ortho-DIMETHOXY EFFECT IN THE CHICHIBABIN REACTION

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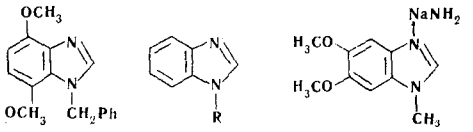
UDC 542.958.3:547.785.5

A phenomenon, called the o-dimethoxy effect, was detected and consists in the fact that, in the sodium amide with aromatic and heterocyclic compounds with an o-dimethoxy grouping, one of the methoxy groups undergoes demethylation to form the corresponding o-methoxyphenol. The formation of an o-methoxyphenoxide anion in the case of N-heteroaromatic compounds hinders their amination by sodium amide. Compounds with m- and p-dimethoxy groups readily undergo the Chichibabin reaction. It is assumed that the nature of the o-dimethoxy effect is associated with sorption factors that are substantial for heterogeneous reactions such as the Chichibabin reaction.

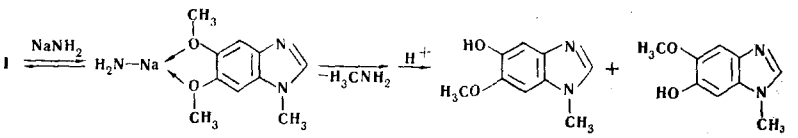
We have previously observed that the two methoxy groups in 1-R-5,6-dimethoxybenzimidazoles completely inhibit the amination of the imidazole ring [1]. A methylenedioxy group has a similar effect. The aim of this paper was a clarification of basically two problems: 1) is this effect peculiar only to the o-dimethoxy grouping or does it apply also to two discrete CH_3O groups in the meta or para positions with respect to one another? In other words, is there really an o-dimethoxy effect? 2) If the latter exists, is it a general phenomenon in the Chichibabin reaction?

As subjects for the investigation, we synthesized the previously unknown II-VII and studied in some detail the behavior of 1-methyl-5,6-dimethoxybenzimidazole (I) toward sodium amide.



II III–VII IX

III R = 3,4-$(MeO)_2C_6H_3$; IV R = 2,4-$(MeO)_2C_6H_3$; V R = 2,5-$(MeO)_2C_6H_3$;
VI R = 3,4-$(MeO)_2C_6H_3CH_2$; VII R = 4-$MeOC_6H_4CH_2$



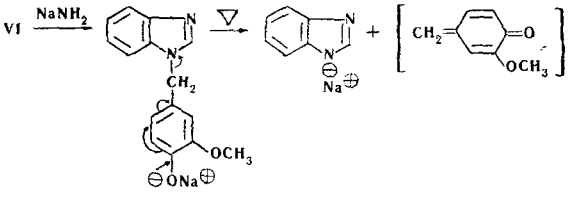
VIII X XI

It turned out that II, IV, and V, with discrete methoxy groups, are aminated in the usual manner by sodium amide to form good yields of the corresponding 2-amino derivatives. On the other hand, I, III, and VI, with an o-dimethoxy grouping cannot be introduced into the Chichibabin reaction from 110-180° in xylene, dimethylaniline, mineral oil, or by heating with $NaNH_2$ without a solvent. Compound I, however, reacts with sodium amide in mineral oil at 180° to give a 35% yield of an alkali-soluble substance to which, on the basis of the results of elemental analysis and the IR spectral data (the IR spectra contain a band at 3540 cm^{-1}, which positively belongs to the hydroxyl group, and bands of N–H stretching vibrations are absent),

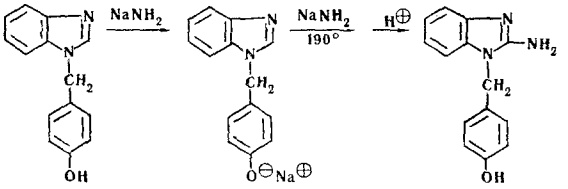
Rostov-on-Don State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1105-1111, August, 1971. Original article submitted November 16, 1970.

we ascribed the 1-methyl-5(6)-hydroxy-6(5)-methoxybenzimidazole structure (X or XI). (We did not establish the precise position of the OH and CH_3O groups.)

