bonyl-4-(2-nitrosophenyl)pyridine was synthesized according to a somewhat modified procedure of [4] and purified by chromatography on a column with aluminum oxide. Nitrobenzene (Janssen) and 2-nitrotoluene (Aldrich) were used without additional purification. The antioxidant activity was determined according to the procedure of [5].

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SYNTHESIS OF 9-CHLOROPYRAZOLO[4,3-b]QUINOLINES

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A series of 1-methyl-4-arylaminopyrazole-3- and -5-carboxylic acids were synthesized by the reaction of 1-methyl-4-halopyrazole-3- and -5-carboxylic acids with aromatic amines in the presence of a copper catalyst; treatment with phosphorus oxychloride converted them to the corresponding 9-chlorosubstituted 1-methyl-1H- and 2-methyl-2H-pyrazolo[4,3-b]quinolines.

Although pyrazolo[4,3-b]quinolines were produced more than 20 years ago [1], up to the present time no convenient method of their synthesis has been found. The method of [2, 3] are characterized by insufficiently high yields or start with difficult-to-obtain compounds.

Yet, among the isomeric pyrazolo[3,4-b]quinolines, effective optical bleaches [4] and substances possessing a broad spectrum of biological activity [5, 6] have been found.

A convenient method for producing pyrazolo[3,4-b]quinolines, consisting of the interaction of 5-amino-1-methylpyrazole with 2-iodobenzoic acid, followed by treatment of 5-(2-carboxyphenylamino)pyrazole with a condensing agent [7], proved inapplicable to the synthesis of pyrazolo[4,3-b]quinolines in view of the sensitivity of 4-aminopyrazoles to the action of atmospheric oxygen.

We have developed a method including aramination of 1-methyl-4-halopyrazole-3- or -5-carboxylic acids by aromatic amines, followed by treatment of the 4-arylaminosubstituted pyrazolecarboxylic acids with phosphorus oxychloride. The method permits the production of 9-chlorosubstituted pyrazolo[4,3-b]quinolines with a yield of 60-70%.

1-Methyl-4-chloropyrazolecarboxylic acids do not react with aromatic amines. Compound Ia, reacting with pyrazole, forms 1-methyl-4-(1-pyrazolyl)pyrazole-5-carboxylic acid (VII); when other pyrazolecarboxylic acids were used, no replacement of a halogen atom by a pyrazole residue was observed.

Together with arylamination in the interaction with aromatic amines, compounds I and IV undergo reductive dehalogenation with the formation of pyrazolecarboxylic acids.

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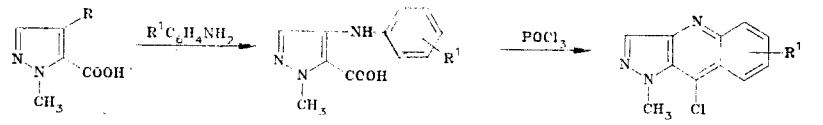
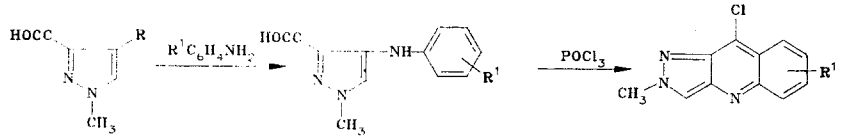
TABLE 1. 4-Arylaminopyrazole-5- and -3-Carboxylic Acids (IIa-g, Va-c)

Compound	mp, °C	Found, %			Empirical formula	Calculated,			Yield, %
		C	H	N		C	H	N	
IIa	185—186	61,3	5,4	19,6	$C_{11}H_{11}N_3O_2$	60,9	5,1	19,4	84
IIb	193—194	62,8	5,6	18,2	$C_{12}H_{13}N_3O_2$	62,5	5,6	18,2	77
IIc	186—188	52,4	3,9	16,7	$C_{11}H_{10}ClN_3O_2$	52,5	4,0	16,7	91
IId	180—181	58,0	5,7	16,6	$C_{12}H_{13}N_3O_3$	58,3	5,3	17,0	73
IIe	237—238	50,1	3,4	21,6	$C_{11}H_{10}N_4O_4$	50,4	3,8	21,4	60
IIf	201—202	58,0	5,7	16,7	$C_{12}H_{13}N_3O_3$	58,3	5,3	17,0	70
IIg	246—248	50,2	3,6	21,2	$C_{11}H_{10}N_4O_4$	50,4	3,8	21,4	58
Va	188—190	60,7	4,9	19,3	$C_{11}H_{11}N_3O_2$	60,9	5,1	19,4	65
Vb	250—251	62,1	5,5	18,0	$C_{12}H_{13}N_3O_2$	62,5	5,6	18,2	71
Vc	187—189	58,0	5,8	16,4	$C_{12}H_{13}N_3O_3$	58,3	5,3	17,0	64

