SYNTHESIS AND PROPERTIES OF SALTS OF 2-SUBSTITUTED DERIVATIVES OF 1,6-DIMETHYL-7-CHLORO-1,6-DIAZAPHENALENIUM SALTS. III.*

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A series of 2-substituted 1,6-diazaphenalene derivatives, the subsequent alkylation of which give 1,6-dimethyl-2-R-7-chloro-1,6-diazaphenalenium salts, was obtained by cyclization of acyl derivatives of 5-amino- and 5-methylamino-8-chlorolepidines. A study of the absorption spectra of the salts attests to the fact that, as in cyanine dyes, electron-donor substituents heighten the color, while electron-acceptor substituents deepen it.

In developing our previous research [1] it was of interest to obtain 1,6-diazaphenalene derivatives and to investigate the effect of substituents on the spectral characteristics of their quaternary salts, which can be considered to be "aromatic cyanines."

As already reported, 7-chloro-1,6-diazaphenalene forms 5-formylamino-8-chlorolepidine during intramolecular condensation. It seemed possible to use this method also for other acylaminolepidines; this would make various 2-substituted 1,6-diazaphenalenes accessible. With this end in mind, we synthesized 2-acetyl- (II) and 2-aroylamino-8-chlorolepidines (III-VI) by acylation of 5-amino-8-chlorolepidine (I). In fact, it was found that II-VI, like 5-formylamino-8-chlorolepidine, are readily converted to the corresponding 2-substituted 1,6-diazaphenalenes (VII-XI) under the influence of phosphorus oxychloride. They were isolated as the perchlorates or hydrochlorides, since bases VII-XI, like the previously described 1H-7-chloro-1,6-diazaphenalene [1], proved to be unstable. The instability of the bases of the diazaphenalene series with an unsubstituted NH group hinders both a study of the properties of these compounds and the preparation of the corresponding quaternary salts. At the same time, as was previously established, N-methyl derivatives of diazaphenalene, which are incapable of ionization to form an anion, are completely stable. In order to obtain such compounds with substituents in the 2 position, we synthesized a series of acyl derivatives (XII-XVI) of 5-methylamino-8-chlorolepidine. We were able to obtain the latter not only by acylation of 5-methylamino-8-chlorolepidine but also by alkylation of 5-aroylaminolepidines (III-VI) in aprotic media by the action of methyl iodide or dimethyl sulfate. This reaction gives good yields and is readily monitored by thin-layer chromatography (TLC).

The cyclization of XII-XVI to 2-substituted 1-methyl-1,6-diazaphenalenes (XVII-XXI) also proceeded without difficulty. As assumed, XVII-XXI proved to be stable in both the salt and base forms.

* See [1] for communication II.

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TABLE 1. Acyl Derivatives of 5-Amino- and 5-Methylamino-8-chlorolepidine

Compound	R	mp, °C	R_f*	Empirical formula	Found, %		Calc., %		Yield, %	λ_{max}, nm	lg ε	λ_{max}, nm	lg ε
					N	Cl	N	Cl					
II	CH_3	216—217	0,7	$C_{12}H_{11}ClN_2O$	11,8	14,9	11,9	15,1	92	235	4,36	300	3,67
III	C_6H_5	236—239	0,54	$C_{17}H_{13}ClN_2O$	9,5	12,1	9,5	12,0	95	235	4,64	300	3,94
IV	$C_6H_4CH_3$	222—223	0,56	$C_{18}H_{15}ClN_2O$	9,1	11,4	9,02	11,7	95	235	4,48	300	3,78
V	$C_6H_4OCH_3$	223	0,55	$C_{18}H_{15}ClN_2O_2$	8,7	10,7	8,6	10,9	80	237	4,56	300	4,00
VI	C_6H_4Cl	229	0,55	$C_{17}H_{12}Cl_2N_2O$	9,0	22,4	8,9	22,4	80	235	4,65	300	3,93
XII	CH_3	185—186	0,4	$C_{13}H_{13}ClN_2O$	11,4	14,3	11,3	14,3	83	233	4,40	295	3,73
XIII	C_6H_5	140	0,4	$C_{18}H_{15}ClN_2O$	8,9	11,3	9,0	11,4	80	236	4,38	303	3,73
XIV	$C_6H_4CH_3$	182	0,45	$C_{19}H_{17}ClN_2O$	8,9	11,1	8,6	10,9	75	237	4,57	303	3,91
XV	$C_6H_4OCH_3$	181	0,36	$C_{19}H_{17}ClN_2O_2$	8,3	10,6	8,2	10,4	75	237	4,53	303	3,87
XVI	$C_6H_4NO_2$	212	0,39	$C_{18}H_{14}ClN_3O_3$	11,9	10,3	11,8	10,6	70	237	4,41	290	3,95

* On activity II Al_2O_3 in chloroform.

