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SYNTHESIS OF 2-HYDROXYMETHYLENE- AND 2-DIMETHYLAMINOMETHYLENE-3-OXOQUINUCLIDINES AND THEIR REACTIONS WITH NUCLEOPHILIC REAGENTS

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The reaction of 3-oxoquinuclidine with ethyl formate in the presence of sodium and with dimethylformamide diethylacetal was used to synthesize 2-hydroxymethylene- and 2-dimethylaminomethylene-3-oxoquinuclidines, which upon reaction with amines from N-substituted 2-aminomethylene-3-oxoquinuclidines and upon reaction with hydrazine hydrate give pyrazolo[3,4-b]quinuclidines. The reaction of 2-aryl- and 2-heteroarylmethylene-3-oxoquinuclidines with hydrazine hydrate and thiourea, which led to the synthesis of pyrazolo[3,4-b]- and pyrimido[5,4-b]quinuclidines with aryl or heteroaryl substituents in the resulting ring, was studied.

One of the methods for the synthesis of condensed quinuclidine derivatives is the conversion of 3-oxoquinuclidine (I) to 2-methylene- and 2-arylidene-3-oxoquinuclidines with subsequent reaction of these compounds of their derivatives with bifunctional nucleophilic reagents [1-5]; new partially or completely hydrogenated rings condensed with the quinuclidine ring are formed as a result of the reaction of the binucleophiles with both the carbonyl group and the olefinic bond of the indicated α,β-unsaturated ketones. It seemed of interest to study the possibility of the synthesis of quinuclidines condensed with unsaturated heterorings on the basis of 2-hydroxymethylene- (II) and 2-dimethylaminomethylene-3-oxoquinuclidines (III), with which nucleophilic reagents should react not only at the olefinic bond but also at the hydroxy or dimethylamino group.

Compounds II and III have not been described in the literature. We obtained 2-hydroxymethylene-3-oxoquinuclidine (II) in 67% yield by the reaction of 3-oxoquinuclidine (I) with ethyl formate in the presence of an equimolar amount of sodium metal, and we prepared 2-dimethylaminomethylene-3-oxoquinuclidine (III) in 58% yield by prolonged refluxing of ketone I in a solution of dimethylformamide diethylacetal with simultaneous removal of the resulting ethanol.

The structures of II and III were confirmed by the ^1H and ^{13}C NMR spectra. In the ^1H NMR spectra (Table 1) the singlets at 8.89 (ketone II) and 6.91 ppm (ketone III) correspond to the protons attached to the exocyclic double bond; in the ^{13}C NMR spectra (Table 2) of these compounds the signals at 180.0 and 137.6 ppm, respectively, correspond to the exocyclic carbon atom.

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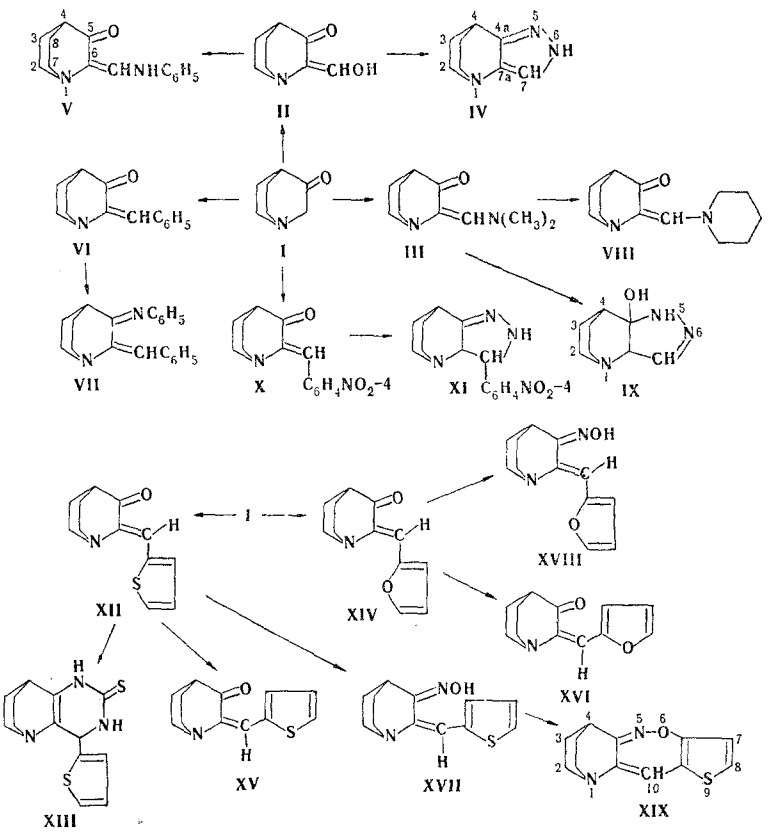


