SYNTHESIS AND THREE-DIMENSIONAL STRUCTURE OF 2-ARYLIDENE-3-OXOQUINUCLIDINE OXIMES

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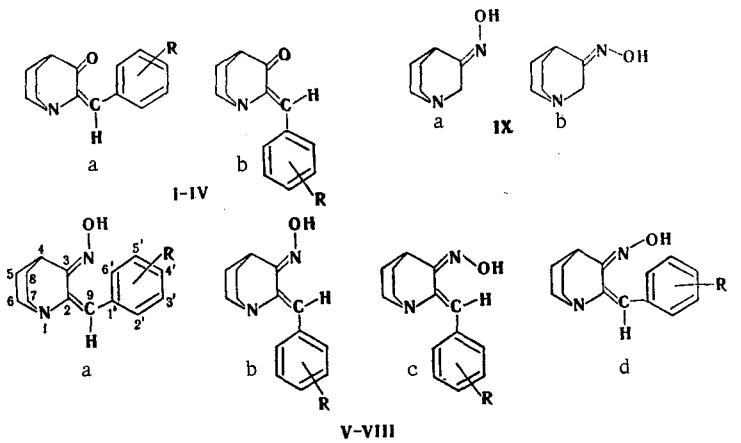
2-Arylidene-3-oxoquinuclidine oximes were obtained from the products of condensation of 3-oxoquinuclidine with aromatic aldehydes. It is shown that three of the four theoretically possible isomers (isomerism involving the C=C and C=N bonds) are formed; their thermal stability was studied. The structures of the isomeric oximes was established on the basis of data from the ^{1}H and ^{13}C NMR spectra and were confirmed by data from chromatographic mass spectrometry and the UV and IR spectra.

In order to synthesize condensed systems that include a quinuclidine ring we obtained the previously unknown 2-arylidene-3-oxoquinuclidine oximes and studied their three-dimensional structures.

2-Arylidene-3-oxoquinuclidines were first synthesized by Clemo and Hoggarth in 1939 [1] and were studied in greater detail by Warawa and co-workers in 1971-1974 [2, 3]. They showed that the cis isomers of 2-arylidene-3-oxoquinuclidines are formed in the reaction of 3-oxoquinuclidine with aromatic aldehydes in the presence of catalytic amounts of alkali hydroxides.* The cis isomers undergo rearrangement to the trans isomers under the influence of hydrogen chloride or when they are allowed to stand in organic solvents.

In the synthesis of 2-arylidene-3-oxoquinuclidines (I-IV) by the Warawa method we showed that in the case of salicylaldehyde the reaction takes place only when 1.15 equivalents of sodium hydroxide are used instead of the catalytic amount of alkali, as in the preparation of I-III.



I, V R=H; II, VI R=4-OCH_3; III, VII R=4-NO_2; IV, VIII R=2-OH

*Here and subsequently, the contiguous orientation of the aryl substituent and the nitrogen atom of the quinuclidine ring is adopted as the cis orientation, and the contiguous orientation of the quinuclidine C_4 atom and the hydroxy part of the oxime group is adopted as the syn orientation.

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TABLE 1. Chemical Shifts in the ^1H NMR Spectra of 2-Arylidene-3-oxoquinuclidines and the Oximes (ppm)

Compound	Positions of the protons[a]									
	2	4	5, 8	6, 7	9	2′	3′	4′	5′	6′
III	—	2,66	~2,1	~3,10	7,02	8,10			8,10	
IV		2,74	~2,1	~3,2	~6,8[b]	4,68 (OH)		6,7—7,4		
Va		3,69	1,76	3,10	6,66	7,1—7,3		7,6—7,8		7,1—7,3
Vb		3,65	~1,7	~3,0	6,75	7,2—7,4		7,8—8,0		7,2—7,4
Vc		2,70	~1,8	~3,0	7,73	7,1—7,3		7,9—8,0		7,1—7,3
VId		3,7	1,7	~3,1	6,62	6,80	7,70	3,78 (OCH_3)	7,70	6,80
VIb[c]		3,65	1,8	3,0	6,69	6,84	7,90	3,78 (OCH_3)	7,90	6,80
VIc[c]		2,72	1,8	3,0	7,76	6,84	7,94	3,8 (OCH_3)	7,94	6,84
VIIa		3,67	1,8	~3,1	6,65	7,72	8,12	—	8,12	7,72
VIIb		3,65	~1,8	~3,1	6,78	8,1			8,1	
VIIIb[c]		3,76	1,86	3,13	~6,8[b]			6,65—7,3		
VIIIc[c]		2,83	1,86	3,13	7,96			6,65—7,3		
IX	4,7	2,5	1,84	2,9						

[a]The solvent was d_1-chloroform. [b]In the multiplet of aromatic protons. [c]Investigated in the mixture of isomers.

