The mass spectra were obtained with an MKh-1303 spectrometer with a system for direct introduction of the substances into the ion source at ionizing voltages of 70 and 20 V and injection temperatures of 30-50°C. The precise masses of the individual fragments were measured with an MS-30 spectrometer.

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REACTION OF 2-METHYLENE-3-OXOQUINUCLIDINE WITH WATER, ALCOHOLS, AND ORGANIC ACIDS

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2-Methylene-3-oxoquinuclidine (I) reacts with alcohols without acidic or alkaline catalysts to give 2-alkoxymethyl-3-oxoquinuclidines. In the case of protonation of I by weak acids (benzoic and barbituric acids) water molecules do not add to the double bond. Condensed heterocyclic systems that include the quinuclidine ring were obtained on the basis of 2-hydroxymethyl-3-hydroxy-Δ^2-dehydroquinuclidine.

According to the data in [1], the 2-methylene-3-oxoquinuclidine (I) base has moderate reactivity: It does not add alcohols and water to the methylene group in the absence of a catalyst. At the same time, it has been noted [2] that unsaturated ketone I reacts with water to give an addition product that has the 2-hydroxymethyl-3-hydroxy-Δ^2-dehydroquinuclidine (II) structure.

Continuing our study of the reactivity of 2-methylene-3-oxoquinuclidine (I) we studied the reaction of I with alcohols, water, and some organic acids. We found that unsaturated ketone I without the addition of acidic or alkaline catalysts is capable of forming addition products with lower alcohols, viz., 2-alkoxymethyl-3-oxoquinuclidines (III). The reactions take place at 20°C with time and depend substantially on the nucleophilicity of the alcohol. Of the four alcohols studied, viz., methanol, ethanol, isopropyl alcohol, and n-butyl alcohol, methanol adds most readily, while isopropyl alcohol adds with the greatest difficulty. The course of the reaction was monitored by means of gas–liquid chromatography (GLC). A mixture of I and the corresponding alcohol (40 equivalents each) was maintained at 20°C for four days; addition was observed only for methanol (IIIa:I = 0.44). In the course of the next

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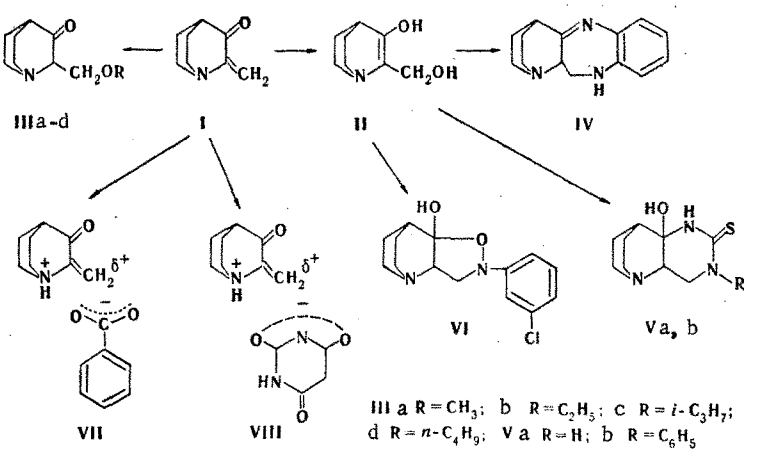
8 days we noted an increase in the amount of the methoxy derivative (IIIa:I = 1.9) and the formation of the ethoxy derivative (IIIb:I = 0.07). The reactions of isopropyl and n-butyl alcohols proceeded extremely slowly, and appreciable amounts of the corresponding addition products were detected only after 4 months. The following ratios of 2-alkoxy derivatives III to starting ketone I were observed after this time: IIIa:I = 2.5, IIIb:I = 0.82, IIIc:I = 0.11, and IIId:I = 0.52.*

The addition of alcohols to the activated double bond of I (the Mannich reaction) is evidently catalyzed in this case by the highly basic quinuclidine molecules, which create a sufficiently high pH value of the medium.

