SYNTHESIS OF BENZIMIDAZOLE DERIVATIVES

V.* PYRIDYLBENZIMIDAZOLES AND CYANINE DYES FROM THEM

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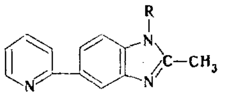
UDC 547.785.5'.828.07: 541.651

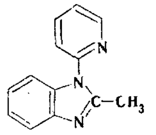
New bases and quaternary salts – 2-methylbenzimidazole derivatives – containing 2-pyridyl residues as a substituent in various positions of the benzimidazole ring were synthesized. Benzimidazolium salts of a new type with hetaryl groups attached to both nitrogen atoms were obtained. Imidacyanines were synthesized from the quaternary salts of pyridyl-substituted 2-methylbenzimidazoles, and the chief light-absorption maxima of these dyes were determined.

2-Methylbenzimidazole derivatives that contain hetaryl groups as substituents in various positions of the benzimidazole ring are of interest for the synthesis of imidacyanine dyes. 1-(2-Pyridyl)-2-methyl-5,6-dichlorobenzimidazole, which is used for the preparation of some imidacyanines, was described in [2].

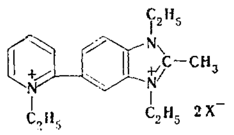
In the present study we have synthesized some 2-pyridylmethylbenzimidazoles as well as 1,3-(2-pyridyl)-2-methylbenzimidazolium salts. The known 2-pyridyl-o-phenylenediamines and N,N'-di(2-pyridyl)-4-chloro-o-phenylenediamine, which was first obtained by us, were the starting materials for the syntheses. These bases were converted to the corresponding 2-pyridyl-2-methylbenzimidazoles (I and III) or pyridylbenzimidazolium salts (VI, VII) by heating with acetyl chloride in toluene or nitrobenzene.



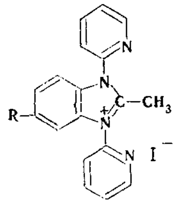
I, II



III



IV, V



VI, VII

I R=H; II R=C_2H_5; IV X=I; V X=ClO_4; VI R=H; VII R=Cl

The 2-pyridyl residue in I-VII displays different basicities as a function of the character of its bonding with the benzimidazole ring. When III is heated with ethyl iodide, a salt is formed only through one of the ring nitrogen atoms of the benzimidazole ring – the 2-pyridyl residue does not participate in salt formation. The interaction of II with ethyl iodide gives IV, and both the benzimidazole and pyridine rings participate in salt formation.

The reduced basicity of the 2-pyridyl residue in II is manifested in the production of imidacyanines from the salt of this base (IV). When the latter is refluxed with ethyl orthoformate and nitrobenzene, partial dealkylation of the 1-ethyl-2-pyridinium residue of this salt occurs, probably as a consequence of the

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*See [1] for communication IV.

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 687-690, May, 1972. Original article submitted May 26, 1971.

TABLE 1. 2-Pyridyl-Substituted Imidadimethylidynemerocyanines, Imidathiacarbocyanines, and Imidacarbocyanines

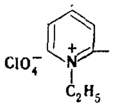
Dye	R	R′	R″	Y	X*	λ_{max}, nm
VIII	2-Pyridyl	C_2H_5	C_2H_5	S	—	521
IX		C_2H_5	C_2H_5	S	—	522
X	H	2-Pyridyl	C_2H_5	O	—	495
XI	H	2-Pyridyl	C_2H_5	S	—	519
XII	H	2-Pyridyl	2-Pyridyl	O	—	498
XIII	H	2-Pyridyl	2-Pyridyl	S	—	521
XIV	Cl	2-Pyridyl	2-Pyridyl	O	—	498
XV	Cl	2-Pyridyl	2-Pyridyl	S	—	522
XVI	2-Pyridyl	C_2H_5	—	—	—	536
XVII	2-Pyridyl	2-Pyridyl	—	—	—	534
XVIII	H	2-Pyridyl	C_2H_5	—	I	512
XIX	H	2-Pyridyl	2-Pyridyl	—	ClO_4	531
XX	Cl	2-Pyridyl	2-Pyridyl	—	I	533

