C) A total of 0.184 g (83%) of 1,2,7-trimethyl-4-ethyldecahydro-4-quinolol (XX) (mp 113-114°; R_f 0.60), which was identical to the alcohol obtained by reaction of ketone XVII with C_2H_5MgBr [3], was synthesized from 0.2 g (1 mmole) of ketone XVII and 0.22 g (2 mmole) of $(C_2H_5)_3Al$ in THF (60° for 5 h).

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STEREOCHEMISTRY OF THE 1,4-REDUCTION OF CHIRAL N-(α-PHENYLETHYL)-$\Delta^{9,10}$-4-KETOOCTAHYDROQUINOLINE*

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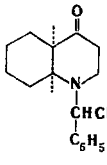
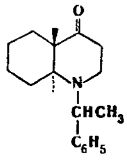
Only trans-N-(α-phenylethyl)-4-ketodecahydroquinoline, which is readily converted to a mixture containing 70% of the thermodynamically more stable cis isomer, is formed in the reduction of chiral N-(α-phenylethyl)-$\Delta^{9,10}$-4-ketooctahydroquinoline with lithium aluminum hydride.

We have previously established [2] that the 1,4-reduction of chiral N-(α-phenylethyl)-$\Delta^{9,10}$-4-ketooctahydroquinoline (I) with lithium aluminum hydride proceeds as an asymmetric synthesis and gives optically active bicyclic 4-piperidones IIa and IIb. The reduction also proceeds to a greater extent to give the corresponding alcohols.



II a



II b

In the present research we have made a detailed analysis of the stereochemical peculiarities of the reduction of enamino ketone I in order to ascertain the primary reaction pathway. The reduction was carried

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TABLE 1. Mass Spectra of cis and trans Isomers IIa and IIb (50 eV)*

Isomer	257 (M)		242 (F_1)		214 (F_3)		110 (F_4)		105 (F_5)	
	IIa	IIb	IIa	IIb	IIa	IIb	IIa	IIb	IIa	IIb
Relative intensity, %	28.4	47	16,3	12,8	23.7	33	21.3	16.2	100	100

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*The five most intense ions are presented.

TABLE 2. Intensities of the Characteristic Ions in the Mass Spectra of Isomers IIa, b

Isomer	W_M*	F_1*	$\frac{F_1}{I_M}$	F_2*	$\frac{F_2}{I_M}$	F_3*	$\frac{F_3}{I_M}$	F_4*	$\frac{F_4}{I_M}$
IIa	10.8	5,4	0,58	1,1	0.11	8	0,84	8,1	1,05
IIb	11,7	2,8	0,27	0.8	0.08	7,3	0.69	3,5	0,49

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*In percent relative to the total ion current.

out by varying the temperature, reaction time, and molar ratios of lithium aluminum hydride and enamino ketone I, but it was found that a change in the conditions does not affect the overall quantitative yield of the reaction products and the percent ratio of piperidones II (69%) and alcohols III (30%). Chromatographic monitoring of the reaction mixture on Silufol immediately after the reaction and during the reaction showed that only trans isomer IIb is present in all cases. If the ether solution obtained after decomposition of the reaction mixture is stored at 0°C, the development of cis isomer IIa is not detected in the course of 3 days, but cis isomer IIa does appear at room temperature. The isomerization proceeds more slowly in the absence of a solvent at room temperature.

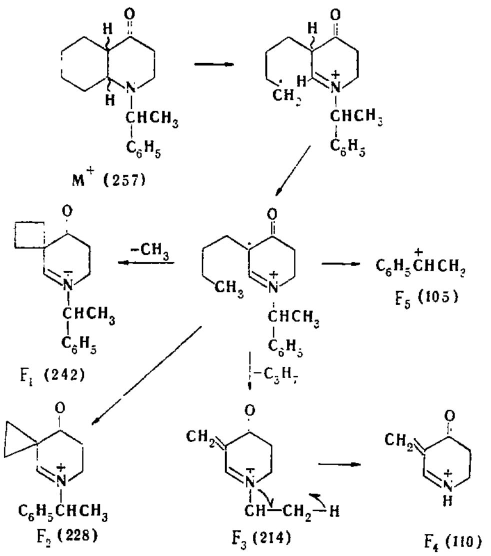
The mixture of isomers of ketones II and alcohols III were isolated with a column filled with silicic acid, inasmuch as the use of aluminum oxide hindered the isolation of the individual compounds [2]. Chromatographic analysis of the fractions obtained showed that a considerable amount of cis isomer IIa is formed after separation, i.e., isomerization is accelerated on silicic acid. The cis and trans isomers of II were separated by cooling a hexane solution of them to −30°, during which the less-soluble crystalline cis isomer precipitates. The cis isomer cannot be separated completely by this method, and trans isomer IIb was therefore isolated from the mixture in the form of the picrate. The chromatographically pure trans isomer was isolated from the picrate by treatment with alkali or by chromatography with a short column filled with silicic acid with elution with hexane−ether (1 : 1). The elution was carried out rapidly in order to avoid possible isomerization. The appearance in the PMR spectra of distinct signals of a methyl group as a doublet (1.3 ppm for IIb and 1.2 ppm for IIa) and of a methylidyne group as a quartet (3.75 ppm for IIb and 4.4 ppm for IIa) for each isomer confirm their diastereomeric purity.