The second possible isomer of this compound could not be isolated because of very pronounced resinification of the reaction mixture. Demethylation of one of the methoxy groups by the action of sodium amide on III was also observed. 1-(3,4-Dimethoxybenzyl)benzimidazole (VI) has an interesting behavior with respect to sodium amide: somewhat unexpectedly in this case, benzimidazole is formed in 75% yield. We suppose that this result is also a consequence of demethylation of the methoxy group (which is apparently in the para position with respect to the CH_2 group) with subsequent elimination, under the severe reaction conditions, of a benzyl radical from the phenoxide (XII)* in the form of an unstable 2-methoxymethylenequinone:

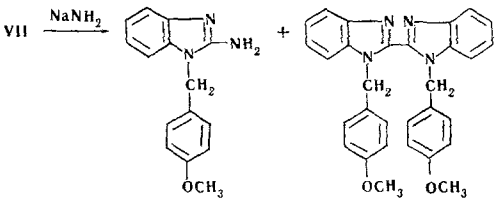


XII



XIII

The similar behavior of the o-hydroxy- and p-hydroxybenzyl derivatives of some tertiary amines in alkaline media [2] as well as an analogy with the transformations of I and III are evidence in favor of this assumption. As expected, 1-(p-methoxybenzyl)benzimidazole (VII) readily enters into the Chichibabin reaction, although a colorless, high-melting substance, to which we ascribed the 1,1'-di(p-methoxybenzyl)-2,2'-dibenzimidazolyl structure on the basis of the analytical data and IR spectrum (absence of absorption at 3100 cm^{-1}), is also formed as a side product in 7% yield.



Attempts to introduce 6,7-dimethoxyisoquinoline into the Chichibabin reaction were unsuccessful. An alkali-soluble product (probably a mixture of the corresponding hydroxy compounds), which however, could not be purified, is formed by the action on it of sodium amide in dimethylaniline at 170°. Isoquinoline itself is readily aminated by sodium amide in dimethylaniline at 120°.

These results indicate that the o-dimethoxy effect really exists and (at least in the benzimidazole series) is general in character.† Outwardly, it consists in the demethylation of one of the CH_3O groups with the formation of the corresponding phenoxide ion, which apparently enters into the Chichibabin reaction with extreme difficulty (this is illustrated in the case of XIII) or does not react at all.

*An attempt to accomplish the analogous elimination of p-methylenequinone in the O-anion of 1-(p-hydroxybenzyl)benzimidazole (XIII) was unsuccessful. This phenoxide is aminated by sodium amide to give 29% yields (although under severe conditions: heating to 190° in dimethylaniline) without decomposition.

†We have established that dimethoxy derivatives of the aromatic series (veratrole, for example) also are demethylated by the action of sodium amide. This material will be published separately.

TABLE 1. Ionization Constants and Behavior of the Compounds Studied toward Sodium Amide

Compound	pK_a (10% aq. soln.), 25 ± 1°C	Behavior toward $NaNH_2$
I	5,90	–
II	4,58	+
III	4,63	–
IV	4,63	+
V	4,62	+
VI	5,24	–
VII	5,42	+

*The + indicates that the compound is aminated, while the – indicates that it is not.

The manifestation of the o-dimethoxy effect is independent of the site at which the o-dimethoxy junction is situated in the molecule, and thus it is not a consequence of the direct electronic effect of two methoxy groups on the reaction center. This is also confirmed by the basicity of all of the substances that we studied, which is completely suitable for the successful occurrence of the Chichibabin reaction [3] (Table 1).