Structure IIIa is confirmed by the ^{13}C NMR spectra of a sample of the reaction mixture, which contains, in addition to IIIa, starting ketone I, methanol, and a very small amount of an impurity with an unestablished structure. The assignment of the ^{13}C signals of the principal components of the reaction mixture, viz., I and IIIa, is presented in Table 1. 2-Methoxymethyl-3-oxoquinuclidine (IIIa) exists in the keto form, as evidenced by the presence in the spectrum of a signal of a CO group at 218.1 ppm (an "unsaturated ketone") and a C_2 signal at 70.4 ppm (a doublet in the spectrum recorded under conditions of incomplete suppression of the spin–spin coupling with the protons). The strong-field shift of the carbon atom signal of the CH_2 group of the substituent attached to C_2 in IIIa as compared with starting ketone I is also significant (Table 1). The chemical shifts and the multiplicity (in the spectrum recorded with incomplete decoupling of the protons) of the remaining signals are also in agreement with the proposed IIIa structure.

In conformity with the data in [2], we obtained diol II and studied its properties. In contrast to unsaturated ketone I, which polymerized on standing, this compound is stable during storage and, like ketone I [3, 4], is capable of reacting under mild conditions with nucleophilic reagents, viz., o-phenylenediamine, thiourea, and m-chlorophenylhydroxylamine, to give condensed quinuclidine derivatives IV-VI in high yields.



It is known that in hydrochloric acid under protonation conditions ketone I adds not one but rather two molecules of water to give 2-hydroxymethyl-3,3-dihydroxyquinuclidine hydrochloride [1, 2]. We demonstrated that addition of water to the olefinic bond does not take place in an aqueous solution of benzoic acid, in which the nitrogen atom also undergoes protonation, and that only salt VII is formed. In the ^{13}C NMR spectrum of salt VII, which was isolated in the monohydrate form, the chemical shifts of all of the carbon atoms (particularly the C_2 and C_3 atoms) are virtually the same as the corresponding shifts for the starting ketone (Table 1). Consequently, the number and character of the carbon bonds in the quinuclidine part of salt VII and in the ketone are identical.

The reaction of I with barbituric acid in dimethylformamide (DMF) proceeds similarly, as a result of which we obtained only salt VIII.

EXPERIMENTAL

The ^{13}C NMR spectra of the compounds were recorded with a Varian XL-100A-12 spectrometer under conditions of complete and incomplete suppression of the spin–spin coupling with the protons with tetramethylsilane as the standard. Gas–liquid chromatographic analysis was

*The analysis was carried out by chromatographic mass spectroscopy.

TABLE 1. ^{13}C NMR Spectra of I, III, and VII

Compound	Solvent	^{13}C NMR spectra, ppm					
		C_2	C_3	C_4	C_5, C_8	C_6, C_7	R (attached to C_2)
I	CD_3Cl	(152,6 s)	(203,3 s)	(40,4 d)	(25,2)	(48,5 t)	(112,7 t) $=CH_2$
I	CD_3OD +	153,0	203,8	41,2	25,4	49,2	113,3
IIIa[a]	$+C_6D_6$ (9 : 1)	70,4 d	218,1 s	40,9 d	25,5 t	43,1 t	70,7 t ($2\text{-}CH_2O$);
					26,3 t	49,2 t	59,0 q. ($-OCH_3$)
VII[b]	d_7-DMF	153,6	203,8	41,1	25,4	48,7	112,4 ($=CH_2$)

[a]This is the spectrum of the reaction mixture. [b]Signals of the ^{13}C atoms of benzoic acid: 1-C 131.8, 2,6-C 129.8, 3,5-C 128.9, 4-C is 133.1, and COO 167.9.

carried out with a Pye-Unicam 104 chromatograph with a catharometer and a 2.1 m by 4 mm column filled with 10% SE-30 silicone elastomer on silanized diatomaceous earth (100-120 mesh); the helium flow rate was 30 ml/min with a 200°C isotherm.

