RING – CHAIN ISOMERISM AND REACTIONS OF 2-(1-ANTHRAQUINONECARBONYL)-1,2,3,4-TETRAHYDROPHTHALAZINE

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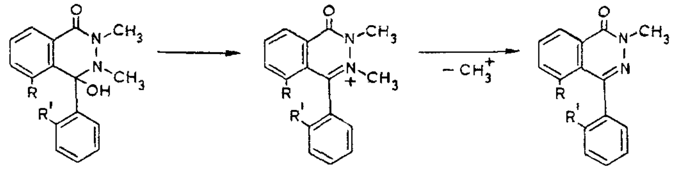
The ring isomer of the corresponding acyl derivative – 5,9-dioxo-17a-hydroxy-9,10,11,16-17,17a-hexahydro-5H-dibenzo[d,e,h]phthalazino[2,3-a]cinnoline – was obtained by acylation of 1,2,3,4-tetrahydrophthalazine with anthraquinone-1-carboxylic acid chloride. Treatment of the product with thionyl chloride or hydrogen chloride gave the deeply colored 5,9-dioxo-9,10,11,16-tetrahydro-5H-dibenzo[d,e,h]phthalazino[2,3-a]cinnolinium chloride. The possibility of charge transfer between the chloride anion and the phthalazinium cation is examined as a reason for the deep coloration. This compound very readily undergoes hydrolytic oxidative cleavage at the C–N bond to give 2-(2-formylbenzyl)-3,7-dioxo-2,3-dihydro-7H-dibenzo[d,e,h]cinnoline.

The N,N'-dimethylhydrazides of 2-benzoylbenzoic [1] and anthraquinone-1-carboxylic acids [2] have ring structure I. Under the influence of electrophilic agents they are demethylated under mild conditions to give phthalazone IIIa or its condensed analog IIIb. It has been assumed [1] that the methyl group is split out in the form of a carbonium ion from intermediately formed immonium ion II.



I–III a R = R' = H; b R–R' = –CO–

To ascertain the mechanism, it was of interest to investigate this reaction in the case of the cyclic N,N'-dialkylhydrazide. In this case the alkyl residue after cleavage of the C–N bond nevertheless remains bonded to the principal fragment of the molecule.

The aim of the present research was the synthesis and study of the structure and reactions with electrophilic agents of 2-(1-anthraquinonecarbonyl)-1,2,3,4-tetrahydrophthalazine, which, like the N,N'-dimethylhydrazide of the same acid, has the hexahydro-5H-dibenzo[d,e,h]phthalazino[2,3-a]cinnoline ring structure (IV). Compound IV was obtained by acylation of tetrahydrophthalazine with anthraquinone-1-carboxylic acid chloride in the presence of triethylamine. Structure IV was vonfirmed by the similarity between the IR and electronic spectra of this compound and the spectra of the previously synthesized [2] dibenzo[d,e,h]cinnoline (Ib).

A derivative with an open structure (V) is formed in the reaction of acetic anhydride with phthalazine IV. An intense (integral intensity 9.42 practical units*) over all absorption band of anthraquinone and acyl C = O groups is observed in the IR spectrum of a solution of V in dioxane at 1678 cm^{-1}. Open structure V is also confirmed by the electronic spectrum of this compound, which is similar to the spectra of other derivatives of anthraquinone-1-carboxylic acid [2].

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*A practical unit is 10^4 liters · $mole^{-1}$ · cm^{-2} (ln).

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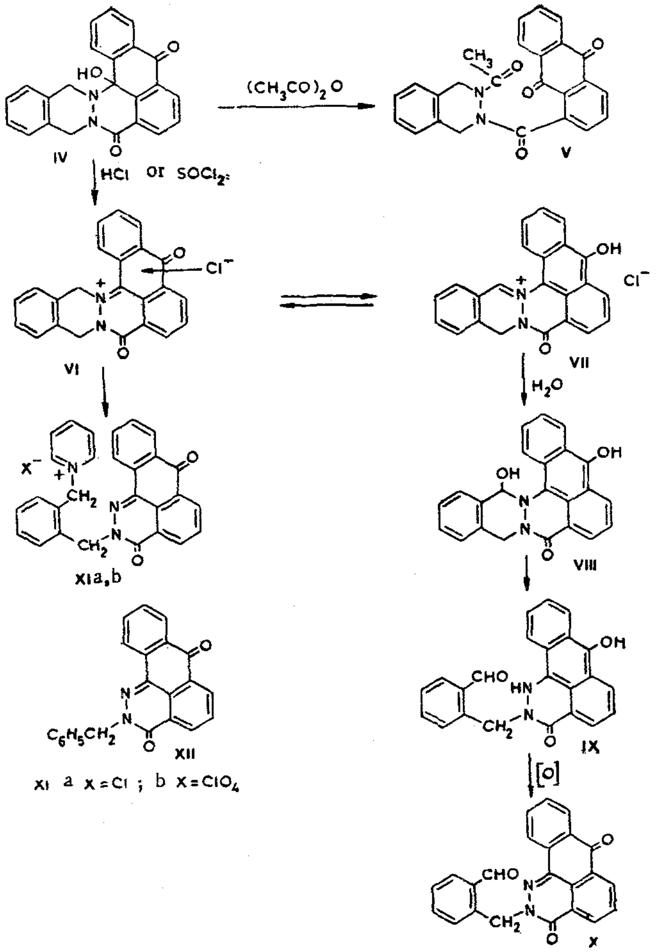
Compound IV differs with respect to its reactivity from previously investigated [1] Ia, which undergoes demethylation when it is treated with acetic anhydride. The formation of V in this reaction can be explained by primary attack of the electrophilic agent on the $N_{(17)}$ atom and subsequent opening of the phthalazine ring. Similar ring opening has been observed [1, 2] in the reaction of phenyl isocyanate with Ia, b.



