CH); 11.29 ppm (1H, s, OH). PMR spectrum of syn-isomer XII: 3.55 (2H, d, J = 5.2 Hz, CH_2), 5.81 (2H, s, NH_2), 7.47 (1H, t, J = 5.2 Hz, CH), 10.82 ppm (1H, s, OH).

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NITRATION OF ACETYL DERIVATIVES OF 1-METHYLPYRAZOLE

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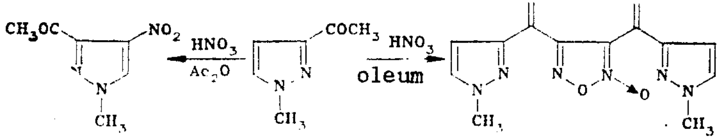
The nitration of acetyl-substituted 1-methylpyrazoles with nitric acid in 20% oleum and in acetic anhydride was studied. Dipyrazoloylfuroxans are formed in the case of nitration in oleum. 4-Nitro-3-acetyl-1-methylpyrazole was obtained by nitration of 3-acetyl-1-methylpyrazole in acetic anhydride.

We have previously studied the peculiarities of the nitration of 1-methylpyrazolecarboxylic acids and their 4-halo-substituted derivatives [1, 2]. In continuing our study of the peculiarities of the nitration of carbonyl derivatives of 1-methylpyrazole we have accomplished the nitration of a number of acetyl-1-methylpyrazoles: 4-acetyl-1,3- and -1,5-dimethylpyrazoles (I, II), 3-acetyl-1-methylpyrazole (III), and 5-acetyl-1-methylpyrazole (IV).

The starting acetylpyrazoles I and II were obtained by direct acetylation of the corresponding pyrazoles with acetic anhydride in the presence of sulfuric acid [3], while III and IV were synthesized by the reaction of 1-methylpyrazole-3- and -5-carboxylic acid nitriles (V, VI) with methylmagnesium iodide [4].

The nitration of acetylpyrazoles I-IV was accomplished with concentrated nitric acid in 20% oleum or in acetic anhydride. In the case of nitration of acetylpyrazoles I-IV in oleum none of the indicated compounds form products with a nitro group in the pyrazole ring; as in the nitration of acetophenone [5], the corresponding 3,4-dipyrazoloylfuroxans VII-X are obtained. The highest yields of VII-X are obtained when the reaction is carried out in the presence of acetic acid and at no higher than 70°C. The nitration of acetylpyrazole IV at higher temperatures leads to 1-methylpyrazole-5-carboxylic acid (XI) as a consequence of oxidative processes.

As demonstrated by our studies, I, III, and IV do not undergo nitration on treatment with concentrated nitric acid in acetic anhydride at 0°C. Under similar conditions II is converted to furoxan in 40% yield. However, 3-acetyl-4-nitro-1-methylpyrazole (XII) was isolated as the only product in the nitration of acetylpyrazole III in acetic anhydride under severe conditions (70°, 3 h).



XII III IX

An attempt to introduce a nitro group into the furoxan VIII molecule was unsuccessful. Compound VIII is not nitrated by an equimolar amount of nitric acid in 20% oleum at 70°C, while the use of a tenfold amount of nitric acid

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TABLE 1. Characteristics of the Synthesized Compounds

Compound	Empirical formula	mp. °C	PMR spectrum, δ, ppm					M⁺	Yield, %
			1-CH_3	3-CH_3 (5-CH_3)	3-H (5-H)	$COCH_3$	4-H, d		
III	$C_6H_8N_2O$	100 (9)	3,91	—	7,35 d	2,49	6,70	—	81
IV	$C_6H_8N_2O$	145 ... 150 (20)	4,06	—	7,40 d	2,48	6,85	—	73
VII	$C_{14}H_{14}N_6O$	138 ... 141	3,80; 3,90	2,36; 2,40	8,44; 8,62	—	—***	330	80
VIII	$C_{14}H_{14}N_6O$	186 ... 187	3,78; 3,80	2,54; 2,56	7,62; 8,20	—	—***	330	84
IX	$C_{12}H_{10}N_6O$	150 ... 152	3,67; 3,80	—	7,51 d; 7,58 d	—	6,72; 6,80	302	53
X	$C_{12}H_{10}N_6O$	108 ... 110	4,05; 4,10	—	7,47 d; 7,55 d	—	6,91; 7,37	302	55
XII	$C_6H_7N_3O_3$	118 ... 121	3,95	—	8,12	2,57	—	—	76

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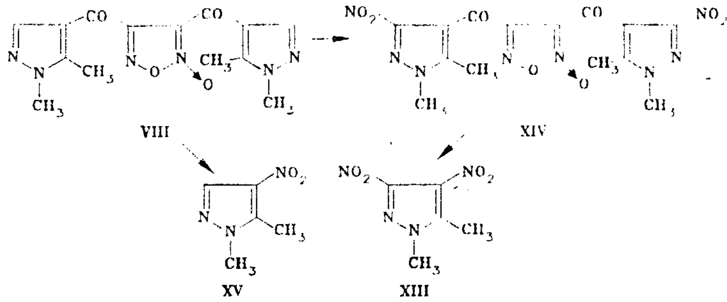
*The boiling points (°C, mm) are presented for III and IV. Compounds VII and VIII were crystallized from isopropyl alcohol—DMF (5:1), while IX, X, and XII were crystallized from ethanol.

under similar conditions leads to a mixture of 1,5-dimethyl-3,4-dinitropyrazole (XIII) and 1,5-dimethyl-4-nitropyrazole (XV) in a ratio of 5:2.

