REACTIVITY OF 4,9-DIAZAPYRENE

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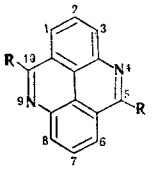
Heating 5,10-dimethyl-4,9-diazapyrene with nitric acid to 200°C does not bring about disruption of the heteroring but leads to the formation of nitro derivatives of 5,10-dioxo-4,5,9,10-tetrahydro-4,9-diazapyrene. 4,9-Diazapyrene is a weak base that forms quaternary salts only under severe conditions. Piperidine replaces two chlorine atoms in 5,10-dichloro-4,9-diazapyrene, whereas only monosubstitution occurs in the case of 1,6-dibromo-5,10-dimethyl-4,9-diazapyrene. Calculations by the Hückel MO method, in agreement with the experimental data, characterize 4,9-diazapyrene as a strong electron acceptor and indicate that the effect of conjugation is propagated primarily along the periphery of the molecule rather than between the heterorings.

The inactivity in electrophilic substitution reactions and the considerable stability with respect to oxidation of 4,9-diazapyrene (Ia) and its derivatives were demonstrated in [1-3]. In a continuation of the studies mentioned above we followed the effect on diazapyrene Ia and 5,10-dimethyl-4,9-diazapyrene (Ib) of a number of strong oxidizing agents. In order to evaluate the electrophilic and nucleophilic reactivities of diazapyrene we measured the basicities of Ia,b, carried out reactions of their halo derivatives with amines, and also made an attempt to nitrate dimethyldiazapyrene N,N'-dioxide. The Hückel MO method in a number of cases enabled us to interpret the experimental data obtained.



Ia, b

Ia R=H; b R=CH_3

In our investigation of the stability of diazapyrene Ia with respect to oxidation, this heterocycle was treated with a chromic acid mixture under the conditions used for the oxidation of pyrene to naphthalenetetracarboxylic acid [4] and also with potassium permanganate in neutral media. In both cases diazapyrene Ia was recovered from the reaction or was purified to remove impurities.

A yellow crystalline substance (III) was isolated under more severe conditions as a result of the action of 54% nitric acid on dimethyldiazapyrene Ib at 170° for 3 h. The strong bands at ~1670 and 1540 cm^{-1} in the IR spectrum of III can be assigned, respectively, to the stretching vibrations of a carbonyl group and the asymmetrical stretching vibrations of a nitro group.* The reduction of III with sodium hydrosulfite gives IV, the IR spectrum of which contains bands of an amino group at ~3350 and 3250 cm^{-1}, whereas the band of a nitro group at 1540 cm^{-1} is absent. The spectral data, in agreement with the results of elementary analysis, make it possible to depict the described transformations as follows:

*In connection with the low solubilities and volatilities of the products of oxidative nitration, it was necessary to restrict ourselves to IR spectroscopy in the establishment of their structures. The IR spectra under discussion are presented in Fig. 1.

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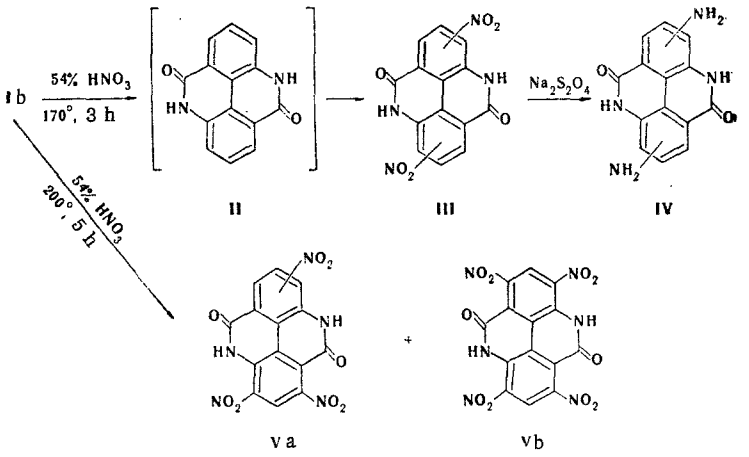


The first step in the oxidative nitration of Ib is probably the formation of 5,10-dioxo-4,5,9,10-tetrahydro-4,9-diazapyrene (II). The fact that we obtained a substance whose chemical properties (in contrast to II, it is soluble in sodium carbonate and alkali solutions) and IR spectrum are very close to those of III by reaction of II [3] with 54% nitric acid at 170° for 3 h serves as a confirmation of this.

