BENZIMIDAZOLE DERIVATIVES WITH ZWITTERION STRUCTURES

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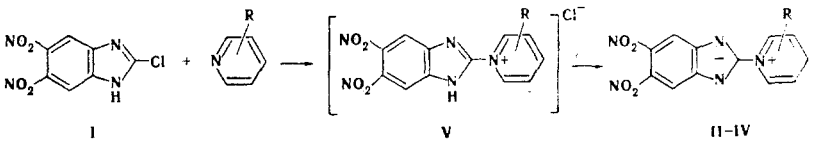
2-Pyridinium and β- and γ-picolinium-5,6-dinitrobenzimidazole betaines were obtained by reaction of 5,6-dinitro-2-chlorobenzimidazole with pyridine and β- and γ-picolines.

In a study of nucleophilic substitution of the chlorine atom in 5,6-dinitro-2-chlorobenzimidazole (I) in pyridine it was observed that benzimidazole I reacts readily with pyridine and also with β- and γ-picolines to give yellow crystalline compounds (II-IV). The reaction does not proceed with α-picoline and 2,6-lutidine under the same conditions.

It is apparent from an analysis of the UV spectra that II-IV (Fig. 1) have similar chromophore systems; moreover, their conjugation chain is increased as compared with the starting chloro derivative (I).

As in the IR spectrum of I, intense absorption bands at 1330-1360 and 1530 cm^{-1}, which are characteristic for aromatic nitro groups, are observed in the IR spectra of II-IV, but the ν_{NH} absorption band at 3290 cm^{-1} that is present in the spectrum of starting benzimidazole I is absent.

Splitting out of HCl and trimerization of the resulting dehydrochlorination product [1] or nucleophilic substitution of the labile chlorine atom to give quaternary salt V may occur in the reaction of I with pyridine and β- and γ-picolines. The molecular weights of III and IV determined by mass spectrometry are 229, which excludes the formation of products with dimeric and trimeric structures. In the case of nucleophilic substitution, the initially formed salt V in excess pyridine (or, respectively, picolines) apparently loses HCl. This may occur either with splitting out of a proton from the NH group of the imidazole ring to give zwitterion compounds II-IV, similar to the reaction of some substituted chloropurines with pyridine [2], or may be accompanied by an intramolecular rearrangement of the Ladenburg type [3], which should lead to different 2-pyridylbenzimidazoles. The IR and PMR spectra, in which the signal of an NH group is absent, constitute evidence against the latter assumption.



I V II-IV

II R=H; III R=3-CH_3; IV R=4-CH_3

The PMR spectrum of chloro derivative I contains two signals (a singlet at 8.33 ppm and a broad signal at 13.7 ppm) with an integral intensity ratio of 2:1, which corresponds to the protons of the condensed benzene ring and the protons of the NH group of the imidazole ring [4]. The PMR spectrum of II (Fig. 2) contains three groups of signals (a doublet at 10.0, a triplet at 8.76 ppm, and a multiplet at 8.18-8.38 ppm) with an intensity ratio of 2:1:4. With respect to their mutual positions and the character of the splitting, these signals can be assigned to the α, γ, and β protons of the pyridine ring, respectively; the triplet of the

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TABLE 1. Characteristics of the Compounds Obtained

Compound		mp, °C	R_f*	Empirical formula	Found, %			Calc., %		
					C	H	N	C	H	N
II	H	327—328	0,34	$C_{12}H_7N_5O_4$	50,3	2,6	24,8	50,5	2,5	24,6
III	3-CH_3	338—339	0,37	$C_{13}H_9N_5O_4$	52,4	3,1	23,5	52,1	3,0	23,4
IV	4-CH_3	304—305	0,40	$C_{13}H_9N_5O_4$	52,3	3,4	22,9	52,1	3,0	23,4

*A butanol–water–acetic acid system (4:1:1) was used for chromatography on Silufol UV-254 plates.