TABLE 2. Chemical Shifts of the ^{13}C NMR Spectra of 2-Arylidene-3-oxoquinuclidines and Their Oximes (ppm)

Compound	Position of the C atoms[a]										
	2	3	4	5, 8	6, 7	9	1′	2′, 6′	3′, 5′	4′	4′-OCH_3
Ia	134,3	204,7	42,9	25,5	49,3	136,1	144,9	131,8	128,8	130,5	
Ib	133,8	205,8	40,2	25,8	47,4	124,9	144,5	131,9	128,2	129,3	
Va	135,2	157,5	24,7	24,7	48,8	124,4	143,2	129,4	127,6	127,1	
Vb	135,3	160,7	24,0	25,2	47,5	118,7	142,4	130,3	128,0	127,5	
Vc	135,4	154,1	31,4	26,1	46,6	128,7	139,3	130,2	127,6	127,4	
VIb[b]	140,3	158,9	24,0	25,3	47,6	118,3	128,2	131,8	113,5	160,2	55,1
VIc[b]			32,6	26,0	47,0						45,8
IXa[b]	53,2		22,0	24,5							
IXb[b]	51,6	161,9	28,2	26,2	46,6						

[a]The following solvents were used: d_1-chloroform for Ia, b, Vb, and VIb, c, and d_6-dimethyl sulfoxide for Va, c and IXa, b. [b]Investigated in a mixture of the isomers.

Oximes V-VIII were obtained by the reaction of cis-2-arylidene-3-oxoquinuclidines I-IV with hydroxylamine hydrochloride. Theoretically speaking, the reaction could proceed with the formation of four isomers, viz., syn,trans (a), syn,cis (b), anti,cis (c), and anti,trans (d). However, we did not observe the formation of all four isomers in a single case: We obtained three isomers for oximes V and VI, one for oxime VII,* and two isomers for oxime VIII.

The three-dimensional structures of oximes V-VIII were established on the basis of data from the ^1H and ^{13}C NMR and UV spectra and chromatographic mass spectrometry.

The ^1H NMR spectral characteristics of oximes V-VIII are basically similar, and only the spectra of the isomeric 2-benzylidene-3-oxoquinuclidine oximes Va-c are therefore examined in detail hereafter (Table 1).

In the spectra of each isomeric oxime Va-c the signals of the α and β protons of the quinuclidine ring are multiplets at 2.9-3.1 and 1.7-1.8 ppm, respectively, and the signals at 6.8-7.4 ppm correspond to the protons of the phenyl ring. A substantial difference in the position of the signals of the isomeric oximes was noted only for the 4-H and 9-H protons: For the Va, b isomers the chemical shift of the 4-H protons is ∿3.7, as compared with 2.7 ppm for isomer Vc, while the corresponding values for the 9-H proton are 6.7 and

*The second isomer of oxime VII was obtained by isomerization of the product of the reaction of ketone III with hydroxylamine in the presence of palladium chloride.

TABLE 3. Specific Shifts of the Protons of 2-Arylidene-3-oxoquinuclidine Oximes (ΔEu, ppm)

Compound	Position of the protons[a]						
	2, 4	5, 8	6, 7	9	2′, 6′	3′, 4′, 5	4′-OCH_3
Va	0,24	0,56	0,22	0,06	0,1	0	
Vb	14,8	7,8	5,3	24,0	2,6	−0,9	
Vc	19,0	4,9	4,6	11,0	3,8	1,8	
VIa	0,25	0,2	0,15	0,15	0	0	−0,05
VIb[b]	3,6	1,9	1,5	6,2	−0,9	−0,2	0
VIc[b]					4,8	2,2	−1,2
IX[b]	18,2; 13,2	5,9	9,8				

[a]The solvent was d_1-chloroform. [b]Investigated in the mixture of isomers.