We were unable to destroy the diazapyrene ring even under the more severe conditions of treatment of dimethyldiazapyrene Ib with 54% nitric acid at 200° for 5 h. As a result of this experiment we isolated a bright-yellow crystalline substance (V), which, judging from its IR spectrum (carbonyl band at ~1710 cm^{-1} and bands of a nitro group at 1550 and 1300 cm^{-1}) and the results of elementary analysis, is a mixture of tri- and tetranitro derivatives of II (Va and Vb).

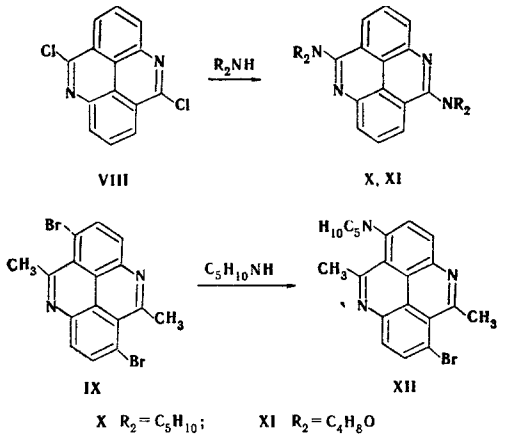
The products of the oxidative nitration of III and V are soluble in aqueous alkali solutions. Proceeding from the assumptions that have been advanced regarding the structures of III, Va, and Vb, this may occur due to ionization in alkaline media of the tautomeric $-NH-CO-$ amide fragment of the $-N=COH-$ hydroxy form. In fact, when we treated V with potassium hydroxide we obtained bright-red crystals of, apparently, the potassium derivative; the band of a carbonyl group is absent in the IR spectrum of this derivative.

The first ionization constants of diazapyrene Ia (pK_a 2.64 ± 0.11) and dimethyldiazapyrene Ib (pK_a 3.52 ± 0.06) were found by potentiometric titration in 50% alcohol. We were unable to determine the second ionization constants because of their low values. For comparison under the same conditions, we also titrated 6-methylphenanthridine (pK_a 4.48 ± 0.02). The low basicity is in agreement with the necessity of severe conditions in the N-alkylation of diazapyrene Ia. Mono- and diquaternary salts of the latter were obtained by the method used to prepare salts of Ib by the action, respectively, of dimethyl sulfate (130°) and methyl p-toluenesulfonate (120°) (salts VI and VII) [5].

The different nucleophilic labilities of halogens in the benzene and pyridine fragments of diazapyrene were demonstrated in reactions of 5,10-dichloro-4,9-diazapyrene VIII* and 1,6-dibromo-5,10-dimethyl-4,9-diazapyrene (IX) with amines. Disubstitution products (X and XI) are formed in high yields as a result of refluxing solutions of dichloride VIII in piperidine and morpholine. Only one halogen is replaced on treatment of dibromo derivative IX with piperidine at 180° to give XII [6].

In view of the inactivity of diazapyrene in electrophilic substitution reactions we made an attempt to subject diazapyrene N-oxide rather than diazapyrene itself to this sort of reaction. With this end in mind, we subjected dimethyldiazapyrene N,N'-dioxide [2] to nitration under the conditions of nitration of pyridine N-oxide [7]. As a result, we obtained an unidentified resinous substance, the IR spectrum of which contained strong bands of carbonyl (1690 cm^{-1}) and nitro (1540 cm^{-1}) groups. The intense band of an N-oxide group that is present in the spectrum of the starting N-oxide at 1250 cm^{-1} is absent here. The spectral data make it possible to assume that although nitration does occur, it is accompanied by profound oxidation of the N,N'-dioxide.

* In view of the unsuccessful attempts to synthesize VIII by reaction of II with phosphorus oxychloride in dimethylaniline [3], dichloride VIII was obtained by reaction of II with phosphorus pentachloride and phosphorus oxychloride under pressure.