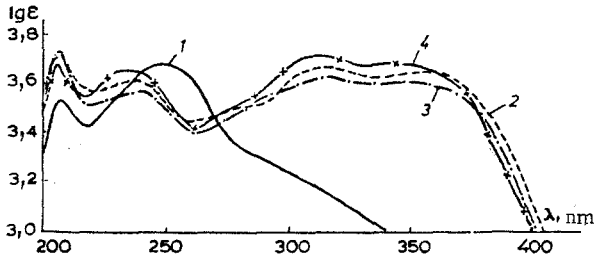

Fig. 1. UV absorption spectra (in ethanol): 1) I; 2) II; 3) III; 4) IV.

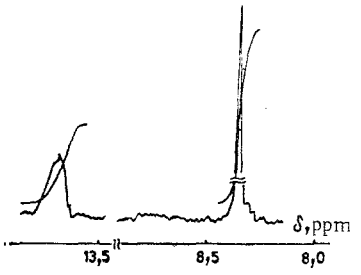

Fig. 2

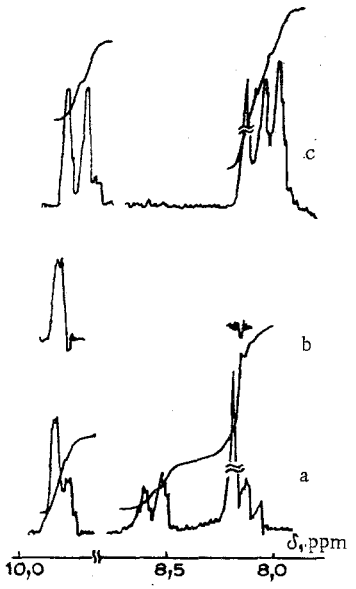

Fig. 3

Fig. 2. PMR spectra of betaine II.

Fig. 3. PMR spectra: a) and b) III; c) IV.

β protons is superimposed on the singlet of the protons of the nitrobenzimidazole ring. This is also confirmed by the double-magnetic resonance data. The number of protons in the pyridine portion of II (2α, 2β, and γ) and the chemical shifts of these signals are characteristic for pyridine derivatives with an electron-acceptor substituent attached to the nitrogen atom of the pyridinium ring [5]. Similar data were obtained from the PMR spectra of III and IV (Fig. 3); the singlets of the methyl groups (at 2.57 and 2.67 ppm) are not presented in these figures.

Thus these data attest to the formation of zwitterion structures with delocalization of the negative charge in the dinitroimidazole portion of the molecule, inasmuch as this entire heterocyclic residue displays electron-acceptor properties, judging from the chemical shifts of the pyridinium protons.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The UV spectra of ethanol solutions of the compounds were recorded with a Specord UV 15 spectrophotometer. The molecular weights were determined with an MS-3302 mass spectrometer. The PMR spectra of solutions of the compounds in deuterodimethyl sulfoxide containing five drops of dimethyl sulfoxide (DMSO) were recorded with a Varian HA-100 spectrometer at 100°; the PMR spectrum of I in deuterodimethyl sulfoxide was recorded with a Varian A56/60A spectrometer. The internal standard was hexamethyldisiloxane.

5,6-Dinitro-2-chlorobenzimidazole (I). A mixture of 5 g of 5,6-dinitro-2-benzimidazolone [6], 30 ml of phosphorus oxychloride, and five drops of concentrated HCl was heated in a sealed ampul at 160° for 4 h, after which a portion of the $POCl_3$ was removed by distillation, and the residue was poured over ice. The resulting precipitate was removed by filtration to give colorless needles with mp 199-200° (from dichloroethane) in 90% yield (according to [7], the yield of a product with mp 190-191° was 40%).

Betaines II-IV. A 0.2-g sample of I was refluxed in 3 ml of pyridine (or β- or γ-picoline) for 1 h, after which the mixture was cooled, and the resulting precipitate was removed by filtration and crystallized from 50% aqueous dimethylformamide (DMF). The yields were almost quantitative. The products were only slightly soluble in the usual organic solvents but were soluble on heating in DMF and DMSO.

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