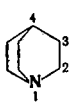
7.7 ppm. The reason for the weak-field shift of the signal of the 4-H proton in the Va, b isomers is evidently the pronounced deshielding effect of the OH group adjacent to this proton. It has been previously shown that substituents attached to the exocyclic double bond in the 3 position of the quinuclidine ring have precisely this effect on the chemical shift of the 4-H proton [4, 5]. These data indicate a syn orientation of the hydroxy group in isomers Va, b and an anti orientation in isomer Vc.

The indicated orientation of the OH groups in isomeric oximes Va-c was confirmed by data from ^{13}C NMR spectroscopy. In these spectra the signals of the unsubstituted carbon atoms of the quinuclidine ring are observed at 25-50 ppm [6]. Signals of the carbon atoms of the exocyclic 2-C=C double bond, the imine carbon atom, and the carbon atoms of the phenyl rings (Table 2).

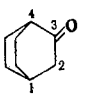
It follows from an analysis of the data in Table 2 that the signals of the C_4 atoms are close to one another in isomers Va, b (24.7 and 24.1 ppm, respectively) but are found at stronger field than the analogous signals for the Vc isomer (31.5 ppm). This sort of strong-field shift (by ∿7 ppm) is characteristic for the signal of a carbon atom that is syn-oriented with respect to an OH group [7]. It hence follows that the OH group and the C_4 atom have a syn orientation in isomers Va, b and an anti orientation in isomer Vc.

The configurations of the isomeric 2-aryldiene-3-oxoquinuclidine oximes relative to the exocyclic C=C bond were established by means of a paramagnetic shift reagent, viz., tris-(dipivaloylmethanato)europium [Eu(DPM)$_3$], the Eu^{3+} ion of which is capable of coordinating with the oxime group and the ring nitrogen atom. Using a similar approach Warawa has previously [2] shown that in cis-2-arylidene-3-oxoquinuclidines the Eu^{3+} ion is coordinated primarily with the oxygen atom of the 3-oxo group, whereas in the trans isomers it is coordinated primarily with the nitrogen atom of the quinuclidine ring.

An analysis of the magnitudes of the specific shifts (ΔEu) of the protons in the isomeric oximes Va-c (Table 3) indicates that in Vb, c the Eu^{3+} ion is coordinated primarily with the nitrogen atom of the oxime group but not with the nitrogen atom of the quinuclidine ring.* Evidence for this is provided by the ratio of the specific shifts of the protons that are closest to the potential coordination centers [ΔEu(6,7-H)]ΔEu(4-H) = A in oximes Va-c and in model compounds X and XI [2], in each of which coordination of Eu^{3+} only at one center, viz., in the 1 and 3 positions, respectively, is possible (Table 4).



X



XI

The close A values in isomers Vb, c and in ketone XI indicate a similar orientation of the Eu^{3+} ion in these compounds.

*The ΔEu_{OH} value of ≈ 12.3 in the spectrum of Vb is comparable with $\Delta Eu_{4-H} \approx 14.8$; this is in agreement to a great degree with coordination of the Eu^{3+} ion with the nitrogen atom rather than with the oxygen atom of the oxime group.

TABLE 4. Ratios of the Specific Shifts of the Protons of Va-c, X, and XI

Compound	Va	Vb	Vc	Xa	XI
$\frac{\Delta Eu\ (6,7\text{-H})}{\Delta Eu\ (4\text{-H})}$	0,92	0,36	0,24	2,5	0,27

[a]Compound IX was calculated on the basis of the data in [2].