We studied the chemical properties of II and III. Ketone II is unstable with respect to the action of alkalis but remains unchanged when it is heated with hydrochloric acid. The reaction of II with ethyl orthoformate in ethanol in the presence of concentrated HCl does not lead to the 2-ethoxymethylene derivative either at room temperature or upon heating, and this distinguishes it substantially from other ketones that contain an α-hydroxymethylene group.

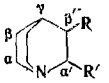
The reactions of II with hydroxylamine, phenylhydrazine, o-phenylenediamine, and thiourea proceed ambiguously to give multicomponent systems. The hydrochloride of II reacts considerably more unambiguously with hydrazine hydrate, and pyrazolo[3,4-b]quinuclidine (IV)is obtained in 64% yield. Aniline reacts with ketone II only at the hydroxymethylene group to give 2-phenylamino-methylene-3-oxoquinuclidine (V). It should be noted that only 2-benzylidene-3-phenyliminoquinuclidine (VII) was synthesized when 2-benzylidene-3-oxoquinuclidine (VI) [6] was heated with aniline. We did not observe the formation of a product of the addition of aniline to the olefinic bond of VI, whereas anilines add readily to the C=C bond of 2-methylene-3-oxoquinuclidine to give 2-arylamino-methyl-3-oxoquinuclidines in high yields [7].

In the ^{1}H NMR spectrum of IV the signal of the 4-H proton (3.41 ppm) is shifted to weak field relative to the analogous signal in the spectrum of II (2.61 ppm) as a consequence of the anisotropic effect of the heteroaromatic pyrazole ring; the signal of the 7-H proton (7.26 ppm), on the other hand, is shifted to strong field (8.89 ppm for ketone II) because of the lower electronegativity of the nitrogen atom as compared with the oxygen atom.

According to the spectral data, ketone V exists in the form of a mixture of isomers, for each of which a signal at ∿190 ppm, which corresponds to the carbon atom of a conjugated keto group, is characteristic in the ^{13}C NMR spectrum. A signal at 172.6 ppm, which indicates the presence of a C=N bond in the molecule, is characteristic for the ^{13}C NMR spectrum of VII.

As compared with II, III displayed lower reactivity in the reaction with amines. Thus III remained unchanged when it was heated with aniline, while 2-(1'-piperidinylmethylene)-3-oxoquinuclidine (VIII) is formed with the more basic piperidine. In contrast to ketone II, the reaction of which with hydrazine hydrate leads to pyrazoloquinuclidine IV, a pyrazoline derivative, viz., 4a-hydroxy-4a,7a-dihydropyrazolo[5,4-b]quinuclidine (IX), was obtained from ketone III in a similar process.

