2-(1-Adamantanyl)-3-hydroxy-3-(4-dimethylaminophenyl)isoindolinone Hydrochloride (VIf). A solution of 0.4 g (1 mmole) of amide III in 10 ml of dioxane was saturated with dry hydrogen chloride, after which it was treated with 30-40 ml of ether. After 24 h, the resulting precipitate was separated to give 0.4 g (92%) of a product with mp 130°C (dec.). IR spectrum in Nujol: 1684 (C=O) and 3270 cm^{-1} (broad O–H band). Found: C 71.8; H 6.8; Cl 8.7; N 6.0%. $C_{26}H_{30}N_2O_2 \cdot HCl$. Calculated: C 71.1; H 7.1; Cl 8.1; N 6.4%.

2-(4-Dimethylaminobenzoyl)benzamide (VIII). A 0.4-g (1 mmole) sample of amide III was dissolved with stirring in 5 ml of concentrated sulfuric acid, and the solution was maintained at room temperature for 1 h. It was then poured over 50 g of finely crushed ice, and the precipitate was removed by filtration to give 0.12 g of a substance that was identified as 1-hydroxyadamantane [9]. The filtrate was neutralized to pH 7-8, and the precipitate was separated, washed with water, dried, and recrystallized to give 0.2 g (75%) of a product with mp 177-179°C (from ethanol). IR spectrum in dioxane: 1688 (C=O), 1650 (amide I), and 3430 cm^{-1} (N–H, in Nujol). UV spectrum in dioxane: λ_{max} 342 nm (log ε 4.39). Found: C 71.5; H 5.8; N 10.3%. $C_{16}H_{16}N_2O_2$. Calculated: C 71.6; H 6.0; N 10.4%.

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SYNTHESIS OF AMINOINDOLES BY THE BUCHERER REACTION

A. N. Kost, V. I. Terenin, and L. G. Yudin

UDC 547.754.07

The reaction of 5-hydroxyindoles with ammonia, alkylamines, or dialkylamines in the presence of sulfites leads to the corresponding 5-aminoindoles. Partial or complete elimination of the substituent is observed in the case of indoles that have an electron-acceptor substituent ($COOC_2H_5$, $COCH_3$).

The Bucherer reaction is well known as a method for the conversion of aromatic amines to hydroxy compounds or the conversion of hydroxy compounds to primary, secondary, or tertiary amines. It has been studied systematically in the naphthalene series and among heterocyclic compounds has been used in the synthesis of quinoline and isoquinoline derivatives [1]. There are also data regarding similar transformations of 4-hydroxy- and 4-aminobenzo-2,1,3-thiadiazoles, as well as 4-hydroxybenzofuran and 4-aminobenzofuran [2-4].

We have attempted to use this method for 5-hydroxyindoles, which are quite easily obtainable but are extremely unstable under the influence of extraneous agents. In particular, one might have expected that addition to the C_2–C_3 bond, as described for some indoles under the influence of sulfurous acid [5], would occur under the conditions of the Bucherer reaction. Our attempts showed that when the conditions are selected successfully, one can convert 5-hydroxyindoles (I) to the corresponding 5-amino- or 5-alkylaminoindoles (II) in good yields. In contrast to the classical conditions of the Bucherer reaction, better re-

M. V. Lomonosov Moscow State University, Moscow 117234.

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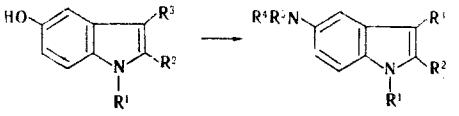
TABLE 1. 5-Aminoindoles

