METHYLATION OF 1-OXO-4-HYDROXYPYRIDAZINO[4,5-b]-QUINOXALINE

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The methylation of 1-oxo-4-hydroxypyridazino[4,5-b]quinoxaline (I) with methyl iodide and diazomethane under various conditions was studied. The structures of the disodium and disilver salts of I were established by means of spectrophotometric methods of analysis.

A study of the methylation of 1-oxo-4-hydroxypyridazino[4,5-b]quinoxaline (I) seemed of interest in connection with the establishment of the structure and with the investigation of the reactivity of this compound. The reaction was carried out with methyl iodide in alkaline solution and with an ether solution of diazomethane; the disodium and disilver salts of I were also methylated with methyl iodide.

The reaction of I with methyl iodide in alkaline solution gave II, while III was obtained with an ether solution of diazomethane.

It is known that metal derivatives of substances that are capable of tautomerism have dual reactivity, which is displayed in alkylation reactions in the formation of both O-alkyl and N-alkyl derivatives. Methylation of the sodium salts leads primarily to N-methyl derivatives, while O-methyl derivatives are the main products in the methylation of silver salts. We therefore assumed that the chief product of the methylation of the disodium salt of I (Ia) would be the N,N-dimethyl derivative, and that the chief product in the case of the disilver salt of I (Ib) would be the O,O-dimethyl derivative.

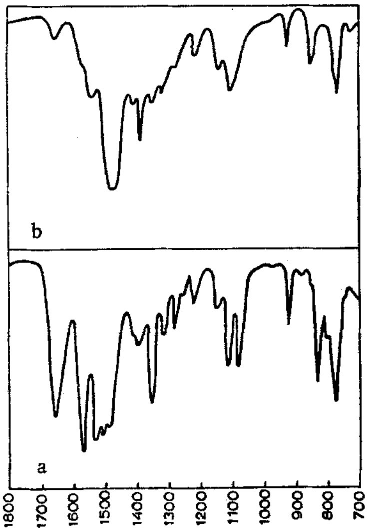
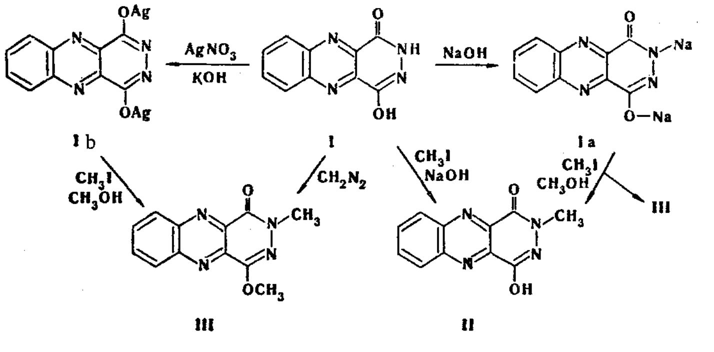


Fig. 1. IR spectra (in the crystalline state): a) disodium salt of I (Ia); b) disilver salt of I (Ib).

We made a preliminary study of the structure of salts Ia and Ib by IR and UV spectroscopy. The IR spectrum of Ia (Fig. 1) in the crystalline state showed the presence of an intense band of carbonyl absorption at 1658 cm^{-1} and a band at 1530 cm^{-1}, which are characteristic for compounds with oxohydroxy forms in this series [1]; this makes it possible to conclude that Ia has a mixed oxo-hydroxy structure.

Only two absorption maxima with λ_{max} 246 and 320 nm appeared in the electronic spectra of an alcohol solution of Ia (Fig. 2, curve 1); this is in accord with a dioxo form [1], and one



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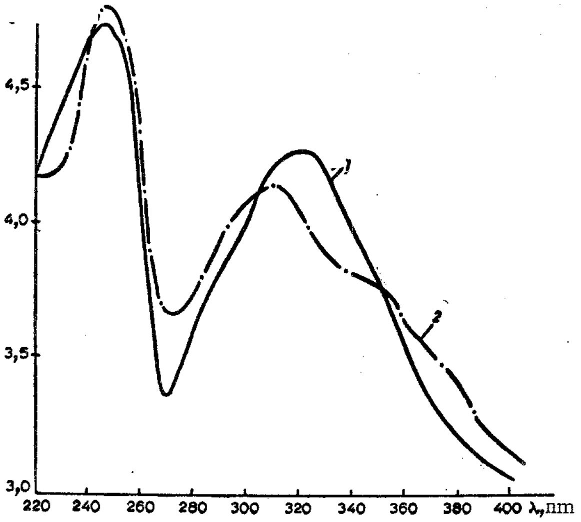

Fig. 2. UV absorption spectra of the disodium salt of I (Ia); 1) in alcohol; 2) in water.

should note the hypsochromic shift of about 10 nm of the absorption maxima as compared with the spectrum of the compound with a known dioxo structure. It is possible that the salt dissociates in alcohol solution and that its anion has the dioxo structure.

