AROMATIC CYANINES

II.* SYNTHESIS AND PROPERTIES OF 1H-1,6-DIAZAPHENALENE DERIVATIVES

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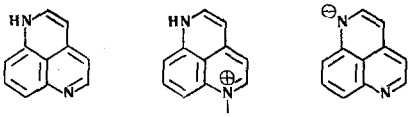
UDC 547.836.3:541.67

The cyclization of 5-formylmethylamino-8-chlorolepidine and subsequent alkylation gave a 1,6-dimethyl-7-chloro-1,6-diazaphenalenium salt, one of the representatives of compounds previously called aromatic cyanines. The spectral characteristics and chemical properties of this salt are in close agreement with the results of calculations by the Hückel MO method.

A theoretical examination of aromatic cations that contain mutually conjugated "pyrrole" and "pyridine" nitrogen atoms demonstrated that they should be stable and deeply colored. We decided to begin our experimental study of this type of compound with the 1,6-diazaphenalenium cation. Since neither this cation nor 1H-1,6-diazaphenalene itself have been described in the literature, we made a preliminary calculation of 1H-1,6-diazaphenalene (I), its cation (II), and anion (III) by the Hückel MO method.



I II III

The calculations of I-III were performed both under the assumption of nonequivalence of the nitrogen atoms and under the assumption that they are equivalent. In the latter case, the parameters for N were taken as the arithmetic mean of the parameters of nitrogen in the corresponding valence states ("averaged parameters"). A comparison of the results of calculations with the application of the heteroatom parameters recommended by Streitwieser [2], by Brown [3], and the "averaged" parameters makes it possible to conclude that the character of the distribution of the electron density, the bond orders (Table 1), and the ratio of the delocalization energy per electron (DE) of I-III do not change substantially when the h_N and k_{CN} values are varied. The calculations also demonstrated that I-III, particularly cation II, should be completely thermodynamically stable: E_π and DE (in β_0 units) were found to be 20.28 and 0.41 for I, 22.59 and 0.62 for II, and 19.93 and 0.53 for III.

It seemed to us that the simplest variant for the synthesis of 1H-1,6-diazaphenalene and its derivatives was intramolecular condensation of 5-formylaminolepidine through the carbonyl group of the acyl residue and the labile hydrogen atoms of the methyl group. However, 5-nitrolepidine is hard to obtain, since the chief product in the nitration of lepidine is 8-nitrolepidine, and only traces of 5-nitrolepidine are formed [4, 5]. 8-Chlorolepidine was therefore taken as the basis of the synthesis. The nitration of 8-chlorolepidine (IV) under conditions similar to those in the nitration of lepidine [6] proceeded unambiguously to give

*See [1] for communication I.

Lensovet Leningrad Technological Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 205-209, February, 1972. Original article submitted May 13, 1971.

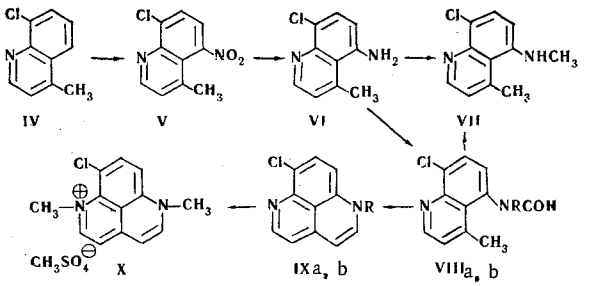
TABLE 1. π-Electron Charges (q_π) and Migratory Bond Orders (p_{ij}) of 1H-1,6-Diazaphenalene (I), Its Cation (II), and Anion (III)*