TABLE 1. Parameters of the ^{1}H NMR Spectra of II-V, VII-IX, XI, XIII, and XVII-XIX



Compound	Chemical shifts, ppm			
	α	β	γ	R and R'[a]
II	3,0—3,7 m	1,9—2,2 m	2,61 qn	8,89 (s, 9-H)
III	2,6—3,1 m	1,7—2,0 m	2,44 qn	6,91 (s, 9-H); 3,18 [$N(CH_3)_2$]
IV	2.5—3.4 m	1,4—2,1 m	3,41 qn	7,26 (s, 7-H)
V[b] (mixture of isomers)	3,2—3,9 m	2,0—2,4 m	2,91 qn	7,87 (d, 9-H), $J_{9HNH} \approx 15$ Hz, 8,83 (d, 9-H), $J_{9HNH} \approx 13$—14 Hz; 11,36 (d, NH) and 10,50 (d, NH)
VII	3,0—3,2 m	2,6—2,9 m	2,87 qn	6,7—8.1 (m, C_6H_5, C_6H_5, 9-H)
VIII	2,7—3,2 m	1,7—2,0 m	2,44 qn	6,91 (s, 9-H), 3,7 (br s, 2′,6′-H_2); 1,6 (br s, 3,4,5-H_2)
IX	2,97 t; 2,62 t	1,4—1,9 m	2,00 qn	6,75 (d, 7-H), $J_{7H7aH} \approx 1$ Hz; 3,80 (s, 7a-H); 5,9 (br, s, NH)
XI	3,3—3,9 m	2,0—2,3 m	3,25 qn	4,82 (d, 7-H), $J_{7H7aH} \approx 12$ Hz; 5,43 (d, 7aH); 7,6—7,8 (m, 2′,6′-H); 8,1—8,2 (m, 3′,5′-H)
XIII	2,6—3,1 m	1,4—1,8 m	2,62 m	5,38 (d, 8-H), $J_{8HNH} \approx 1$ Hz; 6,9—7,1 (m) and 7,3—7,4 (m, 3′,4′,5′-H); 6,8 (br s) and 8,0 (br s, 5-NH and 7-NH)
XVII	3,4—3,9 m	1,8—2,4 m	4,04 q	7,27 (s, 9-H); 7,13 (q, 4′-H); 7,59—7,74 (m, 3′,5′-H)
syn-XVIII	3,4—4,1 m	1,8—2,5 m	3,90 qn	7,16 (s, 9-H); 6,70 (q, 4′-H); 6,92 (d, 3′-H); 7,79 (d, 5′-H)
anti-XVIII			3,08 qn	8,25 (s, 9-H); 6,73 (q, 4′-H); 7,01 (d, 3′-H); 7,85 (d, 5′-H)
XIX	2,6—3,5 m	1,5—2,3 m	4,22 qn	7,82 (7-H); 8,05 (8-H); 7,92 (s, 10-H)

[a]The hydrogen atoms of the R' substituent (piperidinyl, phenyl, furyl, and thienyl) are designated by primes (′). [b]Studied in a mixture of the isomers. The following solvents were used: CD_3OD for II, XVII, and XIX, $CDCl_3$ for III, IV, V, VII, VIII, IX, and XIII, CD_3COOD for XI, and D_2O for XVIII; the abbreviation qn pertains to a quintet ($J_{H\gamma H\beta} \approx 2.5$ Hz).

The virtually complete agreement between the chemical shifts of the 4-H and 9-H protons in VIII and III serves as a confirmation of the structure of VIII.

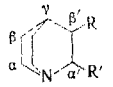
A signal of a quaternary C_{4a} atom at 89.1 ppm, which corresponds to an sp^3-hybridized carbon atom in the 3 position of the quinuclidine ring with two nonequivalent electronegative substituents, is characteristic for the ^{13}C NMR spectrum of IX.

When the hydroxy or dimethylamino group in the methylene residue of II and III is replaced by an aryl (or heteroaryl) group, the reaction with nucleophiles takes place at the olefinic bond, which also leads to the formation of new partially hydrogenated heterocycles but with a different position of the multiple bond. Thus 7-(4′-nitrophenyl-7,7a-dihydropyrazolo[3,4-b]quinuclidine (XI) was obtained from 2-(4′-nitrophenylmethylene)-3-oxoquinuclidine (X) [6] and hydrazine hydrate, whereas 6-thio-8-(2′-thienyl)-5,6,7,8-tetrahydropyrimido[5,4-b]quinuclidine (XIII) was obtained from cis-2-(2′-thienylmethylene)-3-oxoquinuclidine (XII)* [5] and thiourea in the presence of an equimolar amount of sodium ethoxide.

