UDC 547.822.7'781

I. N. Azerbaev,* I. A. Poplavskaya,

R. G. Kurmangalieva, and S. F. Khalilova

2-Amino, 2-amino-3-methyl-, and 4-aminopyridine react with α -chloro- α -isonitrosoacetone at the heteroring nitrogen atom to give salts, which are converted to imidazo[1,2-a]pyridines or, in the case of 4-aminopyridine, to 1-(1-oximino-2oxopropyl)-4-pyridoneimine when they are treated with alkali. Acetylpyridylurea was obtained from chloroisonitrosoacetone and 2-aminopyridine in pyridine.

It has been reported [1, 2] that α -chloro- α -isonitrosoacetone (I) reacts with aromatic amines in the presence of an HCl acceptor (triethylamine) to give the corresponding amidoximes. We have studied the reaction of chloroisonitrosoacetone (I) with 2-amino-, 2-amino-3-methyl-, and 4-aminopyridine. The use of triethylamine as an HCl acceptor in these cases is not always convenient, since, for example, a difficult-to-separate mixture of products is formed in the reaction with 4-aminopyridine, and very pronounced resinification of the reaction mixture is observed in the case of 2-aminopyridine.

2-Amino- and 2-amino-3-methylpyridine react with I in equimolar ratios to give the corresponding pyridinium salts II and III. Cyclization to give 2-methyl- (IV) and, respectively, 2,8-dimethyl-3-nitrosoimidazol[1,2-a]pyridine (V) occurs when aqueous solutions of the salts are made alkaline. Compound V is also obtained in good yield when the reaction is carried out in the presence of an equimolar amount of triethylamine.

The IR spectra of IV and V do not contain absorption bands of carbonyl, OH, and NH groups but do contain a band at 1484 cm^{-1} , which was assigned to the NO group. The position of the absorption maxima in their UV spectra is in good agreement with the literature data for such compounds [3]. The chemical shifts of the signals of the protons in the PMR spectra are also in good agreement with the literature data [4, 5].

As in the case of arylamines, acetylurea VI (12% yield) rather than α -(2-pyridyl)amino- α -isonitrosoacetone, as we previously assumed in [2], is obtained in the reaction of 2-aminopyridine with chloroisonitroso ketone I. N-Acetyl-N'-(2-pyridyl)urea (VI) is formed via the same mechanism as N-acetyl-N'-arylurea [6], and it can be obtained in somewhat higher yield when N-(1-oximino-2-oxopropyl)pyridinium chloride (VII) is treated with a mixture of 2-aminopyridine and triethylamine.

The IR spectrum of urea VI (in KBr) is very similar to the spectra of acetylarylureas: it contains two bands at 1696 and 1716 cm⁻¹, related to two carbonyl groups, and two bands (3140 and 3240 cm⁻¹), which are affiliated with two NH groups [6, 7]. In the IR spectrum of the hydrochloride of VI the NH⁺ band (with two maxima at 2500 and 2590 cm⁻¹) is very distinctly separated from the $v_{\rm CH}$ bands, and there is a group of "imine salt bands" at 1800-2000 cm⁻¹; this constitutes evidence for protonation of the nitrogen atom of the pyridine ring [8].

A salt -4-amino-1-(1-oximino-2-oxopropyl)pyridinium chloride (VIII) - is formed when equimolar amounts of 4-aminopyridine and chloroisonitroso ketone I are mixed in ether. The 1-(1-oximino-2-oxopropyl)-4-pyridoneimine base (IX) is liberated when the salt is made alkaline with sodium carbonate. The base forms a hydrochloride, which can also be obtained by treatment of an alcohol solution of salt VII with hydrogen chloride in ether. Gradual conversion of the base to the hydrochloride is also observed when the salt is refluxed for a long time in alcohol.

*Deceased.

