B) An ether solution (40 ml) of ~1 g of diazomethane was added to a solution of 0.4 g (1.47 mmole) of 2-oxopyridine Ib in 100 ml of acetone, and the mixture was allowed to stand at room temperature for 24 h. It was then vacuum evaporated, and the residue was treated with water and crystallized from ether to give 0.35 g (83%) of pyridine IIIh.

C) This compound was obtained in 93% yield from chloropyridine IVb by method A in the synthesis of IIIa.

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CONFORMATIONAL STUDY OF trans-(+)-(9S,10S)-DECAHYDRO-4-QUINOLONE AND ITS N-SUBSTITUTED DERIVATIVES*

V. M. Potapov, G. V. Grishina, and E. A. Golov

UDC 541.634:547.831.3.8

The spectropolarometric study of trans-(+)-(9S,10S)-decahydro-4-quinolone indicates the existence of invertomers with respect to the nitrogen atom, conformers formed during rotation of the substituent attached to the nitrogen atom about the C–N bond for trans-(9S,10S)-N-(α-phenylethyl)decahydro-4-quinolone, and conformers formed through conversion of the two-ring system for cis-(9R,10S)-N-(α-phenylethyl)decahydro-4-quinolone.

The hydrogenolysis of the two isomeric N-(α-phenylethyl)decahydro-4-quinolones (I) with cis- and trans-fused rings leads to removal of the chiral phenylethyl substituent and the formation of the same trans-(+)-(9S,10S)-decahydro-4-quinolone in both cases [4]. This subsequently made it possible, during the preparation of optically active trans-decahydro-4-quinolone (II), to subject a mixture of the cis and trans isomers of I to hydrogenolysis without their separation. trans-(+)-Decahydro-4-quinolone was recrystallizef from hexane until its melting point was constant. The presence of a second substance, which we assumed to be the cis isomer of II, was detected during a chromatographic study of the mother liquor; however, it was found to be impossible to isolate it because of the small quantity present. The formation of the same substance can be detected chromatographically after UV irradiation or thermal isomerization of a solution of pure trans isomer II.

Both rings in trans-decahydro-4-quinolone are linked rigidly, and ring conversion is impossible. However, different positions of the substituents on nitrogen – equatorial (IIA) and axial (IIB) – are possible as a result of inversion of the nitrogen atom:

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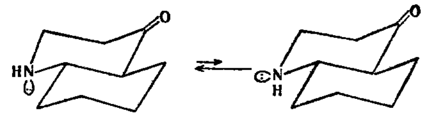
*Communication XXXVIII from the series "Stereochemical Studies"; see [1] for communication XXXVII.

M. V. Lomonosov Moscow State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1093-1097, August, 1976. Original article submitted April 21, 1975.



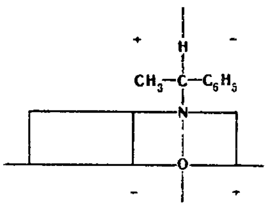
IIA IIB

We attempted to detect the existence of the two invertomers IIA and IIB from the data obtained by UV spectroscopy, circular dichroism (CD), and optical rotatory dispersion (ORD). A positive Cotton effect (CE) at 290 nm, associated with an n→π* transition in the carbonyl chromophore, and the band of a negative CE at 205-225 nm, associated with an n→σ* transition of the electron pair of nitrogen (the assignment of a negative shortwave band is confirmed by its disappearance in the spectrum of the hydrochloride of the trans isomer of II), are observed in the CD spectra of the trans isomer of II in solvents with different polarities. The corresponding transitions are also observed in the UV spectra. It should be noted that the intensity of the absorption in the UV spectra increases as the polarity of the solvent increases in the case of the n→π* transition, during which a decrease in the molecular ellipticity is observed (Table 1).

