The picrate was decomposed with alkali, and the mixture was extracted with methylene chloride. The extract was dried with sodium sulfate and filtered through aluminum oxide. The solvent was evaporated from the filtrate to give 0.62 g (22%) of trans isomer IIb as a light-yellow oil with R_f 0.5 [benzene—acetone (6 : 1)] and 0.6 [petroleum ether—ether (1 : 2)]. PMR spectrum (CCl_4): 1.3 (d, CH_3), 3.75 (q, CH of the phenylethyl substituent), and 7.2 ppm (s, C_6H_5).

Deuteration of cis Isomer IIa. A 0.005-g sample of sodium was added in an argon atmosphere to a solution of 0.036 g of the cis isomer in 4 ml of CD_3OD, after which the solution was allowed to stand at room temperature for 45 h. The solvent was removed in vacuo, 2 ml of D_2O was added to the residue, and the mixture was extracted with methylene chloride. The extract was dried with magnesium sulfate. Chromatography on Silufol showed the presence of a mixture of the cis and trans isomers of II with M^+ 259.

Isomerization of trans Isomer IIb by Irradiation. A solution of 0.022 g of trans isomer IIb in methanol was irradiated with a mercury lamp for 2 days. Chromatography of the solution on Silufol showed the presence of a mixture of isomers with predominance of trans isomer IIb.

Thermal Isomerization of cis Isomer IIa. A 0.01-g sample of cis isomer IIa was heated in benzene in an argon atmosphere for 4 h. Chromatography on Silufol showed the presence of a mixture of isomers.

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9-PHENYL-10-ALKYL(ARYL)PERHYDROACRIDINES FROM 9-PHENYL-10-ALKYL(ARYL)DECAHYDROACRIDINES

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9-Phenyldecahydroacridines with a substituent in the 10 position are reduced stereospecifically to the corresponding perhydroacridines by treatment with formic acid or a mixture of dimethylformamide and concentrated HCl. Perhydroacridines are also formed by disproportionation of the corresponding decahydroacridines.

Continuing our study of the properties of N-substituted decahydroacridines, we investigated their hydride reduction in the case of the 9-phenyl derivatives (IIa-d) [1-3]. Very little study has been devoted to the reduction of compounds with a 1,4-dihydropyridine structure that is not stabilized by electron-acceptor groups; when acceptor groups are present, hydride reduction either does not take place or gives tetrahydropyridine derivatives [4]. Complex hydrides ($LiAlH_4$ and KBH_4) do not reduce IIa-d even under severe conditions. However, the corresponding 9-phenylperhydroacridines (IIIa-c, e) and 9-phenyl-sym-octahydroacridinium salts (IVa-c, e) isolable in the form of the perchlorates, are formed when IIa-d are refluxed with 85% or 100% formic acid. Inasmuch as the yields of III (Table 1) exceed the theoretical yields (33%) for possible

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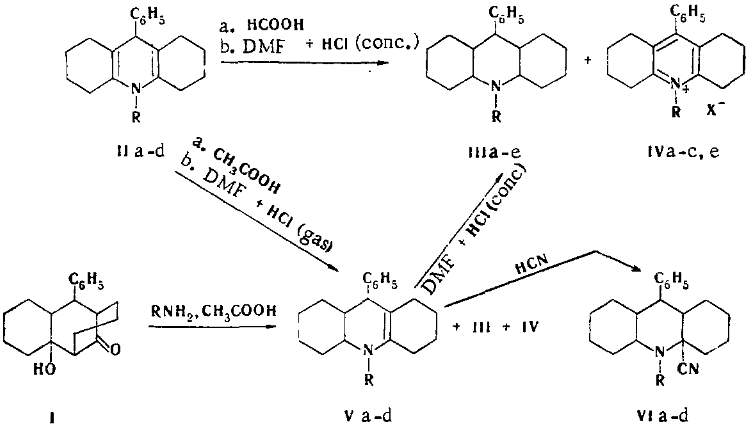
TABLE 1. Ratio of the Yields of III/IV during the Reduction of II