Expt. No.	Aminoindole	Reaction temp., °C (reaction time, h)	mp, °C[a]	PMR spectrum, δ, ppm	IR spectrum (in $CHCl_3$), ν, cm^{-1}	Found, %		Empirical formula	Calculated, %		Yield, %
						C	H		C	H	
1	IIa	170 (6)	158—159[b]								50
2	IIb	170 (12)	105—106	2,0 (3H, s, 2-CH_3), 2,9 (3H, s N—CH_3), 3,0 (1H, s, N—H), 5,9 (1H, s, 3-H), 6,3 (1H, q, J_{67}=9 Hz, J_{64}=2 Hz, 6-H), 6,6 (1H, d, 4-H), 6,8 (1H, d, 7-H), 7,3 (1H, s, 1-H)	3480, 3410 (NH)	75,1	7,6	$C_{10}H_{12}N_2$	75,0	7,5	64
3	IIc	180 (20)	78—79	2,2 (3H, s, 2-CH_3), 3,25 (2H, s, N—H), 3,3 (3H, s, 1-CH_3), 5,8 (1H, s, 3-H), 6,3 (1H, q, J_{67}=8 Hz, J_{64}=2 Hz, 6-H), 6,5 (1H, d, 4-H), 6,75 (1H, d, 7-H)	3440, 3370 (NH)	75,3	7,5	$C_{10}H_{12}N_2$	75,0	7,5	60
4	IId	180 (20)	84—86	2,2 (3H, s, 2-CH_3), 2,7 (3H, s, N—CH_3), 3,0 (1H, s N—H), 3,3 (3H, s, 1-CH_3), 6,3 (1H, q, J_{67}=8 Hz, J_{64}=2 Hz, 6-H), 6,5 (1H, d, 4-H), 6,8 (1H, d, 7-H)	3445, 3405 (NH)	75,4	8,0	$C_{11}H_{14}N_2$	75,4	8,0	37
5	IIe	170 (20)	127—129	1,4 (3H, t, CH_2CH_3), 2,6 (3H, s 2-CH_3), 4,4 (2H, q, CH_2CH_3), 7,2 (1H, q, J_{67}=8 Hz, J_{64}=2 Hz, 6-H), 7,4 (1H, d, 7-H), 8,1 (1H, d, 4-H), 8,6 (3H, s, N—H), 9,5 (1H, s, N—H)	3465, 3400, 3320 (NH) 1665 (CO)[c]	65,5	6,7	$C_{12}H_{14}N_2O_2$	66,1	6,5	50
	IIa		158—159								14
6	IIf	170 (20)	125—126	1,4 (3H, t, CH_2CH_3), 2,65 (3H, s, 2-CH_3), 3,0 (3H, t., N—CH_3), 4,4 (2H, q, CH_2CH_3), 7,2 (1H, q, J_{67}=8 Hz, J_{64}=2 Hz, 6-H), 7,4 (1H, d, 7-H), 8,15 (1H, d, 4-H), 8,7 (2H, s, N—H), 9,5 (1H, s, 1-H)	3465, 3400, 3320 (NH) 1655 (CO)[c]	67,6	7,1	$C_{13}H_{16}N_2O_2$	67,2	6,9	56
	IIb		105—106								12
7	IIg	150 (16)	127—128	1,4 (3H, t, CH_2CH_3), 2,7 (3H, s, 2-CH_3), 3,3 [6H, d, $(CH_3)_2N$], 4,0 (2H, q, CH_2CH_3), 7,1 (1H, q, J_{67}=8 Hz, J_{64}=2 Hz, 6-H), 7,4 (1H, d, 7-H), 8,2 (1H, d, 4-H), 9,5 (1H, s, 1-H)				$C_{14}H_{18}N_2O_2$[d]			28
8	IIh	150 (16)	125—126	1,45 (3H, t, OCH_2CH_3), 1,55 (6H, t, NCH_2CH_3), 2,75 (3H, s, 2-CH_3), 3,7 (4H, q, NCH_2CH_3), 4,45 (2H, q, OCH_2CH_3), 7,1 (1H, q, J_{67}=8 Hz, J_{64}=2 Hz, 6-H), 7,4 (1H, d, 7-H), 8,1 (1H, d, 4-H), 9,4 (1H, s, 1-H)				$C_{16}H_{22}N_2O_2$[e]			28

[a]Compounds IIa, e, f were crystallized from benzene, and IIb-d, g, h were crystallized from heptane. [b]Literature data [7]: mp 157-159°C. [c]The CO band was detected in mineral oil. [d]Molecular weight: Found 246 (by mass spectrometry); calculated 246. [e]Molecular weight: found 274 (by mass spectrometry); calculated 274.