The ratio of the cis and trans isomers in the equilibrium mixture after separation with a column was ~70 : 30; this proves the higher thermodynamic stability of cis isomer IIa. The higher thermodynamic stability of the cis isomer is also confirmed by experiments involving thermal isomerization and deuteration. The appearance of the trans isomers was detected chromatographically when the cis isomer was heated in benzene for 4 h, but the cis isomer predominates in the equilibrium mixture. Deuteration of the cis isomer with CD_3OD-CD_3ONa also leads to a mixture of cis and trans isomers of deuterium-substituted N-(α-phenylethyl)-4-ketodecahydroquinoline. A mass-spectrometric study showed that two hydrogen atoms in the 3 position of the decahydroquinolone systems are exchanged by deuterium in both isomers.

According to the data in [3, 4], trans fusion of the two six-membered rings in 1-decalones and decahydro-4-quinolones is thermodynamically more favorable. Our established fact of the higher thermodynamic stability of the cis isomer is extremely interesting and is probably associated with the steric requirements of the phenylethyl substituent attached to the nitrogen atom.

A mass-spectrometric study of isomeric IIa and IIb (Table 1) made it possible to obtain an additional confirmation of their different three-dimensional structures. The stability of the molecular ion of cis isomer IIa is somewhat lower than that of the trans isomer (Table 2). Under the conditions of the mass-spectrometric determination, the dissociative ionization processes proceed more actively in the case of the cis isomer, and ions F_1–F_4 have higher intensities (the m/e values are presented in parentheses in the scheme following).

The ratio of the intensities of the fragment ions to the intensity of the molecular ion is also higher in the case of cis isomer IIa. Similar dependences were previously observed in the case of stereoisomeric decahydro-4-quinolones [5].



In addition to the F_1-F_4 ions indicated in the scheme, which are common to both isomers and characterize the usual "amine" type of fragmentation, the mass spectrum of isomer IIa also contains an ion with m/e 180 (M − C_6H_5, 2.1%), which is completely absent in the mass spectrum of isomer IIb. Its formation is evidently associated with the higher steric strain of the bicyclic system in the case of the cis isomer, which leads to the development of additional fragmentation pathways. Finally, it should be noted that the relative intensities of the molecular ion and the F_1-F_4 ions increase when the ionizing-electron energy is lowered to 20 eV, and this proves their rearrangement character. The intensity of the fragment ion with m/e 105 decreases simultaneously.

EXPERIMENTAL

The mass spectra were recorded with an MKh-1303 spectrometer with introduction of the substances directly into the ion source at room temperature at ionizing electron energies of 50 and 20 eV and an accelerating voltage of 2 kV. Chromatography was carried out with hydrated silicic acid and Silufol plates.

Enamino ketone I was reduced by the method in [2]. Changes in the molar ratio of lithium aluminum hydride and the enamino ketone (5 : 1, 2.5 : 1, 2 : 1, 1.5 : 1, 1 : 1, and 0.8 : 1), the reaction time (0.5-5 h), and the reaction temperature (20-36°) did not affect the quantitative yields of the reaction products and the percent ratio of piperidones II (69%) and alcohols III (30%). Chromatographic analysis of the reaction mixture during the reaction and after decomposition on Silufol in various systems showed the formation of only trans isomer IIb. Reduction of 4.2 g (16 mmole) of enamino ketone I with 3 g (79 mmole) of lithium aluminum hydride in 180 ml of a mixture of absolute ether and absolute benzene (1 : 3) gave 4.17 g (~ 100%) of a light-yellow oil. The reaction mixture was separated with a column filled with hydrated silicic acid in petroleum ether and eluted successively with petroleum ether, petroleum ether–ether in ratios of 20 : 1, 10 : 1, 5 : 1, and 1 : 1, and ethyl acetate. The chromatographically homogeneous fractions were combined and evaporated to give 2.7 g (64%) of a mixture of the isomers of II: R_f 0.65 (IIa) and 0.5 (IIb) [benzene–acetone (6 : 1)]; 0.7 (IIa) and 0.6 (IIb) [petroleum ether–ether (1 : 2)]. Elution with ethyl acetate yielded 1.4 g (32%) of N-(α-phenylethyl)-4-hydroxydecahydroquinoline, which was found to be a mixture of four isomeric alcohols with R_f 0.4, 0.3, 0.25, and 0.15 [petroleum ether–ether (1 : 2)]. Recrystallization of the mixture of isomeric alcohols from hexane yielded the isomer present in the highest amount in the mixture: R_f 0.15 (same system), mp 139-140°, and M^+ 259.

Isolation of the cis and trans Isomers of II. A mixture of isomers IIa, b (2.8 g) was dissolved in hexane, after which the solution was cooled to −30°, and the resulting crystalline precipitate was removed by filtration and recrystallized from hexane to give 1.44 g (51%) of cis isomer IIa with mp 76-77°, R_f 0.65 [benzene–acetone (6 : 1)], and R_f 0.7 [petroleum ether–ether (1 : 2)]. PMR spectrum (CCl_4): δ 1.21 (d, CH_3), 4.4 (q, CH of the phenylethyl substituent), and 7.2 ppm (s, C_6H_5). A solution of an equivalent amount of picric acid in ether was added to an ether solution of 1.24 g of the mixture of isomers, and the precipitated picrate was removed by filtration and recrystallized from methanol to give 1.2 g of the picrate of trans isomer IIb with mp 185-186°.

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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