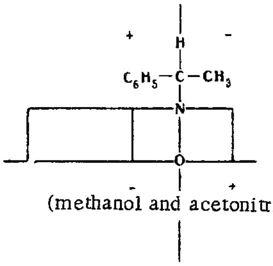
The observed bands in the CD spectra of the trans isomer of II, which contains two isolated chromophores, should, it would seem, exhaust the peculiarities of this system. In fact, however, a positive shoulder is discernible in the CD spectra at 260 nm (Fig. 1). Its appearance provides evidence for the existence of a third band, which, according to the literature data [3], arises in systems with "W-oriented" nitrogen p electrons and carbonyl group π electrons, which interact along σ bonds or through space. In the trans-decahydro-4-quinolone molecule this sort of interaction requires an equatorial orientation of the free electron pair of nitrogen. The weak expression of the positive band of the interaction of the isolated chromophores and its appearance only as a shoulder constitute evidence for the insignificant contribution of invertomer IIB. The existence of a chromophoric interaction in the trans isomer of II is also reflected in an increase in the extinction coefficient of the n→π* transition in the UV spectrum.

When the trans isomer of II is converted to the acetate, methiodide, and hydrochloride, i.e., when the nitrogen atom is quaternized, the character and sign of the CE of the n→π* transition do not change, and the positive shoulder at 260 nm also vanishes. One should also note the decrease in the molecular ellipticity of the n→π* transition in the salts as compared with the free base (Fig. 2). The pronounced decrease in the amplitude of the CE of the hydrochloride and methiodide of the trans isomer of II in methanol can be explained by the formation of an equilibirum between the keto and hemiketal forms [4].

Like trans-decahydro-4-quinolone, the trans isomer of I has a conformationally rigid structure in which axial orientation of the bulky substituent attached to nitrogen is practically not realized. However, the existence of conformers arising upon rotation of the phenylethyl substituent about the C—N bond is possible for the trans isomer of I. A marked change in the molecular ellipticity as a function of the polarity of the medium is observed in the CD spectrum for the n→π* transition (θ+1300° in heptane and +3000 in methanol and acetonitrile) (Fig. 3). This can be explained in conformity with the octant projection by the existence of different conformers in solvents with different polarities:



(heptane)



(methanol and acetonitrile)

TABLE 1. n→π* Transitions in the Spectra of trans-Decahydroquinolone II

Solvent	UV	CD
	λ_{max}, nm (ε)	λ_{max}, nm (ε)
Methanol	290(70)	289(+2400)
Acetonitrile	290(40)	290(+2200)
Heptane	294(35)	295(+2800)

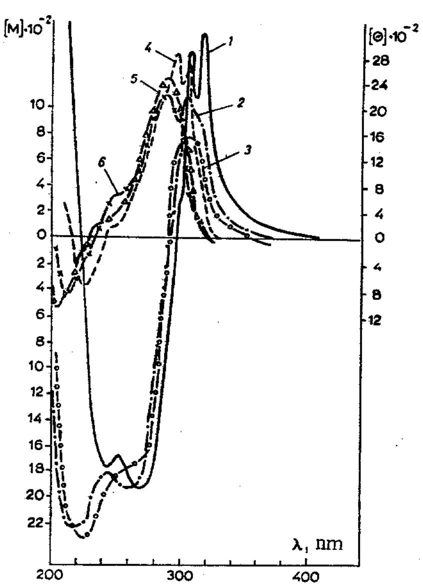


Fig. 1

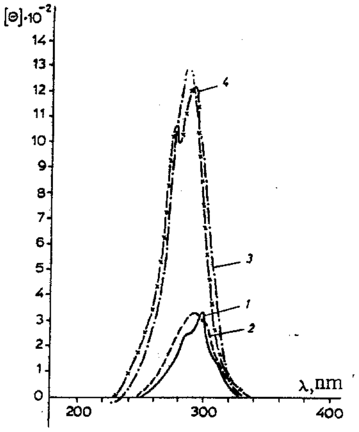


Fig. 2

Fig. 1. ORD of the trans isomer of II in heptane (——, 1) methanol (—·——, 2) and acetonitrile (—O—O—, 3); CD in heptane (— — —, 4), methanol (—Δ—Δ—, 5) and acetonitrile (—X—X—, 6).

Fig. 2. CD of salts of the trans isomer of II: methiodide in methanol (—, 1), hydrochloride in methanol (—, 2) and in water (——·——, 3), and of the acetate in methanol (—X—X—, 4).

