1H-4-Methyl-2,3,4,5-tetrahydrobenz[c]azepine-1-thione (IId). This compound, with mp 141°C, was obtained in 20% yield. Found: C 69.4; H 7.5%. $C_{11}H_{13}NS$. Calculated: C 69.1; H 6.8%.

1H-3-Methyl-2,3,4,5-tetrahydrobenz[c]azepine-1-thione (IIe). This compound was obtained in 20% yield and had mp 134°C and M 191. $C_{11}H_{13}NS$. Mass spectrum, m/e: 191 (M^+).

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SOME SIDE REACTIONS IN THE TEMPLATE SYNTHESIS OF MACROCYCLIC COMPOUNDS FROM o-AMINO-o'-HALOAZOPYRAZOLES

V. M. Dziomko, B. K. Berestevich, A. V. Kessenikh, R. S. Kuzanyan, and L. V. Shmelev

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Pyrazolo[4,5d]-1,2,3-triazoles and 3,4-dimethyl-1,6-diphenyl-dipyrazolo[4,5-b:4',5'-c]-1,6-dihydropyridazine, the structures of which are confirmed by the mass and PMR spectra, were isolated as side products in the preparation of macrocyclic compounds by the template synthesis of o-amino-o'-haloazopyrazoles. The PMR spectra of pyrazolo[4,5-d]-1,2,3-triazoles are examined in comparison with the PMR spectra of the corresponding noncyclic azopyrazoles. All of the compounds obtained were characterized by the results of elementary analysis and data from the IR, UV, mass, and NMR spectra.

Vicinal triazoles are readily formed by cyclization of aromatic o-aminoazo derivatives under both oxidative [1] and reductive [2] conditions. A triazole ring may also be formed in the reaction of an azo group with an o-phenylhydrazono group [3].

In the present research we studied pyrazolo[4,5-d]-1,2,3-triazoles and dipyrazolopyridazine, which were isolated as side products in the preparation of macrocyclic compounds by template synthesis [4, 5].

Azobispyrazoles IIIa-c were obtained by diazotization in hydrochloric acid of 5-amino-4-bromo-3-methyl-1-R-pyrazoles IIa,b and by coupling at pH 1-2 of diazopyrazoles with 5-amino-3-methyl-1-R-pyrazoles Ia,c,d. Diazo coupling of diazopyrazoles with 5-amino-3-methyl-1-R-pyrazoles was also carried out in [6, 7]; however, satisfactory results were not obtained.

All-Union Scientific-Research Institute of Chemical Reagents and Ultrapure Chemical Substances, Moscow 107258.

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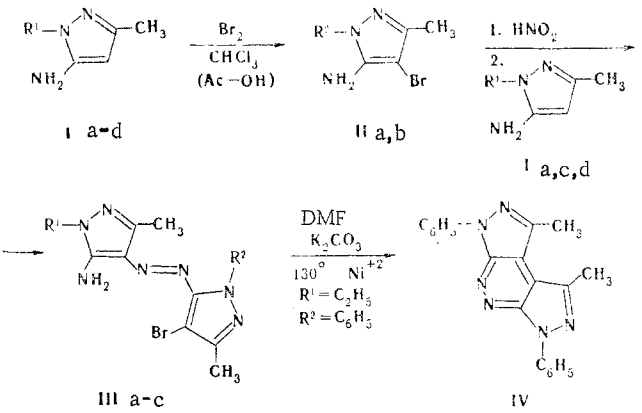


I a R=Et, b R=Pr, c R=*i*-Pr, d R=Ph; II a R=*i*-Pr, b R=Ph; III a R^1=Et, R^2=*i*-Pr; b $R^1=R^2$=*i*-Pr; c R^1=Et, R^2=Ph

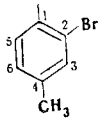
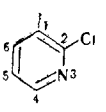
In contrast to N-alkylpyrazole IIa, a nitroso compound is formed in 90% yield in the diazotization of N-arylpyrazole IIb in a small excess of hydrochloric acid [6]. To avoid this process the diazotization of 5-amino-4-bromo(H)-3-methyl-1-arylpyrazoles should be carried out in a strongly acidic medium [6, 7].