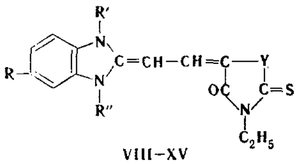
TABLE 1. (Continued)

Dye	Mp, °C	Empirical formula	Element	Found, %	Calc., %	Yield, %
VIII	223—225	$C_{23}H_{24}N_4OS_2$	S	14,5	14,7	16,0
IX	238—239	$C_{25}H_{29}ClN_4O_5S_2$	Cl	5,8	6,2	52,0
X	179—182	$C_{21}H_{20}N_4O_2S$	S	8,2	8,2	85,0
XI	220—222	$C_{21}H_{20}N_4OS_2$	N	13,8	13,7	75,5
XII	214—216	$C_{24}H_{19}N_5O_2S$	N	15,9	15,9	90,0
XIII	208—210	$C_{24}H_{19}N_5OS_2$	N	15,1	15,3	25,0
XIV	228—230	$C_{24}H_{18}ClN_5O_2S$	N	14,9	14,7	40,0
XV	219—221	$C_{24}H_{18}ClN_5OS_2$	Cl	7,1	7,2	45,0
XVI	219—220	$C_{25}H_{25}IN_4S$	I N	22,9 9,7	23,0 10,1	36,0
XVII	211—213	$C_{29}H_{24}N_5SI$	N	11,2	11,6	78,0
XVIII	247—248	$C_{31}H_{29}IN_6$	N	13,6	13,7	26,0
XIX	166—168	$C_{37}H_{27}ClN_8O_4$	N	16,0	16,4	33,8
XX	184—186	$C_{37}H_{25}Cl_2IN_8$	I	16,2	16,3	40,0

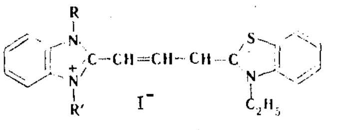
weakened basicity of the 2-pyridyl group, and a mixture of three imidacarbocyanines, which are detected by means of thin-layer chromatography and have very close absorption maxima, is formed. When IV is heated with 3-ethyl-5-acetanilidomethylenerhodanine, formamide, and triethylamine, two imidadimethylidynemerocyanines (VIII and IX) with 2-pyridyl- and 1-ethyl-2-pyridinium residues, which are isolated in pure form, are also formed.

In this connection, it was found that when a nitrobenzene solution of IV is refluxed, the latter partially loses ethyl iodide and is converted to the ethiodide of II. The formation of several dyes in the described cases is also explained by this thermal dealkylation of salt IV.

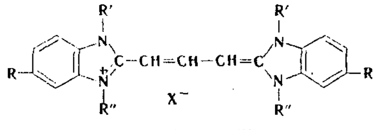
Imidadimethylidynemerocyanines that are derivatives of 3-ethylthiazolidine-2-thione-4-one and 3-ethyloxazolidine-2-thione-4-one (VIII-XV), as well as imidathiacarbocyanines (XVI, XVII) and symmetrical imidacarbocyanines (XVIII-XX) were synthesized from the quaternary salts of 2-pyridylmethylbenzimidazoles.



VIII-XV



XVI, XVII



XVIII, XIX, XX

The significance of R, R', R", X, and Y in formulas VIII-XX is presented in Table 1.

Imidacyanines with 2-pyridyl residues as substituents are distinguished by increased solubility in water and other polar solvents, and this increased solubility is higher, the more such substituents present. A comparison of the light absorption maxima of dyes XVIII and XIX with the absorption maximum of the known 1,1',3,3'-tetraethylimidacarbocyanine iodide (λ_{max} 498 nm) [3] demonstrates that replacement of one ethyl group attached to the nitrogen atom of the imidazole ring in symmetrical imidacarbocyanines by a 2-pyridyl residue leads to a shift in the light absorption maximum to the long-wave portion of the spectrum by an average of 7.8 nm.

EXPERIMENTAL

N,N'-Di(2-pyridyl)-4-chloro-o-phenylenediamine. In analogy with [4], 2.86 g (0.02 mole) of 4-chloro-o-phenylenediamine [5], 6.32 g (0.04 mole) of 2-bromopyridine, and 2.8 g of anhydrous zinc chloride were heated in a sealed glass tube at 200° for 4 h. A solution of the reaction product in 1 liter of water was filtered, decolorized with charcoal, and treated with 30% aqueous sodium hydroxide. The liberated base was extracted with benzene to give 3.9 g of product. This product was used for synthesis without further purification. A sample for analysis was chromatographed (Al_2O_3 and benzene) and crystallized from benzene–petroleum ether to give crystals with mp 99-101°. Found: N 19.1%. $C_{16}H_{13}N_4Cl$. Calculated: N 18.9%.

