IIβ vanished after ∿ 2 h (as monitored by TLC). The isolated IIα was identical to a sample of the compound obtained as described above according to its melting point and IR spectrum.

Similar transformations were observed for isomers IIIβ-Vβ. Analytical samples of the β isomers were not isolated in the case of IV and V, while isomerization was observed for mixtures of the α and β isomers, from which the β isomers vanished.

Action of Sodium Hydroxide on Stereoisomeric N-Hydroxypiperidines VI. Under the conditions presented above, VIα was converted to isomer VIγ in the course of a few hours. Isomer VIβ was also converted to N-hydroxypiperidine VIγ under the influence of NaOH, and monitoring by TLC showed that isomer VIα, which was subsequently converted to isomer VIγ in a few hours, was formed in the first rapid step (∿ 10 min). When NaOH was added, acetoxy derivatives VII underwent decomposition to N-hydroxy derivatives VI, which were isomerized as described above.

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HYDROGENATED AZOLO- AND AZINOPYRIDINES BASED ON 1,5-DIKETONES

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Compounds that contain a hydrogenated azolopyridine structure are formed in the reaction of various types of 1,5-diketones with ethanolamine, o-aminophenol, o-phenylenediamine, and aroylhydrazines; compounds that include a hydrogenated azinopyridine structure were obtained by the reaction of diketones with 3-aminopropanol and anthranilic acid. The hydrocyanation and oxidation of the compounds obtained were studied.

The reactions of alkylidene(arylidene) dicyclohexanones with ethanolamine [1] and o-aminophenol and o-phenylenediamine [2] have been previously studied. To establish the general character of the reactions of 1,5-diketones with primary amines that contain a nucleophilic center in the β or α position relative to the amino group we investigated the action of aliphatic-aromatic (Ia), alicyclic (Ib), "semicyclic" (Ic, d), and other (Ie-j) 1,5-diketones on ethanolamine, 3-aminopropanol, o-aminophenol, o-phenylenediamine, anthranilic acid, and aroylhydrazines. The typical pathway is dual cyclization: when the nucleophilic center is in the β position, derivatives of hydrogenated azolopyridines (II, IV, V, and VII-IX) are formed, whereas derivatives of hydrogenated azinopyridines (III, VI) are formed when the nucleophilic center is in the γ position.

When unsymmetrical diketones Ic-i are used, an azole or azine ring is formed in the direction of the alicyclic fragment of the diketone. However, "dihydropyridine" derivative XIIIh is formed instead of a derivative of the benzoxazinopyridine type (VI) in the reaction of diketone Ih with anthranilic acid, and this indicates the lower tendency for cyclization of the cyclopentanone fragment.

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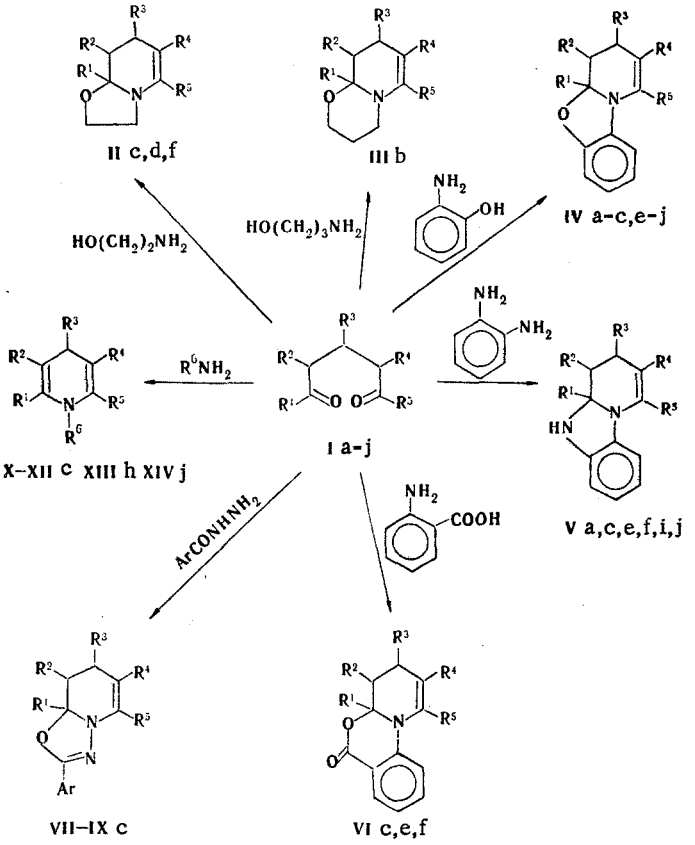
Methylenebis-α-tetralone (Ij) reacts with o-aminophenol and o-phenylenediamine via the general scheme, despite the steric shielding of both carbonyl groups; however, decarboxylatio with the formation of dihydropyridine XIVj, obtained by alternative synthesis from diketone Ij and aniline, occurs in the reaction with anthranilic acid. Compounds VIIc-IXc are not the only products. Thus, dihydropyridine derivative XIc was isolated in addition to VIIc, whereas phenylacetic acid hydrazide and diketone Ic give only dihydropyridine product XIIc; this is probably explained by the very low tendency of this hydrazide to form the hydroxy imine form necessary for cyclization.