When the template condensation of azobispyrazole IIIc was carried out with nickel(II) nitrate hexahydrate, dipyrazolopyridazine IV was isolated from the reaction mixture and identified as the principal product. Its IR spectrum does not contain bands in the region of the stretching vibrations of NH and NH_2 groups. Its PMR spectrum contains a singlet at 2.74 ppm corresponding to two methyl groups (6H) and a well-resolved spectrum of the five-spin N–Ph system (10H), which is possibly associated with the quinoid structure of pyrazoles [8] (the range of the spectrum of the aromatic protons is 1.03 ppm; J^o = 8.0 Hz and J^m = 1.4 Hz are observed distinctly in the spectrum). The molecule has a second-order axis of symmetry, since only two multiplets are present in the PMR spectrum.

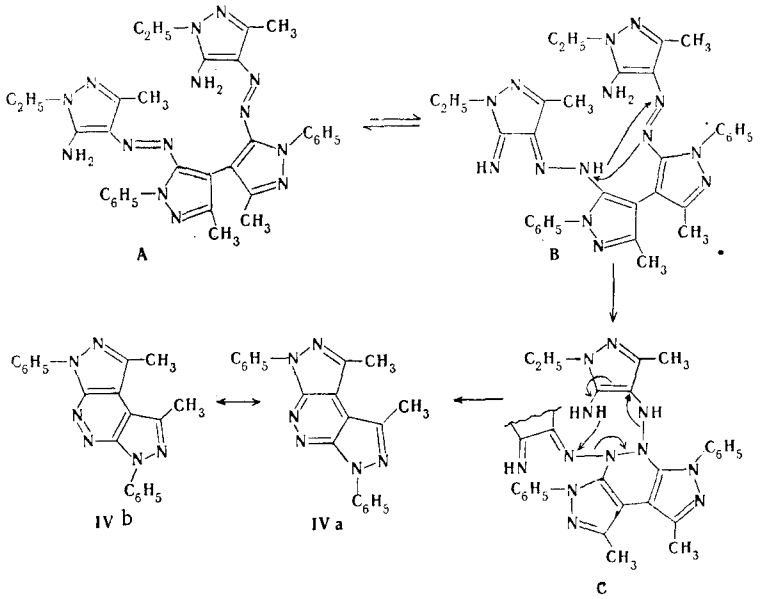
The m/e value of the molecular-ion peaks (M^+) in the mass spectrum of IV [340 mass units (mu)] corresponds to the molecular mass of a substance with the proposed composition. In addition, the spectrum does not contain peaks of ions of the PzN_2^+ and ArN_2^+ type that are characteristic for noncyclic diazo compounds [9] such as arylazopyrazolones [10].

Cleavage of the bonds with the aryl and pyrazole rings is characteristic for noncyclic arylazopyrazolone systems [9], for which the intensities of the resulting PzN_2^+ or ArN_2^+ fragment ions are comparable to the intensities of the molecular-ion peaks [10]. This sort of cleavage is not recorded in the spectrum of the compound under discussion.

TABLE 1. PMR Spectra of VIa-c in $CDCl_3$ (0.2 M)

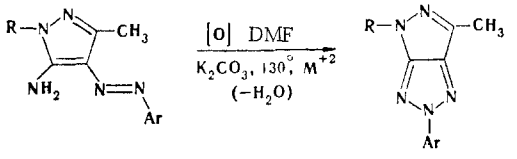
Compound	*T*, °C	R^1	R^2	CH_3	R^1	R^2
VIa	22,5	H		2,52 s	14,93 br s (NH)	2,32 s (CH_3); 7,16 d (5-H, *J*=8,0 Hz); 7,39 br s (3-H); 7,63 d (6-H, *J*=8,0 Hz)
VI b	30	C_3H_7	„	2,55 s	1,59 d ($2CH_3$, *J*=6,0 Hz); 4,59 m (CH, *J*=6,0 Hz)	2,41 s (CH_3); 7,17 dd, q (5-H, *J*=7,9; 1,46; 0,7 Hz); 7,30 dd (6-H, *J*=7,9; 0,28 Hz); 7,33 d, q (3-H, *J*=1,46; 0,38 Hz)
VI c	30	C_6H_5		3,01 s	7,29—7,59 m (3,4,5-H); 7,76—8,14 m (2,6-H)	7,16 dd (5-H, *J*=8,0 Hz); 7,76—8,14 (4-H); 8,51 dd (6-H)

On the basis of the spectroscopic data set forth above it may be assumed that IV has the 3,4-dimethyl-1,6-diphenyldipyrazolo[4,5-b:4',5'-c]-1,6-dihydropyridazine structure. The synthesis of pyridazine IV can be represented by means of the Ullman reaction with the formation of intermediate bisazobispyrazole A or azohydrazone B (semihydrazone form) with subsequent formation of a pyridazine ring. Of the two resonance structures IVa and IVb, we chose IVa.