When the acids IIa-g and Va-c are treated with excess phosphorus oxychloride, the corresponding 9-chlorosubstituted 1-methyl-1H-pyrazolo-[4,3-b]quinolines (IIIa-g) and 2-methyl-2H-pyrazolo[4,3-b]quinolines (VIa-c) are formed (Tables 2 and 3).



I a,b II a-g III a-g



IV a,b V a-c VI a-c

I a R=Br; b R=I; II a R^1=H; b R^1=4-CH_3; c R^1=4-Cl; d R^1=4-OCH_3; e R^1=4-NO_2; f R^1=2-OCH_3; g R^1=2-NO_2; III a R^1=H; b R^1=7-CH_3; c R^1=7-Cl; d R^1=7-OCH_3; e R^1=7-NO_2; f R^1=5-OCH_3; g R^1=5-NO_2; IV b R=Br; b R=I; V a R^1=H; b R^1=4-CH_3; c R^1=4-OCH_3; VI a R^1=H; b R^1=7-CH_3; c R^1=7-OCH_3

The corresponding pyrazolo[4,3-b]quinolin-9-one (VIII) is obtained from compound IIIc by boiling in 50% acetic acid or in a 10% NaOH solution. In the reaction of pyrazoloquinoline IIIa with morphiline, 1-methyl-9-(4-morpholinyl)-1H-pyrazolo[4,3-b]quinoline (IX) was isolated with a 75% yield.

EXPERIMENTAL

The UV spectra were recorded on a Specord UV-vis instrument in ethanol; the mass spectra were recorded on a MX-1303 instrument with energy of ionization 70 eV. The individuality of the compounds obtained was monitored by thin-layer chromatography (silufol UV-254, benzene—ethanol, 5:1).

4-Halopyrazolecarboxylic acids Ia, b, and IVa, b were produced according to [8].

4-Arylamino-1-methylpyrazole-5- and -3-Carboxylic Acids (IIa-g, Va-c). A mixture of 0.02 mole of 4-halo-1-methylpyrazolecarboxylic acid Ia, b, IVa, b, 0.022 mole of the corresponding aniline, and 0.1 g of powdered copper was heated in 100 ml of a 5% soda solution for 6 h at 100°C (80-90°C for compounds Ib and IVb). The catalyst was filtered off, and the filtrate acidified with HCl. The precipitate was filtered off and crystallized from 70% acetic acid. We obtained the corresponding 4-arylamino-1-methylpyrazolecarboxylic acids IIa-g, Va-c (Table 1).

1-Methyl-4-(1-pyrazolyl)pyrazole-5-carboxylic Acid (VII). A mixture of 5.0 g (0.02 mole) of compound Ib, 2.0 g (0.025 mole) pyrazole, and 0.1 g of powdered copper in 100 ml of a 5% soda solution was heated for 8 h at 100°C. The product was isolated analogously to the preceding procedure. Yield 1.85 g (48%) of compound VII, mp 174-175°C (from ethanol). Found: C 49.9; H 4.5; N 28.9%. $C_8H_8N_4O_2$. Calculated: C 50.0; H 4.2; N 29.2%.

TABLE 2. 9-Chlorosubstituted 1-Methyl-1H-pyrazolo[4,3-b]quinolines (IIIa-g) and 2-Methyl-2H-pyrazolo[4,3-b]quinolines (VIa-c)

