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RESEARCH ON IMIDAZO[1,2-a]BENZIMIDAZOLE DERIVATIVES. 22.* SYNTHESIS OF 2,3-DIHYDROIMIDAZO[1,2-a]BENZIMIDAZOLES STARTING FROM 2-IMINO-3-(2-HYDROXYETHYL)BENZIMIDAZOLINES

V. A. Anisimova, M. V. Levchenko, and A. F. Pozharskii

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A β-elimination reaction with the formation of 2-imino-3-vinylbenzimidazolines occurs simultaneously with intramolecular alkylation and the formation of an imidazoline ring in the action of alcoholic alkali on 2-imino-3-(2-chloroethyl) benzimidazolines. The thermolysis of 3-chlorethyl-substituted imines without a solvent or in an inert solvent leads exclusively to 2,3-dihydroimidazo[1,2-a] benzimidazoles. An attempt to obtain the latter directly from 2-imino-3-(2-hydroxyethyl)benzimidazolines by the action of a mixture of thionyl chloride and acetic anhydride on them also leads to ambiguous results.

One of the most widely spread methods for the formation of a condensed imidazoline ring in systems with a bridged nitrogen atom consists in the successive action of thionyl chloride and alcoholic alkali on N-β-hydroxyethyl-substituted nitrogen heterocycles in which there is an amino group in the α position relative to the heteroring nitrogen atom [2,3]. This method was used in 1967 to obtain 9-ethyl-2,3-dihydroimidazo[1,2-a]benzimidazole, the first representative of this hydrogenated system [4,5]. However, it does not always give good results, and the yields of 9-benzyl- [6] and 9-phenyl-substituted compounds [7] synthesized via a similar scheme were only 27% and 36%, respectively. We turned to an investigation of this reaction in order to establish the reasons for the low yields of 2,3-dihydroimidazo-[1,2-a]benzimidazoles and to find more acceptable cyclization conditions, especially since little study has been devoted to the chemical and, particularly, pharmacological properties of this heterosystem [6, 7].

*See [1] for communication 21.

Scientific-Research Institute of Physical and Organic Chemistry, M. A. Suslov Rostov State University, Rostov-on-Don 344090. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 918-925, July, 1986. Original article submitted April 3, 1985.

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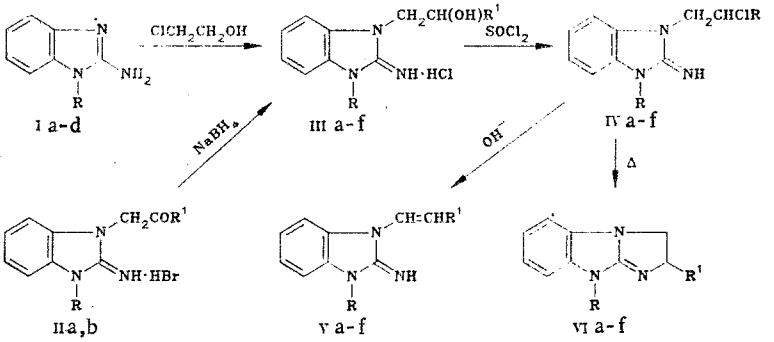
TABLE 1. 2-Imino-3-(2-hydroxyethyl)benzimidazolines III

Compound	mp,* °C	Found, %				Empirical formula	Calc., %				Yield, %
		C	H	Cl	N		C	H	Cl	N	
IIIa	271—272	52,6	6,2	15,4	18,7	$C_{10}H_{13}N_3O \cdot HCl$	57,7	6,2	15,6	18,5	88—96
IIIa-I	133—134	62,9	6,6	—	22,1	$C_{10}H_{13}N_3O$	62,8	6,8	—	22,0	—
IIIb	230—231 (230—231 [12])	54,6	6,7	14,5	17,5	$C_{11}H_{15}N_3O \cdot HCl$	54,7	6,7	14,7	17,4	91,7 (75 [12])
IIIc	254—255 (263—264 [6])	63,0	6,1	11,5	13,8	$C_{16}H_{17}N_3O \cdot HCl$	63,2	6,0	11,7	13,8	94—96 (68 [6])
IIId	233,5—234,5	62,1	5,6	12,0	14,6	$C_{15}H_{15}N_3O \cdot HCl$	62,2	5,6	12,2	14,5	93†
IIIe	280—281	63,2	6,1	11,5	14,0	$C_{16}H_{17}N_3O \cdot HCl$	63,2	6,0	11,7	13,8	95
IIIe-I	153—154	72,1	6,4	—	15,7	$C_{16}H_{17}N_3O$	71,9	6,4	—	15,7	—
IIIf	293	54,5	6,5	15,1	17,2	$C_{11}H_{15}N_3O \cdot HCl$	54,7	6,7	14,7	17,4	90,8
IIIf-I	132—133	64,5	7,4	—	20,6	$C_{11}H_{15}N_3O$	64,4	7,4	—	20,5	—