It was shown that starting cis-ketone XII, like cis-2-(2′-furylmethylene)-3-oxoquinuclidine (XIV) [5], undergoes isomerization to trans-ketone XV (XVI) on treatment with hydrogen chloride. Oximes XVII and XVIII were obtained from cis isomers XII and XIV by reaction with hydroxylamine; a mixture of isomers XVIII with syn and anti orientations of the oxime group and a cis configuration of the furylmethylene group is formed from ketone XIV, whereas one syn isomer XVII with a trans configuration of the thienylmethylene group is formed from ketone XII. To determine the three-dimensional structures of syn-oximes XVII and XVIII and anti-oxime XVIII we compared the chemical shifts of the 4-H and 9-H protons of the indicated

*A drawn-together orientation of the aryl (heteroaryl) substituent and the nitrogen atom of the quinuclidine ring is assumed for the cis configuration.

TABLE 2. Parameters of the ^{13}C NMR Spectra of II-V, VII, and IX



Compound	Chemical shifts, ppm					
	α	α′	β	β′	γ	R and R′[a]
II	51,6 t	118,5 s	22,3 t	192,6 s	38,4 d	170,0 (d, C_9)
III	49,8 t	118,7 s	26,5 t	202,9 s	39,9 d	137,6 (d, C_9); 41,9 [br q, $N(CH_3)_2$]
IV	51,3 t	130,9 s	28,4 t	151,1 s	26,7 d	119,6 (d, C_7)
V (mixture of isomers)	50,8 t	113,1 s	21,8 t	193,7 s	38,4 d	137,9 (s, C_9); 130,5 (d, C_9); 116,5 (d), 116,7 (d, $C_{2''}$, $C_{4''}$); 129,6 (d), 129,7 (d, $C_{3''}$, $C_{5''}$)
	51,4 t	111,8 s		191,1 s	38,1 d	124,7 (d, $C_{1''}$); 125,1 (d, $C_{4''}$); 139,0 (s, $C_{1'}$); 138,1 (d, $C_{1'}$)
VII	47,4 t	151,0 s[b]	26,4 s	172,6 s	29,3 d	119,8 (d), 121,3 (d), 123,1 (d), 128,0 (d), 128,7 (d), 130,9 (d), C_9, $C_{2'}C_{6'}$, $C_{2''}C_{6''}$, $C_{3'}C_{5'}$, $C_{3''}C_{5''}$, $C_{4'}$, $C_{1''}$); 135,2 (s, $C_{1'}$); 145,1 (s, $C_{1''}$)
IX	43,4 t 48,0 t	76,5 d	22,3 t 24,7 t	89,1 s	30,3 d	141,2 (C_7)

[a]The carbons atoms in R' are designated by primes ('), while the carbon atoms in R are designated by two primes (''). The following solvents were used: D_2O for II, $CDCl_3$ for III, IV, V, and VII, and CD_3OD for IX. [b]The reverse assignment of the signals is possible.

compounds with the corresponding values for the previously investigated oximes of 2-arylidene-3-oxoquinuclidines [8].

The oxidative cyclization of 2-(2'-thienylmethylene)-3-oxoquinuclidine oxime (XVII) by means of silver oxide led to thieno[2,3-f][1,2]oxazepino[3,4-b]quinuclidine (XIX). The structure of XIX follows from the presence in the ^1H NMR spectrum of two doublets [7.82 (7-H) and 8.05 ppm (8-H), $J_{7H,8H} \approx 6$ Hz], which correspond to coupling of the protons of the α,β-disubstituted thienyl ring with one another, and the signal of a 10-H proton at 7.92 ppm. The chemical shifts of the protons of the quinuclidine part of the XIX molecule are close to the corresponding values for benz[1,2]oxazepino[3,4-b]quinuclidines [9].

