CONFORMATIONAL TRANSFORMATIONS OF LUPININE IN THE FORMATION OF PROTONATED FORMS AND QUATERNARY SALTS

T. K. Yunusov, T. K. Kasymov, F. G. Kamaev,
V. B. Leont'ev, K. Inoyatova, A. I. Ishbaev,
and A. S. Sadykov

UDC 539.194.538.27

As is well known, quinolizidine, a nitrogen-containing analog of decalin, can exist in cis and trans conformations. cis-Quinolizidine is an unstable form, and the trans conformation, exhibiting inversion about the nitrogen atom in solutions, can generally be converted into the cis form only under severe and specific conditions [1-4]. In a preceding communication [5], we gave the results of an investigation of the processes of inversion in the molecules of lupinine (I) and epilupinine (II) by IR spectroscopy in the liquid and solid states; it was observed that the change in the spectral characteristics was connected with a change in conformations in the phase transition and with the inhibition of inversion processes. In a study of PMR spectra, conformations I and II and an additional six-membered ring of lupinine, formed through an intramolecular hydrogen bond between the CH_2OH group and the nitrogen atom, were determined.

The structural factors through which the spatial structures (I) and (II) are distinguished affect the conformational transition of the trans form of quinolizidine into the cis form. This takes place in reactions affecting the center capable of inversion, since the addition of a carbocation or proton to forms (I) and (II) makes isomerization into the cis conformation probable [6-7].

In order to answer this question, we have considered the PMR and IR spectra of the protonated forms of (I) and (II) and of their methiodides. The methiodides of (I) and (II) were isolated from the bases by direct methylation. Their physical constants have been determined.

The IR spectra of the methiodides of (I) and (II) were obtained (for tablets of 2 mg of salt in 200 mg of KBr) on a UR-10 instrument (K. Zeiss); and the PMR spectra on a H-60 instrument (Hitachi) in D_2O and HCl of various concentrations.

The results of a comparison of the spectra of the protonated forms of (I) and (II) (Fig. 1a, d) taken in conc. HCl to retard the rapid processes of exchange with $>N^+-H$ show that their conformational characteristics under these conditions are different. While in the PMR spectrum of protonated (II) (Fig. 1d) there are a doublet at 3.55 ppm with $J_{vic} = 4$ Hz relating to the protons of an equatorial methyleneoxy (CH_2-O-) group, a pseudodoublet at 3.2 ppm with $J_{gem} = 12$ Hz corresponding to equatorial α-protons located near the nitrogen, and a broad unresolved multiplet at 2.8 ppm (axial α-protons), in the spectrum of protonated (I) (Fig. 1 a) there are two doublets of a methyleneoxy group at 3.75 and 3.40 ppm with $J_{vic} = 5$ and 8 Hz, respectively, and the nature of the signals of the α-equatorial and axial protons differs substantially from that in protonated (II).

The formation of two doublets in protonated (I) unambiguously shows that in an acid medium two protonated forms are produced, the ratio of the integral intensities of the signals depending on the equilibrium constant between these forms and the concentrations of water and free base. Consequently, these forms can be converted into one another reversibly.

We have previously [5] established that in solution compound (I) participates in a labile conformational transformation with inversion of the nitrogen (A). Apparently, the life of the boat-shaped

---

V. I. Lenin Tashkent State University. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 448-452, July-August, 1971. Original article submitted February 22, 1971.