Reagent	Compound			
	IIa	IIb	IIc	IId
100% HCOOH	45/35	68/32	73/25	62/31
85% HCOOH	62/23	88/10	92/7	71/28
Dimethylformamide – conc. HCl	90/5	92/5	93/4	97/3

disproportionation of the decahydroacridine to the perhydroacridine and the octahydroacridinium salt in all cases, one may conclude that reduction of II also occurs in addition to disproportionation. In the case of IId one observes formylation to give N-formyl derivatives IIIe and IVe. Perhydroacridine IIIe was hydrolyzed to IIId by NaOH.

A mixture of dimethylformamide (DMF) in concentrated HCl reduces II even more readily than formic acid; only very small amounts of salts IV are formed in this case (Table 1). This mixture also reduces dodecahydroacridines V (in 92-96% yields), whereas formic acid does not reduce them.

It has been shown that disproportionation of N-alkyldecahydroacridine occurs in acetic acid to give dodecahydroacridine and sym-octahydroacridinium salt [1]. We have established that, in addition to V, perhydroacridines III, the yields of which depend on the disproportionation conditions, are also formed in the disproportionation of II under certain conditions. The percentage of III increases in a mixture of acetic acid with dioxane. Similar results were also obtained in the reaction of ketol I with the appropriate primary amines in the presence of acetic acid and dioxane. We found that decahydroacridines II also undergo disproportionation on treatment with hydrogen chloride in absolute DMF; in this case, in contrast to treatment with DMF–concentrated HCl, perhydroacridines are not formed, and the only reaction products are salts IV and dodecahydroacridines V (Table 2).



II-VI a $R=C_6H_5$, b $R=CH_2C_6H_5$; c $R=o\text{-}OHC_6H_4$, d $R=o\text{-}NH_2C_6H_4$, e $R=o\text{-}NHCHOC_6H_4$

The IR spectra of IIIa-e do not contain the absorption bands of double bonds at 1620-1700 cm^{-1} that are characteristic for the spectra of II and V but do not have a distinct "Bohlmann" absorption band at 2800 cm^{-1}. The spectrum of IIIc contains an absorption band at 3310 cm^{-1} (OH, hydrogen bond), and the spectrum of IIIe contains bands at 1685 (C = O) and 3320 cm^{-1} (secondary amino group); carbonyl absorption vanishes in the spectrum of IIId, and the double bond of a primary amino group (at 3360 and 3470 cm^{-1}) appears. In addition to the absorption at 1100 cm^{-1} characteristic for perchlorates, the spectrum of salt IVe contains carbonyl absorption at 1710 cm^{-1} and absorption of a secondary amino group at 3300 cm^{-1}.

The IR spectra of mineral oil suspensions of Vc and Vd do not contain the absorption characteristic for dodecahydroacridines at 1650 cm^{-1}; the absorption of a OH group is absent in the spectrum of Vc, whereas the spectrum of Vd contains an absorption band of a secondary amino group at 3410 cm^{-1}. This indicates that, like IIc, d [3], Vc, d have five-ring structure B in the solid state. When Vc is dissolved in $CHCl_3$, it is gradually converted to open form A (absorption bands of a C = C bond at 1650 cm^{-1} and of a OH group at 3310 cm^{-1} appear, and their intensities become maximal after 24 h). Compound Vd* is not converted to the open form on dissolving in $CHCl_3$: New absorption bands do not appear in the IR spectrum.

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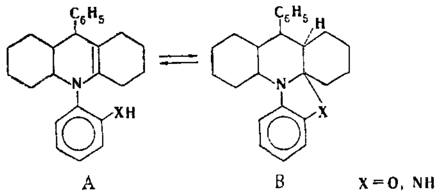
*We were unable to completely purify Vd and VId because of their ready oxidizability. The IR and PMR spectra of these products obtained under various conditions were identical and were in agreement with the proposed structures.