I a-d II a-h

I a $R^1=R^3=H$, $R^2=CH_3$; b $R^1=R^2=CH_3$, $R^3=H$; c $R^1=H$, $R^2=CH_3$, $R^3=COOC_2H_5$; d $R^1=H$, $R^2=CH_3$, $R^3=COCH_3$; II a $R^1=R^3=R^4=R^5=H$, $R^2=CH_3$; b $R^1=R^3=R^4=H$, $R^2=R^5=CH_3$; c $R^1=R^2=CH_3$, $R^3=R^4=R^5=H$; d $R^1=R^2=R^5=CH_3$, $R^3=R^4=H$; e $R^1=R^4=R^5=H$, $R^2=CH_3$, $R^3=COOC_2H_5$; f $R^1=R^4=H$, $R^2=R^5=CH_3$, $R^3=COOC_2H_5$; g $R^1=H$, $R^2=R^4=R^5=CH_3$, $R^3=COOC_2H_5$; h $R^1=H$, $R^2=CH_3$, $R^3=COOC_2H_5$, $R^4=R^5=C_2H_5$

sults are obtained with solutions of neutral salts rather than with bisulfite. The reaction proceeds satisfactorily if a mixture of the amine and a solution of potassium metabisulfite are used.

Indoles that do not contain electron-acceptor groups ($COCH_3$, $COOC_2H_5$) in the 3 position undergo the reaction at 170-180°C to give IIa-d. Thus the known 2-methyl-5-aminoindole (IIa) is obtained in 50% yield from 2-methyl-5-hydroxyindole (Ia).

It should be noted that it is not necessary to prepare the sulfite or bisulfite of methylamine when the hydroxy group is replaced by the methylamino group. A mixture of ammonium bisulfite and methylamine gives the same results; the considerably more nucleophilic methylamine residue consequently undergoes this reaction preferentially.

The 3-carbethoxy group is partially eliminated during the reaction. For example, 2-methyl-3-carbethoxy-5-hydroxyindole (Ic) gave the expected 2-methyl-3-carbethoxy-5-aminoindole (IIe), the PMR spectrum of which (in trifluoroacetic acid) contains a singlet of the 2-CH_3 group (2.6 ppm), a triplet (1.4 ppm) and quartet (4.4 ppm) of the C_2H_5 group, broad singlets of the pyrrole N—H (9.5 ppm) and amine (8.6 ppm) protons, doublets of the 4-H (8.1 ppm, J_{46} = 2 Hz) and 7-H (7.4 ppm, J_{76} = 8 Hz) protons, and a quartet of the 6-H protons (7.2 ppm). However, 2-methyl-5-aminoindole (IIa) was additionally isolated. Similar results were obtained when the hydroxy group was replaced by a methylamino group. Thus a mixture of amines IIf and IIb was obtained from 5-hydroxyindole Ic.

In the case of 2-methyl-3-acetyl-5-hydroxyindole (Id) replacement of the hydroxy group by NH_2 or CH_3NH proceeds primarily with the elimination of the acetyl group, i.e., it leads to amine IIa or IIb. This sort of elimination of a substituent has been frequently noted in the case of various 3-substituted indoles (e.g., see [6]).

The process is more complex with dialkylamines. At 180-200°C we observed the formation of only water-soluble compounds; however, we were able to obtain dialkylaminoindoles IIg and IIh when we lowered the amine concentration and the temperature to 150°C.

Thus hydroxyindoles I, in which the hydroxy group is bonded to the benzene ring, can be converted to aminoindoles II (Table 1).