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded with an XL-100A-12 spectrometer (at 100 MHz for the protons and at 25.2 MHz for the ^{13}C atoms) with tetramethylsilane as the internal standard. The IR spectra of mineral oil pastes of the compounds were recorded with a Perkin-Elmer 599 spectrometer. The mass spectra were obtained with an MAT-112 mass spectrometer with direct introduction of the samples into the source at an ionizing-electron energy of 70 eV and an ionization-chamber temperature of 180°C.

Compound VI was obtained by the method in [6], X was obtained by the method in [8], and XII and XIV were obtained by the method in [5].

2-Hydroxymethylene-3-oxoquinuclidine (II). A mixture of 3 g (24 mmole) of 3-oxoquinuclidine (I), 2.55 g (32 mmole) of ethyl formate, 0.55 g (24 mmole) of sodium, 0.2 ml of ethanol, and 50 ml of dry ether was stirred at 20°C for 25 h, after which the precipitate was removed by filtration, washed with ether, and dried. The precipitate was then dissolved in absolute ethanol, the solution was acidified with an alcohol solution of hydrogen chloride, and the precipitated sodium chloride was removed by filtration. The solution was evaporated, the residue was triturated with ether and acetone, and the precipitate was removed by filtration and washed with ether to give 3 g (67%) of hydrochloride of II with mp 186-188°C (from isopropyl alcohol).

To isolate the base, 0.82 g (4.3 mmole) of the hydrochloride of II was dissolved in a small amount of ethanol, a solution of 0.17 g (4.3 mmole) of sodium hydroxide in 10 ml of ethanol was added, and the precipitated sodium chloride was removed by filtration. The mother liquor was evaporated to give 0.22 g of base II with mp 279-281°C (from ethanol). IR

spectrum: 1590-1633 (C=C–CO) and 2540-2600 cm^{-1} (associated OH). Found: C 62.5; H 7.3; N 8.8%; M^+ 153. $C_8H_{11}NO_2$. Calculated: C 62.7; H 7.2; N 9.1%.

2-(Dimethylaminomethylene)-3-oxoquinuclidine (III). A solution of 3 g (24 mmole) of 3-oxoquinuclidine (I) in 10 ml of dimethylformamide diethylacetal was refluxed for 36 h with simultaneous removal of the resulting alcohol from the reaction mixture. The mixture was then evaporated *in vacuo*, and the residue was triturated with petroleum ether to give 2.5 g (57.8%) of a product with mp 101-102°C (from heptane). IR spectrum: 1587 (C=C) and 1673 cm^{-1} (CO). Found: C 66.5; H 8.8; N 15.3%; M^+ 180. $C_{10}H_{16}N_2O$. Calculated: C 66.6; H 8.9; N 15.5%.

6-H-Pyrazolo[3,4-b]quinuclidine (IV). A mixture of 2 g (10.5 mmole) of the hydrochloride of II and 1.06 g (21 mmole) of hydrazine hydrate in 20 ml of ethanol was maintained at 20°C for 24 h, after which the precipitated hydrazine hydrochloride was removed by filtration, 0.53 g (10.5 mmole) of hydrazine hydrate was added to the solution, and the mixture was refluxed for 5 h. The reaction mass was evaporated *in vacuo*, and the residue was triturated with benzene to give 1 g (63.6%) of product with mp 146-148°C (from benzene). IR spectrum: 1570, 1586 (C=C–C=N); 3050, 3110 cm^{-1} (NH). Found: C 64.3, H 7.2, N 27.9%, M^+ 149. $C_8H_{11}N_3$. Calculated: C 64.4, H 7.4, N 28.2%.

