1108 and 1429 (Si—C_6H_5), 1652 (CO), 3280-3300 cm^{-1} (bound NH). Found, %: C 76.6; H 5.3; N 7.0, M^+ 392. $C_{25}H_{20}N_2OSi$. Calculated, %: C 76.5; H 5.1; N 7.1, M 392.

5,5-Dimethyl-5-sila-5H,10H,11H-benzo[b]pyrido[4,3-e]azepine (VIII). A solution of 3.9 g (102.6 mmoles) lithium aluminum hydride in 200 ml absolute ether was added to a solution of 2.6 g (10.2 mmoles) of a mixture of isomeric lactams III and IV in 200 ml absolute ether over 1 h. The mixture was heated at reflux for 30 h and then decomposed with 15 ml ethyl acetate and 25 ml 20% aqueous NaOH. The ethereal layer was decanted and dried over magnesium sulfate. The residue (2.4 g) after distilling off the ether solvent was subjected to chromatography on a 40 × 3 cm column with 5:1 heptane—ethyl acetate as eluent to yield 0.91 g (37%) VIII as white crystals with mp 157-157.5°C (from ethyl acetate—heptane), R_f 0.42 (ethyl acetate). IR spectrum: 820 and 1260 [$Si(CH_3)_2$], 1525 and 3275 cm^{-1} (NH). PMR spectrum (11 MHz): 8.50 (d, 1H, 3-H), 8.43 (s, 1H, 1-H), 7.44 (m, 2H, 4- and 6-H), 7.12 (m, 1H, 8-H), 6.82 (m, 1H, 7-H), 6.67 (m, 1H, 9-H), 4.45 (s, 3H, NH and CH_2); 0.70 ppm (s, 6H, $SiCH_3$); J_{98} = 8, J_{97} = 1.2, $J_{78} \simeq J_{76} \simeq 7.5$, J_{86} = 1.5 Hz. Found, %: C 70.1; H 6.9; N 11.9, M^+ 240. $C_{14}H_{19}N_2Si$. Calculated, %: C 70.0; H 6.7; N 11.7; M 240.

B. A sample of 0.22 g (43%) VIII with mp 157-157.5°C (from ethyl acetate) was obtained by an analogous procedure by reduction from 0.54 g (2.1 mmoles) lactam III. A mixed melting point with a sample obtained by method A was undepressed.

3-Methyl-5,5-diphenyl-5-sila-5H,10H,11H-benzo[b]pyrido[4,5-e]azepine (IX). The reduction of 2 g (5.1 mmoles) of a mixture of lactams V and VI by the method described above gave 0.6 g (31%) IX as white crystals with mp 193-194°C (from hexane), R_f 0.5 (1:4 hexane—ethyl acetate). IR spectrum: 1108 and 1429 (Si—C_6H_5), 1548 and 3270 cm^{-1} (NH). PMR spectrum (100 MHz): 7.78 (s, 1H, 1-H), 6.83 (s, 1H, 4-H), 4.44 (-, 1H, NH), 4.22 (s, 2H, CH_2), 2.22 ppm (s, 3H, CH_3). Found, %: C 79.7; H 6.0; N 7.2, M^+ 378. $C_{25}H_{22}N_2Si$. Calculated, %: C 79.4; H 5.8; N 7.4, M 378.

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AMINATION OF ISOMERIC BROMO-1-METHYLNITROPYRAZOLES

V. P. Perevalov, L. I. Baryshnenkova,
M. A. Andreeva, Yu. A. Manaev,
I. A. Denisova, B. I. Stepanov,
and V. I. Seraya

UDC 547.772.1'773.07:543.422.25

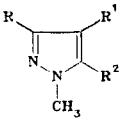
A method was developed for the synthesis of 5-bromo-1-methyl-4-nitropyrazole from 1-methylpyrazole. In the reaction with 25% aqueous ammonia at 180-190°C, 5-bromo-1-methyl-4-nitropyrazole is readily converted to 5-amino-1-methyl-4-nitropyrazole; the production of 4-amino-1-methyl-5-nitropyrazole from 4-bromo-1-methyl-5-nitropyrazole requires the presence of a copper catalyst; under the same conditions in the amination of 4-bromo-1-methyl-3-nitropyrazole, 4-amino-1-methyl-3-nitro- and 1-methyl-3-nitropyrazoles are formed in a 2:3 ratio.

The ability of halopyrazoles to enter into nucleophilic substitution reactions depends on the mutual arrangement of the halogen and substituent that activates its substitution in the heterocycle. Such reactions are used chiefly for the production of 5-substituted pyrazoles, containing an electron acceptor group in the 4-position. There are no data in the literature on the amination of halopyrazoles; the 3- and 5-amino-1-methyl-4-nitropyrazoles described were synthesized by other methods [1, 2].