TABLE 5. Retention Times of 2-Arylidene-3-oxoquinuclidines and Their Oximes

Compound	trans-Ia	trans-IIIa	Va	VIa	VIIa
Retention time	2'25"	2'40"	5'25"	7'30"	13'20"
Compound	cis-Ib	cis-IIIb	Vb, Vc	VIb	VIIb
Retention time	2'40"	2'55"	6'10"	8'50"	15'50"

The problem of the configurations of oximes Va-c relative to the C=C bond was solved on the basis of a comparison of the specific shifts of the protons of the substituent in the 2 position. In isomers Vb, c the specific shift of the 9-H proton exceeds this value for the protons of the benzene ring by a factor greater than 10 (Table 4). This sort of difference can be explained only by the closeness of the 9-H proton to the complexing nitrogen atom of the oxime group and the remoteness from this atom of the phenyl ring, which constitutes evidence for the cis configuration of isomers Vb, c. The differences in the ratios of the $\Delta Eu(9\text{-H})/\Delta Eu(4\text{-H})$ specific shifts for isomers Vb (1.62) and Vc (0.58) can be explained by the different orientations of the 9-H proton relative to the unshared pair of electrons of the nitrogen atom of the oxime group in the syn and anti isomers and, consequently, relative to the axis of the complex formed by these isomers with the Eu^{3+} ion.

Since oximes Vb, c are cis isomers, the configuration of the third isomer Va should be trans relative to the C=C bond. It should be noted that the cis configuration of oxime Vc is confirmed by data from the ^1H NMR spectra recorded without $Eu(DPM)_3$. In fact, the close values of the chemical shifts of the 9-H protons in syn isomers Va, b (Table 1) constitute evidence for the independence of the indicated chemical shift on the configuration relative to the C=C bond. On the other hand, in isomer Vc the signal of the 9-H proton is shifted markedly to weak field, evidently as a consequence of the same effect on this signal as on the signal of the 4-H proton in isomers Va and Vb. Thus our investigation by NMR spectroscopy of the structures of isomeric oximes Va-c showed that these compounds are, respectively, syn,trans-, syn,cis-, and anti,cis-oximes of 2-benzylidene-3-oxoquinuclodine (Va-c).

It was similarly shown that the isomers of oxime V have the following configurations: syn,cis (b, the principal amount obtained), anti,cis (c), and syn,trans (a). The isomers of oxime VII have the following configurations: syn,trans (a) and syn,cis (b, obtained by isomerization of the VIIa isomer). The isomers of oxime VIII have syn,cis (b) and anti,cis (c) configurations.

These conclusions were also confirmed by data from chromatographic mass spectrometry. The orientation of the substituents was determined by a comparison of the chromatographic mobilities of these compounds with the mobilities of model substances (trans and cis ketones Ia, b and IIIa, b) and from the peculiarities of their fragmentation under electron impact.

In analogy with the model substances (Ia, b), the oximes with shorter retention times (Va, VIa, and VIIa) should have a trans orientation of the aryl group, whereas the compounds with longer retention times (Vb, Vc, VIb, and VIIb) should have a cis orientation of the aryl group (Table 5).

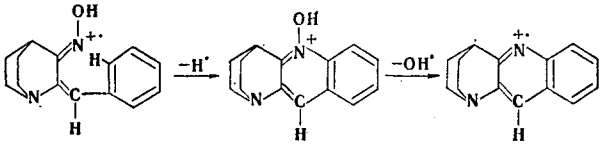
It is interesting to note that Vb, c, which are syn and anti isomers with respect to the oxime group, have identical retention times and give identical mass spectra.

TABLE 6. Relative Intensities of the Ion Peaks of 2-Arylidene-3-oxoquinuclidine Oximes (%)

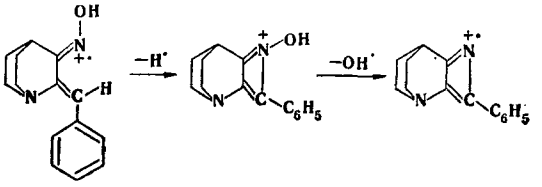
Ions	Substance						
	Va	Vb	Vc	VIa	VIb	VIIa	VIIb
$M^{+\cdot}$	21	50	47,5	22	15,8	14,5	24
$[M-H]^+$	43	32	31,6	18,1	7,2	19,3	8
$[M-OH]^+$	100	100	100	50	100	55	100
$[M-H_2O]^{+\cdot}$	93	32	47	100	58	100	68