2-(Phenylaminomethylene)-3-oxoquinuclidine (V). A solution of 2 g (10.5 mmole) of the hydrochloride of II in 10 ml of aniline was maintained at 20°C for 24 h, after which the excess aniline was removed by distillation *in vacuo*, and the residue was dissolved in 20 ml of water and treated with a 50% solution of potassium carbonate. The mixture was extracted with benzene, the extract was dried with magnesium sulfate and evaporated, and the residue was dissolved in ether. The ether solution was acidified with an alcohol solution of hydrogen chloride, and the liberated oil was triturated with acetone to give 1.02 g (36.5%) of the hydrochloride of V with mp 230-232°C (dec., from isopropyl alcohol). IR spectrum: 1638, 1680, 1710 (C=C–CO), 3240 (NH), 2410-2742 cm^{-1} (NH). Found: C 63.9, H 6.4, Cl 13.3, N 10.4%. $C_{14}H_{16}N_2O \cdot HCl$. Calculated: C 63.5, H 6.5, Cl 13.4, N 10.5%.

2-Benzylidene-3-phenyliminoquinuclidine (VII). A mixture of 3 g (14 mmole) of 2-benzylidene-3-oxoquinuclidine (VI) [6], 1.3 g (14 mmole) of aniline, 80 ml of xylene, and catalytic amounts of p-toluenesulfonic acid was refluxed for 21 h with removal of the water by azeotropic distillation. The solvent was removed by vacuum distillation, and the residue was triturated with petroleum ether to give 3 g (74%) of a product with mp 192-193°C (from isopropyl alcohol). IR spectrum: 1607, 1655 cm^{-1} (C=C–C=N). Found: C 83.0; H 7.0; N 9.6%. M^+ 288. $C_{20}H_{20}N_2$. Calculated: C 83.3; H 7.0; N 9.7%.

2-(1'-Piperidinylmethylene)-3-oxoquinuclidine (VIII). A solution of 1.5 g (8.3 mmole) of 2-(dimethylaminomethylene)-3-oxoquinuclidine (III) in 15 ml of piperidine was maintained at 20°C for 9 days, after which it was heated at 100°C for 2 h. The reaction mass was evaporated *in vacuo*, and the residue was triturated with hot heptane to give 1.2 g (65.6%) of a product with mp 100-102°C (from heptane). IR spectrum: 1572 (C=C) and 1675 cm^{-1} (CO). Found: C 70.6; H 9.2; N 12.9%. M^+ 220. $C_{13}H_{20}N_2O$. Calculated: C 70.9; H 9.2; N 12.7%.

4a-Hydroxy-4a,7a-dihydro-5H-pyrazolo[5,4-b]quinuclidine (IX). A mixture of 1 g (5.5 mmole) of III and 10 ml of hydrazine hydrate was maintained at 20°C for 7 days, after which it was evaporated *in vacuo*, and the residue was triturated with petroleum ether–benzene (10:1) to give 0.4 g (43.4%) of a product with mp 127-129°C (from ethyl acetate). IR spectrum: 1588 (C=N); 3060, 3260 cm^{-1} (OH). Found: C 75.3; H 7.8; N 25.1%; M^+ 167. $C_8H_{13}N_3O$. Calculated: C 57.5; H 7.8; N 25.1%.

7-(4'-Nitrophenyl)-7,7a-dihydro-6H-pyrazolo[3,4-b]quinuclidine (XI). A suspension of 2 g (7.8 mmole) of 2-(4'-nitrobenzylidene)-3-oxoquinuclidine (X) [8] in 20 ml of hydrazine hydrate was maintained at 20°C for 28 days with periodic shaking, during which the gradual disappearance of the yellow starting ketone X and the appearance of almost colorless crystals of three-ring compound XI were observed. The precipitate was removed by filtration and washed thoroughly with ethanol to give 1.37 g (65.3%) of a product with mp 128-129°C (from isopropyl alcohol–ethanol). IR spectrum: 1605 (C=N) and 3293-3300 cm^{-1} (NH, OH). Found: C 57.6; H 6.3; N 19.1%; M^+ 272. $C_{14}H_{16}N_4O_2 \cdot H_2O$. Calculated: C 57.9; H 6.2; N 19.3%.