Synthesis of 2-Pyridyl-Substituted 2-Methylbenzimidazoles and Their Quarternay Salts (General Method). A 0.1 mole sample of acetyl chloride was added to a solution or suspension of 0.03 mole of an o-phenylenediamine (with a 2-pyridyl residue as a substituent in the aromatic ring or attached to one or two nitrogen atoms of the amino groups) in anhydrous benzene, toluene, or nitrobenzene, and the mixture was refluxed for 1.5-2 h. The base was liberated from the hydrochlorides of the 2-pyridyl-substituted 2-methylbenzimidazoles with alkali hydroxides or ammonia. If the reaction product was a quaternary salt – the chloride – it was purified and converted to the iodide or perchlorate.

2-Methyl-5-(2-pyridyl)benzimidazole (I). This compound was obtained in 75% yield (based on the hydrochloride of I) from 4-(2-pyridyl)-o-phenylenediamine [6]. Base I was obtained as crystals with mp 168-169.5° (from xylene). Found: N 20.1%. $C_{13}H_{11}N_3$. Calculated: N 20.1%. I · HCl. The hydrochloride was obtained as colorless crystals with mp 277-281° (from isoamyl alcohol). Found: Cl 14.3%. $C_{13}H_{11}N_3 \cdot HCl$. Calculated: Cl 14.4%.

1-(2-Pyridyl)-2-methylbenzimidazole (III). This compound was obtained in 36% yield from N-(2-pyridyl)-o-phenylenediamine [7] as colorless crystals with mp 130-131° (from chloroform–petroleum ether). Found: N 18.4%. $C_{13}H_{11}N_3 \cdot H_2O$. Calculated: N 18.5%. The product loses water of crystallization on melting. The ethiodide of base III was obtained in 60% yield as colorless needles with mp 209-211° (from water) when III was heated with excess iodide at 100° for 3 h. Found: I 34.3%. $C_{15}H_{16}IN_3$. Calculated: I 34.7%.

1,3-Di(2-pyridyl)-2-methylbenzimidazolium Iodide (VI). This compound was obtained in 42% yield as needles with mp 215-217° (from water) from N,N'-di(2-pyridyl)-o-phenylenediamine [4] and acetyl chloride in anhydrous toluene with subsequent treatment of the resulting aqueous solution of dipyridylbenzimidazolium chloride with excess sodium iodide. Found: I 31.1; N 13.4%. $C_{18}H_{15}IN_4$. Calculated: I 30.7; N 13.5%.

1,3-Di(2-pyridyl)-5-chloro-2-methylbenzimidazolium Iodide (VII). This compound was obtained in 50% yield as fine, colorless crystals with mp 261-263° (from water) from N,N'-di(2-pyridyl)-4-chloro-o-phenylenediamine and acetyl chloride in anhydrous benzene, as in the preparation of VI. Found: I 28.5%. $C_{18}H_{14}ClIN_4$. Calculated: I 28.3%.

1-Ethyl-2-methyl-5-(2-pyridyl)benzimidazole (II) and Its Quaternary Salts (IV, V). A solution of 1.5 g of sodium hydroxide in 12 ml of water was added with stirring to a solution of 0.4 g of the hydrochloride of I in a small amount of water, and 0.4 ml of diethyl sulfate was then added to the mixture. The viscous precipitate of II that formed after heating the mixture on a boiling-water bath for 15 min was extracted with chloroform. The chloroform was removed by distillation, and the residue, without purification, was heated with 2 ml of ethyl iodide in a sealed glass tube at 100° for 4 h. The resulting ethiodide (IV) was washed with ether and, without further purification, was used for the synthesis of dyes or converted to perchlorate V [the yield of the latter was 0.5 g (61%)], which was obtained as fine, colorless crystals with mp 253-255° (dec., from water). Found: Cl 14.4%. $C_{19}H_{25}Cl_2N_3O_8$. Calculated: Cl 14.4%.