The IR spectra of II-IV and VI do not contain the absorption bands of an OH group at 3100-3600 cm^{-1}; only one band at 3400 cm^{-1} (a secondary amino group) is observed in the spectra of V instead of the two bands at 3400-3500 cm^{-1} characteristic for a primary amino group. No NH absorption is observed in the spectra of VII-IX. Instead of the carbonyl absorption at 1680 cm^{-1} that is characteristic for aromatic acids, the spectra of VI contain absorption at 1725 cm^{-1}, which is characteristic of six-membered lactones. On the other hand, the spectrum of XIIIh contains a band at 1680 cm^{-1}, as well as absorption at 3360 cm^{-1} (an OH group with a hydrogen bond), whereas carbonyl absorption is absent in the spectra of VIIc-IXc. On the other hand, the spectra of XIc and XIIc contain the intense absorption of an amide carbonyl group at 1680 cm^{-1} and of an NH group at 3300 cm^{-1}. One peak at 1640 cm^{-1} (at 1665 cm^{-1} for IIIb) is observed in the spectra of II-IX instead of the two peaks at 1640-1690 cm^{-1}



I-XIV a $R^1 = R^5 = C_6H_5$, $R^2 = R^3 = R^4 = H$; b $R^1R^2 = R^4R^5 = (CH_2)_4$, $R^3 = C_6H_5$; c $R^1R^2 = (CH_2)_4$, $R^3 = R^5 = C_6H_5$, $R^4 = H$; d $R^1R^2 = (CH_2)_4$, $R^3 = R^4 = H$, $R^5 = C_6H_5$; e $R^1R^2 = (CH_2)_4$, $R^3 = H$, R^5R^4 = 1,2-benzotetramethylene; f $R^1R^2 = (CH_2)_4$, $R^3 = C_6H_5$, R^5R^4 = 1,2-benzotetramethylene; g $R^1R^2 = (CH_2)_3$, $R^3 = H$, R^5R^4 = 1,2-benzotetramethylene; h $R^1R^2 = (CH_2)_3$, $R^3 = C_6H_5$, R^6R^4 = 1,2-benzotetramethylene; i R^1R^2 = 2,2-dimethyl-3-oxatetramethylene, $R^3C_6H_5$, R^5R^4 = 1,2-benzotetramethylene, j $R^1R^2 = R^5R^4$ = 1,2-benzotetramethylene, $R^3 = H$; VIIc Ar = C_6H_5; VIIIc Ar = C_6H_4Cl-p; IXc Ar = $C_6H_4NO_2$-p; Xc XIVj $R^6 = C_6H_5$; XIc $R^6 = NHCOC_6H_5$; XIIc $R^6 = NHCOCH_2C_6H_5$; XIIIh $R^6 = C_6H_4COOH$-o