All of these results confirm the assumption [1] that the nature of the o-dimethoxy effect is most likely associated with sorption of the o-dimethoxy derivative on the surface of the sodium amide particles (the Chichibabin reaction proceeds under heterogeneous conditions) with the formation of a complex of the VIII type. During this sort of sorption, the molecules of the compound are oriented on the sodium amide surface in such a way that the coordination of the latter with the pyridine nitrogen atom (the first step in the Chichibabin reaction [3]) and, consequently, the amination become geometrically impossible.* Although there is as yet no direct experimental proof of the formation of complexes of the VIII type in our case, there are a number of indirect arguments in favor of this assumption: 1) the coordination of alkali metal ions with o-dimethoxy- and $-OCH_2CH_2O-$ groups is presently a firmly established fact [5-7]; 2) the formation of complex VIII should foster the observed cleavage of the methoxy group with the formation of a phenoxide ion and methylamine. The liberation of methylamine was recorded by means of gas chromatography in all cases when an o-dimethoxy derivative was introduced into the reaction. On the other hand, judging from the absence of methylamine in the gaseous reaction products, demethylation does not occur during the action of sodium amide on compounds that contain one methoxy group or two such groups in the meta and para positions.

It is curious that the demethylation of I, III, and VI proceeds under more severe conditions than those which are usually required for the Chichibabin reaction. This apparently indicates that the sorption of the o-dimethoxy derivative on the surface of $NaNH_2$ particles through the pyridine nitrogen atom to form a complex of the IX type does not occur.

EXPERIMENTAL

2-Benzylamino-3-nitro-1,4-dimethoxybenzene (XIV).† A total of 4.6 g (0.02 mole) of a mixture of 2,3-dinitro- and 2,6-dinitro-1,4-dimethoxybenzene [8, 9] and 4.6 ml (0.044 mole) of benzylamine in 40 ml of absolute o-xylene was refluxed at 140° for 15 h. The mixture was cooled, and the precipitate (0.7 g) of 2,6-dinitro-1,4-dimethoxybenzene was removed by filtration and washed with ether to give orange prisms with mp 205-207° (from ethyl acetate). The filtrate was evaporated in vacuo, and the residual oil was triturated with petroleum ether to give 5.1 g (88%) of XIV as orange prisims with mp 69-70° (from ethanol). Found: C 62.1; H 5.5; N 9.9%. $C_{15}H_{16}N_2O_4$. Calculated: C 62.5; H 5.6; N 9.7%.

4,7-Dimethoxy-1-benzylbenzimidazole (II). A total of 2.88 g (0.01 mole) of XIV was added in portions to a solution of 6.77 g (0.03 mole) of $SnCl_2 \cdot 2H_2O$ in 35 ml of concentrated HCl, and the mixture was heated with stirring on a boiling-water bath for 2 h. The mixture was cooled, and the precipitate of tin complex was removed by filtration, dissolved in 50 ml of water, and decomposed with excess 40% sodium hydroxide solution. The alkaline solution was extracted with chloroform, and the diamine was cyclized without purification by refluxing for 3 h with 10 ml of formic acid and 0.5 ml of concentrated HCl. At the end of the reaction, the solution was diluted to twice its volume with water and clarified by refluxing with activated charcoal. The filtrate was neutralized with 22% ammonium hydroxide and extracted with chloroform. The reaction product was purified by chromatography (Al_2O_3 and chloroform) to give 1.6 g (60%) of colorless prisms of II with mp 95-96° (from benzene–petroleun ether). Found: C 71.8; H 5.9; N 10.6%. $C_{16}H_{16}N_2O_2$. Calculated: C 71.6; H 6.0; N 10.4%.

*Adsorption factors also play an important role in several other reactions that occur under heterogeneous conditions, for example, in the oxidation of organic compounds by active manganese dioxide [4].

†This compound was obtained by V. M. Mar'yanovskii.