The reaction of hydrogen chloride or thionyl chloride with IV gives an easily separable mixture of dark-blue crystalline 9,10,11,16-tetrahydro-5H-dibenzo[d,e,h]phthalazino[2,3-a]cinnolinium chloride (VI) and yellow dibenzo[d,e,h]cinnoline (X). Chloride VI is unstable with respect to the action of moisture and air and is rapidly converted to aldehyde X during storage. The formation of aldehyde X in the course of this reaction and during the reaction of chloride VI with pyridine, which is discussed below, is evidently due to the presence of moisture and oxygen in the reaction mixture. The reaction of chloride VI and pyridine gave a mixture of aldehyde X and 2-[2-(pyridinomethyl)benzyl]-3,7-dioxo-2,3-dihydro-7H-dibenzo[d,e,h]cinnoline chloride (XIa), which for working convenience was converted to the more moisture-resistant perchlorate XIb. The XI structure was confirmed by the similarity between its electronic and IR spectra and the spectra of model compounds – 2-benzyl-3,7-dioxo-2,3-dihydro-7H-dibenzo[d,e,h]cinnoline (XII) and the previously synthesized [2] 2-methyl-substituted analog. Compound XII was obtained by acylation of benzylhydrazine with anthraquinone-1-carboxylic acid chloride. Singlets of CH_2-N^+ and CH_2-N groups are observed in the PMR spectrum of derivative XIb. The formation of pyridinium derivative XI is, in our opinion, a confirmation of the structure of starting chloride VI. The benzylcarbonium ion that is formed after heterolytic cleavage of the CH_2-N^+ bond is captured by pyridine.

The structure of aldehyde X is confirmed by the similarity in the electronic spectra of X-XII. A new band of an aldehyde group at 1688 cm^{-1} appears in the IR spectrum of aldehyde X in addition to the $C=O$ bands (1681 and 1655 cm^{-1}) that are also observed in the spectra of XI and XII. The overall integral intensities of the $C=O$ and $C=N$ bands in the spectrum of aldehyde X are 1.7 practical units higher than the intensities of the $C=O$ and $C=N$ absorption in the spectrum of model compound XII. This difference is in good agreement with the data in [3] on the intensities of the aromatic aldehyde group in the IR spectra. Singlets of a methylene group and aldehyde proton are observed in the PMR spectrum of aldehyde X. The molecular ion peak in the mass spectrum corresponds to the calculated molecular mass of aldehyde X.

To explain the oxidative cleavage of the $C-N^+$ bond under such mild conditions (water and air oxygen) we assumed initial prototropic equilibrium of the cation (VI ⇌ VII), after which nitrogen-containing base VII), is hydrated covalently with ring opening (VII → VIII → IX); this is generally characteristic [4, 5] for immonium heterocycles, which are weak bases. Finally, 9-hydroxy-10-amino derivative of anthracene is oxidized by air oxygen (IX → X).

The problem of the reasons for such intense coloration of immonium salt VI in the crystalline state has not been solved. The long-wave absorption band in the electronic spectrum of crystalline VI, recorded by the method of diffuse reflection, is observed at 590 nm. In our opinion, the appearance of this band can be explained by the formation of a charge-transfer complex (CTC) between the chloride anion and the immonium cation. Charge-transfer complexes of the chloride ion with a number of electron acceptors [6], including cations [7, 8], are known. However, the appearance of new long-wave charge-transfer (CT) bands is possible only if the cation acceptor has a very high electron affinity. For example, the CT band is found at 298 nm in the spectrum of a solution of tropylium chloride [7] in methylene chloride, whereas it is found at 377 nm in the spectrum of the crystalline N,N'-dimethyl-4,4'-dipyridylium dichloride [8]. It is known [9] that the electron affinity of the tropylium cation is 6.24 eV. Since the CT band is found at 590 nm in the spectrum of crystalline VI, it follows that the VI cation has an electron affinity (EA) that is at least 1 eV higher than the EA of the tropylium ion.

