IMIDAZOINDOLES.

2.* SYNTHESIS OF IMIDAZO[4,5-e]INDOLES FROM 5-AMINOBENZIMIDAZOLES

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A method was found for the synthesis of the previously unknown imidazo[4,5-e]-indole heteroaromatic system with angular fusion of the rings. These compounds are obtained by heating 5-hydrazinobenzimidazoles with carbonyl compounds in an acidic medium.

The preparation of linearly linked imidazoindoles by cyclization of 5,6-diaminoindolines with subsequent aromatization of the pyrrole ring has been reported [1]. This method cannot be used for the preparation of angular isomers, since the synthesis of the corresponding 4,5- or 6,7-diamines has not yet been worked out. It was more expedient to use the Fischer synthesis, i.e., to build on a pyrrole ring rather than an imidazole ring starting from hydrazinobenzimidazoles (I), the synthesis of which from the corresponding amines by diazotization with subsequent reduction was not fraught with any difficulties. The direction of heterocyclization was debatable. The mechanism of the Fischer rearrangement is still the subject of debate. The assumption that cyclization under the influence of acidic agents proceeds via a scheme involving electrophilic or nucleophilic attack on the aromatic ring was subsequently advanced, but inexplicable facts were encountered for each scheme [2]. The assumption that cyclization proceeds via a "no-mechanism" scheme [3] or, using the Woodward–Hoffman concepts, via a sigmatropic shift [4] has been advanced. However, this assumption also was not in agreement with the experimental data. Recent research by Ishii and co-workers [5] makes it possible to assume that the reaction takes place both via a scheme involving a sigmatropic shift and via a scheme involving electrophilic attack; the mechanism of the reaction (and the ratio of the reaction products) depend substantially both on the structure of the reacting molecule and the conditions under which the process is carried out [5].

If one proceeds from the assumption that the reaction proceeds primarily via a scheme involving electrophilic attack on the aromatic ring, one should take into account the distribution of the electron density in the benzimidazole ring. It turns out by various methods of calculation to be approximately the same in the 4 and 6 positions (for example, see [6]), but somewhat higher in the 4 position. Data that indicate that the C_4 atom in 5-hydroxy- and 5-aminobenzimidazoles is the preferred center of electrophilic attack [7] are in agreement with this. Steric factors, i.e., the possibility of steric interaction during cyclization with the N_3 atom, should be taken into account. However, in the Fischer synthesis 2-naphthylhydrazones form an angular isomer rather than a linear isomer [8, 9] even if there is a methyl group in the 1 position [10]. Only angular isomers were also obtained from 5-hydrazinobenzofurans [11].

Our experiments showed that imidazol[4,5-e]indoles (II) with angular fusion of the rings (the PMR spectrum contains two doublets of aromatic protons with J = 8-9 Hz) are formed when benzimidazolylhydrazines (I) are heated with carbonyl compounds in acidic media; the presence of linearly fused isomers was not detected in even a single case by thin-layer chromatography (TLC).

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*See [1] for Communication 1.

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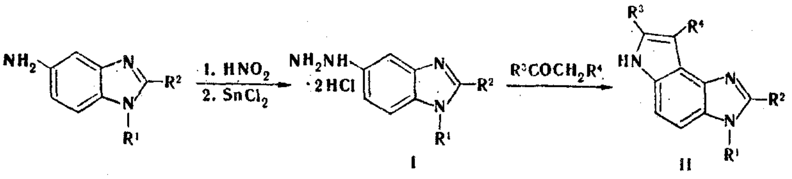
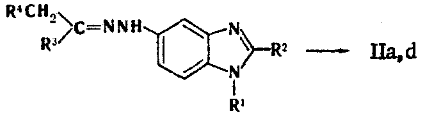


R^4=H, Alk, $CH_2C_6H_5$, CH_2CH_2OH; R^2=H, CH_3; R^3=CH_3, C_6H_5; R^4=CH_3

As a rule, in the Fischer synthesis [2] the degree of unambiguity and, correspondingly, the yield depend substantially on the catalyst used. We obtained hydrazone III in the individual state and found that acetic acid saturated with hydrogen chloride, zinc chloride, boron trifluoride etherate, or polyphosphoric acid can be used for its rearrangement. The formation of ester IIa was established in all cases by TLC, but the process is of preparative value only with polyphosphoric acid, and IIa can be isolated in 30-40% yield. In the remaining cases the chromatograms show the presence of a complex mixture of reaction products, which we did not investigate in greater detail. Imidazo[4,5-e]indole (IIc), which does not have substituents, was obtained by saponification of ester IIa with subsequent decarboxylation of acid IIb.



