TAUTOMERISM OF SOME IMIDAZO[4,5-b]PYRIDINE DERIVATIVES

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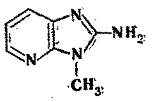
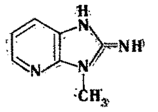
It was shown by means of UV and IR spectroscopy and the ionization constants that the tautomeric equilibrium of 2-amino- and 2-mercapto derivatives of 3-methyl-3H-imidazo[4,5-b]pyridine is shifted to favor the amino and thione forms, respectively.

An extensive amount of literature [1, 2] has been devoted to the investigation of the amine–imine and thione–thiol tautomerism of amino and mercapto derivatives of heterocyclic compounds. The results of investigations in this area attest to the fact that in almost all cases the equilibrium of the tautomeric transformation is shifted practically completely to favor aminoaromatic and thione structures.

The structures of 2-amino-3-methyl-3H-imidazo[4,5-b]pyridine (I) and 2-mercapto-3-methyl-3H-imidazo[4,5-b]pyridine (II) are examined in the present paper for the first time from the point of view of the possibility of prototropic tautomerism for them.

A similarity in the absorption of I and III is observed on comparison of the UV spectra of aqueous solutions of amine I and model compounds III and IV, which correspond to the tautomeric amino and imino forms of I and Ia, whereas the spectrum of imine IV differs considerably from the spectra of I and III; this may serve as evidence for an amino structure for I (Figs. 1-3).


I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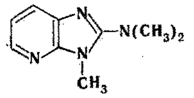
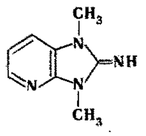

III


IV

The IR spectrum of a dilute solution of I in carbon tetrachloride contains bands at 3394 and 3480 cm^{-1}, which are typical for the absorption of a primary amino group. The results of measurements of the ionization constants of amine I (pK_{BH^+} 5.74) and of amodel compounds – 2-dimethylamino-3-methyl-3H-imidazo[4,5-b]pyridine (III, pK_{BH^+} 5.41) and 1,3-dihydro-1,3-dimethyl-2H-imidazo[4,5-b]pyridine-2-imine (IV, pK_{BH^+} 9.44), which are fixed tautomeric forms of the amine under consideration – are in agreement with this conclusion. As seen from a comparison of the pK_{BH^+} values presented above, the basicity of imine IV is much higher than the basicity of model amine III. In addition, the ionization constants of the latter compound and I are approximately identical. Inasmuch as bases III and IV form a conjugate acid of the same type in acidic media [3],* one can easily calculate the constant of the tautomeric equilibrium for I: $pK_T = 9.44 - 5.21$† $= 4.23$, and $K_T = 5.8 \cdot 10^{-4}$. This is the usual value of the constant for most amino

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* The closeness of the second ionization constants of the conjugate acids of I (pK_{BH^+} − 0.90) and IV (pK_{BH^+} − 1.03) may serve as an additional confirmation of this.

† The effect of one methyl group (0.2 pK) [4] was taken into account in the pK_{BH^+} value of amine III.

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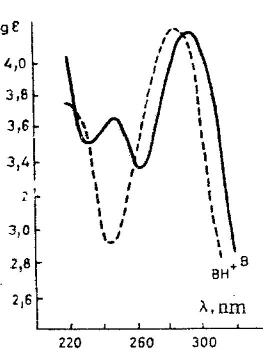


Fig. 1

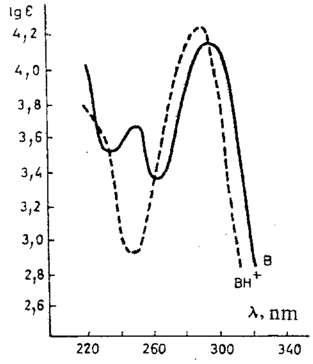


Fig. 2

Fig. 1. UV spectra in water of the neutral (B) and protonated (BH^+) forms of 2-amino-3-methyl-3H-imidazo[4,5-b]pyridine.

Fig. 2. UV spectra in water of the neutral (B) and protonated (BH^+) forms of 2-dimethylamino-3-methyl-3H-imidazo[4,5-b]pyridine.

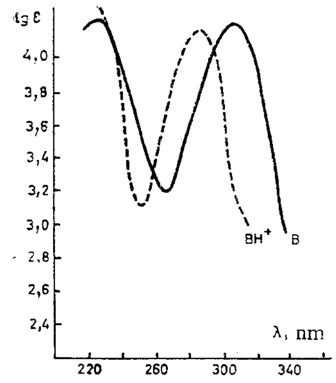


Fig. 3

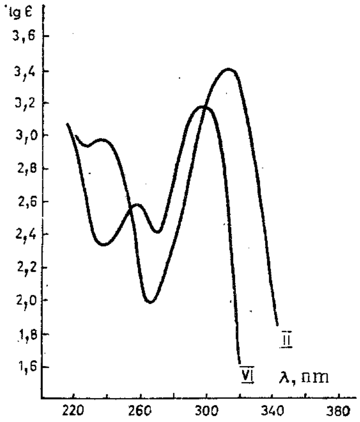


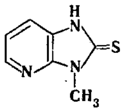
Fig. 4

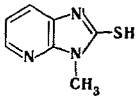
Fig. 3. UV spectra in water of the neutral (B) and protonated (BH^+) forms of 1,3-dihydro-1,3-dimethyl-2H-imidazo[4,5-b]-pyridine-2-imine.

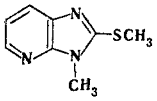
Fig. 4. UV spectra in water of neutral 2-mercapto-3-methyl-3H-imidazo[4,5-b]pyridine (II) and 2-methylmercapto-3-methyl-3H-imidazo[4,5-b]pyridine (VI).

heterocycles and is much lower than the tautomeric equilibrium constant for 2-amino-1-methylbenzimidazole (V) [4], which is the closest structural analog of the investigated amine.

The problem of the thione–thiol tautomerism of II was also studied by various methods. An analysis of the IR spectra of dilute solutions of II in carbon tetrachloride makes it possible to confidently assign a thione form to this compound. In fact, a band of N–H stretching vibrations is recorded distinctly at 3460 cm^{-1}, whereas the corresponding S–H band (2500-2600 cm^{-1}) is absent in the spectrum. The difference in the UV spectra of aqueous solutions of thione II and 2-methylmercapto-3-methyl-3H-imidazo-[4,5-b]pyridine (VI) – the fixed thiol form – indicates the thione structure of mercaptoimidazopyridine II (Fig. 4). A comparison of the ionization constants of II (pK_{BH^+} 0.65) and VI (pK_{BH^+} 2.81) leads to the same conclusion. Such great disparity in the basicities can be linked only to different positions of the site of addition of a proton in these compounds, and inasmuch as VI models mercapto form II, it should have a thione structure.


II a


II b


VI.

Thus I exists in the amino form, whereas II exists in the thione form in solutions in both nonpolar and polar solvents.

EXPERIMENTAL

The substances were synthesized by the method in [6-8]. The IR spectra were recorded with a UR-20 spectrometer. The UV spectra were recorded with an SF-16 spectrophotometer. The basicity constants were determined spectrophotometrically in aqueous solutions at 25° [9].

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