*The hydrochlorides were recrystallized: IIIa-d from alcohol, IIIe from water, and IIIf from 90% alcohol. The imine bases were recrystallized: IIIa-I from benzene, IIIe-I from isooctane, and IIIf-I from ethyl acetate. Compounds IIIa,d,f melted with decomposition.

†According to [7], the yield of the corresponding bromide was 53%.



I a $R=CH_3$, b $R=C_2H_5$, c $R=CH_2C_6H_5$, d $R=C_6H_5$; II a, b $R=CH_3$; a $R^1=C_6H_5$, b $R^1=CH_3$; III—VI a,e,f $R=CH_3$, b $R=C_2H_5$, c $R=CH_2C_6H_5$, d $R=C_6H_5$; a-d $R^1=H$, c $R^1=C_6H_5$, f $R^1=CH_3$

Starting 3-(2-hydroxyethyl)-2-iminobenzimidazolines III were obtained by hydroxyethylation of amines I by means of ethylene chlorohydrin or by reduction of 3-acylmethyl-2-iminobenzimidazolines II with sodium borohydride. It is more convenient to carry out the hydroxyethylation by fusing the starting reagents or by refluxing them in dimethylformamide (DMF) or xylene. This makes it possible to significantly reduce the reaction time as compared with the time described in [4-7] and, in some cases, to increase the yields of imino alcohols III. The chlorination of the latter proceeds successfully under milder conditions than those described in [4-7], viz., by the action of thionyl chloride in chloroform or benzene. The resulting chloro-substituted IV were isolated in high yields in the form of the hydrochlorides and were then converted to the bases by treatment with a solution of ammonia.

The action of alkali on salts IV under the conditions proposed in [4-7] gives mixtures of two compounds, one of which is three-ring base VI; vinyl-substituted structure V was assigned to the second compound, which was identical to the first with respect to the results of elementary analysis, on the basis of the IR and NMR spectra. An absorption band of a free NH group at 3355-3360 cm^{-1} is observed in the IR spectra of imines V; an absorption band at 1660 cm^{-1}, which can be ascribed to the absorption of an exocyclic C=C bond, appears in addition to a band at 1630-1640 cm^{-1}, which is characteristic for the absorption of a C=N group in imines with a similar structure. In the PMR spectra of Va-d signals of the β-cis and β-trans protons of a vinyl group appear in the form of doublets because of the small degree of geminal coupling of these protons; the β-trans proton (δ ~ 5.2-5.5 ppm) is deshielded by the heteroring by ~ 35-40 Hz as compared with the β-cis proton (δ ~ 4.87-5.07

TABLE 2. 2-Imino-3-(2-chloroethyl)benzimidazolines IV and Their Hydrochlorides

Compound	mp,* °C	Found, %				Empirical formula	Calc., %				Yield, %
		C	H	Cl	N		C	H	Cl	N	
IVa·HCl	246—247	49,0	5,3	28,5	17,3	$C_{10}H_{12}ClN_3 \cdot HCl$	48,8	5,3	28,8	17,1	95,9
IVa	65—66	57,1	5,9	16,8	20,3	$C_{10}H_{12}ClN_3$	57,3	5,8	16,9	20,0	—
IVb·HCl	244—245	50,7	5,6	27,0	15,9	$C_{11}H_{14}ClN_3 \cdot HCl$	50,8	5,8	27,3	16,1	100
IVb	93,5—94	59,0	6,4	15,6	18,9	$C_{11}H_{14}ClN_3$	59,1	6,3	15,8	18,1	—
IVc·HCl	248—249	59,5	5,5	22,3	13,2	$C_{16}H_{16}ClN_3 \cdot HCl$	59,7	5,3	22,0	13,0	100
IVc	110	67,3	5,8	12,8	14,5	$C_{16}H_{16}ClN_3$	67,3	5,6	12,4	14,7	—
IVd·HCl	215—216	58,3	5,0	23,3	13,5	$C_{15}H_{14}ClN_3 \cdot HCl$	58,3	4,9	23,0	13,6	100
IVd	oil	66,2	5,0	16,7	15,5	$C_{15}H_{14}ClN_3$	66,3	5,2	16,9	15,4	—
IVe·HCl	270	59,8	5,3	22,3	13,0	$C_{16}H_{16}ClN_3 \cdot HCl$	59,7	5,3	22,0	13,0	95,8
IVe	101	67,0	6,1	12,2	14,9	$C_{16}H_{16}ClN_3$	67,3	5,9	12,4	14,7	—
IVf·HCl	247—248	51,1	5,7	27,5	16,0	$C_{11}H_{14}ClN_3 \cdot HCl$	50,8	5,8	27,3	16,1	97
IVf	66—67	58,8	6,3	16,3	18,5	$C_{11}H_{14}ClN_3$	59,1	6,3	15,8	18,8	—