The structures of the 2-substituted 1,6-diazaphenalenes (VII-XI, XVII-XXI) are confirmed on examination of the spectra of these compounds. While amides II-VI and XII-XVI are colorless substances (λ_{max} < 305 nm,

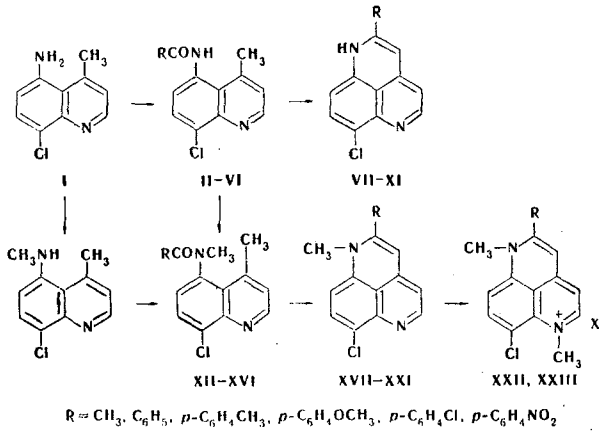

Table 1), the formation of a single conjugated diazaphenalene system leads to a sharp shift in the absorption to the visible region (λ_{max} ~ 430 nm, Table 2). The salts of the diazaphenalene derivatives have an even deeper color, although the bathochromic shift is much lower (~ 20-30 nm) in this case than on passing from the amides to the diazaphenalenes. Moreover, it should be noted that the absorption spectra of the salts of nitrogen-unsubstituted and N-methyl derivatives are similar.

Bands of the stretching and deformation vibrations of the NH groups, and the aromatic C=C and C—H bonds are present in the IR spectra of the salts of VII-XI. The signal of three protons of the methyl group (2.7 ppm) and the signals of the aromatic protons at weaker field (7.5-9.3 ppm) are observed in the PMR spectrum of 1H-2-methyl-7-chloro-1,6-diazaphenalene perchlorate (VII, in CF_3COOH). The band of the stretching vibrations of the CH_3 group (2900-3000 cm^{-1}) and bands of the aromatic C—C and C—H bonds are present in the IR spectra (KBr) of the bases of the N-methyl derivatives of 1,6-diazaphenalene (XVII-XXI). Signals of the N-CH_3 group (δ 4.35 ppm) and of the aromatic protons (7.5-9.3 ppm) are observed in the PMR spectra of solutions of XVII-XXI in CF_3COOH, and the spectrum of the 1,2-dimethyl derivative (XVII) additionally contains the signal of a C—CH_3 group (2.9 ppm) approximately in the same region as for the nitrogen-unsubstituted VII.

The stability of the bases of the N-methyl derivatives of diazaphenalene made it possible to quaternize these compounds. The methylation of 1,2-dimethyl- (XVII) and 1-methyl-2-phenyl-7-chloro-1,6-diazaphenalene (XVIII) with dimethyl sulfate and methyl tosylate, respectively, gave 1,2,6-trimethyl-7-chloro-1,6-diazaphenalenium methosulfate (XXII) and 1,6-dimethyl-2-phenyl-7-chloro-1,6-diazaphenalenium tosylate, which was isolated and purified as the perchlorate (XXIII). The structures of XXII and XXIII are confirmed by their PMR and electronic spectra. One signal of the protons of two N-methyl groups (4.5 ppm), the signal of C—CH_3 protons (2.9 ppm), and the signals of aromatic protons are observed in the PMR spectrum of