TABLE 1. PMR Spectra of Hydrogenated Azolo- and Azinopyridines

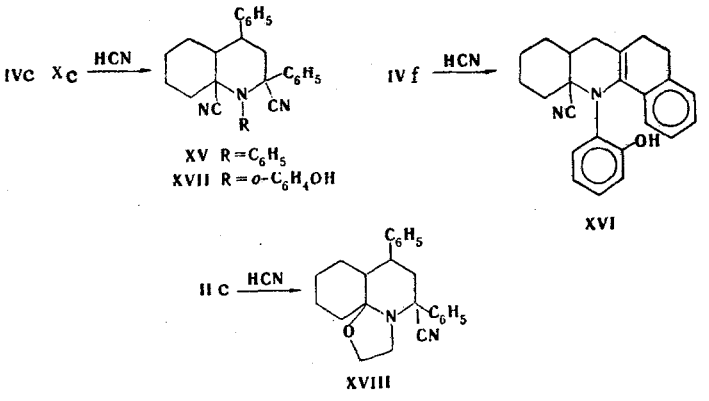
Compound	δ, ppm (J, Hz)		
	C=C–H(1H)	C_6H_5C–H(1H)	 –H(1H)
IIc, VIIc—IXc	4,8—5,4 d (3)	3,5—3,8 dd (8—10, 3)	—
IVa	5,33 q	—	5,82 d
Va*	5,33 q	—	5,82 d
IVc,g,j, Vi	—	—	5,7—6,2 d
IVf,h	—	3,1—3,4 d (8—11)	6,2 d
IVc	5,42 d (3)	3,30 dd (10,3)	6,28 d
VIf	—	3,28 d (8,5)	6,56 d

*The NH signal (broad singlet) is found at 3.94 ppm.

characteristic for dihydropyridine structures [3] (these peaks are present in the spectrum of Xc). This indicates that in these compounds, as well as in IIIb, the double bond is conjugated with the aromatic ring. This band is broadened in the spectra of VIIc-IXc, since the absorption of a C=N bond is also included.

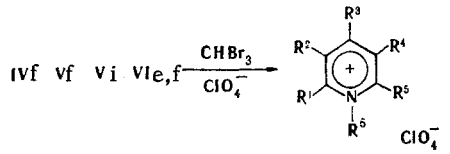
The principal data from the PMR spectra are presented in Table 1. One's attention is drawn to the shift of the signal of one of the aromatic protons of IV-VI to strong field. A similar shift is not observed in the spectra of Xc, N-aryloctahydrobenz[c]acridines [3], and the products of the reaction of alicyclic 1,5-diketones with o-aminophenol and o-phenylenediamine [2]. The strong-field shift is due to shielding of the proton in the 6 position of the aromatic ring attached to the nitrogen atom by the benzene ring in the 2 position of the 2-hydropyridine system.

It has been previously shown [1, 2] that a characteristic feature of hydrogenated azoloacridines is their ability to react in the "dihydropyridine" form with prior opening of the azole ring. Compounds II, IV, and VI also display this tendency, but to a lesser extent. Thus the oxazoline ring of IVc and IVf undergo opening to give, respectively, dinitrile XV and mononitrile XVI when they are heated for a long time with a solution of KCN in acetic acid. These results are in agreement with the fact that 2,4-diphenylhexahydroquinoline Xc adds 2 moles of HCN to give dinitrile XVII, while N-substituted octahydrobenz[c]acridines add only 1 mole of HCN [3] to the double bond that is not conjugated with the benzene ring; in conformity with this, XIVj does not add HCN at all. Under these conditions, IIc forms mononitrile XVIII, undergoing reaction without opening of the oxazolidine ring, whereas IIf, Ve, f, and VIe, f do not add HCN.



An absorption band of an OH group appears in the IR spectra of nitriles XVI and XVII at 3400-3500 cm^{-1}; the spectrum of XVI also contains absorption at 1640 cm^{-1} (C=C). The spectrum of nitrile XVIII does not contain the absorption of either an OH group or a double bond.

In contrast to the analogous products from alicyclic 1,5-diketones [2], II and IV-VI are not oxidized by carbon tetrachloride; some of them could be oxidized by bromoform to the corresponding pyridinium salts XIX-XXIII only under severe conditions.