*The hydrochlorides were recrystallized: those of IVa,c,e from alcohol, those of IVb,f from alcohol—ether, and that of IVd from acetone—ether. Base IVa was recrystallized from petroleum ether, and bases IVb-f were purified by chromatography. Salts IVc·HCl, IVd·HCl, IVe·HCl, and IVf·HCl melted with decomposition.

ppm). The signal of the proton of the —CH= group is deshielded to an even greater extent and appears together with the aromatic protons in the form of a multiplet with the appropriate integral intensity at 6.65-7.2 ppm. The broad singlet of one proton unit at 4.53-4.75 ppm can be assigned to the signal of the proton of the NH group. In the PMR spectrum of Ve the signal of this proton is found at 4.97 ppm; however, the signals of the aromatic and vinyl protons (11H) appear in the form of a poorly resolved multiplet at 6.77-7.31 ppm. The signals of the vinyl protons of Vf are observed at 3.9-4.3 ppm, and the methyl group of the propenyl substituent gives a doublet signal at 1.5 ppm.

Thus two reactions, viz., intramolecular alkylation, which leads to the formation of an imidazoline ring, and β elimination, which leads to vinyl-substituted V, are realized simultaneously under these conditions. Vinyl-substituted V are not intermediates in the synthesis of VI under the selected conditions. However, in the case of prolonged refluxing (30-40 h) in concentrated HBr they undergo cyclization to VI derivatives in ~ 45-50% yields.

In a more detailed investigation of the behavior of chloro imines IV under alkaline conditions we were able to establish that elimination proceeds in high yields under very mild conditions, viz., at room temperature with an equimolar amount of alkali, which serves as an HCl acceptor. However, refluxing the reaction solutions leads to mixtures of V and VI; the yields of dihydroimidazo[1,2-a]benzimidazoles VI increase in some cases on passing from methanol, which serves as the reaction solvent, to ethanol and butanol. This fact, as well as the instability of chloro imine bases IV during storage, led to the idea of the possibility of the occurrence of thermal cyclization in this series.

In fact, when chloro imines IV are maintained briefly at 5-10°C above their melting points, they undergo cyclization to hydrochlorides VI in virtually quantitative yields. The cyclization also proceeds similarly in inert solvents; for faster reactions the solvent should be selected in such a way that its boiling point is close to (or, better yet, somewhat higher than) the melting point of the starting imine. Steric factors, viz., the presence of phenyl or methyl groups in the chloroethyl grouping, do not affect the cyclization (compare with [8]). The characteristic absorption bands of NH and C=N groups that are observed in the spectra of the chloro imines at 3350-3360 and 1635-1640 cm^{-1}, respectively, vanish in the IR spectra of VI, but absorption bands at 1660-1665 cm^{-1}, which are related to the absorption of the endocyclic C=N bond of the 2,3-dihydroimidazo[1,2-a]benzimidazole ring, appear. In the PMR spectra of VIa-d recorded in deuterochloroform the four protons of the external imidazoline ring appear in the form of two symmetrical triplets at 3.55-3.9 and 4.05-4.3 ppm (an AA'BB' system); this is probably associated with the presence in this ring of two types of nitrogen atoms. In the spectra of these compounds or their salts recorded in