TABLE 2. 1-Dimethoxyphenylbenzimidazoles (III-V) and Intermediates

Compound	mp, °C	Crystallization solvent*	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
XVa	173—174	Alcohol	$C_{14}H_{13}N_3O_6$	52,9	4,1	13,3	52,7	4,1	13,2	97
XVb	209—210	Chloroform	$C_{14}H_{13}N_3O_6$	52,9	4,3	13,3	52,7	4,1	13,2	85
XVc	185—186[11]	Acetone	$C_{14}H_{13}N_3O_6$	—	—	—	—	—	—	64
XVIa	209—210	Acetone	$C_{14}H_{15}N_3O_4$	57,8	5,2	14,2	58,1	5,2	14,5	82
XVIb	131—132	Benzene	$C_{14}H_{15}N_3O_4$	58,3	5,4	14,3	58,1	5,2	14,5	87
XVIc	151—152	Benzene	$C_{14}H_{15}N_3O_4$	58,3	5,4	14,2	58,1	5,2	14,5	92
XVIIa	192—193	Alcohol	$C_{15}H_{13}N_3O_4$	58,5	4,2	13,7	58,3	4,2	13,6	90
XVIIb	198—199	The same	$C_{15}H_{13}N_3O_4$	58,5	4,2	13,5	58,3	4,2	13,6	98
XVIIc	178—179	" "	$C_{15}H_{13}N_3O_4$	58,3	4,2	13,8	58,3	4,2	13,6	90
XVIIIa	178—179	" "	$C_{15}H_{15}N_3O_2$	66,6	5,6	15,8	66,9	5,6	15,6	90
XVIIIb	137—138	" "	$C_{15}H_{15}N_3O_2$	67,0	5,6	15,6	66,9	5,6	15,6	71
XVIIIc	180—181	" "	$C_{15}H_{15}N_3O_2$	66,8	5,4	15,6	66,9	5,6	15,6	93
III	146—147	Benzene	$C_{15}H_{14}N_2O_2$	70,5	5,5	11,2	70,8	5,5	11,0	80
IV	158—159	Alcohol	$C_{15}H_{14}N_2O_2$	70,6	5,6	11,1	70,8	5,5	11,0	77
V	110—111	Aqueous alcohol	$C_{15}H_{14}N_2O_2$	70,8	5,4	11,2	70,8	5,5	11,0	65

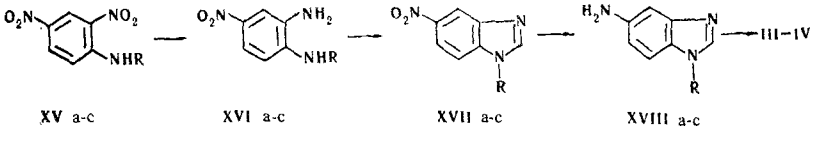
*Compounds XVIIb, III, IV, and V were obtained as colorless crystals; XVa was obtained as orange prisms; XVIa was obtained as brown needles; XVb-c were obtained as red prisms; XVIIa, c were obtained as yellow-green needles; XVIIIa, c were obtained as pale-rose prisms; and XVIIIb was obtained as rose prisms.

1-(3,4-Dimethoxybenzyl)benzimidazole (VI). A solution of 5.6 g (0.03 mole) of 3,4-dimethoxybenzyl chloride in 10 ml of ethanol was added gradually to a warm solution of 3.6 g (0.03 mole) of benzimidazole and 1.7 g (0.03 mole) of potassium hydroxide in 30 ml of alcohol. The mixture was refluxed with stirring for 2 h, the precipitated KCl was removed by filtration, and the alcohol was removed from the filtrate by distillation. The residue was dissolved in chloroform, and the extract was washed several times with water. The reaction product was vacuum-distilled at 250° (4 mm) to give 5.0 g (68%) of colorless prisms of VI with mp 140-141° (from benzene). Found: C 71.7; H 6.2; N 10.7%. $C_{16}H_{16}N_2O_2$. Calculated: C 71.6; H 6.0; N 10.4%.

Compound VII [4.2 g (60%)] was similarly obtained as a colorless oil with bp 215-225° (5-6 mm) that gradually crystallized to give low-melting crystals. The picrate of VII melted at 184-185° (from glacial acetic acid). Found: N 14.9%. $C_{15}H_{14}N_2O \cdot C_6H_3N_3O_7$. Calculated: N 15.0%.

1-(p-Hydroxybenzyl)benzimidazole. A mixture of 2.38 g (0.01 mole) of VII and 7.98 g (0.03 mole) of anhydrous $AlBr_3$ in 75 ml of absolute thiophene-free benzene was refluxed for 4.5 h. The mixture was cooled, 30 ml of concentrated HCl was added, and the benzene layer was separated. The oily mass was dissolved by heating in 70 ml of 20% HCl and decolorized by refluxing with activated charcoal. The filtrate was neutralized with 22% ammonium hydroxide, and the precipitate was removed by filtration and washed well with water to give 1.8 g (80%) of colorless crystals with mp > 360° (purified by reprecipitation from hydrochloric acid solution by the addition of ammonium hydroxide). Found: N 12.3%. $C_{14}H_{12}N_2O$. Calculated: N 12.5%.