Compounds Vc, d add HCN to give 9-phenyl-10a-cyanoperhydroacridines (VIc, d). Compounds Va, b similarly form nitriles VIa, b. The IR spectrum of VIc contains an absorption band at 3310 cm^{-1} (OH with a hydrogen bond), and the spectrum of VId* contains two frequencies of a primary amino group at 3360 and 3470 cm^{-1}. The spectra of nitriles VIa-d contain absorption at 2230 cm^{-1} (CN).

The PMR spectra of IIIa-d contain complex multiplets (2H) at 2.3-2.55 ppm and triplets (1H) at 1.9-2.15 ppm with $J \sim 10$ Hz. The multiplets should be assigned to the protons in the 4a and 10 positions, and the triplets should be assigned to the proton in the 9 position. According to the data in [5], the spectrum of trans, syn,trans-N-phenylperhydroacridine contains a multiplet (2H) at 2.18 ppm, which was assigned to the methylidyne protons adjacent to the nitrogen atoms. In the isomer with cis fusion, these protons give a signal at weaker field at 3.42 ppm. The spin–spin coupling constant (SSCC) for 9-H constitutes evidence for diaxial coupling of this proton. These data, together with the presence of a "Bohlmann" absorption line in the IR spectram, make it possible to assume a trans, syn, trans configuration for perhydroacridines IIIa-d in which the piperidine ring is in the chair conformation with an equatorial orientation of all of the substituents. Thus perhydroacridines IIIa-e are formed as a single stereoisomer, i.e., the synthesis of these compounds is stereospecific.

The spectrum of Va contains a multiplet (2H) consisting of a broad triplet at 3.02 ppm and a doublet at 2.97 ppm ($J = 9$ Hz in both cases). The doublet was assigned to the proton in the 9 position. The SSCC indicates a diaxial orientation of the protons in the 9 and 9a position. The triplet should be assigned to the axial proton in the 10a position, which couples with two axial protons and one equatorial proton; coupling with the latter

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*See footnote on preceding page

TABLE 2. Results of Disproportionation of II

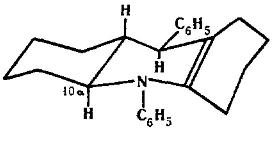
Compound	Solvent	Yields of reaction products, %		
		III	IV	V
IIa	CH_3COOH	Traces	49	43
IIa	CH_3COOH — Dioxane	6	65	12
IIa	abs. DMF–HCl (gas)	0	50	33
IIb	CH_3COOH	5	53	34
IIc	CH_3COOH	0	36	50
IId	CH_3COOH	0	48	50

TABLE 3. 9-Phenylhydroacridines

Compound	mp, °C (crystallization solvent)	Empirical formula	Found, %			Calc., %		
			C	H	N	C	H	N
IIIa	237—238 (ethanol)	$C_{25}H_{31}N$	86,3	9,2	3,8	87,0	9,0	4,1
IIIb	146 (ethanol)	$C_{26}H_{33}N$	86.8	9,1	4,8	86,9	9,2	3,9
IIIc	221—223 (propanol)	$C_{25}H_{31}NO$	83,6	9,1	4,0	83,1	8,6	3,9
IIId	182—183 (ethanol)	$C_{25}H_{32}N_2$	83,3	8,9	7,7	83,3	8,9	7,8
IIIe	170—171 (ethanol–propanol, 4 : 1)	$C_{26}H_{32}N_2O$	79,6	9,0	6,9	80,4	8,2	7,2
IVe	241* (ethanol)	$C_{26}H_{27}ClN_2O_5$	64,2	6,1	6,0	64,7	5,6	5,8
Va	137—138 (petroleum ether)	$C_{25}H_{29}N$	88.3	8,8	4,0	87,6	8,4	4,1
Vb	133—133,5 (petroleum ether)	$C_{26}H_{31}N$	87,8	9,0	4,2	87,4	8,1	3,9
Vc	146—149 (propanol)	$C_{25}H_{29}NO$	83,4	8,5	3,8	83,4	8,1	3.9
VIa	162—164* (ethanol)	$C_{26}H_{30}N_2$	84,5	8,2	8,0	84,3	8,1	7,6
VIb	153* (ethanol)	$C_{27}H_{32}N_2$	84,9	8,8	7,4	84,4	8,3	7,3
VIc	209—211* (ethanol)	$C_{26}H_{30}N_2O$	81,3	8.6	7,0	80,8	7,8	7,3