TABLE 3. 3-Vinyl-2-iminobenzimidazolines V

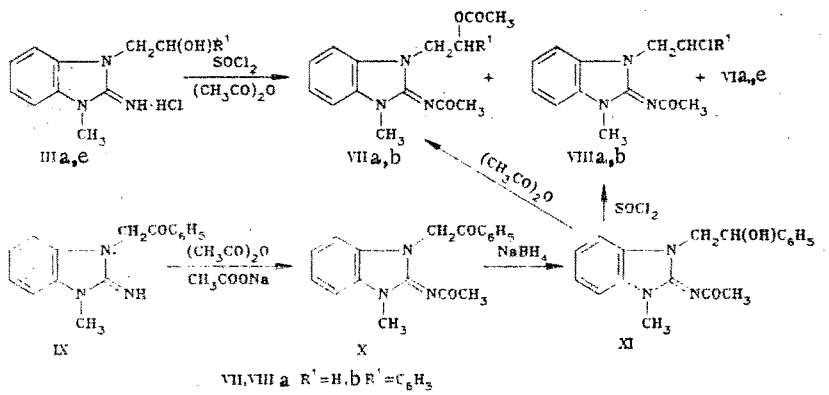
Compound	mp,* °C	Found, %			Empirical formula	Calc., %			Yield, %
		C	H (Hal)	N		C	H (Hal)	N	
Va	62—63	62,6	6,7	22,1	$C_{10}H_{11}N_3 \cdot H_2O$	62,8	6,9	22,0	96
Va-H	220	57,0	6,0 (16,7)	20,2	$C_{10}H_{11}N_3 \cdot HCl$	57,3	5,8 (16,9)	20,0	—
Va-P	246	47,5	3,7	21,1	$C_{10}H_{11}N_3 \cdot C_6H_3N_3O_7$	47,8	3,5	20,9	—
Vb	58—59	70,4	6,8	22,6	$C_{11}H_{13}N_3$	70,6	7,0	22,4	92
Vb-H	212—213	49,0	5,4 (29,5)	15,9	$C_{11}H_{13}N_3 \cdot HBr$	49,3	5,2 (29,8)	15,7	—
Vb-P	199	48,8	4,0	19,9	$C_{11}H_{13}N_3 \cdot C_6H_3N_3O_7$	49,0	3,9	20,2	—
Vc	95—96	76,8	6,2	17,1	$C_{16}H_{16}N_3$	77,1	6,1	16,9	90
Vd	Масло	76,5	5,6	18,0	$C_{15}H_{13}N_3$	76,6	5,6	17,8	97
Vd-H	205—206	57,1	4,2 (25,0)	13,5	$C_{15}H_{13}N_3 \cdot HBr$	57,0	4,4 (25,3)	13,3	—
Ve	154	77,0	6,0	17,0	$C_{16}H_{15}N_3$	77,1	6,1	16,8	89
Vf	49—50	70,5	7,2	22,2	$C_{11}H_{13}N_3$	70,6	7,0	22,4	95
Vf-H	228—229	64,5	5,3 (14,0)	16,3	$C_{11}H_{13}N_3 \cdot HCl$	64,7	5,5 (13,7)	16,2	—

*The compounds were purified: hydrohalides Va-H and Vf-H from alcohol with ether, Vb-H from alcohol, and Vd-H from alcohol, and Vd-H from acetone with ether; picrates Va-P and Vb-P from acetic acid; bases Vb,c,e from ethyl acetate and Va,d,f by chromatography. Compounds Va-H, Va-P, Vb-H, Vb-P, and Vd-H melted with decomposition.

trifluoroacetic acid the ethylene protons appear in the form of a four-proton singlet at 3.2-3.3 ppm (an A_4 system).

We used the thermal cyclization method for the synthesis of the most diverse 2,3-dihydroimidazo[1,2-a]benzimidazole derivatives, including those substituted in the 2 position and in the benzene ring [9]. The yields in most cases were close to quantitative. Lower yields (70-84%) were obtained in the cyclization of hydrochlorides IV in inert solvents in the presence of anhydrous potassium carbonate or sodium carbonate, in which case the reaction proceeds considerably more slowly. When triethylamine is used as the HCl acceptor, the yields decrease to an even greater extent because of resinification of the reaction masses.

In an attempt to arrive at VI directly from hydroxy imines III by the simultaneous action on them of thionyl chloride and acetic anhydride, as in the imidazo[2,1-b]thiazole series [10,11], we obtained mixtures of VI-VIII.