Compounds III-V could not be obtained by the direct arylation of benzimidazole by the appropriate dimethoxyphenyl bromide by the method in [10]. They were obtained by the following scheme (Table 2):



XV a-c XVI a-c XVII a-c XVIII a-c

a R = 3,4-$(CH_3O)_2C_6H_3$; b R = 2,4-$(CH_3O)_2C_6H_3$; c R = 2,5-$(CH_3O)_2C_6H_3$

N-(3,4-Dimethoxyphenyl)-2,4-dinitroaniline (XVa). A mixture of 2.02 g (0.01 mole) of dinitrochlorobenzene, 0.82 g (0.01 mole) of anhydrous sodium acetate, and 1.53 g (0.01 mole) of 4-aminoveratrole in

15 ml of alcohol was refluxed for 3.5 h, and the precipitate was removed by filtration and washed with water and alcohol to give 3.1 g of XVa. XVb was similarly obtained.

2-Amino-4-nitro-N-(3,4-dimethoxyphenyl)aniline (XVIa). A suspension of 3.19 g (0.01 mole) of XVa in 10 ml of alcohol was added gradually to a hot solution of 0.64 g (0.02 mole) of crystalline sulfur and 4.8 g (0.02 mole) of $Na_2S \cdot 9H_2O$ in 10 ml of water. The mixture was refluxed for 2 h, 10 ml of water was added, and the resulting precipitate was removed by filtration and washed with hot water to give 2.4 g of product. Compounds XVIb-c were similarly obtained.

5-Nitro-1-(3,4-dimethoxyphenyl)benzimidazole (XVIIa). A solution of 4.12 g (0.0125 mole) of XVIa in 10 ml of formic acid and 0.5 ml of concentrated HCl was refluxed for 4 h, 30 ml of water and 5 ml of concentrated HCl were added, and the mixture was decolorized by refluxing with activated charcoal. The hot solution was filtered, and the precipitate of the hydrochloride of XVIIa was decomposed with 22% ammonium hydroxide to give 3.4 g of XVIIa. Compounds XVIIb, c were synthesized by the same method.

5-Amino-1-(3,4-dimethoxyphenyl)benzimidazole (XVIIIa). A total of 3.09 g (0.01 mole) of XVIIa was added in portions to a hot solution of 6.77 g (0.03 mole) of $SnCl_2 \cdot 2H_2O$ in 30 ml of concentrated HCl, and the mixture was heated with stirring on a boiling-water bath for 1.5 h. The mixture was cooled, and the precipitate of tin complex was removed by filtration, dissolved in 100 ml of water, and decomposed with excess 40% sodium hydroxide solution. The mixture was extracted with chloroform to give 2.4 g of XVIIIa. Compounds XVIIIb,c were similarly obtained.

1-(3,4-Dimethoxyphenyl)benzimidazole (III). A cooled solution of 1.03 g (0.015 mole) of sodium nitrite in 4 ml of water was added gradually to a cooled (to 0°) solution of 3.05 g (0.0125 mole) of XVIIIa in 18 ml of concentrated HCl and 17 ml of water. Another 7 ml of concentrated HCl was added, followed by the addition, in portions, of a solution of 7.6 g (0.06 mole) of potassium hypophosphite in 10 ml of water. The mixture was stirred with cooling for 1 h and placed in a refrigerator for 20 h to complete the reaction. The solution was made alkaline with 22% ammonium hydroxide, and the precipitate was removed by filtration to give 2.5 g of III. Compounds IV and V were similarly obtained.*