An analysis of the fragmentation of oximes Va-c, VIa, b, and VIIa, b shows that all of the compounds are characterized by relatively intense molecular-ion peaks (M^+) with m/e 228 (Va-c), 258 (VIa, b), and 273 (VIIa, b), the character of the subsequent fragmentation of which is determined basically by the presence of an oxime group in the molecule. As in the mass spectrum of 3-oxoquinuclidine oxime (IX), the $[M-OH]^+$ ion peaks with mass numbers 201 (Va-c), 241 (VIa, b), and 256 (VIIa, b) are the most intense peaks in the spectra of oximes V-VII, while the presence of intense $[M-H]^+$ and $[M-H_2O]^+$ peaks, which are absent in the spectra of the model compounds (Ia, b and IX), is characteristic for the spectra of oximes V-VII. In the case of VI and VII the $[M-H_2O]^+$ peaks (240 and 255, respectively) have the maximum intensities. The intensity of the $[M-H]^+$ ion peaks also increases as the relative intensities of the $[M-H_2O]^+$ ion peaks increase in the spectra of oximes V-VII. It might be assumed that these ions are genetically interrelated and that the elimination of the group of H_2O atoms from M^+ in this case is realized in two stages, i.e., the M^+ ion successively split out a hydrogen atom and a hydroxy group.

It should be noted that the mass spectra of the trans isomers of oximes Va, VIa, and VIIa are characterized by higher intensities of the $[M-H]^+$ and $[M-H_2O]^+$ ion peaks as compared with the cis isomers (Vb, Vc, VIb, and VIIb; see Table 6). This may be explained by the closeness of the exocyclic nitrogen atom and the phenyl group in the trans isomers.



Less favorable elimination of the hydrogen atom of the methylidyne group evidently occurs in the case of the cis isomer:



The three-dimensional structures of the isomeric oximes were also confirmed by data from the UV and IR spectra.

In the UV spectra the long-wave absorption bands of Va (299 nm, log ε 3.99) and VIIa (347 nm, log ε 4.06) have considerably lower intensities as compared with the bands of oximes Vb (293 nm, log ε 4.30) or Vc (292 nm, log ε 3.33) and, respectively, VIIb (352 nm, log ε 4.27).

These data indicate disruption in the Va and VIIa molecules of the coplanarity of the conjugated system of bonds due to steric hindrance, which should occur in the trans isomers.

A difference between the trans isomers (a) and the cis isomers (b, c) was also observed in the IR spectra. In the crystalline state the bands of the OH group of oxime Va (2660 cm^{-1}) and VIIa (2700 cm^{-1}) are shifted to the low-frequency region relative to isomers Vb (3220 cm^{-1}), Vc (3160 cm^{-1}), and VIIb (3340 cm^{-1}); in solutions (1%, in chloroform), the frequencies of the free OH groups of isomers Va-c and VIIa, b coincide (3570 cm^{-1}). This sort of regularity was previously noted for the oximes of other carbonyl compounds [8].

TABLE 7. Thermal Isomerization of 3-Oxoquinuclidine Oximes (isomer content, %)

Oximes	Heating time, h								
	0			2			13		
	isomers								
	a	b	c	a	b	c	a	b	c
Va	100	0	0	100	0	0	40	40	20
Vb	0	100	0	0	70	30	0	65	35
Vc	0	0	100	0	70	30	0	65	35
IX			100		15	85		25	75

In order to determine the stabilities of the oximes obtained, as well as the possibility and conditions for interconversion, oximes Va-c were subjected to thermal isomerization to $C_6D_4Cl_2$ at 150°C. The quantitative ratios of the isomers of the oximes are presented in Table 7.

An analysis of the data obtained shows that oximes V are capable of undergoing isomerization under the indicated conditions; isomerization relative to the C=C and C=N bond takes place at different rates. Isomerization at the C=N bond (Vb $\rightleftarrows$ Vc) proceeds most readily; an equilibrium characterized by the ratio ~2:1 is attained rapidly in this case. A process of the Va $\rightleftarrows$ Vd type is not observed, evidently because of the great energic disadvantageousness of the sterically hindered Vd isomer. Isomerization at the C=C bond occurs only for oxime Va, but the process is slower and is accompanied by the formation (in addition to oximes Vb, c) of unidentified products that are not oximes, the amounts of which increase with time.