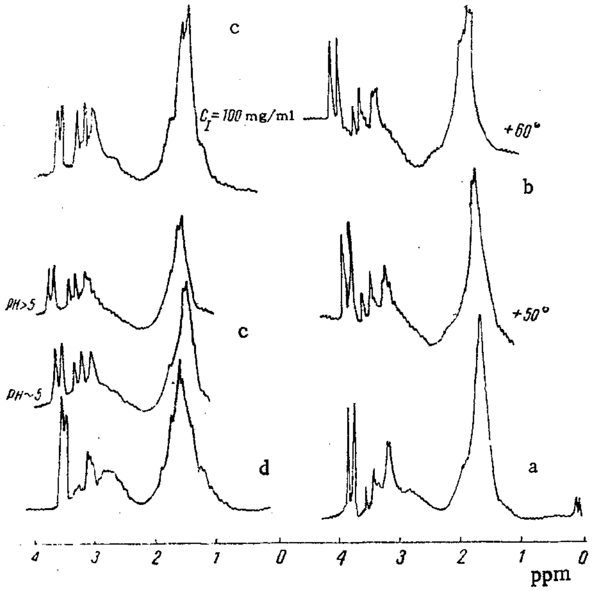
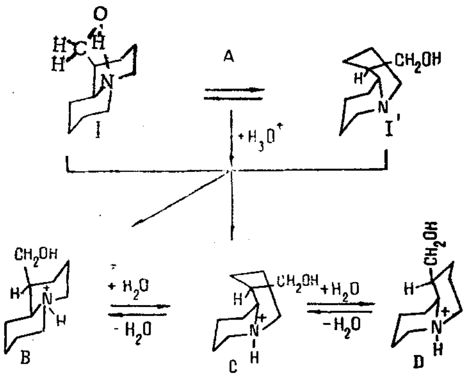


Fig. 1. PMR spectrum of lupinine in concentrated HCl (a); the change in the integral intensity of the CH_2OH doublets with the temperature (b); the same change as a function of the pH of the medium and the concentration of lupinine (c); and the spectrum of epilupinine (d).

conformation is short. However, on protonation the interaction of H^+ with both forms of (I) is possible. Since the axial N^+–H bond in the trans conformation of (I) undergoes a 1,3-diaxial interaction with the axial CH_2OH group, the probability of the protonation of the second form (I') rises. The boat form is unsatable (C) and its transformation is completed by a transition to the cis form with an equatorial CH_2OH group. There is no 1,3-diaxial interaction in (II), and therefore this transformation does not take place.

The interrelationship of the processes of protonation and proton exchange between the molecules of H_2O, H_3O^+, (I) and (I H^+) was revealed as a result of a change in the temperature, in the acidity of the medium, and of the concentration of (I) in D_2O. With an increase in the temperature from +34 to +60°C in solutions in conc. HCl (c_1 = 78 mg/ml), the intensity of the signals of the protons of the equatorial CH_2O group of (I) rose (Fig. 1b); a combined increase in the concentration of (I) to 100 mg/ml and in its pH led to a large relative increase in the concentration of the protonated cis form of (I) (Fig. 1c).

Thus, our experimental results show that compound (I) is converted on protonation into two different protonated conformers (B and D), the ratio between the concentrations of which depends on the rates of the following processes.



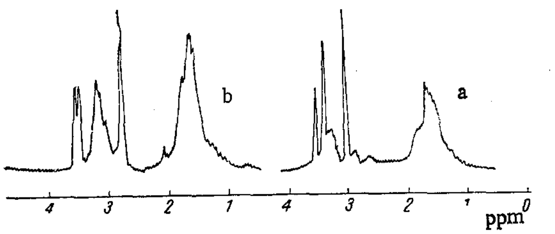


Fig. 2. PMR spectra of the methiodides of lupinine (a) and of epilupinine (b).

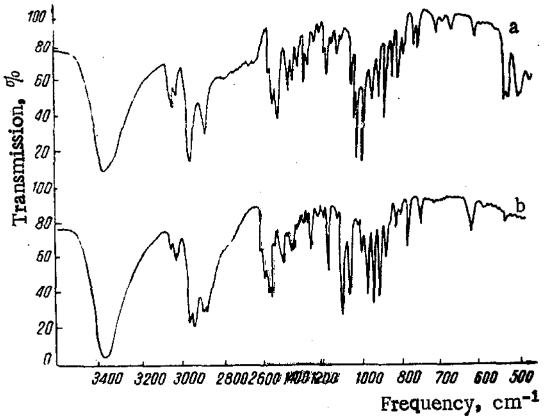


Fig. 3. IR spectra of the methiodides of lupinine (a) and of epilupinine (b).

In more acid media, the equilibrium is shifted in direction of the formation of the trans axial CH_2OH form because of the greater rate of protonation and the inhibition of the exchange of protons through water molecules.