D. I. Mendeleev Moscow Chemical Technology Institute, Moscow 125820. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1672-1675, December, 1983. Original article submitted March 29, 1983.

 0009-3122/83/1912-1322$07.50

TABLE 1. Derivatives of 1-Methylpyrazole I-X



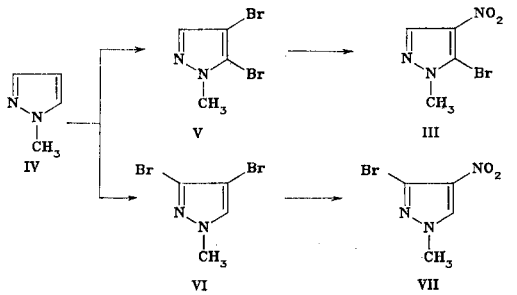
Compound	R	R¹	R²	Mp, °C	PMR spectrum, ppm				Found, %			Empirical formula	Calculated, %			Yield, %
					CH_3	3-H	5-H	NH_2	C	H	N		C	H	N	
I	H	Br	NO_2	56—57[a]	4,13	7,97	—	—	23,6	2,2	20,5	$C_4H_4BrN_3O_2$	23,3	1,9	20,4	89
II	NO_2	Br	H	159—160[a]	3,95	—	8,27	—	23,6	2,1	20,4	$C_4H_4BrN_3O_2$	23,3	1,9	20,4	55
III	H	NO_2	Br	90—92[b]	3,88	8,38	—	—	23,7	2,3	20,7	$C_4H_4BrN_3O_2$	23,3	1,9	20,4	44
V	H	Br	Br	53—55	3,83	7,67	—	—	20,4	1,8	11,9	$C_4H_4Br_2N_2$	20,0	2,3	11,7	42
VI	Br	Br	H	—	3,80	—	7,98	—	—	—	—	—	—	—	—	11
VII	Br	NO_2	H	—	3,90	—	8,92	—	—	—	—	—	—	—	—	—
	H	NO_2	H	—	3,90	8,18	8,80	—	—	—	—	—	—	—	—	—
VIII	H	NO_2	NH_2	257—258[c]	3,55	7,85	—	7,37	—	—	—	—	—	—	—	68
IX	H	NH_2	NO_2	128—129[a]	3,90	7,08	—	6,23	34,1	4,5	39,6	$C_4H_6N_4O_2$	33,8	4,2	39,5	59
					4,05	7,05	—	4,74[d]								
X	NO_2	NH_2	H	151—153	3,70	—	7,18	5,40	34,0	4,4	39,8	$C_4H_6N_4O_2$	33,8	4,2	39,5	—
					3,80	—	7,00	4,53[d]								

[a]From a mixture of methanol with water, 1:1. [b]From a mixture of ethanol with water, 1:1. [c]From ethanol, according to the data of [2], mp 264-265°C. [d]In CD_3Cl.

In view of this we produced some isomeric bromo-1-methylnitropyrazoles and studied the possibility of their conversion to amino-1-methylnitropyrazoles in the interaction with aqueous ammonia. 4-Bromo-1-methyl-5-nitropyrazole (I) was produced by decarboxylation of 4-bromo-1-methyl-5-nitropyrazole-3-carboxylic acid, while 4-bromo-1-methyl-3-nitropyrazole (II) was produced by decarboxylation of 4-bromo-1-methyl-3-nitropyrazole-5-carboxylic acid [3]. The synthesis of 5-bromo-1-methyl-4-nitropyrazole (III) was performed from 1-methylpyrazole (IV); in this case, together with the main compounds V and III, their isomers VI and VII were obtained. We conducted the bromination of 1-methylpyrazole IV with bromine in acetic acid in the presence of sodium acetate, which permits the immediate production of dibromopyrazoles [4].