A similar study of the thermal isomerization of 3-oxoquinuclidine oxime attests to the significant energic preferableness of anti isomer IXb. The energic preferableness of the syn isomer for 2-benzylidene-3-oxoquinuclidine oxime (Vb), which exists in equilibrium with anti isomer Vc, is due to the existence in the latter of an energically unfavorable steric interaction of the oxime hydroxy group with the substituent in the 2 position of the quinuclidine ring.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded with a Varian XL-100A spectrometer with an operating frequency of 100 MHz for the protons and 25.2 MHz for the ^{13}C carbons. The internal standard was tetramethylsilane. The mass spectra were obtained with a Varian MAT-112 chromatographic mass spectrometer at an ionization-chamber temperature of 180°C and an ionizing-electron energy of 70 eV; the chromatograph was a Varian model 1440 with a column length of 180 cm, an inner diameter of 2 mm, a phase consisting of 3% SE-30 on Varoport-30, helium as the carrier gas, a flow rate of 20 ml/min, a vaporizer temperature of 250°C, a column temperature of 230°C (270°C for IIIa, b), and a separator temperature of 260°C. The IR spectra were recorded in the crystalline state in the form of pastes in mineral oil and in solution with a Perkin–Elmer 599 spectrometer. The UV spectra of solutions in alcohol were recorded with a Perkin–Elmer 575 spectrophotometer. Thin-layer chromatography (TLC) was carried out in methanol–chloroform (1:1) with development with iodine.

cis-2-(4'-Nitrobenzylidene)-3-oxoquinuclidine (IIIb). A solution of 10 g (80 mmole) of 3-oxoquinuclidine, 12.1 g (80 mmole) of 4-nitrobenzaldehyde, and 0.1 g of sodium hydroxide in 45 ml of absolute ethanol was refluxed for 3 h. After 20 h, the precipitate was removed by filtration and washed with ethanol to give 13 g (51.3%) of yellow crystals that were quite soluble in alcohol, acetone, and chloroform but insoluble in water and ether and had mp 143-144°C (from methanol). Found: C 65.5; H 5.6; N 10.6%. $C_{14}H_{14}N_2O_3$. Calculated: C 65.1; H 5.5; N 10.8%.

trans-2-(4'-Nitrobenzylidene)-3-oxoquinuclidine (IIIa). A solution of 1 g (4 mmole) of ketone IIIb in 20 ml of chloroform was saturated with gaseous hydrogen chloride for 30 min, after which the solvent was removed *in vacuo*, and the residue was treated with a 25% solution of potassium carbonate and extracted with chloroform. The mass obtained after removal of the chloroform was triturated with ether to give 0.85 g (85%) of a product with mp 158-160°C (from ethanol). Found: C 65.3; H 5.7; N 10.7%. $C_{14}H_{14}N_2O_3$. Calculated: C 65.1; H 5.5; N 10.8%.

cis-2-(2'-Hydroxybenzylidene)-3-oxoquinuclidine (IVb). A solution of 11.25 g (90 mmole) of 3-oxoquinuclidine, 11 g (90 mmole) of salicylaldehyde, and 4.2 g (105 mmole) of sodium hydroxide in 100 ml of methanol was refluxed for 34 h, after which the reaction mixture was evaporated, and the residue was triturated with water. The resulting precipitate was removed by filtration and washed repeatedly with water to give 10.5 g of ketone IVb. The aqueous mother liquors were extracted with chloroform, and the solvent was removed by distillation to give an additional 2 g of the substance for an overall yield of 12 g (58.1%). The yellow crystalline substance was quite soluble in methanol, chloroform, acetone, and benzene but less soluble in ethanol and water and had mp 140-141°C (from isopropyl alcohol) and R_f 0.75. IR spectrum: 1610 (C=C), 1700 (C=O), and 2440-2480 cm^{-1} (associated OH). Found: C 73.4; H 6.6; N 6.0%. $C_{14}H_{15}NO_2$. Calculated: C 73.7; H 6.6; N 6.0%.

The 2-benzylidene- and 2-(4'methoxybenzylidene)-3-oxoquinuclidines (I, II) were obtained by the method in [2, 3].