2-Hydroxymethyl-3-hydroxy-Δ^2-dehydroquinuclidine (II). A solution of 14.78 g (108 mmole) of 2-methylene-3-oxoquinuclidine in 30 ml of water was maintained at 20°C for 48 h, after which 180 ml of acetone was added, and the resulting white precipitate was removed by filtration and washed with acetone to give 14.06 g (75.7%) of a product with mp 79-80°C. IR spectrum: 1667 (C=C); 3190, 3550 cm^{-1} (OH). Found: 56.9; H 8.8; N 8.3%. $C_8H_{13}NO_2 \cdot 0.75\ H_2O$. Calculated: C 56.9; H 8.7; N 8.3%.

In some experiments that were carried out similarly the amount of crystallization water in II was 2.75 equivalents; this crystal hydrate had mp 64-66°C. Found: C 47.2; H 10.4; N 6.8%. $C_8H_{13}NO_2 \cdot 2.75\ H_2O$. Calculated: C 47.1; H 10.6; N 6.9%. (The ability of diol II to form crystal hydrates with various percentages of water has also been previously noted [2].)

11,11a-Dihydro-10H-benzodiazepino[3,4-b]quinuclidine (IV). A mixture of 3.37 g (20 mmole) of 2-hydroxymethyl-3-hydroxy-Δ^2-dehydroquinuclidine and 2.16 g (20 mmole) of o-phenylenediamine in 15 ml of ethanol was shaken for 10-15 min until the starting compounds dissolved and a new precipitate developed. The reaction mixture was then allowed to stand at 20°C for 48 h, and the precipitate was removed by filtration and washed with a small amount of alcohol to give 4 g (88%) of a product with mp 215-216°C (from ethanol) [3]. IR spectrum: 1648 (C=N) and 3240 cm^{-1} (NH). Found: C 74.2; H 7.5; N 18.4%. $C_{14}H_{17}N_3$. Calculated: C 74.0; H 7.5; N 18.5%.

4a-Hydroxy-6-thio-4a,5,6,7,8,8a-hexahydropyrimido[5,4-b]quinuclidine (Va). An aqueous solution of sodium hydroxide [0.9 g (39 mmole) of sodium hydroxide in 15 ml of water] was added to a mixture of 1.52 g (20 mmole) of thiourea and 3.37 g (20 mmole) of diol II, and the reaction mixture was then stirred until the starting compounds dissolved. The clear solution was cooled to 20°C, during which a precipitate began to form. The reaction mixture was allowed to stand at 4°C for 18 h, after which the precipitate was removed by filtration and washed with water to give 2.77 g (56.7%) of a product with mp 205-206°C (dec.) [4]. IR spectrum: 3210 and 3160 cm^{-1} (NH, OH). Found: 50.6; H 7.1; N 19.6; S 15.0%. $C_9H_{15}N_3OS$. Calculated: C 50.7; H 7.1; N 19.7; S 15.0%.

4a-Hydroxy-6-thio-7-phenyl-4a,5,6,7,8,8a-hexahydropyrimido[5,4-b]quinuclidine (Vb). A 0.45-g (2.96 mmole) sample of phenylthiourea and 0.5 g (2.96 mmole) of diol II were added to a solution of 0.12 g (2.96 mmole) of sodium hydroxide in 15 ml of water, and the mixture was heated to the boiling point, during which the starting compounds dissolved, and a precipitate of different character formed. The mixture was maintained at 20° for 1 h, after which the precipitate was removed by filtration and washed with water to give 0.8 g (93%) of a product with mp 224-225°C (dec.) [4]. IR spectrum: 3200 and 3340 cm^{-1} (NH and OH). Found: C 62.2; H 6.6; N 14.5; S 11.1%. $C_{15}H_{19}N_3OS$. Calculated: C 62.2; H 6.6; N 14.5; S 11.1%.