Action of Sodium Amide on 1-Methyl-5,6-dimethoxybenzimidazole (I). A mixture of 0.96 g (0.005 mole) of I and 0.78 g (0.02 mole) of finely ground sodium amide in 10 ml of mineral oil was stirred at 175-180° for 1.5 h with collection of the evolved gas in a gas burette. The mixture was cooled, and 20 ml of petroleum ether and 10 ml of water were added. The aqueous layer was separated, neutralized with concentrated HCl, and evaporated to dryness. The residue was extracted with hot alcohol. A total of 10 g of Al_2O_3 was added to the alcohol solution, the alcohol was removed by distillation, and the aluminum oxide was mixed with chloroform and poured into a column containing 15 g of pure Al_2O_3. The mixture was eluted with chloroform with collection of the last portions to give 0.31 g (35%) of X (or XI) as colorless needles with mp 209-210° (from chloroform). IR spectrum, cm^{-1}: ν_{OH} 3540. Found: C 60.5; H 5.5; N 15.5%. $C_9H_{10}N_2O_2$. Calculated: C 60.7; H 5.7; N 15.7%. Ammonia (57%) and methylamine (43%) were detected during analysis of the collected gas.

Action of Sodium Amide on 1-(3,4-Dimethoxyphenyl)benzimidazole (III). A mixture of 2 g (0.008 mole) of III and 1.46 g (0.04 mole) of sodium amide in 10 ml of mineral oil was stirred at 150° for 1 h. The method used for the isolation was similar to that in the previous experiment. An alcohol solution of picric acid was added to a hot alcohol solution of the reaction product, and the precipitated picrate of the hydroxy derivative was filtered and washed with alcohol to give 2.5 g (66%) of a product with mp 269-270° (dec., from alcohol). IR spectrum, cm^{-1}: ν_{OH} 3620 and 3548; bands of the valence vibrations of the NH_2 group were absent. Found: N 15.0%. $C_{14}H_{12}N_2O_2 \cdot C_6H_3N_3O_7$. Calculated: N 14.9%. The picrate was not decomposed by liquid ammonia by the method in [12].

Action of Sodium Amide on 1-(3,4-Dimethoxybenzyl)benzimidazole (VI). A mixture of 1.34 g (0.005 mole) of VI and 0.97 g (0.025 mole) of sodium amide in 6 ml of dimethylaniline was stirred at 130° for 1.5 h. The mixture was cooled, 8 ml of water was added, and the aqueous layer was separated and neutralized with concentrated HCl. The oil that separated was purified by chromatography (Al_2O_3 and chloroform) with selection of the last portions of the eluent to give 0.3 g (75%) of colorless crystals that were identical with respect to spectral characteristics and melting point [171-172° (from benzene)] to benzimidazole. This product did not depress the melting point of a known sample of the benzimidazole.

* Compound IV was purified by chromatography (Al_2O_3 and chloroform), while V was triturated with hot n-octane.

2-Amino-4,7-dimethoxy-1-benzylbenzimidazole. A mixture of 1.34 g (0.005 mole) of II and 0.97 g (0.025 mole) of finely ground sodium amide in 9 ml of dimethylaniline was stirred at 145° for 1 h. The mixture was cooled, 10 ml of water was added, and the precipitate was removed by filtration and washed with benzene and petroleum ether to give 0.88 g (65%) of colorless prisms with mp 203-204° (from benzene). IR spectrum, cm^{-1}: δ_{NH_2} 1660; ν_{NH_2} 3310, 3460. Found: C 67.6; H 6.3; N 14.9%. $C_{16}H_{17}N_3O_2$. Calculated: C 67.8; H 6.1; N 14.8%.

2-Amino-1-(2,4-dimethoxyphenyl)benzimidazole. Sodium amide [1.46 g (0.04 mole)] was added to a solution of 2 g (0.008 mole) of IV in 10 ml of dimethylaniline, and the mixture was stirred at 130° for 1 h. The mixture was then cooled, 10 ml of water was added, and the dimethylaniline was removed by steam distillation. The dark-brown residue was filtered and washed with benzene to give 1.4 g (66%) of colorless prisms with mp 240-241° (from alcohol). IR spectrum, cm^{-1}: δ_{NH_2} 1660; ν_{NH_2} 3330, 3410. Found: C 66.8; H 5.8; N 15.6%. $C_{15}H_{15}N_3O_2$. Calculated: C 66.9; H 5.6; N 15.6%.