6-Thio-8-(2'-thienyl)-5,6,7,8-tetrahydropyrimido[5,4-b]quinuclidine (XIII). A mixture of 3 g (13.7 mmole) of cis-2-(2'-thienylmethylene)-3-oxo-quinuclidine (XII) [5], 1.04 g (13.7 mmole) of thiourea, and 30 ml of an ethanol solution of sodium ethoxide [from 0.31 g

(13.4 mmole) of sodium] was refluxed for 26 h. The resulting precipitate was removed by filtration and washed with ethanol. The combined ethanol solutions were evaporated, and the residue was dissolved in a small amount of water. The aqueous solution was extracted with chloroform, the extract was dried with magnesium sulfate and evaporated, and the residue was triturated successively with petroleum and diethyl ether to give 1.6 g (42%) of a product with mp 231-232°C [from 2-propanol–ethanol (2:1)]. IR spectrum: 1695 (C=C) and 3100-3200 cm^{-1} (NH). Found: C 56.0, H 5.8, N 15.0, S 22.9%, M^+ 277. $C_{13}H_{15}N_3S_2$. Calculated: C 56.3, H 5.5, N 15.1, S 23.2%.

trans-2-(2'-Thienylmethylene)-3-oxoquinuclidine (XV). A solution of 0.98 g of cis-2-(2'-thienylmethylene)-3-oxoquinuclidine (XII) in 20 ml of methylene chloride was treated for 10 min with gaseous hydrogen chloride, after which the mixture was evaporated *in vacuo*, and the residue was dissolved in water. The aqueous solution was made alkaline with potassium carbonate, and the precipitate was removed by filtration and washed with water to give 0.8 g (82%) of a product with mp 118-120°C (from 2-propanol). Found: C 65.7, H 6.0, N 6.6, S 14.5%; M^+ 219. $C_{12}H_{13}NO_2$. Calculated: C 65.7, H 6.0, N 6.4, S 14.6%.

trans-2-(2'-Furylmethylene)-3-oxoquinuclidine (XVI). The isomerization of cis-2-(2'-furylmethylene)-3-oxoquinuclidine (XIV) [5] was carried out as in the preceding experiment. To isolate the trans isomer of XVI the alkaline solution was extracted with chloroform. The extract was dried with magnesium sulfate and evaporated, and the residue was dissolved in 2-propanol. The solution was decolorized with charcoal and evaporated *in vacuo*, and the residue was triturated with heptane to give a product with mp 94-96°C in 67% yield. Found: C 70.8, H 6.5, N 6.8%; M^+ 203. $C_{12}H_{13}NO_2$. Calculated: C 70.9, H 6.5, N 6.9%.

trans-2-(2'-Thienylmethylene)-3-oxoquinuclidine syn-Oxime (XVII). A mixture of 2 g (9 mmole) of cis-2-(2'-thienylmethylene)-3-oxoquinuclidine (XII), 0.63 g (9 mmole) of hydroxylamine hydrochloride, and 60 ml of ethanol was maintained at 20°C for 10 days, after which it was evaporated *in vacuo*, and the residue was triturated with ether and acetone to give 1.66 g (72%) of the hydrochloride of XVII with mp 221-222°C (from 2-propanol). Found: C 52.4, H 5.8, Cl 12.9, N 9.8, S 11.3%. $C_{12}H_{14}N_2OS \cdot HCl \cdot H_2O$. Calculated: C 52.8, H 6.2, Cl 13.0, N 10.2, S 11.7%.

cis-2-(2'-Furylmethylene)-3-oxoquinuclidine syn- and anti-Oximes (XVIII). These compounds were obtained by the method described for the synthesis of oxime XVIII from cis-2-(2'-furylmethylene)-3-oxoquinuclidine (XIV). The reaction time was 5 days, and the yield of the hydrochloride, with mp 182-183°C (from 2-propanol), was 84%. Found: C 56.1, H 6.2, Cl 14.2, N 10.7%. $C_{12}H_{14}N_2O_2 \cdot HCl$. Calculated: C 56.5, H 5.9, Cl 13.9, N 11.0%.