2-Benzylidene-3-oxoquinuclidine Oximes (Va-c). A mixture of 10 g (47 mmole) of cis-2-benzylidene-3-oxoquinuclidine (Ib) and 3.26 g (47 mmole) of hydroxylamine hydrochloride in 75 ml of absolute ethanol was refluxed for 4 h, after which it was cooled, and the resulting precipitate was removed by filtration and washed with ethanol to give 5.32 g of the hydrochloride of oxime Va with mp 221-223°C (from ethanol) as colorless crystals that were only slightly soluble in organic solvents and water. Found: C 59.2; H 6.6; Cl 12.6; N 10.0%. $C_{14}H_{16}N_2O \cdot HCl$. Calculated: C 59.5; H 6.8; Cl 12.5; N 9.9%.

The mother liquor was evaporated, and the residue was triturated with diethyl ether to give 7.08 g of a mixture of the hydrochlorides of oximes Va (the principal product), Vb, and Vc. The overall yield was 12.4 g (99.6%).

The isolation of the bases and the separation of the isomeric oximes were carried out as follows.

A) A suspension of 5.25 g (19 mmole) of the hydrochloride of oxime Va in 30 ml of water was treated with 30 ml of a 50% solution of potassium carbonate and extracted with chloroform (24 50-ml portions). The residue obtained after evaporation of the extract was recrystallized from isopropyl alcohol to give 3.1 g (59%) of oxime base Va as colorless crystals that were only slightly soluble in ethanol, acetone, and chloroform but more soluble in dimethylformamide (DMF) and pyridine and had mp 225-226°C and R_f 0.6. IR spectrum: 1690 (C=C, C=N) and 2660 cm^{-1} (OH). Found: C 73.5; H 6.9; N 11.9%. $C_{14}H_{16}N_2O$. Calculated: C 73.5; H 7.0; N 12.2%.

B) A mixture of the hydrochlorides of oximes Va-c (7.08 g) was treated as in the preceding experiment. The residue obtained after removal of the chloroform by distillation was triturated with heptane to give 6 g (86.4%) of a heptane-insoluble mixture of bases, which was refluxed with 50 ml of isopropyl alcohol. The insoluble part was removed by filtration, and the isopropyl alcohol solution was cooled to precipitate 2.2 g of oxime Va with mp 225-226°C and R_f 0.6. The precipitate that was insoluble in isopropyl alcohol was refluxed with 50 ml of ethanol and filtered, and the filtrate was cooled to give another 1.74 g of oxime Va with R_f 0.6. The substance that was insoluble in ethanol was recrystallized from methanol—chloroform. Cooling precipitated 0.8 g of oxime Vb with mp 215-216°C and R_f 0.75. IR spectrum: 1610 (C=C, C=N) and 3220 cm^{-1} (OH). Found: C 73.7; H 6.9; N 12.2%. $C_{14}H_{16}N_2O$. Calculated: C 73.5; H 7.0; N 12.2%.

When the mother liquor obtained after separation of oxime Vb was allowed to stand for 48 h at 4°C, 0.5 g of isomer Vc, with mp 168-170°C and R_f 0.75, precipitated. Found: C 73.5; H 7.0; N 12.0%. $C_{14}H_{16}N_2O$. Calculated: C 73.5; H 7.0; N 12.2%.

2-(4'-Methoxybenzylidene)-3-oxoquinuclidine Oximes (VIa-c). A mixture of 4 g (16 mmole) of cis-2-(4'-methoxybenzylidene)-3-oxoquinuclidine (IIc) and 1.08 g (16 mmole) of hydroxylamine hydrochloride in 50 ml of absolute ethanol was refluxed for 7 h, after which it was cooled, and the precipitate was removed by filtration to give 3 g (65.5%) of a mixture of hydrochlorides of oximes VIb, c with considerable preponderance of the VIb isomer. (The minor amount of the VIc isomer was not separated by crystallization.) The yellow crystals were only slightly soluble in water and organic solvents and had mp 212-213°C (from ethanol) and R_f 0.7. IR spectrum: 1600, 1662 (C=C, C=N); 2700-2860 ($\overset{+}{N}H$); 3070 cm^{-1} (OH). Found: C 61.3; H 6.6; Cl 11.9; N 9.5%. $C_{15}H_{18}N_2O_2 \cdot HCl$. Calculated: C 61.1; H 6.5; Cl 12.0; N 9.5%. The mother liquor was evaporated, and the residue was triturated with