*With decomposition.

broadens the triplet line. The shift of the 10a-H signal by 0.47 ppm to weak field as compared with signal of the analogous proton in IIIa indicates that this proton falls in the region of double bond deshielding. Of the two possible three-dimensional structures, this makes it possible to choose structure I in which the proton in the 10a position is closer to the double bond. In this case, a half-chair form in which interconversion of the rings occurs without serious deformations of the ethylene group [6] is most favorable for the cyclohexene and tetrahydropyridine rings. In our case only conversion of the cyclohexene ring can probably be realized, since the tetrahydropyridine ring is trans-fused to the cyclohexane ring. In fact, the 9-H doublet should have a lower SSCC in the case of conversion of the central ring.



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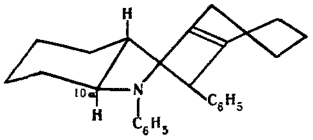

2

The PMR spectrum of Vb contains a multiplet consisting of a doublet at 2.84 ppm (J = 9.4 Hz), which was assigned to 9-H^{a}, and a doublet of triplets at 2.79 ppm (J = 9.5, 9.5, 4 Hz), which was assigned to 10a-H^{a}. Hence it should be concluded that Vb also has structure I. The fact that the 10a-H signal is shifted to strong field to a greater extent than the 9-H signal ($\Delta\delta$ 0.23 and 0.13 ppm, respectively) when the phenyl group is replaced by a benzyl group is in complete agreement with the proposed structure. The resonance signals (3H) at 2.1-2.8 ppm in the spectra of Vc, d are considerably broadened and differ from the signals in this region in the spectra of Va, b; this is explained by intramolecular cyclization.

Two triplets (1H) at 3.15 ppm (J = 10 Hz) and 2.48 ppm (J = 10.9 Hz) are isolated in the spectrum of VIa. The lines of the first triplet are broadened, and this makes it possible to assign it to 10a-H^{a}; the triplet at 2.48 ppm was assigned to 9H^{a}. The cyano group is evidently axially oriented, since the 9-H and 10a-H signals are shifted to weak field as compared with the signals of the corresponding protons in the spectrum of IIIa; this is in agreement with the deshielding contribution of the axial cyano group [7]. The spectra of VIb contain a doublet of triplets (1H) at 2.54 ppm (J = 9.0, 9.0, 3.0 Hz) and a triplet (1H) at 2.31 ppm (J = 10.8 Hz); the spectrum of VIc contains a broad triplet (1H) at 3.18 ppm (J = 9.5 Hz) and a triplet (1H) at 2.52 ppm (J = 10.5 Hz), i.e., an analogy with the spectrum of VIa is observed. The spectrum of VId also contains a signal with an intensity of 2H at 2.4-3.3 ppm, but its assignment is not possible because of its strong broadening. The interpretation of the PMR spectra of nitriles VIa-c makes it possible to assume a trans,cis,trans configuration for the perhydroacridine structure for them.

The protons of the N-benzyl group in IIb and IIId give singlets at 4.53 and 3.86 ppm, respectively; this is in agreement with the symmetry of the molecules of these compounds. In the spectra of Vb and VIb these protons give quartets (2H) at 3.93 ppm ($\Delta\delta$ 0.23 ppm, J = 18 Hz) and at 4.32 ppm ($\Delta\delta$ 0.18 ppm, J = 17.5 Hz), respectively.

