazoles IIIa, e, g, j–*l*. Dehydration of the β-hydroxyalkylpyrazoles IIk, *l* to the alkenylpyrazoles IVk, *l* occurs with sulfuric acid at 40°C. The iodoalkylpyrazoles Va, c are formed by nucleophilic substitution of the hydroxyl group in IIa, c,. Oxidation of β-hydroxyalkylpyrazoles IIc, g using pyridinium chlorochromate gives the 3(5)-acetylpyrazoles VIc, g instead of the expected β-pyrazolylcarbonyl compounds. The constants for these compounds are given in Table 1.

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