VII,VIII a R'=H, b R'=C_6H_5

The structures of VII and VIII were proved by independent syntheses. Chloro acetylimines VIII are intermediates in the synthesis of VI; this is confirmed by their conversion to VI when the time of this reaction is increased. The quantitative ratios of VI and VII depend on many factors (for example, on the amount of thionyl chloride and the way it is introduced into the reaction, the reaction conditions, etc.) and are not very reproducible. We were unable to select conditions that would completely exclude the for-

TABLE 4. 2,3-Dihydroimidazo[1,2-a]benzimidazoles VI

Compound	mp,* °C	Found, %				Empirical formula	Calc., %			
		C	H	Hal	N		C	H	Hal	N
VIa	68	69,1	6,3	—	24,5	$C_{10}H_{11}N_3$	69,3	6,4	—	24,3
VIa-H	276—277	57,0	6,0	16,7	20,2	$C_{10}H_{11}N_3 \cdot HCl$	57,3	5,8	16,9	20,0
VIb	Oil	70,3	7,2	—	22,2	$C_{11}H_{13}N_3$	70,6	7,0	—	22,4
VIb-H	256	59,0	6,5	15,6	18,8	$C_{11}H_{13}N_3 \cdot HCl$	59,1	6,3	15,8	18,8
VIb-P	268—268,5 †	49,2	4,0	—	20,0	$C_{11}H_{13}N_3 \cdot C_6H_3N_3O_7$	49,0	3,9	—	20,2
VIc	Oil	76,9	6,3	—	16,5	$C_{16}H_{15}N_3$	77,1	6,1	—	16,8
VIc-H	257—258 (262—264 [6])	67,1	5,6	12,2	14,7	$C_{16}H_{15}N_3 \cdot HCl$	67,3	5,6	12,4	14,7
VIc-P	203,5—204 (204—206 [6])	55,2	4,0	—	17,7	$C_{16}H_{15}N_3 \cdot C_6H_3N_3O_7$	55,2	3,8	—	17,6
VId	115—116	76,6	5,5	—	17,6	$C_{15}H_{13}N_3$	76,6	5,6	—	17,8
VId-H	226—227 (225—228 [7])	57,2	4,4	25,0	13,5	$C_{15}H_{13}N_3 \cdot HBr$	57,0	4,4	25,3	13,3
VIe-H	258 (258 [13])	67,3	5,8	12,7	14,9	$C_{16}H_{15}N_3 \cdot HCl$	67,3	5,6	12,4	14,7
VIf	121—122	70,3	6,8	—	22,5	$C_{11}H_{13}N_3$	70,6	7,0	—	22,4
VIf-H	275—276	58,9	6,4	15,5	19,0	$C_{11}H_{13}N_3 \cdot HCl$	59,0	6,3	15,9	18,8

*Hydrohalides VIa-H—VIf-H were purified by recrystallization from alcohol, picrates VIb-P and VIc-P were purified by recrystallization from glacial acetic acid, bases VIf,d were purified by recrystallization from ethyl acetate, VIa was purified by recrystallization from benzene, and VIb,c were purified by chromatography. All of the hydrohalides and picrates melted with decomposition.

†According to the data in [5], this compound had mp 267-268, 265-268, and 263-266°C (dec.).

mation of VII. However, the successive action on hydroxy imines III of excess thionyl chloride and acetic anhydride without isolation of intermediate chloro imine IV leads to the formation of three-ring product VI in high yield.

The absorption bands of NH and OH groups vanish in the IR spectra of VII and VIII; the band of carbonyl absorption of the $NCOCH_3$ group is shifted significantly to the low-frequency side and appears at 1535-1550 cm^{-1}. This fact, as well as the absence of the absorption at 1630-1640 cm^{-1} that is characteristic for the stretching vibrations of the C=N bond of imine bases III and IV, indicates a decrease in the multiplicities of the C=O and C=N bonds in these compounds. On passing to the hydrochlorides of VII and VIII the double bond character of the C=O groups increases, and its absorption is observed at 1725-1755 cm^{-1}.

EXPERIMENTAL

The IR spectra of chloroform solutions of bases III-XI and mineral oil suspensions of their salts were recorded with a UR-20 spectrometer. The PMR spectra of solutions in deuterochloroform and trifluoroacetic acid were obtained with a Tesla BS-487 C spectrometer (80 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The course of the reaction and the purity of the compounds obtained were monitored by thin-layer chromatography (TLC) on aluminum oxide with elution by chloroform or benzene and development with iodine vapors in a moist chamber.

1-R-3-(2-Hydroxyethyl)-2-iminobenzimidazoline Hydrochlorides IIIa-d (Table 1). A) A mixture of 10 mmole of amine Ia-d and 2.5-3 ml of freshly distilled ethylene chlorohydrin was heated at 130-135°C for 30-40 min, after which the melt was cooled and triturated with 10 ml of ether. Precipitated salts IIIa-d were removed by filtration, washed with ether and acetone, and crystallized from alcohol.