The indicated results provide evidence that the nitration of VIII proceeds both via direct ipso attack at the 4 position of the pyrazole fragment of the starting compound and through a step involving the formation of 3,4-bis(1,5-dimethyl-3-nitro-4-pyrazoloyl)furoxan (XIV), which then undergoes ipso substitution. Evidence in favor of the possibility that the reaction proceeds through a step involving the formation of nitrofuroxan XIV is provided by the presence among the reaction products of dinitropyrazole XIII, which, according to the data in [6], is not formed from 1,5-dimethyl-4-nitropyrazole under similar conditions.



EXPERIMENTAL

The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Tesla BS spectrometer [100 MHz, hexamethyldisiloxane (HMDS)]. The mass spectra were obtained with an MKh-1303 spectrometer at an ionization energy of 70 eV. Chromatographic monitoring was accomplished on Silufol UV-254 plates [elution with chloroform—alcohol (20:1)].

The characteristics of III, IV, VII-X, and XII are presented in Table 1. The results of elementary analysis of the newly obtained compounds were in agreement with the calculated values.

3-Acetyl-1-methylpyrazole (III). A solution of 10.7 g (0.1 mole) of 1-methylpyrazole-3-carboxylic acid nitrile (V) in 150 ml of absolute ether was added to a solution of methylmagnesium iodide obtained by the reaction of 3.58 g (0.14 mmole) of magnesium and 20.7 g (0.14 mole) of methyl iodide in 100 ml of absolute ether, after which the mixture was refluxed for 30 min. It was then cooled and treated with 50 ml of 15% ammonium chloride solution. The ether layer was separated from the aqueous layer, and the latter was extracted with ether (5 × 50 ml). Workup gave acetylpyrazole III.

5-Acetyl-1-methylpyrazole (IV). This compound was obtained in the same way as III from 1-methylpyrazole-5-carboxylic acid nitrile (VI).

3,4-Bis(1,2-dimethyl-4-pyrazoloyl)furoxan (VII). A solution of 2 g (0.015 mole) of acetylpyrazole I in 5 ml of acetic acid was added with cooling to a nitrating mixture consisting of 4 ml (0.1 mole) of nitric acid (d 1.51) and 4 ml of 20% oleum, after which the temperature was cautiously raised to 70°C, and the mixture was maintained at this temperature for 1 h and then poured over ice.

3,4-Bis(1,5-dimethyl-4-pyrazoloyl)furoxan (VIII). This compound was obtained in the same way as VII by nitration of II.

3,4-Bis(1-methyl-3-pyrazoloyl)furoxan (IX). This compound was obtained in the same way as VII by nitration of III.

3,4-Bis(1-methyl-5-pyrazoloyl)furoxan (X). A 1.24-g (0.01 mole) sample of IV was dissolved in 1 ml of 20 oleum, the solution was cooled to 0°C, and 0.5 ml (0.012 mole) of nitric acid (d 1.51) in 1 ml of 20% oleum was added with stirring. The temperature was cautiously raised to 50°C, and the mixture was maintained at this temperature for 30 min. The reaction was completed by heating at 70°C for 1 h. When the indicated conditions were not adhered to, the reaction mixture heated up spontaneously to 150°C, and 0.5 g (40%) of carboxylic acid XI was isolated as a result of the reaction.

Nitration of 4-Acetyl-1,5-dimethylpyrazole (II) in Acetic Anhydride. A 3-g (0.02 mole) sample of II was dissolved in 4 ml of acetic anhydride, a mixture of 2.5 ml (0.06 mole) of nitric acid (d 1.51) in 3 ml of acetic anhydride was added with cooling and stirring, and the mixture was maintained at 0°C for 1 h. Workup gave 3.1 g of a mixture of II and III (in a ratio of 3:2, according to the PMR spectral data).

4-Nitro-3-acetyl-1-methylpyrazole (XII). A solution of 0.83 g (0.02 mole) of nitric acid (d 1.51) in 3 ml of acetic anhydride was added with cooling to a solution of 1.24 g (0.01 mole) of III in 25 ml of acetic anhydride, after which the mixture was heated at 65-70°C for 3 h and then poured over ice.

Nitration of Furoxan VIII. A. A 1.65-g (0.005 mole) sample of furoxan VIII was added to a nitrating mixture consisting of 0.4 ml (0.01 mole) of nitric acid (d 1.51) and 4 ml of 20% oleum, and the mixture was heated at 70°C for 1 h. Workup gave 1.60 g of the starting compound.

B. A 3-mmole sample of furoxan VIII was added to a nitrating mixture consisting of 4 ml (0.1 mole) of nitric acid (d 1.51) and 4 ml of 20% oleum, after which the mixture was heated at 70°C for 1 h and then poured over 50 g of ice to precipitate XIII. The yield was 0.63 g (52%). The aqueous solution remaining after separation of the precipitate was neutralized with sodium carbonate and extracted with chloroform (5 × 20 ml). Removal of the solvent by distillation gave XV. The yield was 0.20 g (21%).

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