III, IV

IIa, III R^1=R^2=R^4=H, R^3=$COOC_2H_5$; IId, IV R^1=$CH_2C_6H_5$, R^2=CH_3, R^3=C_6H_5, R^4=H

If the ring nitrogen atom in the 1 position of the starting benzimidazolylhydrazine (I) is alkylated, virtually no effect on the yields of the corresponding imidazoindoles (Table 2, compounds 1 and 8, 10, 16; 2 and 7; 4 and 9, 11, 15) is observed.

Thus we have found a method for the synthesis of the previously unknown heteroaromatic imidazo[4,5-e]indole system. The UV spectra of these substances are quite characteristic.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil or solutions in chloroform were recorded with a UR-10 spectrometer. The UV spectra of alcohol solutions (10^{-3} M) were recorded with a Hitachi EPS-3T spectrophotometer. The PMR spectra of solutions in DMSO were recorded with an RS-60 spectrometer with hexamethyldisiloxane as the external standard.

5-Hydrazinobenzimidazoles (I). A solution of 0.1 mole of sodium nitrite in 18 ml of water was added with vigorous stirring at −5 to −3°C to a solution or suspension of 0.1 mole of the corresponding benzimidazolylamine in 300 ml of concentrated HCl. After all of the sodium nitrite solution had been added, the mixture was stirred for 30 min, and a solution of 0.21 mole of stannous chloride in 35 ml of concentrated HCl was added dropwise at −5 to 0°C. The mixture was then stirred for 1 h, and the precipitate was removed by filtration and washed with alcohol and ether. The complex salt obtained was dissolved in water and decomposed with hydrogen sulfide. The tin sulfide was separated, and the solution was evaporated to give the hydrazine dihydrochloride (I). The results of elementary analysis, the melting points, and the yields are presented in Table 1.

Imidazo[4,5-e]indoles (II, Table 2). An equimolar amount of the ketone was added to a solution of the corresponding 5-hydrazinobenzimidazole (Table 1) in water, and the mixture was refluxed for 4-10 h while monitoring the course of the reaction and the individuality of the compounds obtained by TLC on Al_2O_3 (activity II) in a benzene–ethanol system (5:1) and on Silufol UV-254 plates in a chloroform–ethyl acetate–diethylamine system (50:40:10). The precipitate that formed after cooling was separated. The hydrochloride of imidazo[4,5-e]indole was purified by reprecipitation from aqueous solution by the addition of excess concentrated HCl and ether. The hydrochlorides of the compounds that have a substituent attached to the N_3 atom were washed with acetone. The bases were isolated by alkalization of aqueous or aqueous alcohol solutions with concentrated ammonium hydroxide and were recrystallized from alcohol.

TABLE 1. 5-Hydrazinobenzimidazole Dihydrochlorides (I)

R^1	R^2	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N		C	H	N	
H	H	235 (dec.)	38,0	4,7	25,4	$C_7H_8N_4 \cdot 2HCl$*	38,0	4,6	25,3	60
H	CH_3	225 (dec.)	40,7	5,1	23,8	$C_8H_{10}N_4 \cdot 2HCl$*	40,9	5,1	23,8	65
CH_2CH_2OH	H	200—202	40,4	5,3	21,1	$C_9H_{12}N_4 \cdot 2HCl$	40,8	5,3	21,1	56
n-C_4H_9	H	190—192	48,1	6,2	20,6	$C_{11}H_{16}N_4 \cdot 2HCl$	47,6	6,6	20,2	46
$CH_2C_6H_5$	H	215 (dec.)	54,4	5,4	17,8	$C_{14}H_{14}N_4 \cdot 2HCl$	54,0	5,2	18,0	56
CH_3	H	290 (dec.)	40,6	5,3	23,5	$C_8H_{10}N_4 \cdot 2HCl$	40,9	5,1	23,8	44
$CH_2C_6H_5$	CH_3	213 (dec.)	55,8	5,9	16,9	$C_{15}H_{16}N_4 \cdot 2HCl$	55,4	5,6	17,2	54