B) A solution of 10 mmole of amine Ia-d and 0.8-0.9 ml (a 10-20% excess) of ethylene chlorohydrin in 4-5 ml of dry DMFA was refluxed for 0.5-1 h, after which it was cooled. Precipitated salts IIIa-d were removed by filtration and washed with ether and acetone.

The reaction time was 1-2 h when the process was carried out in absolute xylene.

2-Imino-1-methyl-3-(2-hydroxyethyl)benzimidazoline. A 0.46-g (2 mmole) sample of salt IIIa was treated with 5 ml of 40% NaOH solution, and the liberated oil was extracted with

hot benzene. The benzene was evaporated, and the residue was triturated with petroleum ether to give 0.39 g of the imine in the form of snow-white crystals (Table 1). IR spectrum: 1500, 1610 (C=C); 1630 (C=N); 3380 (NH); 3100-3300 cm^{-1} (OH, broad band).

2-Imino-1-methyl-3-(2-hydroxyl-2-phenylethyl)benzimidazoline Hydrochloride (IIIe). A 0.4-g (10 mmole) sample of sodium borohydride was added in small portions at room temperature to a stirred suspension of 2.7 g (10 mmole) of imine IIa or the corresponding amount of its hydrobromide in 40 ml of methanol. At the end of the addition (~20-30 min), the resulting solution was stirred for another 2-3 h, and the excess borohydride was decomposed by acidification of the solution with 10% HCl solution to pH 2-3. The methanol was evaporated, and the residue was treated with 20 ml of cold water. The undissolved hydrochloride IIIe was removed by filtration and washed with water to give 2.85 g of product. Information on IIIe, imino alcohol IIIf, which was similarly obtained from 3-acetonyl-2-imino-1-methylbenzimidazoline hydrobromide (IIb), and the corresponding bases is presented in Table 1. The absorption band of a C=O group that appears in the IR spectra of the starting imines at 1690-1695 cm^{-1} vanished in the IR spectra of the salts obtained. The IR spectra of imine bases IIIe,f, which were liberated by treatment of the corresponding salts with 22% NH_4OH, contained bands at 1635 (C=N), 3375 (NH), and 3150-3300 cm^{-1} (OH).

2-Imino-1-R-3-(2-chloroethyl)benzimidazolines IVa-f (Table 2). A 1-ml sample of freshly distilled thionyl chloride was added to a suspension of 10 mmole of hydrochloride IIIa-f in 10-15 ml of dry chloroform or benzene, and the mixture was refluxed for 1-2 h. It was then cooled, and the precipitated hydrochloride of IV was removed by filtration and washed with petroleum ether. If no precipitate was formed from the cooled solution, the solution was evaporated, and the residue was treated several times with petroleum ether until crystallization was complete. The yields of the hydrochlorides of IVa-f were close to quantitative.

Chloro imine bases IVa-f were isolated in quantitative yields by treating the salts with 22% NH_4OH in the cold. The liberated imine was removed by filtration or extracted with some solvent (chloroform, benzene, or ethyl acetate). The melting points of bases IVa-f were determined by placing a capillary tube containing the substance in a heated device for determination of the melting point.

3-Vinyl-2-imino-1-R-benzimidazolines Va-f (Table 3). A mixture of 5 mmole of the hydrochloride of IVa-f and 10 ml of a 5% solution of NaOH in alcohol (or the corresponding amount of sodium ethoxide) was maintained at room temperature until the reaction was complete. The NaCl was separated, the alcohol was evaporated, and the residue was purified by recrystallization from ethyl acetate or by means of column chromatography (Al_2O_3, elution with chloroform).

When the reaction solutions were heated, the yields of imines V decreased due to the formation of VI. Imines Va-f are snow-white low-melting crystals or oils, which were converted to salts by dissolving them in acetone and adding the corresponding acid to the solutions up to pH 2-3.

2,3-Dihydroimidazo[1,2-a]benzimidazoles VIa-f (Table 4). A) Imines IVa-f were maintained at 5-15°C above their melting points until the resulting melts crystallized completely (~5-20 min). The melts were then cooled and crystallized from suitable solvents to give the products in 93-97% yields.

B) A 2-mmole sample of chloro imine IVa-f was refluxed in 5-7 ml of absolute xylene, toluene, octane, benzene, or ethyl acetate for 20-60 min, during which the completion of the reaction was followed by means of TLC (the starting imines had R_f ~ 0.15-0.2, and the final three-ring products had R_f ~ 0.3-0.4). The mixtures were then cooled, and the precipitated hydrochlorides of VIa-f were removed by filtration and washed with the appropriate solvent and ether. The yields were quantitative.