Institute of Chemical Sciences, Academy of Sciences of the Kazakh SSR, Alma-Ata 480100. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1525-1529, November, 1978. Original article submitted March 1, 1977; revision submitted March 15, 1978. Compound IX is bright-yellow and soluble in water, and its IR spectrum contains a broad band at 2700-2900 cm⁻¹, from which it can be assumed that it has an inner salt structure:



The band at 1660 cm⁻¹ with a shoulder at approximately 1700 cm^{-1} in the IR spectrum of IX probably corresponds to the C=N and C = 0 stretching vibrations. The very strong band at 1233 cm^{-1} should apparently be assigned to =N-O⁻ vibrations. The color vanishes on passing from the base to the hydrochloride, and a carbonyl band appears in the IR spectrum at 1705 cm^{-1} , and a C=N band is observed at 1662 cm⁻¹. Also in agreement with the salt structure of IX is the PMR spectrum, which contains a singlet of a CH₃ group at 2.4 ppm, two doublets at 6.67 and 7.5 ppm with J = 7 Hz which are the signals of the α and β protons of a pyridine ring, and a singlet of two protons at 8 ppm, which can be assigned to an NH₂⁺ group. In the PMR spectrum of the hydrochloride the signals of the ring protons and the protons of the NH₂⁺ group are shifted, respectively, to weak field to 7.0, 8.0, and 9.0 ppm, and a very broad signal of the proton of an NOH group appears at 14.2 ppm.



11, 1V R = H; 111, V, X $R = CH_3$; XI $R = C_6H_5$

We carried out the acetylation and benzoylation of IX assuming that, the imino or oximino group would be acylated depending on the conditions. However, 4-acylaminopyridines (X, XI) were isolated in all cases. The initial product in the acylation of the imino group is evidently pyridinium salt A, which undergoes decomposition under the influence of alkaline agents to give 4-acylaminopyridines X and XI.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were obtained with a UR-20 spectrometer. The PMR spectra* were obtained with a ZKR-60 spectrometer with tetramethylsilane as the internal standard. The UV spectra of solutions of the compounds were recorded with a Specord spectrophotometer.

<u>1-(1-0ximino-2-oxopropy1)-2-aminopyridinium Chloride (II).</u> A solution of 2.6 g (0.021 mole) of chloroisonitrosoacetone in ether was added with stirring and cooling to 2 g (0.021 mole) of 2-aminopyridine, and the mixture was stirred for 3-4 h. The next day, the precipi-</u>

*The PMR spectra were analyzed in accordance with first-order principles. The assignment of the signals in the more complex spin systems was made by comparison with the literature data [4, 5, 9] and by comparison of the areas of the signals.

tate was removed by filtration and washed with ether to give 4.31 g (94%) of salt II with mp 107-109°C. Found: C1 16.3%. $C_8H_{10}ClN_3O_2$. Calculated: C1 16.5%.

<u>2-Methyl-3-nitrosoimidazo[1,2-a]pyridine (IV)</u>. A saturated solution of sodium carbonate was added to a solution of 3 g of salt II in the minimum amount of water until the mixture was alkaline, after which it was extracted with chloroform. The extract was evaporated to a minimal volume, and the resulting precipitate was removed by filtration to give 1.3 g (44%) of green IV with mp 127-128°C (from ethyl acetate). IR spectrum: 728 (pyridine ring CH) and 1484 cm⁻¹ (C-N=O). UV spectrum, λ_{max} (log ε): 249 (4.56), 278 (4.66), 322 (4.49), 377 nm (4.68). PMR spectrum, δ (CDCl₃): 3.03 (s, 3H, CH₃), ~7.16 (1H, 6-H), ~7.65 (2H, 7-and 8-H), and 9.7 ppm (d, J_{5,6} = 6 Hz, 1H, 5-H). Found: C 59.5; H 4.3%. C₆H₇N₃O. Calculated: C 59.6; H 4.1%. The hydrochloride was obtained by treatment of a solution of base IV in absolute acetone with an ether solution of HCl. The brown hydrochloride had mp 194-196°C. Found: C1 17.4%. C₆H₇N₃O·HCl. Calculated: C1 17.9%.

 $\frac{1-(1-0ximino-2-oxopropyl)-2-amino-3-methylpyridinium Chloride (III). A solution of 2.66 g (0.022 mole) of chloroisonitrosoacetone in ether was added gradually to a solution of 2.37 g (0.022 mole) of 2-amino-3-methylpyridine in ether, and the mixture was stirred for several hours. The next day the precipitate was separated and washed with ether to give 4.6 g (91%) of III with mp 125°C. Found: Cl 15.1%. C₉H₁₂ClN₃O₂. Calculated: Cl 15.5%.$

<u>2,8-Dimethyl-3-nitrosoimidazo[1,2-a]pyridine (V).</u> A) A 0.25-g (2.4 mmole) sample of sodium carbonate was added to a solution of 1 g (4.4 mmole) of salt III in water, and the solution was stirred for a certain time. The reaction product was extracted from the aqueous solution with chloroform, and the extract was dried with magnesium sulfate and evaporated to give 0.68 g (89%) of base V with mp 142-143°C (from alcohol).