*The compositions were also confirmed by determination of the chlorine content.

Ethyl Pyruvate 5(6)-Benzimidazolylhydrazone (III). A mixture of 27.91 g (0.126 mole) of 5-hydrazinobenzimidazole dihydrochloride, 11.45 g (0.13 mole) of pyruvic acid, and 140 ml of water was heated with stirring at 50-60°C for 1 h, after which it was cooled, and the precipitate was removed by filtration and washed with water. The hydrazone hydrochloride obtained was suspended in 200 ml of water, and the suspension was made alkaline to pH 8-9 with concentrated ammonium hydroxide. Base III was removed by filtration, washed with water, and dried. A 28.6-g sample of hydrazone III was added to a solution of 27 ml of concentrated H_2SO_4 in 425 ml of absolute ethanol, and the mixture was refluxed for 8 h. The alcohol was evaporated, and the residue was neutralized to pH 8-9 with ammonia. The precipitated III was removed by filtration and washed with water. The yield was 16.4 g (49.2%). The yellowish powder had mp 145-146°C (from ethanol). Found: C 54.7; H 5.8; N 21.2%. $C_{12}H_{14}N_4O_2 \cdot H_2O$. Calculated: C 54.5; H 6.1; N 21.2%.

Ethyl Imidazo[4,5-e]indole-7-carboxylate (IIa). A mixture of 2 g (8 mmole) of III and 16 g of polyphosphoric acid (PPA) was heated in a porcelain dish with vigorous stirring at 130-140°C for 5-10 min, after which the hot reaction mixture was poured over ice, and the resulting solution was purified with charcoal and neutralized to pH 7 with concentrated ammonium hydroxide. The precipitate was removed by filtration and purified by passing an ethanol solution through a column filled with aluminum oxide (elution with benzene) to give 0.72 g (40%) of light-yellow powdered ester IIa with mp 215-217°C. UV spectrum, λ_{max} (log ε): 249-251 (4.22), 302 nm (4.37). Found: C 63.4; H 5.0; N 18.6%. $C_{12}H_{11}N_3O_2$. Calculated: C 62.8; H 4.8; N 18.3%.

Imidazo[4,5-e]indole-7-carboxylic Acid (IIb). An 8-ml sample of a 20% solution of potassium hydroxide was added to a suspension of 2.25 g (9.8 mmole) of ester IIa in 15 ml of water, and the mixture was heated on a water bath for 30 min. The resulting solution was purified with charcoal and neutralized to pH 7 with hydrochloric acid to give 1.67 g (85%) of product. The product was purified by reprecipitation from DMF by the addition of water. The white powder sublimed when it was heated above 300°C. Found: C 54.5; H 4.5; N 19.3%. $C_{10}H_7N_3O_2 \cdot H_2O$. Calculated: C 54.8; H 4.1; N 19.2%.

Imidazo[4,5-e]indole (IIc). A 0.5-g (2.5 mmole) sample of IIb was heated with copper powder at 310-315°C for 13 min in a sublimation apparatus. The sublimed white substance was collected, washed with alkali, and crystallized from water containing a few drops of alcohol to give 0.14 g (60%) of white needles with mp 202-203°C. UV spectrum, λ_{max} (log ε): 272 (3.97): 287 (3.98); 297 nm (3.95). Found: C 69.3; H 4.5; N 26.4%. $C_9H_7N_3$. Calculated: C 68.8; H 4.5; N 26.7%.