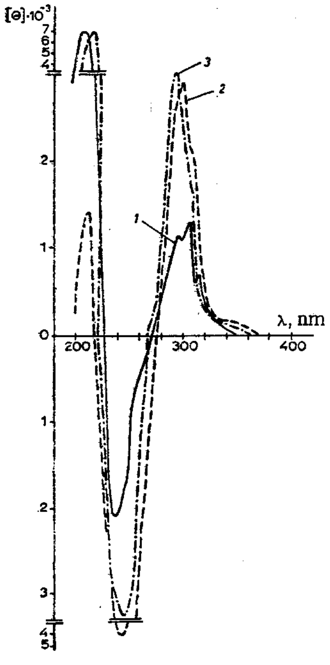


Fig. 3

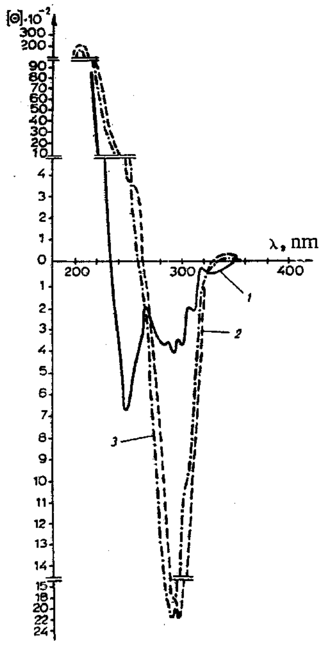
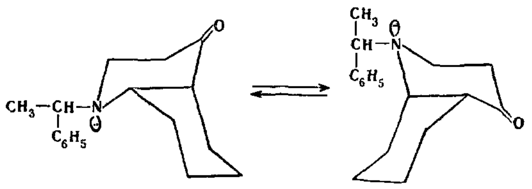


Fig. 4

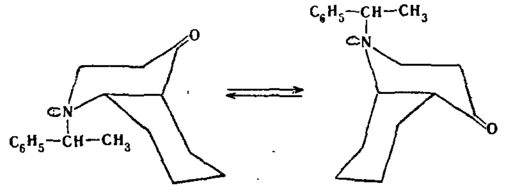
Fig. 3. CD of the trans isomer of I in heptane (—, 1), methanol (—, 2), and acetonitrile (——·——, 3).

Fig. 4. CE of the cis isomer of I in heptane (—, 1), acetonitrile (—, 2), and methanol (——·——, 3).

Not only inversion of nitrogen but ring conversion also is possible for the cis isomer of I, which is a conformationally labile system:

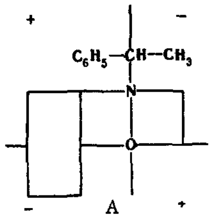


IA IB

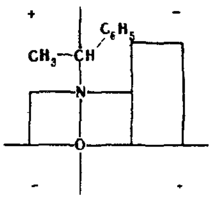


IC ID

Conformers IC and ID with an axial phenylethyl group are unlikely, and we will not consider them further. A negative CE with a relatively small amplitude is observed in the region of the n→π* transition in the CD spectra of the cis isomer of I in heptane, and a strong negative CE is observed in methanol and acetonitrile (Fig. 4). The application of the octant rule to the cis isomer of I shows that a weak negative CE should be observed for conformation IA and a strong CE should be observed for conformation IB.



A



B

Thus conformer Ia evidently predominates in nonpolar solvents, and conformer IB predominates in polar solvents.

EXPERIMENTAL

The CD and ORD spectra were recorded with a J-20 spectropolarimeter. trans-Decahydro-4-quinolone (II) and cis- and trans-N-(α-phenylethyl)decahydro-4-quinolones (I) were obtained by the method in [2, 3].

Isomerization of trans-Decahydro-4-quinolone (II). A) A 50-mg sample of the trans isomer of II was heated in benzene for 4 h, after which the solution was chromatographed on Silufol in an ammonia-saturated chloroform system, which revealed the presence of two substances with R_f 0.65 (trans isomer of II) and 0.8 (identical to the substance found in the mother liquor from recrystallization of the trans isomer of II).

B) A solution of 20 mg of the trans isomer of II in methanol was irradiated with a mercury lamp for 2 h, after which it was chromatographed on Silufol, which revealed the presence of two substances formed during thermal isomerization.