X $R_2 = C_5H_{10}$; XI $R_2 = C_4H_8O$

The molecular diagram calculated with the parameters in [8] (Fig. 2) is in agreement with the experimental data regarding the clearly expressed electrophilicity of diazapyrene Ia. It follows from an examination of Fig. 2 that nucleophilic substitution reactions should be characteristic for diazapyrene Ia, and the 5 and 10 positions should be the most active positions.

The molecular diagrams of halo derivatives VIII and XI and of monosubstitution products A and XII (Fig. 3) make it possible to evaluate the effect of conjugation between the nitrogen atom of the piperidine substituent and the diazapyrene ring.* It is apparent from Fig. 3 that replacement of the chlorine atom attached to C_5 by a piperidine residue in dichloride VIII leads to a very insignificant increase in the electron density on C_{10} in A (0.0011 charge unit). It follows from the experiments that this is not reflected in the lability of the residual chlorine atom. At the same time, replacement of the bromine atom attached to C_1 in dibromo derivative IX causes a sharp increase in the electron density on C_6 (~0.0155 charge unit), as a consequence of which replacement of the remaining bromine atom becomes difficult. Let us note that the electron density in the 13 and 14 positions remains practically unchanged on passing from IX to XII.

The results presented above and the data in [5] on the insignificant character of conjugation between heteroatoms in cations of the quaternary salts of dimethyldiazapyrene Ib constitute evidence that the effect of conjugation is propagated mainly along the periphery of the diazapyrene molecule and to a considerably lesser degree between the heterorings.

This conclusion is also confirmed by the closeness of the reactivities of diazapyrene Ia, phenanthridine, dimethyldiazapyrene Ib, and 6-methylphenanthridine during oxidation [9, 10] and in condensations involving the activated methyl group. The indexes, calculated by the Hückel MO method, that characterize the heteroatom and the non-nodal C_6 atom bonded to it in phenanthridine [11] (according to our data, A_n 2.045, A_e 2.539, and A_r 2.292 for the C_6 atom in phenanthridine) are very close to the indexes for diazapyrene Ia.†

EXPERIMENTAL METHOD

Thin-layer chromatography (TLC) on activity II aluminum oxide was used to monitor the homogeneity of the substances, and the spots were detected by means of UV irradiation. The IR spectra of KBr pellets of the compounds were obtained with an IKS-22 spectrometer. Potentiometric titration was accomplished with an LPU-01 pH-meter at 25 ± 0.1°.

Dinitro-5,10-dioxo-4,5,9,10-tetrahydro-4,9-diazapyrene (III). A 0.5-g sample of dimethyldiazapyrene Ib [2] and 15 ml of 54% nitric acid were heated in a sealed tube at 170° for 3 h, after which the mixture was filtered to give 0.45 g (64%) of III. Crystallization of the product from dimethyl sulfoxide (DMSO) (1 : 2000) gave colorless crystals with mp > 360°. The product was soluble in dimethylformamide (DMF), hexametapol,

*The inductive effect exerted by the heteroatom on the adjacent carbon atom in VIII, IX, A, and XII and the hyperconjugation of the methyl groups with the diazapyrene ring in IX and XII were disregarded.

†The electron distribution in the 4,9-diazapyrene molecule found by the self-consistent-field (SCF) method [12] is in qualitative agreement with the data presented in the present paper. This, it seems to us, confirms the possibility of the use of the Hückel MO method for the evaluation of the reactivities and electronic effects in 4,9-diazapyrene and closely related heterocycles.