On the other hand, the UV spectrum of an aqueous solution of Ia with three absorption maxima (246, 310, and 340 nm) proved to be similar to the electronic spectrum of an alcohol solution of I [1]. Only the long-wave bands of I (294 and 322 nm) are bathochromically shifted to 310 and 340 nm, respectively, in the spectrum of Ia, and there is a simultaneous increase in the intensity of all of the absorption maxima. Since I has the oxo-hydroxy structure, we have assigned an electron structure corresponding to the oxo-hydroxy form also to the anion of Ia in water.

Thus, from the IR spectra, Ia has a lactam-lactim form in the crystalline state. The electron-density distribution in the anion of the salt in water corresponds to this same mixed structure. Dissociation of the salt also apparently occurs in alcohol solution, but its anion has the dioxo structure.

The IR spectrum of disilver salt Ib (Fig. 1) at 700-1800 cm^{-1} proved to be substantially different from the spectrum of Ia with respect to the position of many of the absorption bands. The character of the spectrum also differs sharply from the spectrum of the N,N-dimethyl derivative of I [1]; this provides a possibility for assuming the dihydroxy form for Ib. The low-intensity band at 1660 cm^{-1} is apparently related to the $-\mathrm{C}=\mathrm{N}-$ stretching vibrations, since it is present in the spectra of other derivatives of I that do not contain carbonyl groups. We were unable to obtain the electronic spectrum of Ib because it is not soluble in either water or organic solvents.

The reaction products in the methylation of Ia with methyl iodide in methanol proved to be II and III. Reaction of Ib with methyl iodide under the same conditions gave only one compound – III. According to their melting points and IR spectra, II and III were identical to the compounds of known structure described in [1].

EXPERIMENTAL

The IR spectra of KBr pellets of the substances were recorded with a UR-10 spectrophotometer. The UV spectra of $2 \cdot 10^{-4}$ M solutions in alcohol and water (layer thickness 0.5 cm) were recorded with a VSU-1 spectrophotometer.

Methylation of I with Methyl Iodide in Alkaline Solution. A 4-ml (28 mmole) sample of methyl iodide was added to a solution of 0.2 g (1 mmole) of I in 25 ml of 1.25 N NaOH, and the mixture was refluxed for 1 h, cooled, and concentrated in vacuo. The residue was acidified with acetic acid or concentrated HCl, and the precipitate was removed by filtration and reprecipitated twice from dilute NaOH solution by the addition of concentrated HCl to give 0.15 g (70%) of bright-yellow crystals of 1-oxo-2-methyl-4-hydroxypyridazino[4,5-b]quinoxaline (II) with mp 300°. Found,%: C 57.7; H 3.2; N 24.4. $C_{11}H_8N_4O_2$. Calculated, %: C 57.9; H 3.5; N 24.6.

Methylation of I with Diazomethane. An ether solution of diazomethane [2], obtained from 10 g (100 mmole) of nitrosomethylurea, was added to a suspension of 0.2 g (1 mmole) of I in 30 ml of ether and 30 ml of methanol, and the mixture was allowed to stand at room temperature for 24 h. The filtrate was evaporated to dryness, and the residue was crystallized from heptane to give 0.15 g (70%) of yellow crystals of 1-oxo-2-methyl-4-methoxypyridazino[4,5-b]quinoxaline (III) with mp 240°. Found,%: C 59.4; H 4.0; N 22.9. $C_{12}H_{10}N_4O_2$. Calculated,%: C 59.5; H 4.2; N 23.1.

Methylation of the Sodium Salt of I (Ia) with Methyl Iodide. A 1-g (4.7 mmole) sample of I was added with stirring to a solution of 0.38 g (9.5 mmole) of NaOH in 10 ml of water, and the precipitate was removed by filtration and dried to give 1.2 g of Ia with mp > 300°. Found,%: C 46.3; H 1.3; N 21.4. $C_{10}H_4N_4Na_2O_2$. Calculated,%: C 46.5; H 4.6; N 21.7.

A 1.2-g (4.7 mmole) sample of Ia was refluxed with 5 ml (35 mmole) of methyl iodide in 100 ml of methanol for 3 h. The solvent was removed by distillation, and the residue was extracted with acetone. Removal of the acetone gave 0.7 g of a mixture of II and III. It was treated with a dilute solution of NaOH. The insoluble portion [0.3 g (30%)] was isolated as yellow crystals of III with mp 240°. Acidification of the alkaline filtrate with concentrated HCl precipitated 0.4 g (40%) of II with mp 300°.

Methylation of the Silver Salt of I (Ib) with Methyl Iodide. A 0.2-g (1 mmole) sample of I and 0.35 g (2 mmole) of silver nitrate were added with stirring to a solution of 0.11 g (2 mmole) of KOH in 4 ml of water, and the resulting precipitate was removed by filtration, washed with water, alcohol, and acetone, and dried to give 0.4 g of Ib with mp > 300°. Found,%: C 28.0; H 1.0; N 13.1. $C_{10}H_4Ag_2N_4O_2$. Calculated, %: C 28.1; H 0.9; N 13.1.

A 0.4-g (1 mmole) sample of Ib was refluxed with 2 ml of methyl iodide in 10 ml of methanol for 1 h. The mixture was filtered, and the filtrate was evaporated to give 0.11 g (50%) of III with mp 240° (from heptane).

LITERATURE CITED

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