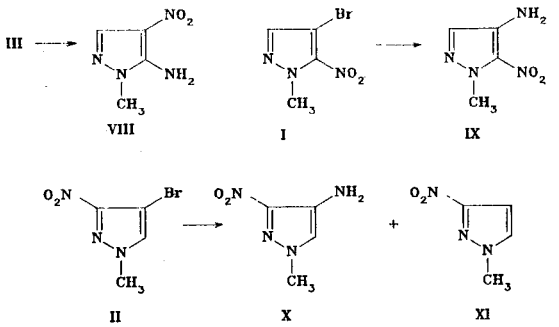
The PMR spectrum of the bromination product contains two signals of the protons of the pyrazole ring at 7.67 and 7.98 ppm with a 4:1 ratio of the integral intensities, which are shifted by the same amount in the strong-field direction ($\Delta\delta$ 0.3 ppm), respectively, in comparison with the signal of the proton $H_{(3)}$ (δ 7.97 ppm) in the spectrum of 4-bromo-1-methyl-5-nitropyrazole (I) and the proton $H_{(5)}$ (δ 8.27 ppm) in the spectrum of compound II (Table 1). These data are evidence that in the bromination of 1-methylpyrazole IV, 4,5-dibromo-1-methylpyrazole (V) and 3,4-dibromo-1-methylpyrazole (VI) are formed in a 4:1 ratio. Such a pattern agrees with the results of the bromination of 1,3-dimethylpyrazole and 1,5-dimethylpyrazole under analogous conditions: The production of 4,5-dibromo-1,3-dimethylpyrazole requires 2 h [4]; 1,5-dimethylpyrazole is entirely converted to 3,4-dibromo-1,5-dimethylpyrazole in 10-12 h.

The production of bromonitropyrazole III requires the nitrodebromination of compound V. However, the isomers V and VI could not be separated by crystallization and thin-layer chromatography; therefore, we used a mixture of them for further conversions. It is known that the nitrodebromination of 4-bromopyrazoles occurs using nitrating mixtures based on sulfuric acid, containing water [5], or 20% oleum [4]. In view of this, the nitration of a mixture of dibromopyrazoles V and VI by a nitrating mixture [5] was conducted under similar conditions. The product obtained in this way, according to the data of thin-layer chromatography, contained three compounds. Individual 4,5-dibromo-1-methylpyrazole (V), 5-bromo-1-methyl-4-nitropyrazole (III), and 3-bromo-1-methyl-4-nitropyrazole (VII) with a small admixture of the isomer III were isolated by preparative thin-layer chromatography. The ratio of compounds V, III, and VII was approximately 7:5:1 according to the data of the PMR spectrum.



The structure of bromonitropyrazoles III and VII was confirmed by a comparison of the data of their PMR spectra with the spectrum of 1-methyl-4-nitropyrazole (Table 1). In the nitration of dibromopyrazoles V and VI in 20% oleum, the reaction proceeded more rapidly; the precipitate isolated after nitration contained only compound III. The latter is evidently due to the complete destruction of 3,4-dibromo-1-methylpyrazole VI, supported, in our view, by the following data: 4,5-Dibromo-1,3-dimethylpyrazole was converted to 5-bromo-1,3-dimethyl-4-nitrophyrazole under analogous conditions with a good yield [4]; in the nitration of 3,4-dibromo-1,5-dimethylpyrazole abundant evolution of gases was observed, and the corresponding bromonitropyrazole was not isolated; the product of nitrodebromination also could not be obtained as a result of the nitration of 3,4-dibromopyrazole [5].

Heating the bromonitropyrazole III with 25% aqueous ammonia at 180-190°C for 5 h produced 5-amino-1-methyl-4-nitropyrazole (VIII) with a yield of about 70%; it was synthesized earlier with a yield of 24% in the nitration of 5-amino-1-methylpyrazole [2]. The amination of 4-bromo-1-methyl-5-nitropyrazole (I) was conducted under the same conditions, resulting in the isolation (data of thin-layer chromatography) of the initial bromonitropyrazole I with an admixture of 4-amino-1-methyl-5-nitropyrazole (IV). The individual aminonitropyrazole IX was produced by amination of the bromonitropyrazole I in the presence of a copper catalyst at 140°C.



The arrangement of substituents most unfavorable for amination occurs in the 4-bromo-1-methyl-3-nitropyrazole (II) molecule. This compound does not react with aqueous ammonia at 180-190°C and at 140°C in the presence of a catalyst. When the bromonitropyrazole II is heated with 25% aqueous ammonia at 180-190°C in the presence of copper powder, simultaneously with amination leading to the formation of 4-amino-1-methyl-3-nitropyrazole (X) there is a debromination of compound II, resulting in the formation of 1-methyl-3-nitropyrazole (XI).

Aminonitropyrazole X and nitropyrazole XI were separated by preparative thin-layer chromatography; the data of the PMR spectrum of 1-methyl-3-nitropyrazole (XI) coincide with the literature data [6].

EXPERIMENTAL

The PMR spectra were measured on a Tesla BS-467 instrument (60 MHz, HMDS) in DMSO-D_6. The data of the spectra are cited in Table 1.