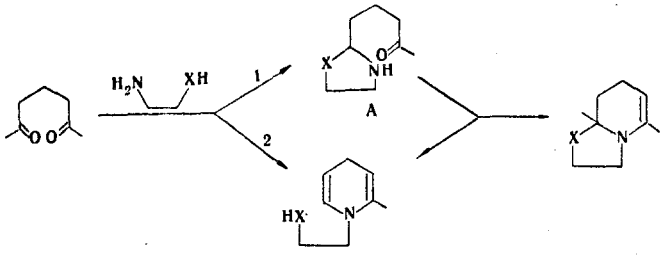
XIX f $R^6 = o\text{-}C_6H_4OH$; XX f, XXI j $R^6 = o\text{-}C_6H_4NH_2$;
XXII e, XXIII f $R^6 = o\text{-}C_6H_4COOH$

A broad band of absorption of an OH group linked by a hydrogen bond appears in the IR spectra of perchlorates XIX, XXII, and XXIII at 3200-3300 cm^{-1}, while two absorption bands of a primary amino group at 3400 and 3500 cm^{-1} appear in the spectra of perchlorates XX and XXI. The band of carbonyl absorption of the COOH group is found at 1720 cm^{-1} in the spectra of salts XXII and XXIII (as a result of the effect of a quaternary nitrogen atom).

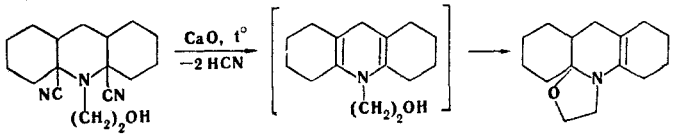
In contrast to the analogous products from alicyclic 1,5-diketones, IV and Vc, e, f do not undergo disproportionation under the influence of acetic acid.

The oxadiazoline ring of VII is opened very easily. Bands characteristic for XIc at 1680 (C=O) and 3410 cm^{-1} (NH) appear after a solution of this compound in chloroform is allowed to stand at room temperature for an hour. When VIIc is heated in chloroform and subsequently treated with perchloric acid, it is easily oxidized to the corresponding 1-benzamido-2,4-diphenyl-5,6,7,8-tetrahydroquinolinium perchlorate (XXIV).

Two possible schemes for the formation of II-IX can be proposed. 1) The amine containing an additional nucleophilic center initially reacts with one carbonyl group with the formation of an azole or azine ring. Ring formation of this sort has been described for the reactions of monocarbonyl compounds with ethanolamine [4], o-phenylenediamine [5], o-aminophenol [6], and anthranilic acid [7]. Intermediate A subsequently undergoes cyclodehydration with the participation of the second carbonyl group. 2) The primary amino group of the reagent reacts with both carbonyl groups of the diketone via the usual scheme to give a 1,4-dihydropyridine with subsequent nucleophilic addition.



We demonstrated the possibility of this sort of addition in the case of the dehydrocyanation of dinitrile XXV, in which four-ring compound XXVI is formed instead of N-hydroxydecahydroacridine.



XXV XXVI

Moreover, we were unable to observe conversion of hexahydroquinoline derivative XIc to VIIc. It is possible that various schemes of double cyclization are realized for different reacting partners.

EXPERIMENTAL

The IR spectra of solutions of the compounds in chloroform or suspensions in mineral oil were recorded with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in