Atom	q_π			Bond	p_{ij}		
	I	II	III		I	II	III
1	+0,242	+0,277 (+0,323)	−0,138 (−0,265)	1—2	0,405	0,452 (0,490)	0,683 (0,654)
2	+0,137	+0,191 (+0,206)	+0,004 (+0,041)	2—3	0,813	0,771 (0,747)	0,657 (0,684)
3	−0,098	−0,083 (−0,099)	−0,146 (−0,155)	3—4	0,480	0,531 (0,543)	0,578 (0,552)
4	+0,074	+0,149 (+0,166)	+0,019 (+0,024)	4—5	0,611	0,549 (0,543)	0,524 (0,552)
5	−0,089	−0,087 (−0,099)	−0,159 (−0,155)	5—6	0,659	0,747 (0,747)	0,714 (0,684)
6	+0,094	+0,226 (+0,206)	+0,068 (+0,041)	6—7	0,667	0,468 (0,490)	0,613 (0,654)
7	−0,292	+0,286 (+0,323)	−0,381 (−0,265)	7—8	0,526	0,379 (0,398)	0,512 (0,536)
8	+0,041	+0,098 (+0,092)	+0,038 (+0,021)	8—9	0,570	0,628 (0,624)	0,592 (0,566)
9	−0,089	−0,087 (−0,099)	−0,159 (−0,155)	9—10	0,700	0,669 (0,666)	0,657 (0,670)
10	+0,018	+0,037 (+0,034)	+0,005 (+0,006)	10—11	0,634	0,660 (0,666)	0,684 (0,670)
11	−0,098	−0,083 (−0,099)	−0,146 (−0,155)	11—12	0,658	0,642 (0,624)	0,552 (0,566)
12	+0,067	+0,079 (+0,092)	0,000 (+0,021)	12—13	0,549	0,548 (0,540)	0,527 (0,527)
13	−0,007	−0,011 (−0,012)	0,000 (0,000)	8—13	0,527	0,543 (0,540)	0,529 (0,527)
				4—13	0,514	0,509 (0,509)	0,525 (0,526)
				1—12	0,338	0,359 (0,398)	0,552 (0,536)

*The results of calculations with parameters from [1-3] are presented; the results of calculations with "averaged" parameters are given in parentheses.

good yields. The nitro group was reduced with stannous chloride in hydrochloric acid. 5-Amino-8-chlorolepidine (VI) is readily diazotized and undergoes azo coupling. The amine was formylated with a mixture of 85% formic acid and acetic anhydride at room temperature [7].

We found that the crucial step in the synthesis – cyclization of 5-formylamino-8-chlorolepidine (VIIIa) – proceeds readily when the latter is heated with phosphorus oxychloride at 200°C. 1H-7-Chloro-1,6-diazaphenalene (IXa) was isolated and purified as the stable perchlorate (orange needles). The structure of the salt was proved by IR and UV spectra [8].



Potentiometric titration of a solution of the perchlorate of IXa in 50% alcohol was used to determine the basicity constant of IXa (pK_a^{25} 7.83 ± 0.04). The high basicity attests to conjugation between the two nitrogen atoms. Compound IXa could not be isolated in pure form. The yellow compound obtained when solutions of the perchlorate of IXa were made alkaline darkened rapidly in air, and the compound could not be purified by crystallization. The direct alkylation of IXa by dimethyl sulfate in alkaline media gave a dark-colored substance with a polymeric structure. Using thin-layer chromatography on Al_2O_3, we were able to establish that the substance also contains the mono- and dimethyl derivatives. We assumed that the instability of the 1H-7-chloro-1,6-diazaphenalene base (IXa) and the appearance of side products during its alkylation in alkaline media are caused by the chemical instability of the anion formed under these conditions. Compounds V and VIIIa could not be alkylated at the heteroatom, although various alkylating agents

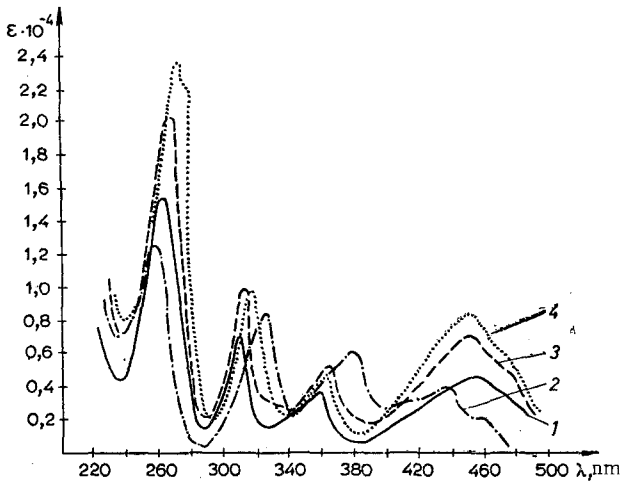


Fig. 1. Absorption spectra of 1,6-diazaphenalene derivatives (in alcohol, c $0.3 \cdot 10^{-4}$ M): 1) 1H-7-chloro-1,6-diazaphenalenium perchlorate (IXa); 2) 1-methyl-7-chloro-1,6-diazaphenalene (IXb); 3) 1-methyl-7-chloro-1,6-diazaphenalenium perchlorate (IXb); 4) 1,6-dimethyl-7-chloro-1,6-diazaphenalenium methylsulfate (X).

were used, and the reaction conditions were varied. This is apparently due to the low basicity of V and the hydrolysis of VIIIa under the alkylation conditions.