The base was isolated by treatment of an aqueous solution of the hydrochloride with potassium carbonate and had mp 138-140°C (from heptane). Found: C 65.6, H 6.4, N 12.6%; M^+ 218. $C_{12}H_{14}N_2O_2$. Calculated: C 66.0, H 6.4, N 12.8%.

Thieno[2,3-f][1,2]oxazepino[3,4-b]quinuclidine (XIX). A mixture of 2 g (7.6 mmole) of 2-(2'-thienylmethylene)-3-oxoquinuclidine oxime (XVII) hydrochloride and 2 g of silver oxide in 50 ml of chloroform was stirred at 20°C for 7 days, after which 1 g of silver oxide was added, and the mixture was stirred under the same conditions for 10 days. Another gram of silver oxide was added, and stirring was continued for 7 days. The liberated silver and excess silver oxide were removed by filtration, the solution was evaporated *in vacuo*, and the residue (1.4 g) was chromatographed with a column filled with 40/100 silica gel by elution with chloroform–methanol (10:1).

The fraction containing reaction product XIX was evaporated *in vacuo*, and the residue was triturated with petroleum ether to give 0.5 g (25%) of a product with mp 225-226°C (dec., from heptane). IR spectrum: 1550 and 1630 cm^{-1} (C=C–C=N). Found: C 59.8, H 5.4, N 11.6, S 13.3%; M^+ 232. $C_{12}H_{12}N_2OS \cdot 0.5H_2O$. Calculated: C 59.9, H 5.7, N 11.6, S 13.6%.

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ELECTROPHILIC SUBSTITUTION OF 1-METHYLINDENO-1H-[2,1-b]PYRIDINE

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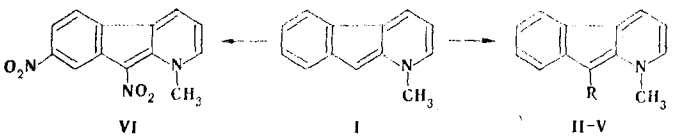
It is shown that electrophilic substitution of 1-methylindeno-1H-[2,1-b]pyridine takes place at the C_9 atom in the case of acylation (acetylation, benzoylation, and formylation), bromination, and nitration. Data from the ^{13}C NMR spectrum of this pseudoazulene confirm sp^2 hybridization of the C_9 atom.

1-Methylindeno-1H-[2,1-b]pyridine (I), which is formed by treatment of 1-azafluorene methiodide with 40% potassium carbonate solution [1], is classified as an aromatic system. In order to study its structure we used ^{13}C NMR spectroscopy. The spectra were obtained under conditions with and without proton decoupling; in this way we were able to assign the signals from five carbon atoms [the chemical shifts and ^{13}C and H spin-spin coupling constants (SSCC) are presented in Table 1].

It is apparent from Table 1 that the signal of the C_9 atom is localized at stronger field; however the $^1J_{C,H}$ value of 166 Hz constitutes evidence for its sp^2 hybridization [2], just as does the $^3J_{9-C,\ 8-H}$ value of 4 Hz. Thus the aromatic character of the five-membered ring of this pseudoazulene is confirmed. With respect to the chemical shift of 85.4 ppm for the C_9 atom (according to the established correlation of the chemical shifts of the ^{13}C nuclei with the π density in aromatic systems [3]), this ring fits into the category of aromatic anions. Quantum-chemical calculations of the pseudoazulene system [4] also show increased π-electron density on the C_9 atom, from which it follows that it would be the center of electrophilic substitution.

In order to obtain substituted 1-methylindeno-1H-[2,1-b]pyridines and to experimentally confirm the direction of its electrophilic substitution pseudoazulene I was subjected to acylation, formylation, bromination, and nitration.



VI I II-V

II R=$COCH_3$; III R=COC_6H_5; IV R=CHO; V R=Br

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