QUATERNIZATION CENTERS OF N-METHYL DERIVATIVES OF IMIDAZO[4,5-b]PYRIDINE

T. N. Pliev, R. M. Bystrova,
and Yu. M. Yutilov

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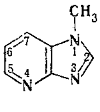
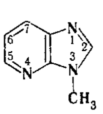
It is shown that quaternization of isomers of 1-methylimidazo[4,5-b]pyridine and 3-methylimidazo[4,5-b]pyridine proceeds at different reaction centers – at the nitrogen atom of the imidazole ring in the first case and at the nitrogen atom of the pyridine ring in the second case.

The structures and reactivities of compounds of the imidazo[4,5-b]pyridine series are of great interest in connection with the close structural analogy of this class of polyheterocyclic systems, which contain two or more reaction centers, with the benzimidazole derivatives and the biologically important purine derivatives. The present research is devoted to the determination of the quaternization center of the 1-methylimidazo[4,5-b]pyridine (I) molecule in the reaction with methyl chloride. Isomeric compounds I and 3-methylimidazo[4,5-b]pyridine (II) each have two basic centers, and it is therefore difficult to predict the direction of quaternization.


I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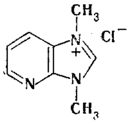
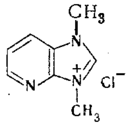
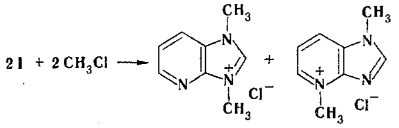

III


IV

It has been previously shown [1] for 3-methylimidazo[4,5-b]pyridine (II) that alkyl halides add to the N_1 atom. These results indicated that the most nucleophilic atom in isomer II is the nitrogen atom of the imidazole ring. The question of the reaction center in isomeric compound I was investigated by IR and UV spectroscopy. In the general case, four possible directions of quaternization can be assumed for I on reaction with methyl chloride: at the nitrogen atom of the imidazole ring, at the nitrogen atoms of the imidazole ring and pyridine ring to give a dichloride, at the nitrogen atom of the imidazole ring and partially at the pyridine ring to give a mixture of two isomeric chlorides, and at the nitrogen atom of the pyridine ring.



The second direction is unlikely, since simultaneous reaction of the nitrogen atoms of the imidazole and pyridine rings is sterically hindered. For this reason, the previously obtained data on the quaternization of isomer I could be interpreted unambiguously as proof of the formation of 1,3-dimethylimidazolio[4,5-b]pyridine chloride (III). If the positive charge is not localized on a definite nitrogen atom but uniformly distributed between the two nitrogen atoms of the imidazole ring, the molecular structures of III and the isomeric IV should be identical. In this case, the IR spectra of the quaternary salts – the products of quaternization of isomers I and II – should be identical. In fact, differences in the region of the chief characteristic frequencies [β-ring, γ-ring, β-(CH), γ-(CH), δ_s, δ_{as}] are observed in the IR spectra of the compounds obtained; this is evidence for different molecular structures of these compounds (see Fig. 1). But

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Severo-Osetinsk State Medical Institute, Ordzhonikidze. All-Union Scientific-Research Institute of Reagents and Chemically Pure Materials for Electronic Technology, Donetsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1686-1688, December, 1973. Original article submitted February 28, 1972.

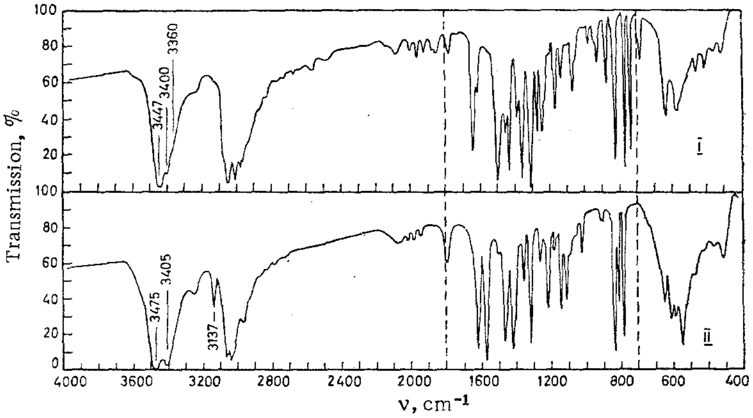

Fig. 1. IR absorption spectra of 1,4-dimethylimidazo[4,5-b]-pyridinium chloride and 1,3-dimethylimidazolio[4,5-b]pyridine chloride (III).

localization of the positive charge should not have led to such large changes in the vibrational frequencies and distribution of the intensities of the absorption bands. Consequently, the first direction is also unlikely. Moreover, the III and IV structures can be considered to be the limiting structures of the mesomeric cation formed.

The spectra show that the investigated methochlorides cannot be considered to be mixtures of one and the same isomeric chlorides with a different ratio of these isomers (the third direction): a number of intense bands observed in the spectrum of one methochloride are completely absent in the spectrum of the other, and vice versa. The methochlorides obtained also differ with respect to other characteristics – melting point and UV spectra: methochloride of I has mp 238-239° and λ_{max} 292 nm (ε 12,800); the methochloride of II has mp 226-227° and λ'_{max} 242 nm (ε' 4102), and λ''_{max} 274 nm (ε'' 8892). Proceeding from the experimental data and also from reasons that substantiate the unreality of the first direction, the reaction with the formation of a mixture of two isomeric chlorides also should be excluded. The experimental data indicate that the quaternization center in I is the nitrogen atom of the pyridine ring. The distribution of the intensities of the components of the broad band at 3350-3500 cm^{-1} and localization of the maxima themselves within this interval, just as the different multiplicity and distribution of the relative intensities of the bands of the stretching vibrations of the C–H bond at 2900-3150 cm^{-1}, constitute evidence that the synthesized methochlorides have different molecular structures, and quaternization of 1-methyl-1H-imidazo[4,5-b]-pyridine is consequently realized at the nitrogen atom of the pyridine ring.

EXPERIMENTAL

The IR spectra of the synthesized compounds were obtained with a UR-20 spectrometer. The UV spectra of ethanol solutions were measured with an SF-4 spectrophotometer.

1,3-Methyl-3H-imidazolio[4,5-b]pyridine Chloride (III). A 1-g sample of II was heated in a sealed tube with 8 ml of methyl chloride at 70-90° for 4 h and at 120-125° for 2 h. The tube was then cooled and opened, and the solid material [1.3 g (95% of the theoretical yield), mp 222-223°] was recrystallized from isopropyl alcohol, initially with charcoal and then twice without the sorbent. The product was dried in vacuo to give a material with mp 226-227°. Found: C 52.4; H 5.4; Cl 19.3%. $C_8H_{10}N_3Cl$. Calculated: C 52.3; H 5.5; Cl 19.3%.

1,4-Dimethyl-1H-imidazo[4,5-b]pyridinium Chloride. Reaction of 0.45 g of I with 4 ml of methyl chloride under conditions similar to those in the preceding experiment gave 0.602 g (97%, mp 234-235°) of product. The latter was recrystallized from ethanol containing charcoal and then twice from isopropyl alcohol, after which it was dried in vacuo to give a product with mp 239-239°. Found: 22.6%. $C_8H_{10}N_3Cl$. Calculated N 22.9%. A mixture of this product with III gives a melting point depression (196-200°C).

LITERATURE CITED

1. Yu. M. Yutilov and R. M. Bystrova, Khim. Geterotsikl. Soedin., 954 (1968).