4-Bromo-1-methyl-5-nitropyrazole (I). We heated 5.0 g (0.02 mole) 4-bromo-1-methyl-5-nitropyrazole-3-carboxylic acid [3] in an atmosphere of inert gas to 240°C and exposed until the liberation of carbon dioxide ended. Yield 3.7 g.

4-Bromo-1-methyl-3-nitropyrazole (II). In an autoclave we heated 1.03 g (5 mmoles) 4-bromo-1-methyl-3-nitropyrazole-5-carboxylic acid [3] in 20 ml of water to 190°C and exposed

for 5 h; after cooling the precipitate was filtered off and washed with a small amount of methanol. Yield 0.45 g.

1-Methylpyrazole (IV). We heated 15.0 g (0.12 mole) 1-methyl-pyrazole-5-carboxylic acid until the beginning of decarboxylation (235-250°C) and exposed for 40 min until the liquid ceased to distill off. Yield 8.0 g (81%), bp 128-130°C; according to the data of [7], bp 125-127°C.

Bromination of 1-Methylpyrazole. To a solution of 16.4 g (0.2 mole) 1-methylpyrazole V and 37.0 g sodium acetate trihydrate in 125 ml acetic acid, 64.0 g (0.40 mole) bromine was added dropwise over a period of 1 h at 30°C. The mass was heated to 90°C and exposed for 2 h; after cooling it was poured out into 500 ml of water. The oil liberated was washed with water (2 × 100 ml), 200 ml of water and 5.0 g sodium sulfite were added to it, and it was mixed until decolorization and pulverization of the precipitate. The precipitate was filtered off and washed with water. We obtained 25.2 g (53%) of a mixture of 4,5-dibromo-1-methylpyrazole (V) and 3,4-dibromo-1-methylpyrazole (VI) in a 4:1 ratio (according to the date of the PMR spectrum).

Nitration of a Mixture of Dibromopyrazoles V and VI. A. To the nitrating mixture, consisting of 5 ml of 99% nitric acid, 10 ml 80% sulfuric acid, and 5 ml of the monohydrate was gradually added 7.2 g (0.03 mole) of a mixture of the dibromopyrazoles V and VI, produced in the preceding experiment, at 30°C. The reaction mass was heated to 80°C and exposed for 2 h, then heated to 100°C and exposed for 1 h. After cooling the nitro-mass was poured out into 100 g of ice; the precipitate was washed with ice water and dried. We obtained 3.5 g of a precipitate which, according to the data of thin-layer chromatography (Silufol UV-254, benzene–ethyl acetate–petroleum ether, 1:1:1), contained three compounds – 4,5-dibromo-1-methylpyrazole V (R_f 0.82), 5-bromo-1-methyl-4-nitropyrazole III (R_f 0.62), and 3-bromo-1-methyl-4-nitropyrazole VII (Rf 0.44). Compounds V and III were isolated by preparative chromatography on silica gel; the bromonitropyrazole VII was produced with an admixture of the isomer III.

B. To a nitrating mixture consisting of 8 ml of 99% nitric acid and 12 ml of 20% oleum we added 7.2 g (0.03 mole) of a mixture of dibromopyrazoles V and VI, so that the temperature did not exceed 25°C, heated slowly to 100°C, and exposed for 1 h. After cooling the mixture was poured out onto 100 g of ice. We obtained 2.7 g bromonitropyrazole III.

5-Amino-1-methyl-4-nitropyrazole (VIII). In an autoclave we heated 2.06 g (0.01 mole) bromonitropyrazole III in 30 ml of 25% aqueous ammonia to 190°C and exposed for 5 h; after cooling the precipitate was filtered off and washed with a small amount of ether. Yield 0.95 g.

Amination of 4-Bromo-1-methyl-5-nitropyrazole (I). A. We heated 1.03 g (5 mmoles) of the bromonitropyrazole I and 30 ml of 25% aqueous ammonia in an autoclave to 190°C, exposed for 5 h, and filtered off the precipitate; according to the data of thin-layer chromatography (Silufol UV-254, benzene–ethyl acetate–petroleum ether, 1:1:1) it contains compound I (R_f 0.85) with a small admixture of the aminonitropyrazole IX (R_f 0.39).

B. A mixture of 1.03 g (5 mmoles) bromonitropyrazole I, 0.1 g copper powder, and 30 ml 25% aqueous ammonia was heated in an autoclave to 140°C, exposed for 4 h, and after cooling the precipitate was filtered off and washed with water. We obtained 0.4 g of 4-amino-1-methyl-5-nitropyrazole, an additional amount of which (0.1 g) was isolated after extraction of the filtrate with ether and distillation of the solvent.