B) A solution of 2.16 g (0.018 mole) of chloroisonitrosoacetone in ether was added with cooling to a mixture of 2.1 g (0.019 mole) of 2-amino-3-methylpyridine and 1.81 g (0.018 mole) of triethylamine in ether, and the mixture was stirred at room temperature for several hours. The resulting precipitate was removed by filtration and washed with water to remove the triethylamine hydrochloride. This procedure gave 1.3 g of product. Evaporation of the ether solution gave an additional 1.61 g of reaction product for an overall yield of 2.64 g (85%) of green needles with mp 144-145°C (from alcohol). The product was soluble in chloroform, alcohol, and ethyl acetate, less soluble in ether, and only slightly soluble in water. IR spectrum: 765 (pyridine ring CH) and 1460 cm⁻¹ (C-N=O). PMR spectrum, δ (CDCl₃): 2.62 (s, 3H, 8-CH₃), 3.05 (s, 3H, 2-CH₃), 7.06 (1H, 6-H), 7.55 (d, J_{7,6} = 7.2 Hz, 1H, 7-H), and 9.57 ppm (d, J_{5,6} = 6.7 Hz, 1H, 5-H). UV spectrum, λ_{max} (log ε): 250 (4.38), 279 (4.43), 322 (4.33), 384 nm (4.38). Calculated: C 61.7; H 5.1; N 23.7%. C9H9N3O. Calculated: C 61.7; H 5.1; N 24.0%. The hydrochloride was obtained by treatment of an ether solution of the base with an ether solution of HCl and had mp 179-180°C (from alcohol containing ether). Found: C1 16.6%. C9H9N3O.HCl. Calculated: C1 16.8%.

<u>1-(1-Oximino-2-oxopropyl)pyridinium Chloride (VII)</u>. A 3-g sample of chloroisonitrosoacetone was added with stirring and cooling (with ice water) to 5-10 ml of pyridine, and the mixture was stirred for 3-4 h. The resulting precipitate was separated and washed several times with ether to give pyridinium salt VII in quantitative yield. The white powder had mp 125-126°C. PMR spectrum, δ (CD₃OD): 2.53 (s, 3H, CH₃), 8.20 (2H, H_β), 8.75 (t, J = 7.6 Hz, 1H, H_γ), and 8.85 ppm (d, J = 6.6 Hz, 2H, H_α). Found: N 14.4%. C₉H₉ClN₂O₂. Calculated: N 13.9%.

<u>N-Acety1-N'-(2-pyridy1)urea (VI).</u> A) A 3.4-g (0.028 mole) sample of α -chloro- α -isonitrosoacetone was added gradually at room temperature to a solution of 2.62 g (0.028 mole) of 2-aminopyridine in 15-20 ml of pyridine, and the mixture was stirred for several hours and allowed to stand overnight. The next day, it was diluted with two to three volumes of water and extracted repeatedly with ether. The ether solution was evaporated, and the resulting precipitate was removed by filtration, washed with a small amount of water, and dried to give 0.6 g (12%) of a substance with mp 196-197.5°C (from ethanol). IR spectrum: 1690, 1716 (C=0); 3140, 3240 cm⁻¹ (NH). Found: C 52.9; H 5.0%. CeHeNsO2. Calculated: C 53.6; H 5.0%. The hydrochloride was obtained by the action of an ether solution of HCl on an ether solution of the base. The white hydrochloride had mp 209-210°C. IR spectrum:

1695, 1725 (C=O); 3140, 3240 (NH); ~2500-2600, 1800-2000 cm⁻¹ (C=NH⁺). Found: C 44.2; H 4.6; C1 16.0; N 18.6%. C₈H₉N₃O₂•HC1. Calculated: C 44.6; H 4.8; C1 16.4; N 19.5%.

B) A 2.1-g (0.011 mole) sample of pyridinium salt VII was added gradually to a solution of 1 g (0.011 mole) of 2-aminopyridine and 1.07 g (0.011 mole) of triethylamine in ether, and the mixture was stirred for 3-4 h. The resulting precipitate was separated and washed with water to give 0.27 g of urea VI. An additional 0.14 g of VI was obtained from the ether solution for an overall yield of 0.41 g (22%) of a product with mp 195°C (from alcohol).