In order to make an indirect estimate of the EA for ion VI, we calculated the EA for its nonquaternized analog XII from the equation [10]

$$h\nu_{CT} - h\nu^0_{CT} = EA_0 - EA,$$

where $h\nu_{CT}$ and $h\nu^0_{CT}$ are the CT energies, respectively, for the CTC of the investigated acceptor and chloranil with the same donor, and EA and EA_0 are the electron affinities of the investigated acceptor and chloroanil. According to the data in [11], the EA of chloranil is 2.45 eV. As the common donor we used dibenzotetrathiofulvalene. To estimate the $h\nu_{CT}$ and $h\nu^0_{CT}$ values we measured the wavelengths of the maxima of the CT bands in the spectra of solutions in chloroform: λ_{CT} 550 nm for XII–dibenzotetrathiofulvalene, and λ_{CT} 885 nm for chloranil–dibenzotetrathiofulvalene. The EA for XII is 1.6 eV. Calculations by the CNDO/2 (complete neglect of differential overlap) method in [12] showed that quaternization of nitrogen heterocycles leads to an increase of 5.5-10 eV in their electron affinities. An increase in the π-electron system of the bases and an increase in their electron-acceptor ability lower this difference; however, since EA = 1.6 eV for XII, one may fully expect that its quaternized analog VI has an electron affinity on the order of 7 eV. Consequently, the long-wave absorption of VI may be due to the formation of a CTC with the chloride ion.

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EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil and hexachlorobutadiene and of solutions in dioxane ($c = 2.5 \cdot 10^{-2}$ M, $l = 0.01$ cm) were recorded with UR-20 and IKS-14A spectrometers. The integral intensities of the bands were calculated by the Wilson–Wells method with corrections for the Ramsay wings [13]. The electronic spectra of solutions of the compounds in ethanol and dioxane ($c = 10^{-4}$ M, $l = 0.4$ and 1 cm) were obtained with a Specord UV-vis spectrophotometer. The diffuse reflection spectrum was obtained with an SFD-2 apparatus with a PDO-1 adapter. The compound was ground with magnesium oxide. The PMR spectra were obtained with a Perkin–Elmer R-12A (60 MHz) spectrometer with tetramethylsilane as the internal standard. The mass spectrum was obtained with an MS-905 spectrometer at an ionizing-electron energy of 70 eV.

5,9-Dioxo-17a-hydroxy-9,10,11,16,17,17a-hexahydro-5H-dibenzo[d,e,h]phthalazino[2,3-a]cinnoline (IV). A solution of 1.35 g (5 mmole) of anthraquinone-1-carboxylic acid chloride in 15 ml of dioxane was added to a solution of 1.34 g (10 mmole) of tetrahydrophthalazine and 1.4 ml (10 mmole) of triethylamine in 15 ml of dioxane. After 2 h, the mixture was diluted with water, and the precipitate was separated to give 0.8 g (45%) of colorless crystals with mp 180°C (dec., from benzene). IR spectrum in Nujol: 1677 (anthrone C = O), 1632 (hydrazide C = O), and 3215 cm^{-1} (O–H); in dioxane: 1675 shoulder, 1657 cm^{-1}. UV spectrum (in ethanol), λ_{max}(log ε): 227 (4.35) and 272 nm (4.14). Found: C 75.3; H 4.5; N 7.4%. $C_{23}H_{16}N_2O_3$. Calculated: C 75.2; H 4.4; N 7.6%.

2-Acetyl-3-(1-anthraquinonecarbonyl)-1,2,3,4-tetrahydrophthalazine (V). A solution of 0.25 g (0.7 mmole) of IV and 0.5 ml (5 mmole) of acetic anhydride in 5 ml of dioxane was heated at 100°C for 1 h, after which it was diluted with water, and the precipitate was separated to give 0.2 g (78%) of light-yellow crystals with mp 236-237°C (from benzene–cyclohexane). IR spectrum in Nujol: 1685 cm^{-1} (C = O); in dioxane: 1678 cm^{-1} ($A_{C=O}$ = 9.42 practical units). UV spectrum (in dioxane), λ_{max} (log ε): 253 (4.51) and 325 nm (3.69). Found: C 72.3; H 4.4; N 6.6%. $C_{25}H_{18}N_2O_4$. Calculated: C 72.6; H 4.5; N 6.9%.