C) A 2-mmole sample of imine IVa,d,f was refluxed in 5 ml of water for 20-30 min (with monitoring by TLC), after which the solution was cooled and made alkaline to pH 8-9 with ammonium hydroxide. Imidazobenzimidazoles VIa,d,f were extracted with chloroform. The yields were quantitative.

D) A solution of 0.84 g (4 mmole) of chloro imine IVa in 15 ml of acetic anhydride was refluxed for 1 h, after which it was cooled and poured into 50 ml of water, and the aqueous mixture was neutralized to pH 7-8 with sodium carbonate. The liberated oil was extracted with chloroform and purified by column chromatography to give 0.62 g (90%) of a colorless

oil. The oil crystallized when it was triturated with petroleum ether to give a product with mp 68°C.

Compound VIe was also obtained in 85% yield when the hydrochloride of IVe was refluxed for 2 h in acetic anhydride.

E) A mixture of 2 mmole of the salt of imine IVa,e and 8-10 mmole of finely ground anhydrous potassium carbonate or sodium carbonate in 10 ml of absolute benzene, toluene, or xylene was refluxed until the reaction was complete (5-7 h), after which the mixture was filtered, and the solvent was evaporated from the filtrate. The residue was purified by chromatography. The yields ranged from 70% to 84%.

2-Acetylimino-1-methyl-3-phenacylbenzimidazoline (X). A 1.14-g (4 mmole) sample of imine IX was maintained in 15 ml of acetic anhydride at room temperature until the solid had dissolved completely (∿24 h). The solution was diluted with 50 ml of water, and, after decomposition of the excess acetic anhydride, the mixture was neutralized to pH 7-8 with sodium carbonate. The resulting precipitate was removed by filtration, washed thoroughly with water, air dried, and crystallized from alcohol to give 0.9 g (75%) of silky fibrous crystals with mp 179-180°C. IR spectrum: 1545, 1705 cm^{-1} (C=O). Found: C 70.2; H 5.6; N 13,9%. $C_{18}H_{17}N_3O_2$. Calculated: C 70,3; H 5,6; N 13,7% . The hydrochloride of X, with mp 210-211°C (from alcohol), was obtained by acidification of an alcohol solution of the base to pH 2-3 with concentrated HCl. IR spectrum: 1700, 1728 (C=O); 3250-3400 cm^{-1} (NH). Found: C 62.7; H 5.2; Cl 10.0; N 12.4%. $H_{17}N_3O_2 \cdot HCl$. Calculated: C 62.9; H 5.3; Cl 10,3; N 12,2% .

2-Acetylimino-1-methyl-3-(2-hydroxy-2-phenylethyl)-benzimidazoline (XI). A 0.2-g sample of $NaBH_4$ was added in small portions with stirring to a suspension of 7 mmole of imine X in 30 ml of methanol, after which the mixture was stirred at room temperature for 3-4 h. The solution was acidified carefully to pH 1-2 with concentrated HCl, the methanol was evaporated, and the residue was treated with 10 ml of water. The hydrochloride of XI, which was only slightly soluble in water, was removed by filtration and washed with water to give 1.39 g (80.2%) of snow-white needles with mp 217-218°C (from alcohol). IR spectrum: 1725 (C=O); 3200, 3370 cm^{-1} (OH, NH). Found: C 62.4; H 5.3; Cl 10.1; N 12,2%. $C_{18}H_{19}N_3O_2 \cdot HCl$. Calculated: C 62,5; H 5,5; Cl 10,3; N 12,2% .

The salt obtained was treated with NH_4OH, and the mixture was extracted with chloroform. The chloroform was evaporated, the residue was triturated with petroleum ether until it crystallized from acetone to give a product with mp 156-157°C. IR spectrum: 1545 (C=O), 3150-3300 cm^{-1} (broad OH band). Found: C 69.9; H 6,0; N 13.7%. $C_{18}H_{19}N_3O_2$. Calculated: C 69,9; H 6,2; N 13,6% .