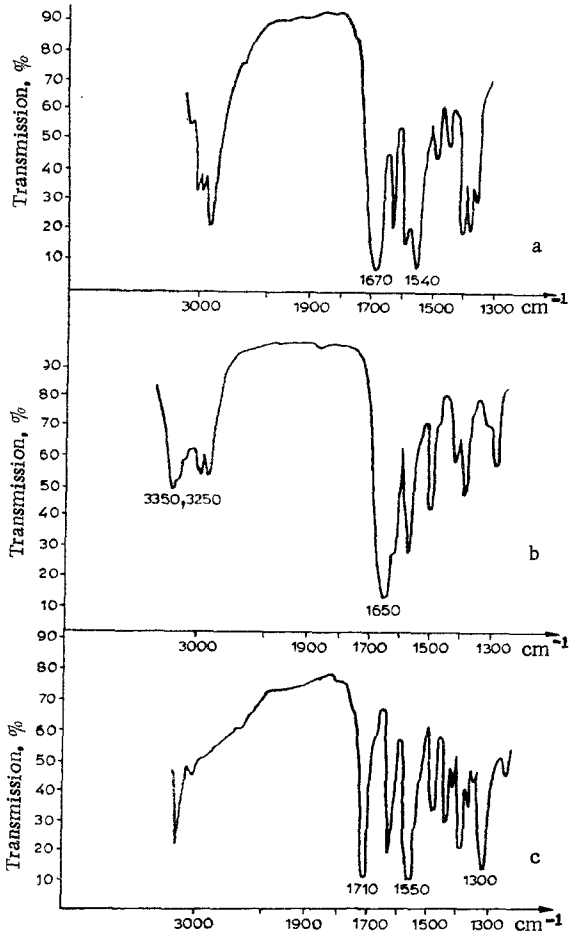
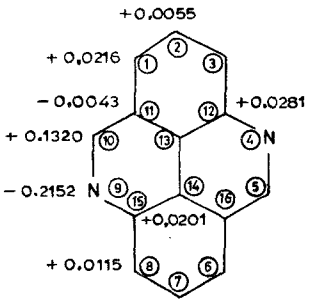


Fig. 1. IR spectra (KBr pellets): a) dinitro-5,10-dioxo-4,5,9,10-tetrahydro-4,9-diazapyrene (III); b) diamino-5,10-dioxo-4,5,9,10-tetrahydro-4,9-diazapyrene (IV); c) product of oxidative nitration (V).



C-atom	A_n	A_r	A_e
1	2.114	2.190	2.260
2	2.526	2.545	2.563
3	2.129	2.195	2.265
5	2.029	2.264	2.499

Fig. 2. Molecular diagram of 4,9-diazapyrene (Ia); A_n, A_r, and A_e are, respectively, the energies of anionic, radical, and cationic localization in $(-\beta_0)$ units.

alkalis, and concentrated H_2SO_4 (1 : 75). IR spectrum, cm^{-1}: 3180, 3050, 2950, 2900, 1670 (C=O), 1620, 1570, 1540 (NO_2), 1470, 1430, 1380, 1355, 1270, 1180, 1140, 1090, 960, 870, 740, 710, and 670. Found: C 51.8; H 2.4; N 17.0%. $C_{14}H_6N_4O_6$. Calculated: C 51.5; H 1.9; N 17.2%.

Diamino-5,10-dioxo-4,5,9,10-tetrahydro-4,9-diazapyrene (IV). A 0.2-g sample of III was dissolved by refluxing in 100 ml of 10% KOH solution, after which 0.8 g of $Na_2S_2O_4$ was added, and the mixture was refluxed for 3-5 min. It was then cooled, and 0.1 g (70%) of IV was removed by filtration. Three reprecipi-

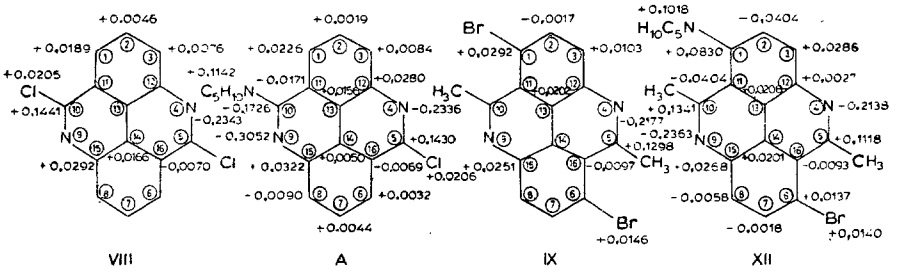


Fig. 3. Molecular diagrams of VIII, A, IX, and XII.

tations from CF_3COOH (1 : 600) by the addition of ammonia (with decolorization by activated charcoal) gave yellow crystals with mp > 360°. The product was insoluble in alkalis but soluble in concentrated H_2SO_4. IR spectrum, cm^{-1}: 3350, 3250 (NH_2), 3050, 2950, 2980, 1650 (C=O), 1560, 1490, 1410, 1380, 1270, 1160, 1040, 860, and 820. Found: C 63.3; H 4.0; N 21.0%. $C_{14}H_{10}N_4O_2$. Calculated: C 63.2; H 3.8; N 21.1%.