The hydrochloride of the trans isomer of II was obtained by mixing an alcohol solution of 200 mg of base II with an alcohol solution of hydrogen chloride. Workup yielded 240 mg (97%) of the salt with mp 215-216° (from ethanol). IR spectrum: 1730 (C=O), 2700 cm^{-1} ($>NH_2$). UV spectrum, λ_{max}, nm (ε): 203 (224), 280 (20) (methanol); 245 (50), 278 (90) (water).

The methiodide of the trans isomer of II was obtained from 100 mg of base II in 1 ml of acetone and 0.5 ml of methyl iodide. The yield of product, with mp 189-190° (dec., from CH_3COOH), was 170 mg (88%). IR spectrum: 2400 ($\overset{+}{N}HCH_3$) and 1735 cm^{-1} (C=O). UV spectrum, λ_{max}, nm (ε): 220 (15850) and shoulder 300 (60) (methanol).

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RESEARCH ON 1-AZABICYCLIC SYSTEMS

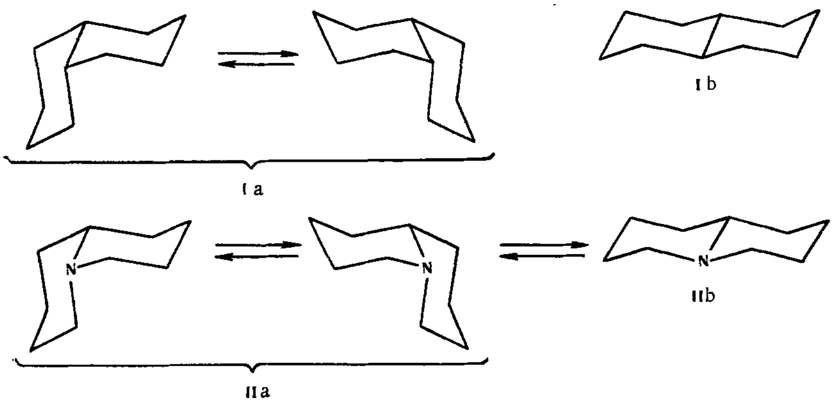
XIV.* DIFFERENCE IN THE ENTHALPIES OF THE cis- AND trans-FUSED FORMS OF QUINOLIZIDINE

I. M. Skvortsov

UDC 547.834.2:541.634'11

The enthalpy of the cis–trans conversion of quinolizidine was calculated by two independent methods on the basis of the literature data on the heat content of decalins, the difference in the enthalpies of the N–H-axial and N–H-equatorial conformations of piperidine, and the hydrogen bond energies in the quinuclidine–phenol and quinolizidine–phenol systems. The calculations yielded ΔH values of 3.7 and 4.3 kcal/mole for gaseous quinolizidine and 3.3 kcal/mole in favor of the **trans-fused** form for the liquid.

The differences in the thermodynamic properties of cis- (Ia) and trans-decalin (Ib) [2-6] have been the starting point and basis for comparisons and calculations [3, 7, 8] of the parameters of the conformational equilibrium between the cis- (IIa) and trans-fused (IIb) conformations of quinolizidine.



The results of a determination of the difference in the thermodynamic parameters that characterize the Ia⇌Ib and IIa⇌IIb equilibria are presented in Table 1. Except for [11], all of the determinations of the ΔH° or ΔG° values of the cis-trans conversion of quinolizidine presented in Table 1 are indirect, and their results deviate considerably from one another. Data on the entropy of the process under consideration has not been obtained in any of the studies. If one takes into account the fact that IIa is an unseparable d,*l*-pair, the cis-fused conformation is preferred from an entropy point of view by no more than R ln 2, i.e., 1.38 $\mathrm{cal \cdot deg^{-1} \cdot mole^{-1}}$. Relative to the conclusions drawn in [7], it has been noted that the calculations were based on erroneous notions of the dimensions of the unshared electron pair of nitrogen [8, 12]. The data of [8, 9] met with disapproval [13, 14], but Aaron subsequently [10] rejected his previously obtained ΔG° value of −4.6 kcal/mole [8] and proposed a new ΔG° value of −2.6 kcal/mole. The latter determination found support in a communication by Crabb and Newton, who made an attempt to explain the unexpected closeness of the free energies of cis-trans conversion of quinolizidine (II) and indolizidine (III) [15].

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*See [1] for communication XIII.

N. G. Chernyshevskii Saratov State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1098-1102, August, 1976. Original article submitted December 23, 1974.