The results of [11], in which nonequivalence of structures IVa and IVb and higher stability of structure IVa were established on the basis of energy calculations of pyridazine, confirm our conclusion.

When the template cyclization of 5-amino-4-arylazo-3-methyl-1-propylpyrazoles Va-c was carried out in a solution in dimethylformamide (DMF) that was 2.5 times more concentrated than in [4] (all other things being equal), in addition to the formation of macrocyclic metal chelates, we observed the formation of triazepines [12], as well as 2,6-dihydro-2-aryl-4-methyl-1H-pyrazolo[4,5-d]-1,2,3-triazoles VIa-c. The formation of triazoles VIb and VIc has been previously observed in template syntheses [5, 13]; however, dealkylation of the pyrazole N_1 atom of azo compound Va occurred only in this case. The synthesis of pyrazolotriazoles VIa-c can be represented by the following scheme:



V a-c VI a-c

V a R = C_3H_7; V, VI b R = *i*-C_3H_7; c R = C_6H_5; a,b Ar = 2-Br-*p*-tolyl

c Ar = 2-Cl-3-pyridyl, VI a R = H

On passing from azo compounds V to pyrazolo[4,5-d]-1,2,3-triazoles VIa-c, the signals of the protons that are closest to the newly formed ring are shifted to weak field in the PMR spectra (Table 1) (this is most clearly evident in the case of VIc; see Table 2): the signals of the peripheral protons are shifted to stronger field. The shift of the 6-H signal of VIb ($\Delta\delta$ = —0.33) can probably be explained by the weak shielding of the bromotolyl substituent by the triazole ring; consequently, the substituent attached to the triazole N_2 atom does not lie in the plane of the pyrazolotriazole system (Fig. 1).

On the basis of the mass spectra recorded at various ionizing-electron energies it was established that VIa,b are individual substances. The m/e values and the ratios of the M^+ isotope peaks confirm the molecular masses of the substances and the presence of a bromine atom in the molecules. The relative intensities of the M^+ peaks in the spectra of VIa and

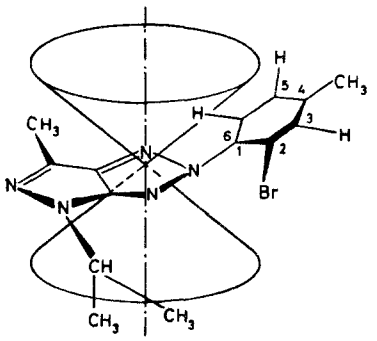


Fig. 1. Magnetic anisotropy of the triazole rings.

TABLE 2. Difference in the Chemical Shifts (CS) ($\Delta\delta$) of Triazoles and Azo Compounds (CS_{VI}—CS_V)

Group of protons	VI a		VIb		VIc	
CH_3		+0,02		+0,08		+0,49
R^2	3-H	−0,06		−0,13	4-H	−0,11
	5-H	+0,10		+0,03	5-H	−0,10
	6-H	+0,07		−0,33	6-H	+0,27
	CH_3	+0,21		+0,08		—
R^1			$2CH_3$	+0,15	2,6-H	+0,48
			CH	**+0,48**	3,4,5-H	−0,03

VIc are 100 and 54%, respectively. The presence of an isopropyl group attached to the pyrazole N_1 atom in VIb is recorded from the characteristic cleavage of the β-C—C bond with splitting out of a methyl group from M+ and the formation of $[M - CH_3]^+$ ions (m/e 318-320, 100%). Similar cleavage is also observed in the case of 5-amino-4-bromo-3-methyl-1-isopropylpyrazole [10]. The principal pathways of fragmentation of the molecular ions of triazoles VIa and VIb are similar to those in the fragmentation of triazole VIc [5]: splitting out of a halogen atom and the formation of ions of the corresponding iminopyrazoles, as well as aryl cations.