Acetophenone 1-Benzyl-2-methyl-5-benzimidazolylhydrazone (IV). A 1.2-ml (1 mmole) sample of acetophenone was added to a solution of 2.5 g (8 mmole) of 1-benzyl-2-methyl-5-hydrazinobenzimidazole (I, $R^1 = C_6H_5CH_2$, $R^2 = CH_3$) in 20 ml of water, and the mixture was stirred at room temperature for 3 h. The precipitate was removed by filtration and washed with ether to give 2.03 g (67%) of the hydrazone hydrochloride with mp 230°C. Found: C 70.3; H 5.6; N 14.3%. $C_{23}H_{22}N_4 \cdot HCl$. Calculated: C 70.7; H 5.7; N 14.4%.

2-Methyl-3-benzyl-7-phenylimidazo[4,5-e]indole (IId). A mixture of 1.5 g (4 mmole) of IV and 12 g of PPA was heated in a porcelain dish at 120°C for 5 min and at 150-170°C for 15 min, after which the hot mixture was poured over ice. The precipitate was removed by filtration and washed with water. A suspension of the precipitate in water was treated with

TABLE 2. Imidazo[4,5-e]indoles (II)

No.	R^1	R^2	R^3	R^4	mp, °C[a]	UV spectrum (in alcohol), λ_{max}, nm (log ε)	IR spectrum,[b] ν_{NH}, cm^{-1}	Found, %			Empirical formula	Calc., %			Yield,[c] %
								C	H	N		C	H	N	
1	H	H	CH_3	CH_3	240—241	280—285 (4,03), 293 (4,07), 303 (4,06)	3467 (3400)	71,6	6,1	22,5	$C_{11}H_{11}N_3$	71,3	6,0	22,7	74
2	H	H	—$(CH_2)_4$—		236	281—284 (4,03), 294 (4,07), 303 (4,06)	3463 (3416)	71,0	6,1	18,9	$C_{13}H_{13}N_3$[d]	70,9	6,4	19,1	58
3	H	H	—$(CH_2)_3$—		291	280 (4,06), 294 (4,12), 303 (4,09)	(3400)	72,8	5,7	21,0	$C_{12}H_{11}N_3$	73,1	5,6	21,3	37
4	H	H	C_6H_5	CH_3	260	255 (4,25), 313 (4,42)	(3440)	77,5	5,5	16,8	$C_{16}H_{13}N_3$	77,7	5,3	17,0	47
5	CH_2CH_2OH	H	CH_3	CH_3	231—233	300—302 (4,22)	3475	68,2	6,2	17,9	$C_{13}H_{15}N_3O$	68,1	6,6	18,3	78
6	H	CH_3	C_6H_5	CH_3	258	256 (4,27), 313 (4,41)	3430	77,7	5,7	16,1	$C_{17}H_{15}N_3$	78,1	5,8	16,1	44
7	*n*-C_4H_9	H	—$(CH_2)_4$—		210—211	300—303 (4,24)		76,5	8,3	15,8	$C_{17}H_{21}N_3$	76,4	7,9	15,7	78
8	*n*-C_4H_9	H	CH_3	CH_3	181—182	301 (4,21)		74,5	7,5	17,4	$C_{15}H_{19}N_3$	74,7	7,9	17,4	58
9	*n*-C_4H_9	H	C_6H_5	CH_3	211—212	252 (inf., 4,08), 318-320 (4,48)	3475	79,3	6,9	13,9	$C_{20}H_{21}N_3$	79,2	7,0	13,8	53
10	$CH_2C_6H_5$	H	CH_3	CH_3	263	302—304 (4,41)		78,8	6,2	15,1	$C_{18}H_{17}N_3$	78,5	6,2	15,3	41
11	$CH_2C_6H_5$	H	C_6H_5	CH_3	283	253 (inf., 4,11), 318-321 (4,51)		82,3	5,7	12,7	$C_{23}H_{19}N_3$	81,9	5,7	12,5	45
12	$CH_2C_6H_5$	C_6H_5	C_6H_5	CH_3	132—133	290—292 (4,34)		84,7	5,4	9,8	$C_{29}H_{21}N_3$	84,6	5,1	10,2	51
13	$CH_2C_6H_5$	CH_3	CH_3	CH_3	258	300 (4,30)		79,3	6,8	15,0	$C_{19}H_{19}N_3$	78,9	6,6	14,5	72
14	$CH_2C_6H_5$	CH_3	C_6H_5	CH_3	278	253 (inf., 4,20), 316-320 (4,52)		82,6	6,1	12,1	$C_{24}H_{21}N_3$	82,0	6,0	11,9	
15	CH_3	H	C_6H_5	CH_3	271	255 (inf., 4.09), 318-321 (4,46)	3480	78,3	5,7	16,3	$C_{17}H_{15}N_3$	78,1	5,8	16,1	40
16	CH_3	H	CH_3	CH_3	300	301—303 (4,28)	3482	72,4	6,4	21,3	$C_{12}H_{13}N_3$	72,3	6,6	21,1	73
17	H	CH_3	CH_3	CH_3	247	278—280 (4,03), 293 (4,07), 303 (4,08)	(3380)	72,4	6,5	21,0	$C_{12}H_{13}N_3$	72,3	6,6	21,1	56
18	$CH_2C_6H_5$	C_6H_5	CH_3	CH_3	226			82,6	6,1	12,0	$C_{24}H_{13}N_3$	82,0	6,0	12,0	