Product of Oxidative Nitration (V). A 0.3-g sample of dimethyldiazapyrene Ib and 10 ml of 54% nitric acid were heated in a sealed tube at 200° for 5 h, after which the mixture was filtered to give 0.2 g of bright-yellow crystals with mp ~380° (dec.). The product was soluble in DMF, pyridine, alkali, and concentrated H_2SO_4. A sample was purified for elementary analysis by reprecipitation from potassium carbonate solution by the addition of hydrochloric acid. IR spectrum, cm^{-1}: 3300, 3100, 1710 (C=O), 1620, 1550 (NO_2), 1470, 1430, 1380, 1350, 1330, 1300 (NO_2), 1230, 1170, 1000, 900, 890, 840, 810, 790, 770, 740, 680. Found: C 41.5; H 1.6; N 19.4%. $C_{14}H_5N_5O_8$ (Va). Calculated: C 45.3; H 1.4; N 18.9%. $C_{14}H_4N_6O_{10}$ (Vb). Calculated: C 40.4; H 1.0; N 20.2%.

4-Methyl-4-azonia-9-azapyrene Methosulfate (VI). A solution of 0.3 g (1.5 mmole) of diazapyrene Ia [2] in 20 ml of chlorobenzene was refluxed with 1 ml (10 mmole) of dimethyl sulfate for 4 h, after which the substance that precipitated during the reaction was removed by filtration to give a quantitative yield of product. Colorless crystals with mp 297-310° (dec.) were isolated by reprecipitation of the product from a solution in 90% alcohol (1 : 60) by the addition of acetone. Found: N 8.7%. $C_{16}H_{14}N_2O_4S$. Calculated: N 8.5%.

4,9-Dimethyl-4,9-diazoniapyrene Ditosylate (VII). A mixture of 0.1 g of diazapyrene Ia and 5 g of methyl p-toluenesulfonate was heated at 180° for 1.5 h, after which it was worked up to give a quantitative yield of pale-yellow crystals with mp 268-270° (from alcohol, 1 : 100). Found: N 4.7%. $C_{30}H_{28}N_2O_6S_2$. Calculated: N 4.9%.

5,10-Dichloro-4,9-diazapyrene (VIII). A mixture of 0.3 g of dioxo derivative II, 1 g of phosphorus pentachloride, and 1 ml of phosphorus oxychloride was heated in a sealed tube at 160° for 3 h, after which it was treated with ice water, and the resulting precipitate was removed by filtration. Sublimation of the product at 280° and 3 mm gave 0.06 g (20%) of shiny colorless needles with mp >360° and R_f 0.8 (chloroform, blue luminescence). The product was soluble in DMF and chlorobenzene but insoluble in alcohol. Found: N 10.3%. $C_{14}H_6Cl_2N_2$. Calculated: N 10.3%.

5,10-Dipiperidino-4,9-diazapyrene (X). A solution of 0.12 g of dichloride VIII in 10 ml of piperidine was refluxed for 1 h, after which the mixture was treated with water, and 0.15 g (93%) of X was removed by filtration. Crystallization of the product from 1-butanol (1 : 100) gave shiny yellow crystals with mp 234-235° and R_f 0.8 [ether–chloroform (7 : 3), blue luminescence]. The product was soluble in alcohol, carbon tetrachloride, and benzene. IR spectrum, cm^{-1}: 1370 (C–N). Found: N 15.1%. $C_{24}H_{26}N_4$. Calculated: N 15.1%.

5,10-Dimorpholino-4,9-diazapyrene. The method in the preceding experiment was used to obtain this compound in 94% yield. Two crystallizations from 1-butanol gave yellow crystals with mp 244-255° and R_f 0.8 [benzene–ethyl acetate (2 : 1), blue luminescence]. IR spectrum, cm^{-1}; 1360 (C–N) and 1110 (C–O). Found: N 14.8%. $C_{22}H_{22}N_4O_2$. Calculated: N 15.0%.

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