Compound	mp, °C	Found, %				Empirical formula	Calculated, %				M^+	Yield, %
		C	H	N	Cl		C	H	N	Cl		
IIIa	145—146	60,4	3,6	19,2	16,5	$C_{11}H_8ClN_3$	60,7	3,7	19,3	16,3	217/219	89
IIIb	172—173	62,6	4,3	18,0	15,0	$C_{12}H_{10}ClN_3$	62,2	4,3	18,1	15,3	231/233	90
IIIc	176—178	52,0	2,9	16,1	28,8	$C_{11}H_7Cl_2N_3$	52,4	2,8	16,5	28,4	251/253/255	93
IIId	164—165	57,9	3,8	17,4	14,0	$C_{12}H_{10}ClN_3O$	58,2	4,0	17,0	14,3	247/249	95
IIIe	211—212	50,5	3,6	20,9	13,8	$C_{11}H_7ClN_4O_2$	50,3	3,8	21,3	13,5	262/264	71
IIIf	155—157	58,0	4,1	17,3	14,1	$C_{12}H_{10}ClN_3O$	58,2	4,0	17,0	14,3	247/249	97
IIIg	199—201	49,9	3,6	21,2	13,8	$C_{11}H_7ClN_4O_2$	50,3	3,8	21,3	13,5	262/264	64
VIa	175—178	61,0	3,6	19,6	16,0	$C_{11}H_8ClN_3$	60,7	3,7	19,3	16,3	217/219	82
VIb	199—200	61,8	4,0	18,0	15,7	$C_{12}H_{10}ClN_3$	62,2	4,3	18,1	15,3	231/233	94
VIc	215—216	58,0	4,3	17,4	14,0	$C_{12}H_{10}ClN_3O$	58,2	4,0	17,0	14,3	247/249	92

TABLE 3. UV Spectra of Pyrazoloquinolines III and VI

Compound	UV spectrum, λ_{max}, nm (log ε)
IIIa	246 (5,08), 318 (3,71), 333 (3,92), 373 (3,82), 390 (3,81)
IIIb	248 (4,90), 326 (3,58), 339 (3,81), 371 (3,64), 389 (3,60)
IIIc	250 (5,03), 328 (3,69), 341 (3,93), 375 (3,77), 392 (3,74)
IIId	251 (4,84), 349 (4,10), 366 (3,80), 386 (3,75)
IIIe	246 (4,25), 296 (3,81), 328 (3,41), 341 (3,39), 406 (3,30)
IIIf	251 (4,84), 349 (4,54), 369 (3,74), 389 (3,74), 406 (3,30)
IIIg	246 (4,12), 333 (3,61), 392 (3,54)
VIa	242 (4,91), 326 (3,98), 340 (4,07), 389 (3,94), 411 (3,83)
VIb	246 (4,91), 330 (3,98), 347 (4,07), 389 (3,85), 411 (3,83)
VIc	246 (4,81), 336 (4,07), 352 (4,31), 390 (3,88), 413 (4,07)

9-Chlorosubstituted 1-Methyl-1H-pyrazolo[4,3-b]quinolines (IIIa-g) and 2-Methyl-2H-pyrazolo[4,3-b]quinolines (VIa-c). A 0.01 mole portion of the corresponding acid IIa-g or Va-c was boiled in 10 ml of $POCl_3$ for 30 min. After cooling the solution was poured out into a 10% soda solution; the precipitate formed was removed and recrystallized from ethanol. The corresponding pyrazolo[4,3-b]quinolines IIIa-g, VIa-c were obtained (Tables 2 and 3).

7-Chloro-1-methyl-1H,4H,9H-pyrazolo[4,3-b]quinolin-9-ones (VIII). A. We boiled 1.25 g (0.005 mole) of compound IIIc with 20 ml of 10% NOH for 2 h. The mixture was cooled and diluted with 100 ml of water. The precipitate was removed and crystallized from DMFA. Yield 1.1 g (95%), mp 354-356°C (358-360° [2]).

B. For 30 min 1.25 g (0.005 mole) of compound IIIc was heated with 20 ml of 50% acetic acid, neutralized with soda solution, the precipitate removed and dried. Yield 1.0 g (86%).

1-Methyl-9-(4-morphilinyl)-1H-pyrazolo[4,3-b]quinoline (IX). We heated 2.17 g (0.01 mole) of the pyrazoloquinoline IIIc in 10 ml of morphiline for 3 h at 120°C. After cooling the reaction mass was diluted with 20 ml of water. The precipitate was filtered off and dried. Yield 2.0 g (75%), mp 204-205°C (from ethanol). Found: C 66.8; H 5.4; N 21.3%. $C_{15}H_{16}N_4O$. Calculated: C 67.2; H 5.6; N 20.9%.

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