TABLE 2. 2-Aryl Derivatives of 1,6-Diazaphenalene

Compound	R	mp, °C	R_f*	Empirical formula	Found, %		Calc., %		λ_{max}, nm (lg ε)†
					Cl	N	Cl	N	
VII · $HClO_4$	CH_3	254—255	0,5	$C_{12}H_9ClN_2 \cdot HClO_4$	22,5	8,9	22,4	8,9	270, 305, 355, 442, (4,23; 3,85; 3,68; 3,84)
VIII · HCl	C_6H_5	298—299	0,62	$C_{17}H_{11}ClN_2 \cdot HCl$	22,7	8,4	22,5	8,6	245, 290, 363, 464 (4,03; 4,25; 3,57; 3,51)
IX · $HClO_4$	$C_6H_4CH_3$	298—300	0,60	$C_{18}H_{13}ClN_2 \cdot HClO_4$	18,0	7,4	18,1	7,1	247, 300, 363, 464 (4,22; 4,40; 3,69; 3,83)
X · $HClO_4$	$C_6H_4OCH_3$	>300	0,64	$C_{18}H_{13}ClN_2O \cdot HClO_4$	17,8	7,0	17,4	6,9	253, 312, 364, 462 (4,39; 4,47; 3,74; 3,95)
XI · HCl	C_6H_4Cl	299—302	0,69	$C_{17}H_{10}Cl_2N_2 \cdot HCl$	29,5	7,8	29,8	8,0	250, 293, 364, 468 (4,19; 4,43; 3,71; 3,59)
XVII	CH_3	222—223	0,47	$C_{13}H_{11}ClN_2$	15,2	12,4	15,4	12,3	255, 325, 380, 425 (4,30; 3,99; 3,88; 3,85)
XVIII	C_6H_5	219	0,35	$C_{18}H_{13}ClN_2$	12,4	9,8	12,1	9,6	260, 328, 376, 435 (4,23; 3,87; 3,83; 3,69)
XIX	$C_6H_4CH_3$	207	0,30	$C_{19}H_{15}ClN_2$	11,2	9,5	11,6	9,2	260, 328, 378, 435 (4,28; 3,92; 3,90; 3,76)
XX	$C_6H_4OCH_3$	207	0,26	$C_{19}H_{15}ClN_2O$	10,9	8,5	11,0	8,7	260, 328, 378, 436 (4,36; 4,03; 4,02; 3,92)
XXI	$C_6H_4NO_2$	209—211	0,35	$C_{18}H_{12}ClN_3O_2$	10,4	12,2	10,5	12,4	267, 325, 376, 458 (4,33; 4,13; 4,00; 3,72)
XVIII · $HClO_4$	CH_3	>300	0,35	$C_{13}H_{11}ClN_2 \cdot HClO_4$	21,2	8,6	21,4	8,5	265, 310, 360, 440 (4,20; 3,95; 3,69; 3,96)
XVIII · HCl	C_6H_5	—	—	$C_{18}H_{13}ClN_2 \cdot HCl$	—	—	—	—	285, 310, 360, 455 (4,36; 4,05; 3,78; 4,07)
XIX · HCl	$C_6H_4CH_3$	—	—	$C_{19}H_{15}ClN_2 \cdot HCl$	—	—	—	—	260, 295, 360, 455 (4,22; 4,31; 3,75; 4,08)
XX · HCl	$C_6H_4OCH_3$	—	—	$C_{19}H_{15}ClN_2O \cdot HCl$	—	—	—	—	255, 312, 360, 455 (4,04; 4,02; 3,45; 3,80)

* On activity II Al_2O_3, in chloroform.

† The electronic absorption spectra of the hydrochlorides of XVIII-XX were recorded in acidic alcohol solutions of the corresponding bases.

XXII (in CF_3COOH). Thus the PMR spectra make it possible to conclude that the N-methyl groups in the quaternary salts are equivalent and, consequently, that the distribution of positive charge between the nitrogen atoms is uniform.

The electronic spectra of XXII and XXIII are characterized by four intense absorption maxima, and, just as in 1H-7-chloro-1,6-diazaphenalene, alkylation of the nitrogens does not have a substantial effect on the position of the long-wave maximum but does increase its intensity considerably. An electron-acceptor substituent (phenyl) in the 2 position causes deepening of the color, while an electron-donor substituent (methyl) heightens the color. The same shift of the absorption maximum of the long-wave band is also observed in cyanine dyes when substituents enter into the outer ring. Thus, the 1,6-diazaphenalenium salts obtained are stable and have intense color; this justifies calling them aromatic cyanines.

EXPERIMENTAL

5-Acetamido-8-chlorolepidine (II). A solution of 0.8 g (4 mmole) of 5-amino-8-chlorolepidine (I) in 8 ml of acetic acid and 0.6 ml (6.4 mmole) of acetic anhydride was refluxed for 1 h, after which the excess acetic acid was removed by distillation, and 20 ml of water was added. The resulting precipitate was removed by filtation and dried to give 0.9 g (100%) of II as colorless needles with mp 216-217° [from ethanol (1 : 50)]. Found: C 56.1; H 5.4; Cl 14.9; N 11.8%. $C_{12}H_{11}ClN_2O$. Calculated: C 56.2; H 4.7; Cl 15.1; N 11.9%.

5-(4-R-Benzamido)-8-chlorolepidines (III-VI, Table 1). A 1-g (5 mmole) sample of I was heated in 10 ml of anhydrous toluene, 8 mmole of the appropriate acid chloride (benzoyl chloride or p-chloro-, p-methyl-, or p-methoxybenzoyl chloride) was added, and the mixture was stirred and refluxed for 1 h. The precipitate was removed by filtration, dried, and crystallized from butanol. Compounds III-VI were obtained as colorless plates that were quite soluble in dimethylformamide but insoluble in low-polarity solvents.