In this connection, we carried out the methylation of the tosyl derivative of VI with subsequent saponification of the 5-tosylmethylamino-8-chlorolepidine to VII. This synthesis proceeds unambiguously and gives completely satisfactory yields. 5-Formylmethylamino-8-chlorolepidine (VIIIb) is formed under conditions similar to those in the formylation of VI. The cyclization of VIIIb to form a phenalene ring was also readily accomplished by heating with phosphorus oxychloride in sealed ampuls. The cyclizability of VIIIb demonstrates that preliminary enolization of the carbonyl group, which many investigators have proposed in similar cases [9], is not necessary for this reaction. 1-Methyl-7-chloro-1,6-diazaphenalene (IXb) was also isolated as the perchlorate and the base. The stability of the base confirms the validity of the assumption that the lability of the unalkylated compound (IXa) is due to the formation of an anion of the III type. Although the latter also has a rather high delocalization energy, it should readily undergo oxidative-reductive transformations apparently because of the elevated electron density (Table 1).

The structure of 1-methyl-7-chloro-1,6-diazaphenalene (IXb) was proved by IR, UV, and PMR spectroscopy. The IR spectrum (KBr) contains a band of the stretching vibration of the methyl group (2900 cm^{-1}), the vibration of the aromatic rings (1600-1630 cm^{-1}), and deformation out-of-plane vibrations of the aromatic CH groups (780, 830, and 870 cm^{-1}). A signal of the protons of the $N-CH_3$ group at 4.35 ppm and signals of the aromatic protons at 7.4-9.3 ppm are observed in the PMR spectrum (acetic acid). The basicity constant of IXb proved to be the same as that for IXa (pK_a^{25} 7.83 ± 0.03). This is evidence that protonation of both compounds proceeds at the pyridine nitrogen atom. In contrast to IXa, the corresponding quaternary salt (X) is formed when IXb is heated with dimethyl sulfate. Its structure was proved by the IR, UV, and PMR spectra. The IR spectrum (KBr) contains an absorption band of the stretching vibrations of the methyl group (2900 cm^{-1}), vibrations of the aromatic rings (1600 cm^{-1}), and out-of-plane deformation vibrations of the aromatic CH groups (800, 820, and 850 cm^{-1}). Signals of aromatic protons at weak field and one intense peak of six protons of the two $N-CH_3$ groups at 4.5 ppm are observed in the PMR spectrum (acetic acid), which attests to the equivalency of these groups. The PMR spectrum thus makes it possible to conclude that the positive charge in 1,6-dimethyl-7-chloro-1,6-diazaphenalenium methylsulfate (X) is not localized on a single nitrogen atom but is distributed between two atoms.

The absorption spectra of 1-methyl-7-chloro-1,6-diazaphenalene and its perchlorate, the perchlorate of the unalkylated product, and of 1,6-dimethyl-7-chloro-1,6-diazaphenalenium methylsulfate are presented in Fig. 1. It is apparent that all of the compounds have four absorption maxima, while base IXb has

a shoulder in the long-wave region, the λ_{max} of which corresponds to the position of the long-wave absorption maximum of the salts. The introduction of methyl groups into the nitrogen atoms does not have a substantial effect on the position of the long-wave maximum but increases its intensity considerably.

EXPERIMENTAL

8-Chlorolepidine (IV). This compound was obtained from o-chloroaniline and methyl vinyl ketone via the method in [10]. The dark mass formed after alkalinization was evaporated to dryness and extracted with benzene. The benzene was removed by distillation, and the residue was vacuum distilled in a sword-shaped flask at 215-220°C(5-6 mm) to give 60% of a product with mp 103-105°.