EXPERIMENTAL

The IR spectra of solutions of the compounds in $CHCl_3$ were recorded with a UR-20 spectrometer. The UV spectra were obtained with Unicam-100A and SF-4a spectrophotometers. The PMR spectra were recorded with Varian XL-100-12 and Tesla-80 BS-487c spectrometers with tetramethylsilane as the internal standard. The mass spectra were obtained with an MS-702 mass spectrometer with direct introduction of the samples into the ion source; the temperature of the sample-vaporization block was 160-170°C; and the ionizing-electron energy was 70 eV. Thin-layer chromarography (TLC) was carried out on Silufol UV-254 plates for Ia-d in acetone—petroleum ether (5:1) with development with iodine vapors.

5-Amino-3-methylpyrazoles (Ia-d). These compounds were obtained by the methods in [4, 6, 14, 15]. The constants of the compounds obtained were in agreement with the literature data: Ia, mp 99-101°C (mp 100-101°C [14]); Ib, bp 150°C (27 mm) [bp 150°C (27 mm) [4]]; Ic, mp 110-112°C (mp 111-112°C [15]); Id, mp 114-115°C (mp 116°C [6]).

5-Amino-4-bromo-3-methylpyrazoles (IIa,b). These compounds were obtained by the methods in [16, 17]. The constants of the compounds obtained were in agreement with the literature data: IIa, mp 109-110°C (mp 109-110°C [16]); IIb, mp 103-104°C (mp 106.5°C [17]).

5-Amino-4'-bromo-3,3'-dimethyl-4,5'-azobis-1,1'-diisopropylpyrazole (IIIb). A diazonium solution prepared from 10.9 g (0.05 mole) of pyrazole IIa in 200 ml of water, 10 ml (0.1 mole) of concentrated HCl, and 3.45 g (0.05 mole) of sodium nitrate in 15 ml of water was added dropwise with stirring to a solution of 6.95 g (0.05 mole) of pyrazole Ic and 2.0 g of sodium acetate in 250 ml of acetic acid, after which the pH was brought up to 3-5 and the resulting precipitate was removed by filtration, washed with water, dried, and recrystallized from isopropyl alochol to give 2.2 g (11%) of azo compound IIIb with mp 110-112 °C as a yellow crystalline substance that was quite soluble in acetone, ethanol, isopropyl

alcohol, trichloromethane, DMF, and DMSO. Thin-layer chromatography was carried out in acetone–pentane (1:4). PMR spectrum (0.2 M in $CDCl_3$): 1.41 (12H, d, J = 7.0 Hz, $4CH_3$), 4.14 (1H, p, CH), 5.00 (1H, p, CH), 2.25 and 2.41 (6H, s, $2CH_3$), and 5.59 ppm (2H, broad s, NH_2). UV spectrum (in methanol), λ_{max} (log ε): 390 (4.57) and 410 nm (4.57). Found: C 45.7; H 6.0; N 26.7%; M^+ 366. $C_{14}H_{22}N_7Br$. Calculated: C 45.7; H 6.0; N 26.6%; M 367.27.

Compound IIIa was similarly obtained. Thin-layer chromatography in an acetone–pentane system (1:5) gave a product with mp 110-112°C (dec.). PMR spectrum (0.4 M in d_6-acetone): 1.29 (3H, t, J = 7.0 Hz, CH_3), 1.37 (6H, d, J = 6.8 Hz, $2CH_3$), 2.11 (3H, s, CH_3), 2.21 (3H, s, CH_3), 3.89 (2H, q, J = 7.0 Hz, CH_2N); 5.00 (1H, p, J = 6.8 Hz, CH); and 6.70 ppm (2H, broad s, NH_2). UV spectrum (in methanol), λ_{max} (log ε): 385 (4.71) and 410 nm (4.71). Found: C 44.1; H 5.7; N 27.8%; M^+ 353. $C_{13}H_{20}N_7Br$. Calculated: C 44.1; H 5.7; N 27.7%; M 354.26.