A comparison of the spectra of the protonated forms of (I) and (II) shows that the doublet signals at 3.55-3.47 ppm relate to the equatorial CH_2O group and the signal at 3.75 ppm to the axial CH_2O group in the cis and trans forms. The unambiguous nature of such an assignment follows from the PMR spectra of the methiodides of (I) and (II) with equatorial CH_2-O- groups, which contain almost equivalent methylene groups and the chemical shifts of which correspond to the doublet of the protonated form of (I), which is located in the weak field.

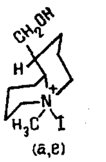
It can be seen from the spectra of the methiodides of (I) and (II) in conc. HCl (Fig. 2) that the methiodide of (I) has the chemical shift of the hydroxymethylene protons at 3.45 ppm with $J_{vic} = 5$ Hz and the methiodide of (II) has it at 3.45 ppm with $J_{vic} = 4$ Hz; the chemical shift of N^+-CH_3 in (I) resonates at 3 ppm and in (II) at 2.75 ppm.

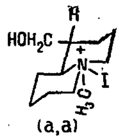
In addition, the nature of the signals of the α protons adjacent to the nitrogen differs substantially. Consequently, in the methiodides of (I) and (II) the CH_2OH group is equatorial and the N^+-CH_3 occupies the axial-equatorial position in (I) and the axial-axial position in (II). Consequently, on interaction with the methyl cation isomerization of the quinolizidine system of lupinine takes place.

The differences in the conformations of the methiodides of (I) and (II) are additionally confirmed by their IR spectra (Fig. 3). Thus, in the region of the deformation and pulsation vibrations of the ring (500-1000 cm^{-1}), the methiodides of (I) and (II) give different characteristic features. The deformation and stretching vibrations of the CH_2OH groups in (I) and (II) are comparatively different from one another.

Since in the methiodides of (I) and (II) the group is equatorial (PMR spectra), the differences in the region of the deformation and stretching vibrations of the CH_2OH group are apparently connected with the different conformations of the rings of (I) and (II). The methiodide of (I) exhibits bands at (cm^{-1}):500, 525, 555, 560, 640, 690, 785, 800, 855, 870, 900, 925, 935, 960, 980 and 1025, 1055, 1065, 1080, 1090 (deformation vibration of CH_2OH group) and 3350 (stretching vibration of CH_2OH), and the methiodide of (II) at 540, 625, 720, 785, 820, 835, 865, 885, 910, 940, 970, 1000, 1055, 1090 (deformation vibration of CH_2OH) and 3370 (stretching vibration of CH_2OH).

On studying the PMR and IR spectra, we came to the conclusion that the methiodide (I) exists in the cis conformation because of the conformational transition in the reaction process, reducing the 1,3-diaxial interaction. Consequently, the methiodides of (I) and (II) have the following conformations:





SUMMARY

1. The results of a study of IR and PMR spectra have shown that in solution protonated lupinine exists in two interconverting cis-trans conformations the relative amounts of which depend on the temperature, the concentrations of base and water, and the pH of the medium. This process is possible because of a change in the direction of the unshared pair of the nitrogen atom in the inversion process.

2. On the basis of the PMR and IR spectra, lupinine methiodide has the a,e conformation with an e-CH_2OH group and epilupinine methiodide has the a,a conformation with an e-CH_2OH group.

LITERATURE CITED

1. H. I. Aaron, Chem. Ind. (London), 30, 1338 (1965).
2. E. Eliel, N. Allinger, S. Angyal, and G. Morrison, Conformational Analysis, Interscience (1965).
3. F. Galinovsky and V. Nesvadba, Monatsh., 85, 1300 (1954).
4. A. Thomas, H. Vipond, and L. Marion, Canad. J. Chem., 33, 1290 (1955).
5. T. K. Yunusov, A. I. Ishbaev, V. B. Leont'ev, and A. S. Sadykov, Khim. Prirodn. Soedin., 7, 49 (1971).
6. T. Moynehean, K. Schofield, A. V. Jones, and A. R. Katritzky, J. Chem. Soc., 2637 (1962).
7. W. Grow, Austral. J. Chem., 11, 366 (1958).