4a-Hydroxy-6-(m-chlorophenyl)quinuclidino[4,5-b]isoxazolidine (VI). A) A mixture of 2.04 g (10 mmole) of diol II and 1.44 g (10 mmole) of m-chlorophenylhydroxylamine in 10 ml of ethanol was shaken for 10-15 min until the starting compounds dissolved and a new pre-

cipitate developed. It was then maintained at 20°C for 16 h, after which the precipitate was removed by filtration and washed with alcohol to give 2.58 g (91.6%) of a product with mp 152-153°C (from ethanol). IR spectrum: 2640-2660 cm^{-1} (OH). Found: C 59.9; H 6.1; Cl 12.8; N 9.8%. $C_{14}H_{17}ClN_2O_2$. Calculated: C 60.0; H 6.1; Cl 12.7; N 10.0%.

B) A solution of 1.44 g (10 mmole) of m-chlorophenylhydroxylamine in 10 ml of acetone was added to a solution of 2.04 g (10 mmole) of diol II in 10 ml of water, and the mixture was allowed to stand at 20°C for 16 h. The resulting precipitate was removed by filtration and washed with acetone to give 2.5 g (88.8%) of a product with mp 152-153°C (from ethanol).

2-Methylene-3-oxoquinuclidine Benzoate (VII). A 0.45-g (3.28 mmole) sample of 2-methylene-3-oxoquinuclidine in 2 ml of water was added to a suspension of 0.4 g (3.28 mmole) of benzoic acid in 4 ml of water, and the mixture of reagents was stirred, during which a precipitate with a new structure formed. The reaction mixture was allowed to stand at 20°C for 4 h, after which the precipitate was removed by filtration and washed with water to give 0.66 g of salt VII with mp 134-136°C (dec.). Found: C 65.8; H 7.1; N 5.1%. $C_8H_{11}NO \cdot C_7H_6O_2 \cdot H_2O$. Calculated: C 65.5; H 6.9; N 5.1%. The aqueous mother liquor was evaporated, and the residue was triturated with acetone to give an additional 0.11 g of salt VII with mp 134-136°C for an overall yield of 83.6%.

2-Methylene-3-oxoquinuclidine Barbiturate (VIII). A solution of 1.37 g (10 mmole) of quinuclidine I in 10 ml of dimethylformamide (DMF) was added to a solution of 1.28 g (10 mmole) of barbituric acid in 50 ml of DMF, and the precipitate that formed immediately was removed by filtration after 1 h to give 2.6 g (98.1%) of a product with mp 277-279°C (dec., from DMF). Found: C 54.6; H 6.0; N 15.6%. $C_8H_{11}NO \cdot C_4H_4N_2O_3$. Calculated: C 54.4; H 5.7; N 15.8%.

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SYNTHESIS, STEREOCHEMISTRY, AND ISOMERIC TRANSFORMATIONS OF cis- AND trans-1,2-DIMETHYL-4-ARYL-5-AROYL-2-IMIDAZOLINES

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The corresponding trans- and cis-1,2-dimethyl-4-aryl-5-aroyl-2-imidazolines were obtained from complexes of cis- and trans-1-methyl-2-aryl-3-aroylaziridines with BF_3 by heating with acetonitrile. The reaction proceeds with inversion of the configuration of the starting 3-aroylaziridines. In the presence of bases the complexes of cis-1,2-dimethyl-4-aryl-5-aroyl-2-imidazolines readily undergo isomerization to the corresponding trans analogs. The structures of the products were established on the basis of the IR, PMR, and mass spectra and the results of elementary analysis. The configurations of the compounds were determined by means of the Overhauser nuclear effect.

Preparations based on 2-imidazolines are widely used in medicine and pharmacology [1, 2]. However, the known methods for the synthesis of 2-imidazolines [3] make it virtually

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