EXPERIMENTAL

The IR spectra of chloroform solutions of all of the compounds and of mineral oil suspensions of Vc, d were recorded with a UR-20 spectrometer. The PMR spectra of $CDCl_3$ solutions of all of the compounds were recorded with a ZKR-60 spectrometer and with an HX-90 Brucker spectrometer in the case of II-VIa, b and IIIc. The course of the reactions and the individuality of the substances were monitored by thin-layer chromatography (TLC) on activity II Al_2O_3 and on Silufol.

10-Substituted 9-Phenylperhydroacridines (IIIa-c, e). A) A mixture of 0.01 mole of IIa-d and 5 ml of HCOOH was refluxed for 1-2.5 h, after which it was cooled, diluted to twice its volume with water, and made alkaline with ammonium hydroxide or sodium carbonate solution. Compounds IIIa-c, e were removed by filtration, washed with water, and dried. In the case of IVa-c, e, ammonium perchlorate solution was added to the filtrate, and the precipitates were removed by filtration, washed with water, and dried. Compounds IVa-c were identified from a comparison of their IR spectra with those of the compounds previously obtained in [1-3] (see Table 3 for data on IIIa-c, e and IVe).

B) A 0.01-mole sample of IIa-d or Va-d was dissolved in 15 ml of DMF, 3 ml of concentrated HCl (sp. gr. 1.19) was added, and the mixture was heated on a water bath for 1-2 h. The mixture was then worked up as described above. See Table for the yields of the products in the reduction of II; salts IV were not formed in the reduction of Va-d, and the yields of IIIa-d ranged from 90 to 95%.

9-Phenyl-10-(o-aminophenyl)perhydroacridine (IIId). A 3.6-g (0.01 mole) sample of IIIe was refluxed for 2 h with a solution of 2.5 g of NaOH in 75 ml of ethanol, after which the mixture was cooled and filtered to give 1.8 g (50%) of IIId. The filtrate was diluted with water and filtered to give another 1.5 g (40%) of IIId. The product was washed with water and vacuum dried thoroughly, since it readily forms crystal solvates (see Table 3 for data on IIId).

Disproportionation of IIa-d. A 0.04-0.05 mole sample of IIa-d was added in an argon atmosphere to 80 ml of refluxing acetic acid or a refluxing mixture of 50 ml of acetic acid and 30 ml of dioxane, after which the mixture was refluxed for 1-2.5 h (up to 12 h in the case of IId).

A) The reaction mixture was poured into a mixture of 100 g of ice and 50 ml of 25% ammonium hydroxide, and the amorphous precipitate was removed by filtration after 24 h. A solution of NH_4ClO_4 was added to the filtrate, and the precipitated IVa-d, which were identical to the samples obtained by reduction, were removed by filtration. The previously isolated amorphous precipitate was washed with water and dried. In the case of the disproportionation of IIa, b the precipitate was placed in a column containing 250 g of activity II Al_2O_3 and chromatographed with elution of Va, b with petroleum ether and of IIIa, b with petroleum ether containing 1% ethyl acetate. See Table 2 for the yields.

B) A solution of 0.03 mole of KCN in 20 ml of 80% acetic acid was added to the cooled reaction mixture, and the mixture was allowed to stand for 24 h. The precipitated nitriles VIa-d were removed by filtration, washed with water, and dried. The yields ranged from 40 to 48%.

Reaction of Ketone I with Primary Amines. A 20-mmole sample of ketole I was refluxed with 25 ml of acetic acid or dioxane–acetic acid (2 : 1) until it dissolved completely, after which 22 mmole of the appropriate amine was added, and the mixture was refluxed for 3-9 h. It was then worked up by method A or B. The yields of the products were on the order of the yields in the disproportionation of II.

Reaction of 10-Substituted 9-Phenyldodecahydroacridines (Va-d) with HCN. A 2-mmole sample of Va-d was dissolved in 5 ml of acetic acid, and a solution of 3 mmole of KCN in 20 ml of 75% acetic acid was added. The mixture was then stirred magnetically for 24 h, after which it was diluted with water, made alkaline with sodium carbonate, and dried. The yields ranged from 85 to 95%.

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