5-Amino-4'-bromo-3,3'-dimethyl-4,5'-azobis-1-ethyl-1'-phenylpyrazole (IIIc). A diazonium solution prepared from 1.2 g (5 mmole) of pyrazole IIb in 20 ml of water, 20 ml of acetic acid, 1.0 ml of concentrated HCl, and 0.35 g of sodium nitrite in 5 ml of water was added to a solution of 0.625 g (5 mmole) of pyrazole Ia in 25 ml of acetic acid, and the mixture was allowed to stand for 30 min. The pH was then adjusted to 3-5 and the resulting precipitate was removed by filtration, washed with water, dried, and recrystallized from DMF to give 1.40 g (38%) of azo compound IIIc as a yellow crystalline substance that was quite soluble in trichloromethane and acetone. Thin-layer chromatography was carried out in an acetone–pentane system (1:5). PMR spectrum (0.1 M in d_6-acetone): 1.25 (3H, 6, J = 7.0 Hz, CH_3), 3.85 (2H, q, J = 7.0 Hz, CH_2N), 2.23 (6H, s, $2CH_3$), and 7.30-7.67 ppm (5H, m, Ph). UV spectrum (methanol), λ_{max}(log ε): 390 (4.52) and 420 nm (4.53). Found: C 49.5; H 4.7; N 25.3%; M^+ 387. $C_{16}H_{18}N_7Br$. Calculated: C 49.5; H 4.7; N 25.3%: M 388.27.

3,4-Dimethyl-1,6-diphenyldipyrazolo[4,5-b:4',5'-c]-1,6-dihydropyridazine (IV). A mixture of 3.30 g (0.024 mole) of potassium carbonate, 1.54 g (2 mmole) of nickel(II) nitrate hexahydrate, and 0.588 g (17 mmole) of azobispyrazole IIIc was heated in 120 ml of DMF at 130-140°C for 4 h [with monitoring by TLC in an acetone–petroleum ether system (1:5)]. The reaction mixture was then cooled, and the resulting precipitate was removed by filtration. Water (300 ml) was added to the mother liquor, and the newly formed precipitate was removed by filtration, washed successively with water, DMF–H_2O (1:5), water, 10% HCl solution, and water, and air dried. The second fraction from repeated column chromatography on neutral Al_2O_3 (activity II, elution with benzene) was collected, the benzene was evaporated, and the residue was recrystallized from trichloromethane to give 0.042 g (15%) of yellow finely crystalline IV with mp 107-109°C. The product was quite soluble in DMF, DMSO, and trichloromethane. Thin-layer chromatography was carried out in an acetone–hexane system (1:5). PMR spectrum (0.2 M in $CDCl_3$): 2.74 (3H, s, CH_3), 7.21 (1H, dd, J = 8.0 and 1.4 Hz, 4H), 7.48 (2H, d, J = 8.0 Hz, 3,5-H), 8.24 (2H, dd, J = 8.0 and 1.4 Hz, 2,6-H). UV spectrum ($CHCl_3$), λ_{max}(log ε): 420 (3.70). Found: C 70.5; H 4.7; N 24.8%; M^+ 340. $C_{20}H_{16}N_6$. Calculated: C 70.6; H 4.7; N 24.7%; M 340.39.

2,6-Dihydro-2-(2-bromo-4-methyl)-4-methyl-6H-pyrazolo[4,5-d]-1,2,3-triazole (VIb). This compound was obtained in the synthesis of [1,10,11,20-tetrahydro-1,11-dipropyl-3,8,13,18-tetramethyldibenzo[c,j]dipyrazolo[3,4-f:3',4'-m][1,2,5,8,9,12]hexaazacyxlotetradecenato(2-)-$N^{4(5)}$, N^{10}, $N^{14(15)}$, N^{20}]nickel. A mixture of 2.016 g (6 mmole) of 5-amino-4-(2-bromo-4-methylphenylazo)-3-methyl-1-propylpyrazole, 0.87 g (3 mmole) of nickel(II) nitrate hexahydrate, 4.84 g (0.035 mole) of potassium carbonate, and 500 ml of DMF was stirred at 150°C for 10 h. The course of the reaction was monitored by TLC [acetone–pentane (1:5)]. The reaction mixture was cooled and filtered, and the filtrate was diluted with 500 ml of water. The resulting precipitate was removed by filtration, and the mother liquor was acidified to pH 3-5 with 5% HCl solution. The precipitate was removed by filtration, washed with water, air dried, and recrystallized twice from a small amount of $CHCl_3$ or $CHCl_3$–CCl_4 (1:2) to give 0.38 g (22%) of yellow finely crystalline VIa with mp 129-130°C. The product was quite soluble in trichloromethane, DMF, and DMSO but insoluble in water. Thin-layer chromatography was carried out in an acetone–petroleum ether system (1:5). UV spectrum ($CHCl_3$), λ_{max}(log ε), 430 (3.25). Found: C 45.3; H 3.4; N 23.9%; M^+ 291. $C_{11}H_{10}N_5Br$. Calculated: C 45.2; H.3.5; N 24.0%; M 292.14.

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