EXPERIMENTAL

The IR spectra of the compounds were recorded with an IKS-22 spectrometer. The UV spectra of ethanol solutions were recorded with a Specord UV-vis spectrophotometer. The PMR spectra of IIa-d (in CCl_4) and IIe-h (in CF_3COOH) were recorded with a Varian T-60 spectrometer with hexamethyldisiloxane as the standard. The mass spectra were recorded with an MKh-1303 spectrometer with direct introduction of the samples into the ion source. Preparative separation was accomplished in a thin layer of Al_2O_3 (Brockmann activity II) in a benzene—methanol system (9:1).

Method for the Preparation of Aminoindoles IIa-d. A mixture of 3.5 mmole of hydroxyindole Ia, b, 4 g of ammonium bisulfite, and 20 ml of 20% ammonium hydroxide (experiments Nos. 1 and 3) or 33% aqueous methylamine solutions (experiments Nos. 2 and 4) was heated in an autoclave test tube, after which the mixture was extracted with ethyl acetate, and the extract was treated with 2 N HCl solution. The resulting hydrochloric acid solution was made alkaline with 2 N NaOH solution, and the precipitate was removed by filtration and recrystallized.

Method for the Preparation of Aminoindoles IIe, f. A mixture of 10 mmole of hydroxyindole Ic, 4 g of ammonium bisulfite, and 20 ml of 20% ammonium hydroxide (experiment No. 5)

or 33% aqueous methylamine solution (experiment No. 6) was heated in an autoclave test tube, after which the mixture was extracted with ethyl acetate, and the solution was dried with magnesium sulfate. The solvent was removed by evaporation, and the residue was crystallized to give amine IIe or IIf. The same amine, as well as an aminoindole that did not contain a carbethoxy group in the 3 position, was additionally obtained from the mother liquor after separation on Al_2O_3.

Method for the Preparation of Aminoindoles IIg, h. A mixture of 2.25 mmole of hydroxyindole Ic, 4 g of potassium metabisulfite, and 15 ml of 15% aqueous dimethylamine solution (experiment No. 7) or 15% aqueous diethylamine solution (experiment No. 8) was heated in an autoclave test tube, after which the mixture was extracted with ethyl acetate, and the extract was dried with magnesium sulfate. The solvent was removed by evaporation, and the residue was separated preparatively by chromatography on Al_2O_3. The isolated aminoindole was then recrystallized. The yield given is based on the converted hydroxyindole.

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PYRROLOCARBAZOLES.

1. SYNTHESIS AND SOME PROPERTIES OF 3H-PYRROLO[2,3-c]CARBAZOLE

T. E. Khoshtariya, M. I. Sikharulidze, L. G. Tret'yakova, T. K. Efimova, and N. N. Suvorov

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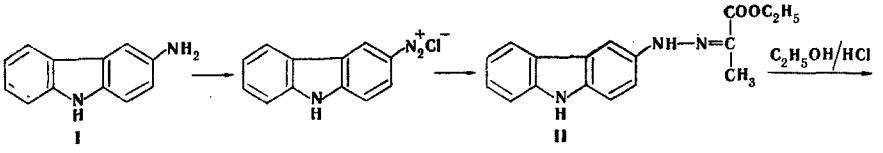
3H-Pyrrolo[2,3-c]carbazole was synthesized from 3-aminocarbazole by means of the Japp–Klingemann reaction. The structure of this heterocycle was proved by a study of the absorption, fluorescence, IR, PMR, and mass spectra. A great analogy between 3H-pyrrolo[2,3-c]carbazole and carbazole as compared with indole in the case of formation of hydrogen bonds was observed; this was indicated by the shift of the absorption band of the NH group in the IR spectra of the investigated compound in the presence of various proton-acceptors.

Despite the large number of studies devoted to the synthesis of indole derivatives, no data on the preparation and properties of 3H-pyrrolo[2,3-c]carbazole are available in the literature.

We accomplished the synthesis of this compound by means of the Japp–Klingemann reaction [1]:



I II

D. I. Mendeleev Moscow Institute of Chemical Technology, Moscow 125047.

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