1H-2-R-7-Chloro-1,6-diazaphenalenium Salts (VII-XI, Table 2). A 1-g sample of the appropriate acyl derivative of I (II-VI) and 10 ml of $POCl_3$ were heated in sealed ampuls at 150-200° for 3 h. The excess $POCl_3$ was removed by vacuum distillation, water was added to the residue, and the resulting solution was boiled with activated charcoal. Addition of the appropriate acid yielded the perchlorates or hydrochlorides of 2-substituted 1,6-diazaphenalenes, which were crystallized from ethanol.

5-Acetylmethylamino-8-chlorolepidine (XII). This compound was obtained in 83% yield by acetylation of 5-methylamino-8-chlorolepidine, as in the preparation of II. The colorless needles had mp 185-186° [from CCl_4 (1 : 50)]. Found: C 62.9; H 5.4; Cl 14.3; N 11.4%. $C_{13}H_{13}ClN_2O$. Calculated: C 63.0; H 5.3; Cl 14.3; N 11.3%.

5-(4-R-Benzoylmethylamino)-8-chlorolepidines (XII-XVI, Table 1). A. A 1-g (4.9 mmole) sample of 5-methylamino-8-chlorolepidine was dissolved in a mixture of 10 ml of toluene and 1 ml of pyridine, and the solution was heated to 80°. A 7.2-mmole sample of the appropriate acid chloride (benzoyl chloride or p-nitro-, p-methyl-, or p-methoxybenzoyl chloride) was added, and the mixture was refluxed for 1 h. The pyridine hydrochloride was removed by filtration, the solvent was removed by vacuum distillation, and the residue was crystallized from ethanol (1:30). Compounds XII-XVI were obtained as colorless plates.

B. A solution of 0.68 ml (6.8 mmole) of dimethyl sulfate in 4 ml of acetone was added to a hot mixture of 3.4 mmole of the appropriate aroyl derivative of I (III-VI), 0.4 g (10 mmole) of finely ground sodium hydroxide, and 20 ml of acetone, and the mixture was refluxed for 1 h. The precipitate was removed by filtration, a large portion of the solvent was removed from the filtrate by distillation, and 20 ml of water was added to the residue. The precipitate was removed by filtration and crystallized from ethanol (1:30) to give a product in 70% yield. The compounds obtained by methods A and B were identical.

1-Methyl-2-R-7-chloro-1,6-diazaphenalenes (XVII-XXI, Table 2). A 1-g sample of the appropriate acyl derivative of I (XII-XVI) and 10 ml of freshly distilled phosphorus oxychloride were heated in a sealed ampul at 200° for 3 h. A large portion of the $POCl_3$ was removed by vacuum distillation, water was added to the residue, and the solution was boiled with activated charcoal. The base was precipitated by the addition of alkali solution. The compounds were crystallized from ethanol and were obtained as bright-yellow plates.

1,2,6-Trimethyl-7-chloro-1,6-diazaphenalenium Methosulfate (XXII). A 1-g (4.4 mmole) sample of XVII and 4 ml (44 mmole) of dimethyl sulfate were heated in a test tube with a calcium chloride tube at 140° for 2 h. The dimethyl sulfate was washed out with ether, and ethanol was added to the residue to precipitate the product. It was removed by filtration and dried to give 1.1 g (71%) of XXII. Crystallization from ethanol (1:40) gave bright-yellow needles. UV spectrum, nm (log ε): 278 (4.38), 315 (3.92), 360 (3.62), 440 (3.96). Found: Cl 9.8; N 7.5%. $C_{15}H_{17}ClN_2O_4S$. Calculated: Cl 9.7; N 7.9%.

1,6-Dimethyl-2-phenyl-7-chloro-1,6-diazaphenalenium Perchlorate (XXIII). A 1.5-g (5.1 mmole) sample of XVIII and 4.8 g (25 mmole) of methyl p-toluenesulfonate were fused at 130° for 4 h. The mixture was cooled and dissolved in 30 ml of 0.1 N HCl, and the solution was boiled with activated charcoal and filtered. The addition of 56% $HClO_4$ precipitated 1.7 g (70%) of XXIII. Crystallization from acetic acid (1:50) gave yellow needles with mp 255-255.5°. UV spectrum, nm (log ε): 285 (4.36), 316 (4.02), 366 (3.72), 456 (4.12). Found: Cl 17.5; N 6.9%. $C_{19}H_{16}Cl_2N_2O_4$. Calculated: Cl 17.5; N 6.9%.

The electronic absorption spectra of alcohol solutions of II-XXI ($c = 0.4 \cdot 10^{-4} - 0.6 \cdot 10^{-4}$ M) were recorded with an SF-8 spectrometer.

LITERATURE CITED

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