<u>1-(1-Oximino-2-oxopropyl)-4-aminopyridinium Chloride (VIII).</u> A 2-g (0.021 mole) sample of 4-aminopyridine was dissolved in the minimum amount of alcohol, the solution was poured into 100-150 ml of ether, and an ether solution of 2.6 g (0.021 mole) of chloroisonitrosoacetone was added with cooling and stirring. The precipitate of quaternary salt VIII that formed after stirring at room temperature for 4 h was separated to give 3.8 g (83%) of a product with mp 110-111°C. Found: Cl 16.3%. $C_{eH_{10}ClN_{3}O_{2}}$. Calculated: Cl 16.4%.

<u>1-(1-0ximino-2-oxopropyl)-4-pyridoneimine (IX)</u>. A saturated solution of sodium carbonatewas added to a solution of 4.6 g of salt VIII in water until the mixture was alkaline, andthe resulting precipitate was separated and washed with water until the washings were freeof chloride ions. This procedure gave 0.82 g of product. The aqueous solution was evaporated to a minimal volume, and the precipitate was separated, washed to remove chloride ions,and dried to give another 1.3 g of product for an overall yield of 2.12 g (55%) of a brightyellow product with mp 175-176°C. The product was soluble in alcohol but only slightly</u>

soluble in water. IR spectrum: (cm^{-1}) : 1660 s,~1700 sh (C=N and C=O), and ~2700 br (NH₂). PMR spectrum (d_-DMSO): 2.4 (s, 3H, CH₃), 6.58 (d, J = 7 Hz, 2H, H_β), 7.3 (d, J = 7 Hz, 2H, H_α), and 7.9 ppm (s, 2H, NH₂). UV spectrum, λ_{max} (10gε): 250 (3.56) and nm 259 nm (4.15). Found: C 52.8; H 5.1; N 23.1%. C_gH₉N₃O₂. Calculated: C 53.6; H 5.0; N 23.4%. The hydrochloride was a colorless substance with mp 170°C (dec., from alcohol with ether) and was soluble in water. IR spectrum: 1707 (C=O) and 1663 cm⁻¹ (C=N). PMR spectrum (DMSO): 7.04 (d, J = 7.5 Hz, 2H, H_β), 8.04 (d, J = 7.5 Hz, 2H, H_α), 9.08 (s, 2H, NH₂), and 14.25 ppm (broad s, 1H, NOH). Found: C 45.0; H 4.7; Cl 15.9%. C_gH₉N₃O₂•HCl. Calculated: C 44.5; H 4.6; Cl 16.5%.

<u>4-Acetamidopyridine (X).</u> A 1.8-ml (0.03 mole) sample of acetic anhydride was added with cooling to a mixture of 0.45 g (0.0025 mole) of salt IX and 1.65 ml of pyridine. After the solid dissolved, the mixture was heated on a water bath for 3 h, subjected to vacuum evaporation with a water aspirator, treated with 2-3 ml of water, and evaporated to dryness. Water was added to the residue, and the mixture was neutralized with NaHCO₃. The next day, the precipitate was separated to give 0.126 g of X with mp 146-147°C (from alcohol); the product was identical to 4-acetamidopyridine (no melting-point depression was observed for a mixture with a genuine sample). The filtrate was evaporated to dryness, and the residue was washed with absolute ethanol. An ether solution of HCl was added to the ethanol washes, and the mixture was worked up to give 0.03 g of 4-acetamidopyridine hydrochloride with mp 231-233°C (from alcohol). The overall yield of amide X was 43%.

<u>4-Benzamidopyridine (XI)</u>. A solution of 0.16 g (0.004 mole) of NaOH in water was added to a solution of 0.35 g (0.002 mole) of salt IX in 30 ml of water, and 0.47 ml (0.004 mole) of benzoyl chloride was added gradually to this mixture with stirring and cooling (with ice). The solution was stirred for a few minutes, and the resulting precipitate was separated and dried to give 0.25 g (68%) of XI with mp 202-203°C, which was identical to 4-benzamidopyridine (no melting-point depression was observed for a mixture with a genuine sample).