2-Amino-1-(2,5-dimethoxyphenyl)benzimidazole. This compound [1.2 g (60%)] was similarly obtained with the only difference that the precipitate after removal of the dimethylaniline by distillation was purified by chromatography (Al_2O_3 and chloroform). The colorless prisms melted at 227-228° (from benzene). IR spectrum, cm^{-1}: δ_{NH_2} 1665; ν_{NH_2} 3310, 3445. Found: C 66.7; H 5.4; N 15.9%. $C_{15}H_{15}N_3O_2$. Calculated: C 66.9; H 5.6; N 15.6%.

Amination of 1-(p-Methoxybenzyl)benzimidazole (VII). A mixture of 2 g (0.0084 mole) of VII and 1.46 g (0.04 mole) of sodium amide in 8 ml of dimethylaniline was stirred at 140° for 1.5 h. The mixture was cooled, 6 ml of water was added, and the precipitate was removed by filtration and washed with benzene to give 0.15 g (7%) of 1,1'-bis(p-methoxybenzyl)-2,2'-dibenzimidazolyl as colorless plates with mp 295-296° (dec., from butanol). Found: C 76.1; H 5.2; N 12.0%. $C_{30}H_{26}N_4O_2$. Calculated: C 75.9; H 5.5; N 11.8%. The dimethylaniline was removed from the filtrate after filtration by steam distillation, and the amine was extracted from the residue with chloroform. The compound was purified by chromatography (Al_2O_3 and chloroform) to give 1.3 g (61%) of colorless prisms of 1-(p-methoxybenzyl)-2-aminobenzimidazole with mp 177-178° (from benzene). IR spectrum, cm^{-1}: δ_{NH_2} 1660; ν_{NH_2} 3375, 3470. Found: C 70.9; H 6.1; N 16.6%. $C_{15}H_{15}N_3O$. Calculated: C 71.1; H 6.0; N 16.6%.

2-Amino-1-(p-hydroxybenzyl)benzimidazole. A mixture of 1 g (4.4 mmole) of 1-(p-hydroxybenzyl)-benzimidazole and 0.78 g (20 mmole) of sodium amide in 7 ml of dimethylaniline was stirred at 190° for 2 h. The mixture was cooled, 5 ml of water was added, and the dimethylaniline was removed by steam distillation. The residue was acidified with concentrated HCl to pH 2-3, and the solution was refluxed with activated charcoal. The mixture was filtered, and the filtrate was made alkaline with 22% ammonium hydroxide to give 0.8 g of colorless crystals that were a mixture of the starting compound and the amination product. The amine was extracted with hot butanol to give 0.3 g (29%) of product. An alcohol solution of the amine gave an intense color with sodium hypochlorite solution. The colorless needles melted above 360° (from butanol). Found: C 70.5; H 5.6; N 17.7%. $C_{14}H_{13}N_3O$. Calculated: C 70.3; H 5.5; N 17.6%.

2-Aminoisoquinoline. A mixture of 3 g (0.023 mole) of isoquinoline and 4.5 g (0.11 mole) of sodium amide in 15 ml of dimethylaniline was stirred at 120° for 1.5 h. The mixture was cooled, 15 ml of water was added, and the precipitated amine was removed by filtration and washed with benzene and petroleum ether to give 3.2 g (98%) of colorless needles with mp 124-125° (from water) [13]. The yield was 38 and 70%, respectively, when the amination was carried out in toluene [13] and liquid ammonia [14].

Ionization Constants. These were measured with an LPU-01 pH meter at 25 ± 1°. The solvent was water–alcohol (9:1). A 0.001 M solution of the base was titrated with 0.01 N hydrochloric acid. The scatter did not exceed ± 0.06 pK_a units. The IR spectra of mineral oil suspensions were measured with a UR-20 spectrophotometer.

The authors sincerely thank Professor L. N. Yakhontov and Candidate of Chemical Sciences V. A. Azimov for their assistance in the chromatographic determination of the gases.

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