Thermal Decomposition of 1-Ethyl-2-methyl-5-(2-pyridyl)benzimidazole Diethiodide (IV). A solution of 0.3 g of diethiodide IV in 5 ml of nitrobenzene was refluxed for 5 h, and excess ether was added. The precipitate was washed with ether and heated with 10 ml of water. The aqueous mixture was filtered, and excess sodium perchlorate was added to the hot filtrate. The precipitated 1-ethyl-2-methyl-5-(2-pyridyl)benzimidazole ethylperchlorate (II) was washed with water to give 0.05 g (21.5%) of colorless needles with mp 186-188°. Found: Cl 9.8%. $C_{17}H_{20}ClN_3O_4$. Calculated: Cl 9.7%. The salt forms an imidacarbocyanine with λ_{max} 518 nm (in ethanol) on heating with ethyl orthoformate in nitrobenzene.

3-Ethyl-5-{β-[1,3-diethyl-5-(2-pyridyl)benzimidazolinylidene-2]ethylidene}thiazolidine-2-thione-4-one (VIII) and Its Ethylperchlorate (IX). A mixture of 0.37 g of V, 0.3 g of 3-ethyl-5-acetanilidomethylenerhodanine, 2 ml of formamide, and 0.4 ml of triethylamine was refluxed for 75 min. The precipitated dye was washed with water and crystallized from the minimum amount of alcohol to give 0.2 g of IX. A green, crystalline precipitate of VIII gradually separated out from the mother liquor, from which this dye was removed by filtration. Compound VIII was removed by filtration after 3 days and crystallized from alcohol. Data on dyes VIII and IX are presented in Table 1.

Reaction of 1-Ethyl-2-methyl-5-(2-pyridyl)benzimidazole Diethiodide (IV) with Ethyl Orthoformate in Nitrobenzene. A mixture of 0.55 g of IV, 0.6 ml of ethyl orthoformate (or 0.5 ml of diethoxymethyl acetate), and 4 ml of nitrobenzene [or nitrobenzene–pyridine (4 : 1)] was refluxed for 1.5 h. The dye was precipitated with ether, washed with ether, and dissolved in dimethylformamide. The solution was salted out with aqueous sodium iodide solution to give 0.35 g of product. The product was crystallized from alcohol or alcohol–ether. Found: N 10.45%. $C_{37}H_{42}I_2N_6$. Calculated: N 10.2%. From its nitrogen content, the dye corresponded to an imidacarbocyanine, which could have been formed from salt IV with subsequent loss of one molecule of ethyl iodide. However, thin-layer chromatography [Al_2O_3, acetone–methanol (14 : 1)] attested to the presence of a mixture of three dyes (R_f 0.05, 0.2, and 0.5). One of them (R_f 0.5) has the same absorption maximum (λ_{max} 518 nm) as the imidacarbocyanine formed from the salt obtained as a result of thermal cleavage of ethyl iodide from diethiodide IV and, consequently, it is extremely likely that it is 1,1',3,3'-tetraethyl-5,5'-di(2-pyridyl)imidacarbocyanine.

Cyanine dyes were obtained from the quaternary salts of 2-pyridyl-substituted 2-methylbenzimidazoles by known standard methods: imidadimethylidynemerocyanines X-XV were obtained by heating the corresponding quaternary salts with acetanilidomethylene derivatives of 3-ethylthiazolidine-2-thione-4-one or 3-ethyloxazolidine-2-thione-4-one in anhydrous pyridine or alcohol in the presence of triethylamine; unsymmetrical imidathiacarbocyanines XVI and XVII were obtained from the quaternary salts and 2-(β-acetanilidovinyl)-3-ethylbenzothiazolium iodide in acetic anhydride with triethylamine; and the symmetrical imidacarbocyanines XVIII-XX were obtained from the quaternary salts and ethyl orthoformate in nitrobenzene with subsequent precipitation with excess ether. Dye XIX was purified by dissolving it in excess hot water, precipitating it as the perchlorate, and crystallizing it. Dyes X-XX were crystallized from alcohol. Data on dyes VIII-XX are presented in Table 1. The light absorption maxima of the dyes in ethanol solution were determined with an SF-10 spectrophotometer.

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