Amination of 4-Bromo-1-methyl-3-nitropyrazole (II). A. In an autoclave 1.03 g (5 mmole) bromonitropyrazole II was aminated as described in the production of the aminonitropyrazole VIII. The product isolated (0.76 g) was the initial compound II.

B. We aminated 0.75 g (3.6 mmoles) of the bromonitropyrazole II as described in the production of the aminonitropyrazole IX. The product isolated (0.55 g) was the initial compound II.

C. A mixture of 0.70 g (3.4 mmoles) of the bromonitropyrazole II, 0.1 g of copper powder, and 20 ml of 25% aqueous ammonia was heated in an autoclave to 190°C and exposed for 5 h; after cooling the solution was extracted with ether (3 × 20 ml), the extract dried over sodium sulfate, and the ether distilled off. We obtained 0.31 g of a mixture of 4-amino-1-methyl-3-nitropyrazole (X) and 1-methyl-3-nitropyrazole (XI) in a 2:3 ratio (according to the data of the PMR spectrum). The mixture was separated by preparative thin-layer chromatography

(silica gel, benzene–ethanol, 5:1), and 0.18 g of the aminonitropyrazole X and 0.07 g of the nitropyrazole XI, mp 86-88°C (ethanol–water, 1:2) were obtained; according to the data of [6], mp 80-84°C. PMR spectrum ($CDCl_3$): 3.80 (3H, s, 1-CH_3); 6.82 (1H, d, 4-H); 7.42 ppm (1H, d, 5-H).

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SYNTHESIS OF 3-AMINO-4-NITROPYRAZOLES

V. P. Perevalov, M. A. Andreeva, L. I. Baryshnenkova, Yu. A. Manaev, G. S. Yamburg, B. I. Stepanov, and V. A. Dubrovskaya

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3-Bromo-1,5-dimethyl-4-nitropyrazole does not react upon heating with aqueous ammonia, while 1,5-dimethyl-3,4-dinitropyrazole under the same conditions yields 3-amino-1,5-dimethyl-4-nitropyrazole, which is formed from 3-bromo-1,5-dimethyl-4-nitropyrazole in the presence of a copper catalyst. The amination of 1-methyl-3,4-dinitropyrazole-5-carboxylic acid is accompanied by decarboxylation, which is characteristic for 4-substituted 1-methylpyrazole-5-carboxylic acids upon heating in aqueous ammonia or water.

3- and 5-Amino-1-methyl-4-nitropyrazoles (I and II) were first obtained by the reaction of 4-methoxy-5-nitropyrimidine with methylhydrazine. However, Porter et al. [1] made a mistake in the structure assignment using the PMR spectra. Subsequently, 5-amino-1-methyl-4-nitropyrazole (II) was obtained as the result of a planned but rather complicated synthesis [2]. The simplest method for the synthesis of 5-amino-4-nitropyrazoles is the ammonolysis of 4-nitro-5-halopyrazoles, which has yielded 5-amino-1,3-dimethyl-4-nitropyrazole [3] and aminonitropyrazole II [4]. The possibility of obtaining 3-amino-4-nitropyrazoles by this method had not been examined, apparently, since 3-halopyrazoles, even with an electron-withdrawing group at C-4, do not undergo nucleophilic substitution in contrast to the corresponding 4,5-isomers [5]. To check this hypothesis in the case of ammonolysis, we synthesized 3-bromo-1,5-dimethyl-4-nitropyrazole (III).

The bromination of 1,5-dimethylpyrazole in acetic acid in the presence of sodium acetate yields, 3,4-dibromo-1,5-dimethylpyrazole (IV) which was synthesized previously by the bromination of 4-bromo-1,5-dimethylpyrazole in nitric acid [6]. Nitrodebromination of IV by a mixture of concentrated nitric acid and 95% sulfuric acid yielded bromonitropyrazole III. The position of the nitro group in this molecule is indicated unequivocally by the coincidence of the methyl group proton signals in its PMR spectrum with the same signals in the spectrum of 4-nitro-1,5-dimethylpyrazole (Table 1). 3-Bromo-1,5-dimethyl-4-nitropyrazole was isolated unchanged after heating for 5 h at 200°C with excess 25% aqueous ammonia. 3-Amino-1,5-dimethyl-4-nitropyrazole (VI) was obtained under the same conditions from 3-bromo-1,5-dimethyl-4-nitropyrazole in the presence of copper powder in high yield.

D. I. Mendeleev Moscow Chemical Technology Institute, Moscow 125820.

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