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[a] The temperatures at which melting begins are indicated for the substances that melt with decomposition.
[b] The spectra were obtained from solutions in chloroform or suspensions in mineral oil (in parentheses).
[c] These are the yields of hydrochlorides. [d] The hydrate, which retained water after vacuum drying. Calculated for $C_{13}H_{13}N_3 \cdot \frac{1}{2}H_2O$.

a solution of sodium carbonate, and the resulting precipitate was removed by filtration. The yellowish precipitate was purified by reprecipitation from DMF by the addition of water, after which it melted above 300°C with decomposition. UV spectrum, λ_{max} (log ε): 253 (4.24); 328 nm (4.54). Found: C 81.8; H 5.7; N 12.7%. $C_{23}H_{19}N_3$. Calculated: C 81.9; H 5.7; N 12.5%.

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SYNTHESIS AND ABSORPTION—FLUORESCENCE PROPERTIES OF 1,4-BIS(Δ^2-PYRAZOLIN-3-YL)- AND 1,4-BIS(3-PYRAZOLYL)BENZENES

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1,4-Bis(Δ^2-pyrazolin-3-yl)benzene derivatives were synthesized by the reaction of dibenzal-p-diacetylbenzene or 1,4-bis(β-dimethylaminopropionyl)benzene with various hydrazines. Some of these derivatives were converted to the corresponding 1,4-bis(3-pyrazolyl)benzene derivatives by oxidative dehydrogenation with sulfur. The absorption and fluorescence spectra of the synthesized compounds were measured, and the fluorescence quantum yields were determined.

Of the known organic luminophores, Δ^2-pyrazoline derivatives are widely used [1]. Of particular interest are 1,4-bis(Δ^2-pyrazolin-3-yl)benzenes (I), solutions of which not only luminesce intensely, but also are capable of generating laser emission [2]. The compounds of this type that are described in the literature generally contain aromatic substituents in the 1, 1', 5, and 5' positions. All of these compounds luminesce at 470-510 nm, whereas compounds that luminesce in the UV and blue-violet regions are of great interest today for laser technology. In this connection it seemed of interest to study the effect of substituents in the 1 and 5 positions of the pyrazoline rings on the luminescence spectra in order to obtain compounds of the I type that luminesce in the UV region. In addition, it was of interest to synthesize analogous dehydrogenated (aromatic) compounds, viz., 1,4-bis(3-pyrazolyl)benzenes (III, V), the luminescence properties of which have not been described in the literature.

Compounds Ia-c were obtained by reaction of dibenzal-p-diacetylbenzene (II) with substituted hydrazines [3]. In the case of the reaction of II with unsubstituted hydrazine in isopropyl alcohol we were unable to isolate any individual compound from the reaction mix-

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