5-Nitro-8-chlorolepidine (V). A solution of 5 g (0.028 mole) of IV in 6.1 ml (0.11 mole) of concentrated H_2SO_4 was cooled to −5°, and a mixture of 3.1 ml (0.075 mole) of HNO_3 (sp. gr. 1.51) and 3.1 ml (0.058 mole) of H_2SO_4 was added to it with stirring while maintaining the temperature at −5 to 0°. The mixture was stirred at 0° for 2 h, allowed to stand at room temperature for 5 h, and poured over ice. The resulting precipitate was removed by filtration to give 5.6 g (89%) of V. This product was crystallized from acetone (1 : 50) to give light-yellow needles with mp 187-187.5° and R_f 0.57 (chloroform).* Found: C 54.0; H 3.4; N 12.5%. $C_{10}H_7ClN_2O_2$. Calculated: C 54.1; H 3.1; N 12.6%.

5-Amino-8-chlorolepidine (VI). To a solution of 3.5 g (0.016 mole) of stannous chloride in 7.5 ml of concentrated HCl, 1.0 g (0.005 mole) of V was added gradually and the mixture was stirred for 1 h. The precipitated complex was removed by filtration and dissolved in 50 ml of hot water. The resulting dark-red solution was treated with 20% NaOH to pH ~ 8. The precipitate was removed by filtration, washed with water, and dried to give 0.52 g (60%) of VI as slightly yellowish needles with mp 142-143.5° [from ethanol (1 : 30)] and R_f 0.7 (chloroform). Found: C 62.3; H 5.2; Cl 18.1; N 14.2%. $C_{10}H_9ClN_2$. Calculated: C 62.5; H 4.7; Cl 18.4; N 14.5%.

5-Methylamino-8-chlorolepidine (VII). A solution of 10 g (0.052 mole) of VI in 25 ml of pyridine was heated to 60°, and a solution of 20 g (0.104 mole) of p-toluenesulfonyl chloride in 50 ml of pyridine was added. The mixture was stirred for 1 h, the major portion of the solvent was removed by vacuum distillation, and 20% NaOH was added to the residue to pH ~10. The precipitate was separated, and the solution was refluxed with activated charcoal and filtered. The filtrate was cooled to precipitate 12.1 g (61%) of yellowish needles of the sodium salt of 5-tosylamino-8-chlorolepidine. A solution of 6 g (0.016 mole) of the sodium salt and 1.3 g (0.033 mole) of NaOH in 30 ml of water was heated to 70°, and 15.2 ml (0.16 mole) of dimethyl sulfate was added with stirring while maintaining the pH at ~ 9. The resulting precipitate was removed by filtration, washed with water, and dried to give 5.9 g (97%) of 5-tosylmethylamino-8-chlorolepidine as colorless plates with mp 230-231° [from benzene (1 : 30)]. Found: C 60.5; H 4.8; Cl 10.1; N 7.7; S 9.02%. $C_{18}H_{17}ClN_2O_2S$. Calculated: C 60.2; H 4.7; Cl 9.9; N 7.8; S 8.9%. A solution of 3.75 g (0.01 mole) of 5-tosylmethylamino-8-chlorolepidine in 10 ml (0.19 mole) of concentrated H_2SO_4 was held at room temperature for 12 h and poured into ice water. Ammonium hydroxide was added gradually to pH ~ 7, and the precipitate was removed by filtration and dried to give 2.1 g (100%) of VII as yellowish needles with mp 135-137° [from benzene (1 : 40)] and R_f 0.4 (chloroform). Found: C 64.0; H 5.04; N 13.7%. $C_{11}H_{11}ClN_2$. Calculated: C 64.1; H 5.4; N 13.6%.

5-Formylamino-8-chlorolepidine (VIIIa). Acetic anhydride [16 ml (0.17 mole)] was added to 1 g (0.005 mole) of VI in 9.5 ml (0.25 mole) of 85% formic acid, and the mixture was stirred at room temperature for 2 h. The acetic acid was removed by vacuum distillation, 20 ml of water was added to the residue, and the resulting precipitate was removed by filtration and dried to give 0.88 g (77%) of VIIIa as colorless plates with mp 245-246° [from butanol (1 : 30)] and R_f 0.5 [chloroform–acetone (4 : 1)]. Found: C 59.6; H 4.2; Cl 16.2; N 12.7%. $C_{11}H_9ClN_2O$. Calculated: C 60.0; H 4.1; Cl 16.1; N 12.7%.