ethyl acetate to give 0.8 g (25.7%) of a mixture of the hydrochlorides of oximes VIa-c with mp 170-206°C. The mixtures of hydrochlorides of oximes VIb, c and VIa-c obtained were converted to the bases by the action of an aqueous solution of potassium carbonate and repeated extraction with chloroform. a) A 3-g sample of the hydrochlorides yielded 1.85 g (90.5%) of the oxime bases VIb, c with mp 170-171°C (from isopropyl alcohol) and R_f 0.81. IR spectrum: 1608 (C=C, C=N) and 3220-3280 cm^{-1} (OH). Found: C 69.8; H 7.0; N 10.9%. $C_{15}H_{18}N_2O_2$. Calculated: C 69.7; H 7.0; N 10.8%. b) Crystallization of the mixture of oxime bases VIa-c isolated from 0.8 g of the hydrochlorides gave 0.26 g of oxime VIa with mp 192-193°C and R_f 0.62. Found: C 69.7; H 7.2; N 10.9%. $C_{15}H_{18}N_2O_2$. Calculated: C 69.7; H 7.0; N 10.8%.

2-(4'-Nitrobenzylidene)-2-oxoquinuclidine Oximes (VIIa, b). A) A mixture of 2.47 g (10 mmole) of cis-2-(4'-nitrobenzylidene)-3-oxoquinuclidine (IIIb) and 0.67 g (10 mmole) of hydroxylamine hydrochloride in 25 ml of ethanol was refluxed for 4 h, after which it was cooled, and the precipitate was removed by filtration to give 2.06 g (70.3%) of the hydrochloride of oxime VIIa with mp 227-228°C (from ethanol) and R_f 0.418. IR spectrum: 1595 (C=C, C=N), 2480-2540 ($\overset{+}{N}H$), and 3030-3120 cm^{-1} (OH). Found: C 54.7; H 5.6; Cl 11.5; N 13.8%. $C_{14}H_{15}N_3O_2 \cdot HCl$. Calculated: C 54.6; H 5.3; Cl 11.5; N 13.6%. The base was isolated in 95.9% yield from the hydrochloride of oxime VIIa. The yellow crystals were quite soluble in chloroform and acetone and in hot ethanol and methanol but insoluble in ether and water and had mp 214-216°C and R_f 0.68. IR spectrum: 1700 (C=C, C=N) and 2640-2710 cm^{-1} (OH). Found: C 61.7; H 5.7; N 15.5%. $C_{14}H_{15}N_3O_2$. Calculated: C 61.5; H 5.5; N 15.4%.

B) A 0.77-g (4.3 mmole) sample of palladium chloride and 0.4 g (3.8 mmole) of sodium carbonate were added to a solution of 1 g (4 mmole) of oxime VIIa in 70 ml of methylene chloride, and the mixture was stirred at room temperature for 50 h. It was then filtered, and the mother liquor was evaporated *in vacuo* to give 0.8 g (80%) of oxime VIIb with mp 249-250°C (from isopropyl alcohol) and R_f 0.92.

2-(2'-Hydroxybenzylidene)-3-oxoquinuclidine Oximes (VIIIb, c). A mixture of 10.5 g (46 mmole) of cis-2-(2'-hydroxybenzylidene)-3-oxoquinuclidine (IVb) and 3.18 g (46 mmole) of hydroxylamine hydrochloride in 80 ml of ethanol was refluxed for 8 h, after which 6.08 g of a mixture of the hydrochlorides of oximes VIIIb, c was separated, and another 2.65 g of the mixture was obtained from the mother liquor after removal of the ethanol by distillation for an overall yield of 8.73 g (68.4%) of a product with mp 206-208°C (from isopropyl alcohol). Found: C 60.0; H 5.9; Cl 12.9: N 9.8%. $C_{14}H_{16}N_2O_2 \cdot HCl$. Calculated: C 59.9; H 6.1; Cl 12.6; N 9.9%. A mixture of bases VIIIb, c with preponderance of the VIIIb isomer was isolated from the mixture obtained. The yellow crystals were quite soluble in chloroform, methanol, and acetone but insoluble in water and ether and had mp 176-178°C (from isopropyl alcohol). Found: C 69.0; H 6.7; N 11.2%. $C_{14}H_{16}N_2O_2$. Calculated: C 68.8; H 6.6; N 11.2%.

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