LITERATURE CITED

- 1. I. N. Azerbaev, I. A. Poplavskaya, and R. G. Kurmangalieva, Zh. Org. Khim., <u>4</u>, 590 (1968).
- 2. I. N. Azerbaev, R. G. Kurmangalieva, and I. A. Poplavskaya, Zh. Org. Khim., 6, 66 (1970).
- N. O. Saldabol, S. A. Giller, L. N. Alekseeva, and I. V. Dipan, Khim.-Farm. Zh., No. 6, 12 (1972).
- 4. J. G. Lombardino, J. Org. Chem., <u>30</u>, 2403 (1965).
- 5. J. P. Paolini and R. K. Robins, J. Org. Chem., <u>30</u>, 4085 (1965).
- 6. I. N. Azerbaev, I. A. Poplavskaya, R. G. Sharipova, and S. F. Khalilova, Izv. Akad. Nauk Kaz. SSR, Ser. Khim., No. 4, 59 (1973).
- 7. R. C. Raul, S. Sood, and S. L. Chadcha, J. Inorg. Nucl. Chem., 33, 2703 (1971).

- 8. K. Nakanishi, Infrared Spectra and the Structure of Organic Compounds [Russian translation], Mir, Moscow (1965), p. 47.
- 9. B. I. Ionin and B. A. Ershov, NMR Spectroscopy in Organic Chemistry [in Russian], Khimiya, Moscow (1967), p. 239.

MOLECULAR-ORBITAL SELF-CONSISTENT FIELD CALCULATIONS OF QUINOLINE

AND ITS DERIVATIVES.

II.* CALCULATION OF THE ELECTRONIC STRUCTURE AND SPECTRA OF

8-MERCAPTOQUINOLINE

Z. P. Bruvers and L. V. Zuika

UDC 543.422.6:547.831.78

The electronic spectra of the thiol, anionic, protonated, and mesoionic forms of 8-mercaptoquinoline and the mesoionic form of 5-mercaptoquinoline and the 5mercapto-N-methylquinolinium ion were calculated within the CNDO (complete neglect of differential overlap) approximation. The inclusion of the d orbitals of the sulfur atom in the AO basis has virtually no effect on the energies of the electron transitions of these compounds.

In the present research we calculated the various forms of 8-mercaptoquinoline in order to ascertain the electronic structures and nature of the electron transitions and to compare them with the analogous data for 8-hydroxyquinoline.

The spectral properties of these compounds are also of interest in connection with the problems of the structures of the chelate compounds of 8-mercaptoquinoline and 8-hydroxyquinoline. On the basis of electronic absorption spectra it has previously been assumed [1] that the ligands in 8-mercaptoquinoline complexes of nontransition metals have structures analogous to the thiol form, whereas the ligands in the corresponding complexes of transition metals have structures analogous to the mesoionic form of the reagent.

The thiol (I), anionic (II), cationic (III), and mesoionic (IV) forms of 8-mercaptoquinoline and the mesoionic form of 5-mercaptoquinoline (V) and the 5-mercapto-N-methylquinolinium cation (VI) were calculated within the CNDO (complete neglect of differential overlap) approximation (with an sp basis for the AO). Twenty-five lower singly excited configurations were taken into account in the calculation of the electronic spectra. The $u_{\mu\mu}$ and γ_{AA} values were borrowed from [2], and the β_A° values were varied for reproduction of the electronic spectra of the thiol and mesoionic forms of 8-mercaptoquinoline ($\beta_H^{\circ} =$ -12, $\beta_C^{\circ} = -16$, $\beta_N^{\circ} = -24$, and $\beta_S^{\circ} = -18$ eV). The contribution of the d orbitals of the sulfur atom to the formation of the bonds was examined in the case of the thiol and mesoionic forms of 8-mercaptoquinoline (with an spd' basis for the AO of the sulfur atom).

The udd value was calculated from the data in [3], and the β_{AB}° (d) value for the orbitals was calculated on the basis of β_{AB}° (d) = $0.5\beta_{AB}^{\circ}$ (sp). The two-center two-electron integrals were calculated from the Mataga formula. The geometry of the molecules was selected in accordance with the data in [4], the C-S and S-H bond lengths were 1.75 and 1.35 Å, respectively, and the CSH angle was 100°.

The observed and calculated energies and oscillator forces of the singlet-singlet electron transitions of I-VI are compared in Table 1. In the case of the thiol form of 8mercaptoquinoline the calculation satisfactorily conveys the energies of the electron transitions and the oscillator forces, which correspond to $\alpha + p$, β , and β ' transitions (π - π * bands) of quinoline and 8-hydroxyquinoline. An n- π * band is not observed in the spectrum because of overlapping with the intense π - π * absorption.

*See [4] for communication I.

Institute of Inorganic Chemistry, Academy of Sciences of the Latvian SSR, Riga 226934. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1530-1534, November, 1978. Original article submitted December 1, 1977.