5-Formylmethylamino-8-chlorolepidine (VIIIb). A solution of 1 g (0.005 mole) of VII in 9 ml (0.24 mole) of 85% formic acid and 21 ml (0.22 mole) of acetic anhydride was stirred at room temperature for 1 h and refluxed for 1 h. The major portion of the acetic acid was removed by distillation, 20 ml of water was added to the residue, and the precipitate was removed by filtration to give 0.8 g (70%) of VIIIb as colorless plates with mp 133-134° [from CCl_4 (1 : 50)] and R_f 0.6 [chloroform–acetone (3 : 1)]. Found: C 61.2; H 4.8; Cl 15.3; N 12.1%. $C_{12}H_{11}ClN_2O$. Calculated: C 61.5; H 4.7; Cl 15.2; N 12.0%.

*All of the R_f values presented are for thin-layer chromatography on activity II Al_2O_3.

1H-7-Chloro-1,6-diazaphenalenium Perchlorate (IXa · $HClO_4$). A mixture of 1 g (0.0046 mole) of VIIIa and 10 ml of freshly distilled $POCl_3$ was heated in a sealed ampul at 150° for 3 h. The excess $POCl_3$ was removed by vacuum distillation, 30 ml of water was added to the residue, and the resulting solution was refluxed with activated charcoal. The gradual addition of 56% $HClO_4$ to the filtrate precipitated 0.32 g (23%) of IXa · $HClO_4$ as orange plates with mp 279-281° [from ethanol (1 : 40)] and R_f 0.33 (chloroform); λ_{max}, nm (log ε): 260 (4.2), 308 (3.86), 358 (3.58), 454 (3.68). Found: C 43.6; H 3.2; N 8.9%. $C_{11}H_7ClN_2 \cdot HClO_4$. Calculated: C 43.6; H 2.6; N 9.2%.

1-Methyl-7-chloro-1,6-diazaphenalene (IXb). A mixture of 1 g (0.0043 mole) of VIIIb and 10 ml of $POCl_3$ was heated at 150° for 3 h in a sealed ampul. The resulting precipitate was removed by filtration and dissolved in water. The solution was refluxed with activated charcoal, and NaOH solution was added to the cooled solution. The resulting bright-yellow precipitate was removed by filtration and dried to give 0.74 g (80%) of IXb with mp 233-235° [from benzene (1 : 40)] and R_f 0.45 (chloroform); λ_{max}, nm (log ε): 255 (4.1), 325 (3.94), 380 (3.81), 435 (3.62). Found: C 66.5; H 4.4; Cl 16.4; N 13.1%. $C_{12}H_9ClN_2$. Calculated: C 66.7; H 4.2; Cl 16.5; N 13.0%.

1,6-Dimethyl-7-chloro-1,6-diazaphenalenium Methylsulfate (X). A mixture of 1 g (0.005 mole) of IXb and 4.5 ml (0.05 mole) of freshly distilled dimethyl sulfate was heated in a test tube with a calcium chloride stopper at 120° for 1 h. The resulting viscous mass was washed with ether. The addition of alcohol to it gave 0.98 g (62%) of X as bright-yellow plates [from ethanol (1 : 40)] with mp > 300°; λ_{max}, nm (log ε): 268 (4.37), 315 (4.02), 360 (3.67), 450 (3.97). Found: Cl 10.2; N 8.0; S 9.4%. $C_{14}H_{15}ClN_2O_4S$. Calculated: Cl 10.4; N 8.2; S 9.5%.

LITERATURE CITED

1. L. S. Éfros, L. A. Ezhova, É. R. Zakhs, and V. M. Treiger, Khim. Geterotsikl. Soedin., 202 (1972).
2. A. Streitwieser, Molecular Orbital Theory for Organic Chemists, Wiley (1961).
3. R. D. Brown and M. L. Heffernan, Austr. J. Chem., 12, 319 (1959).
4. E. Roberts and E. E. Turner, J. Chem. Soc., 1832 (1927).
5. M. Ishikawa and K. Kikkawa, J. Pharm. Soc. Japan, 75, 33 (1955); Chem. Abstr., 50, 1008a (1956).
6. E. R. Buchman, C. M. McCloskey, and J. A. Senecer, J. Am. Chem. Soc., 69, 380 (1947).
7. É. R. Zakhs and T. R. Strelets, Khim. Geterotsikl. Soedin., 1387 (1970).
8. L. S. Éfros and L. A. Ezhova, Zh. Organ. Khim., 6, 403 (1970).
9. R. Elderfield, Heterocyclic Compounds, Wiley (1961).
10. K. N. Campbell and I. J. Shaffner, J. Am. Chem. Soc., 67, 86 (1945).