TABLE 2. Products of the Reaction of 1,5-Diketones with Primary Amines

Compound	mp, °C	Found, %			Empirical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
IIc	122—124	83,5	7,7	4,2	$C_{23}H_{25}NO$	83,3	7,2	4,2	60
IId	64—65	79,8	8,5	5,3	$C_{17}H_{20}NO$	80,0	8,2	5,5	61
IIf	124—125	85,0	7,9	4,7	$C_{25}H_{27}NO$	84,0	7,6	3,9	98
IIIb	118—119	82,4	10,0	4,7	$C_{22}H_{29}NO$	81,7	9,0	4,3	32
IVa	166—168[a]	84,6	6,0	4,5	$C_{23}H_{19}NO$	85,0	5,9	4,3	80
IVc	179—180	85,1	6,9	3,9	$C_{27}H_{25}NO$	85,5	6,6	3,7	79
IVe	188—189	83,6	7,5	4,4	$C_{23}H_{23}NO$	83,9	7,0	3,7	90
IVf	181—183	85,6	6,8	3,5	$C_{29}H_{27}NO$	85,9	6,7	3,5	82
IVg	135—136	84,3	6,5	3,8	$C_{22}H_{21}NO$	83,8	6,7	4,4	55
IVh	149—150	85,2	6,6	3,4	$C_{28}H_{25}NO$	85,7	6,6	3,6	67
IVi	201—203	83,4	6,4	2,7	$C_{30}H_{29}NO_2$	82,7	6,2	3,2	58
IVj	226—227[b]	85,8	6,2	4,2	$C_{27}H_{29}NO$	86,0	6,1	3,7	88
Va	160—162[a]	84,7	6,5	8,7	$C_{23}H_{20}N_2$	85,2	6,2	8,8	89
Vc	227—228	85,3	6,8	8,0	$C_{27}H_{26}N_2$	85,7	6,9	7,4	62
Ve	204—205	83,7	7,9	8,6	$C_{23}H_{24}N_2$	84,2	7,3	8,6	90
Vf	213—214	86,9	6,9	7,4	$C_{29}H_{28}N_2$	86,1	7,0	6,9	95
Vi	211—212	83,6	8,8	6,3	$C_{30}H_{30}N_2O$	82,9	7,0	6,4	70
Vj	214—218	85,8	6,5	7,2	$C_{27}H_{24}N_2$	86,1	6,5	7,5	70
VIc	184—185	82,6	6,2	3,5	$C_{28}H_{25}NO_2$	82,7	6,1	3,4	51
VIe	178—180	80,4	6,5	3,9	$C_{24}H_{23}NO_2$	80,4	6,5	3,9	54
VIf	222—224	82,9	6,3	3,5	$C_{30}H_{27}NO_2$	83,1	6,3	3,2	39
VIIc	171—172[c]	83,0	6,6	6,8	$C_{28}H_{26}N_2O$	82,7	6,4	6,9	66
VIIIc	163—164	76,3	5,8	6,2	$C_{28}H_{25}ClN_2O$	76,2	5,6	6,3	35
IXc	174—176[d]	74,8	5,8	9,2	$C_{28}H_{25}N_3O_3$	74,5	5,5	9,3	22
Xc	109—110	90,1	7,1	4,0	$C_{27}H_{25}N$	89,4	6,9	3,9	57
XIc	127d	82,2	6,4	7,3	$C_{28}H_{26}N_2O$	82,7	6,4	6,9	30
XIIc	145—146	83,1	6,7	7,0	$C_{29}H_{28}N_2O$	82,9	6,7	6,9	19
XIIIh	162—163	83,6[f]	—	3,2	$C_{29}H_{25}NO_2$	83,1	6,3	3,5	54
XIVj	239—244[b]	89,0	6,4	4,2	$C_{27}H_{23}N$	89,7	6,4	3,9	50
XV	208—210[e]	83,1	7,9	10,1	$C_{29}H_{27}N_3$	83,4	7,4	10,0	70
XVI	161—162	82,7	6,5	6,4	$C_{30}H_{28}N_2O$	83,2	6,2	6,4	68
XVII	204—206	79,9	7,1	9,1	$C_{29}H_{27}N_3O$	80,4	6,3	9,7	100
XVIII	198—199	80,5	7,5	8,7	$C_{24}H_{26}N_2O$	80,7	7,0	7,9	100
XIXf[e]	228[e,g]	69,2	5,3	2,5	$C_{29}H_{26}ClNO_5$	69,2	5,2	2,8	28
XXf	261[e]	69,3	5,5	5,6	$C_{28}H_{27}ClN_2O_4$	69,2	5,4	5,6	80
XXIj	239—241	68,6f	—	5,7	$C_{27}H_{23}ClN_2O_4$	68,2	4,8	6,1	40
XXIIe	232—234	64,1	5,2	3,5	$C_{24}H_{22}ClNO_6$	63,3	4,8	3,1	40
XXIIIf	179[e]	69,6	4,9	2,6	$C_{30}H_{26}ClNO_6$	69,6	4,9	2,6	8
XXIV	219—220	66,7	5,2	5,2	$C_{28}H_{25}ClN_2O_5$	66,6	4,9	5,6	44

[a]From ethanol—ethyl acetate (2 : 1). [b]From xylene. [c]From ethyl acetate. [d]From benzene. The remaining compounds were recrystallized from ethanol. [e]With decomposition. [f]Analysis by the damp combustion method. [g]From ethanol—water (1 : 1).

deuterochloroform were recorded with a Brücker HE-90X spectrometer. Data on II-XXIV are presented in Table 2.