2-Acetylimino-1-methyl-3-(2-phenyl-2-chloroethyl)-benzimidazoline (VIIIb). A 0.4-ml sample of $SOCl_2$ was added dropwise to a suspension of 0.9 g (2.5 mmole) of the hydrochloride of XI in 10 ml of dry $CHCl_3$, after which the mixture was stirred until the solid had dissolved completely, and the solution was allowed to stand at room temperature for 24 h. The solvent was evaporated to give 0.95 g of white crystals of the hydrochloride of VIIIb with mp 197-198°C (dec., from alcohol with ether). IR spectrum: 1720 cm^{-1} (C=O). Found: C 59.1; H 5.3; Cl 19.2; N 11,6%. $C_{18}H_{18}ClN_3O \cdot HCl$. Calculated: C 59.3; H 5.3; Cl 19,5; N 11,5% . Base VIIIb was obtained by treatment of the salt with 10% NH_4OH and had mp 142°C (dec., from acetone). IR spectrum: 1555 cm^{-1} (C=O). Found: C 65.8; H 5.7; Cl 10.5; N 12,9%. $C_{18}H_{18}ClN_3O$. Calculated: C 66.0; H 5,5; Cl 10.8; N 12.8%.

Compound VIIIb was also obtained by acylation of imine IVe with acetic anhydride at room temperature and by brief refluxing of IIIe with excess [1:(7-10)] $SOCl_2$ in $(CH_3CO)_2O$.

2-Acetylimino-3-(2-acetoxy-2-phenylethyl)-1-methyl-benzimidazoline (VIIb). A mixture of 0.6 g (2 mmole) of hydrochloride IIIe, 0.5 g of fused sodium acetate, and 6 ml of $(CH_3CO)_2O$ was refluxed for 2 h, after which it was cooled and poured into 20 ml of cold water. The aqueous mixture was neutralized with $NaHCO_3$, and the precipitate was removed by filtration, washed with water, dried, and crystallized from benzene–petroleum ether to give 0.62 g (88.6%) of colorless plates with mp 131°C. IR spectrum: 1550, 1740 cm^{-1} (C=O). Found: C 68,2; H 6.1; N 12.2%. $C_{20}H_{21}N_3O_3$. Calculated: C 68.3; H 6.0; N 12.0%. . The hydrochloride of VIIb was isolated d by acidification of an acetone solution of the base with concentrated HCl and had mp 208-209°C (from alcohol). IR spectrum: 1735, 1755 cm^{-1} (C=O). Found: C 61,7; H 5.7; Cl 9.0; N 10,9%. $C_{20}H_{21}N_3O_3$. Calculated: C 61,9; H 5.7; Cl 9.2; N 10,8% .

Compound VIIb was also obtained in a mixture with VIe when hydroxy imine IIIe was refluxed with excess $SOCl_2$ in $(CH_3CO)_2O$ for 2-3 h.

2-Acetylimino-3-(2-acetoxyethyl)-1-methylbenziimdazoline (VIIa). A 0.68-g (2 mmole) sample of hydrochloride IIIa was refluxed in 5 ml of $(CH_3CO)_2O$ for 2-2.5 h, after which the mixture was diluted with water. The aqueous mixture was neutralized to pH 7-8 with sodium carbonate and extracted with chloroform. The $CHCl_3$ was evaporated, and the residual oil crystallized slowly on standing to give 0.78 g (94%) of a product with mp 92-93°C (from ethyl acetate). IR spectrum: 1545, 1740 cm^{-1} (C=O). PMR spectrum: 1.88 (3H, s, $NCOCH_3$), 2.13 (3H, s, $OCOCH_3$), 3.47 (3H, s, NCH_3), 4.79 (4H, s, CH_2CH_2), and 7.15 ppm (4H, s, aromatic protons). Found: C 61,1; H 6,2; N 15,3%. $C_{14}H_{17}N_3O_3$. Calculated: C 61,0; H 6,2; N 15,3%.

Compound VIIa was also obtained in a mixture with VIa and VIIIa when salt IIIa was refluxed with $SOCl_2$ and $(CH_3CO)_2O$.

2-Acetylimino-1-methyl-3-chloroethylbenzimidazoline (VIIIa). This compound was obtained in the form of a colorless oil by acylation of imine IVa with acetic anhydride at room temperature or by refluxing alcohol IIIa with $SOCl_2$ and $(CH_3CO)_2O$. The hydrochloride was isolated by acidification of an acetone solution of the oil with an ether solution of HCl to pH 1-2 and had mp 257-258°C (dec., from alcohol with ether). IR spectrum: 1740 cm^{-1} (C=O). Found: C 49,9; H 5,5; Cl 24,2; N 14,5%. $C_{12}H_{14}ClN_3O \cdot HCl$. Calculated: C 50,0; H 5,3; Cl 24,6; N 14,6%.

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