5,9-Dioxo-9,10,11,16-tetrahydro-5H-dibenzo[d,e,h]phthalazino[2,3-a]cinnolinium Chloride (VI) and 2-(2-Formylbenzyl)-3,7-dioxo-2,3-dihydro-7H-dibenzo[d,e,h]cinnoline (X). A) A solution of 1.8 g of IV in 100 ml of anhydrous benzene was saturated with dry hydrogen chloride, during which a precipitate formed rapidly. The mixture was worked up to give 0.3 g (17%) of dark-blue crystals of VI with mp > 150°C (dec.). IR spectrum (in Nujol): 1682, 1646, 1596, 1556, and 1537 cm^{-1}. Diffuse reflection UV spectrum: λ_{max} 390 and 590 nm. Found: C 71.6; H 4.1; Cl 9.8; N 6.9%. $C_{23}H_{15}ClN_2O_2$. Calculated: C 71.4; H 3.9; Cl 9.2; N 7.2%.

The filtrate after separation of salt VI was evaporated to give 1.2 g (63%) of yellow crystals of X. For purification, it was dissolved in chloroform, and the solution was chromatographed through a column filled with silica gel (L100/250μ) as the support with elution by chloroform. Evaporation of the eluate gave 0.8 g (42%) of X with mp 214-216°C. IR spectrum in Nujol: 1688, 1681, and 1655 cm^{-1} (C = O); in dioxane: 1694, 1657 cm^{-1} ($A_{C=X}$ = 9.71 practical units). UV spectrum (in dioxane), λ_{max} (log ε): 310 (3.78), 340 (3.69), and 390 nm (3.97). PMR spectrum in DMSO: 10.4 (1H, s, CH= O), 7-9 (11H, m, aromatic), and 5.92 ppm (2H, s, CH_2–N); in CF_3COOH: 7-9 (11H, m, aromatic) and 6.29 ppm (2H, s, CH_2–N). Found: C 75.5; H 4.1; N 7.4%; M^+ 366. $C_{23}H_{14}N_2O_3$. Calculated: C 75.4; H 3.9; N 7.7%; M 366.

B) A solution of 0.2 g of IV in 10 ml of anhydrous benzene was heated to the boiling point, and 0.2 ml of thionyl chloride was added. The solution was cooled, and 0.01 g of salt VI was separated. Evaporation of the filtrate gave 0.15 g of dibenzocinnoline X.

2-[(2-Pyridinomethyl)benzyl]-3,7-dioxo-2,3-dihydro-7H-dibenzo[d,e,h]cinnoline Perchlorate (XIb). A 0.2-g sample of VI was dissolved in 5 ml of anhydrous pyridine, and the resulting red solution was vacuum evaporated in a stream of argon. The dry resinous residue was washed with hot benzene until a colorless wash solution was obtained. The benzene solution was vacuum evaporated to give 0.08 g (40%) of aldehyde X. The residue was washed with a few drops of pyridine and dissolved in 5 ml of ethanol, and one to two drops of perchloric acid were added to the solution. It was then cooled to –10°C, and the precipitate was separated to give 0.045 g (16%) of yellow crystals of perchlorate XIb, which decomposed explosively at 250°C. IR spectrum (in Nujol): 1672 and 1643 cm^{-1}. UV spectrum (in ethanol), λ_{max} (log ε): 310 (3.99), 335 (3.75), and 385 nm (3.89). PMR spectrum (in DMSO): 7-9.15 (16H, m, aromatic), 6.23 (2H, s, CH_2–N^+), and 5.64 ppm (2H, s, CH_2–N). Found: Cl 7.2%. $C_{28}H_{20}ClN_3O_6$. Calculated: Cl 6.7%.

2-Benzyl-3,7-dioxo-2,3-dihydro-7H-dibenzo[d,e,h]cinnoline (XII). A solution of 0.5 g (2 mmole) of anthraquinone-1-carboxylic acid chloride in 15 ml of dioxane was added to a solution of 2 ml (20 mmole) of benzylhydrazine and 1 ml (7 mmole) of triethylamine in 10 ml of dioxane. After 2 h, the mixture was diluted with water, and the precipitate was separated to give 0.4 g (63%) of yellow crystals of XII with mp 232-235°C (from dioxane). IR spectrum in Nujol: 1677 and 1661 cm^{-1}; in dioxane: 1654 cm^{-1}. (A = 8.03 practical units). UV spectrum (in dioxane), λ_{max} (log ε): 312 (3.90), 340 (3.66), and 390 nm (397). PMR spectrum (in CF_3COOH): 7-9 (12H, m, aromatic) and 5.80 ppm (2H, s, CH_2–N). Found: C 76.8; H 4.2; N 8.0%. $C_{22}H_{14}N_2O_2$. Calculated: C 78.1; H 4.2; N 8.3%.

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