Reaction of 1,5-Diketones with Primary Amines. A) A solution of 0.01 mole of the diketone, 0.011 mole (0.03 mole for the preparation of VIc and VIf) of the amine, and 20 mg of p-toluenesulfonic acid in 40-50 ml of xylene (benzene for the preparation of IIc) was refluxed with water separation for 5-10 h (30 h for the preparation of VIe, f) until water separation ceased. In the reaction of diketone Ic with benzoylhydrazine, VIIc precipitated immediately after cooling, and XIc precipitated after the mother liquor was allowed to stand for an hour. In the remaining cases the solvent was removed by distillation at reduced pressure, the residue was treated with 10 ml of ethanol (petroleum ether in the case of IIc), and II-VI were removed by filtration.

B) A 0.02-mole sample of diketone Ic was dissolved by heating in 50 ml of ethyl acetate, 5 ml of CH_3COOH and 0.02 mole of aroylhydrazine or phenylacetylhydrazine were added, and the solution was refluxed for 2-3 h and allowed to stand at 0°C for 24 h. Compounds VIIc, VIIIc, and XIIc were removed by filtration.

C) A 0.01-mole sample of aroyl hydrazine was added to a heated (to 90°C) solution of 0.01 mole of diketone Ic in 15 ml of CH_3COOH, and the mixture was allowed to stand at room temperature for 24 h. Compounds VIIc and IXc were removed by filtration.

Hydrocyanation of the Products of the Reaction of Diketones with Primary Amines. A) A

0.02-mole sample of IVc or Xc was added in portions with stirring to a solution of 0.08 mole of KCN in 2 ml of water and 3 ml of CH_3COOH, and the mixture was maintained at room temperature for 18 h. Compounds XV and XVII, respectively, were removed by filtration.

B) Solutions of 0.01 mole of KCN in 2 ml of water and 10 ml of CH_3COOH and 0.03 mole of IIc or IVf in 5 ml of dioxane were mixed, and the mixture was heated on a water bath for 15 h. It was then diluted with water, and products XVIII and XVI, respectively, were removed by filtration. The starting compounds were recovered in 80-90% yields in attempts to hydrocyanate Ve, Vf, VIf, and XIVj under these conditions.

Oxidation of the Products of the Reaction of 1,5-Diketones with Primary Amines. A) A mixture of 0.5 g of IVf, Vf, Vj, VIe, and VIf, 0.5 g of bromoform, and 5 ml of xylene was refluxed for 5-10 h, during which a resinous precipitate formed. Water (10 ml) was added, and the mixture was refluxed for 30 min. The aqueous layer was separated, and extraction with water was repeated twice. The combined aqueous extracts were extracted with ether, a saturated solution of NH_4ClO_4 was added to the clear aqueous layer, and perchlorates XIX-XXIII were removed by filtration. Only traces of perchlorates were formed in attempts to oxidize IVe and Ve under these conditions.

B) A 5-g sample of VIIc was refluxed in 100 ml of chloroform for 10 h, after which the chloroform was removed by distillation, and the residue was dissolved in 20 ml of ethanol. A 20-ml sample of 57% perchloric acid was added to the ethanol solution, and the liquid was removed from the resulting precipitate by decantation. Ethanol (20 ml) was added to the precipitate, and product XXIV was removed by filtration.

Dehydrocyanation of 10-(N-Hydroxyethyl)-4a,10a-dicyanoperhydroacridine. A 10-g sample of XXV [1] was triturated with 5 g of CaO, and the mixture was subjected to dry distillation at 1 mm with collection of the fraction with bp 145-158°C. This fraction was redistilled to give a product with bp 135-137°C (1 mm) in 30% yield. With respect to its IR spectrum, the product was identical to 4a,10a-oxazolidinodecahydroacridine [1].

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