Thus the data obtained in this study completely unambiguously attest to the unexpectedly small effect of two acetyl groups on the probability of the primary ions. Cleavage of the alkyl chain at the β-carbon–carbon bond to give the corresponding immonium ion turns out to be more favorable energically than detachment of the methyl group adjacent to the carbonyl group and formation of an acylium ion.

The subsequent fragmentation of ions A and B involves elimination of an acetyl group. The removal of ketene is only slightly probable in the case of ions A and is practically unrealizable in the case of ions B.

The formation of an ion with mass 43, evidently corresponding to the $CH_2=C=\overset{+}{O}H$ or CH_3CO^+ structure, is characteristic for all of the examined compounds. The intensity of the peak of this ion is almost identical and does not exceed 5.5% of the total current. The ion with mass 43 has the primary composition C_3H_7 only in the case of XI. This process requires considerable energy expenditure and is not observed when the ionizing-electron energy is lowered.

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PYRROLOINDOLES

I. SYNTHESIS OF 1H,6H-PYRROLO[2,3-e]INDOLE

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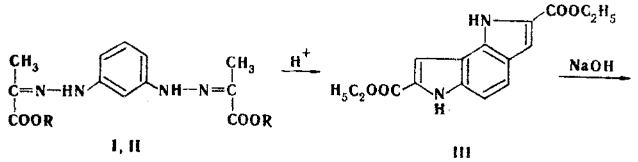
UDC 547.759.3'5.07:541.63:543.422.25.4.6

1H,6H-Pyrrolo[2,3-e]indole was obtained by Fischer cyclization of the m-phenylenedihydrazone of ethyl pyruvate. The structure of the product was proved by analysis of the PMR spectra and mass spectrum. Bands characteristic for the corresponding spectra of indole were observed in the absorption, luminescence, and IR spectra of the pyrroloindole. The geometrical isomers of ethyl pyruvate m-phenylenedihydrazone were isolated.

Despite the fact that pyrroloindoles are the closest analogs of indole, this class of compounds remains practically uninvestigated. The synthesis of pyrroloindole derivatives has been reported in individual studies [1-4], but up until now no one has been able to obtain even enough of the unsubstituted heterocycle to investigate its physicochemical properties.

To obtain 1H,6H-pyrrolo[2,3-e]indole we used Fischer cyclization of pyruvic acid m-phenylenedihydrazone (II) and ethyl pyruvate m-phenylenedihydrazone (I) via the scheme



D. I. Mendeleev Moscow Chemical-Engineering Institute, Moscow 125047. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 938-944, July, 1977. Original article submitted July 8, 1976; revision submitted November 17, 1976.

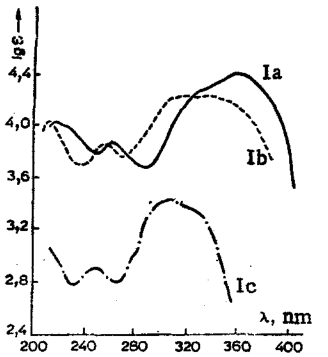
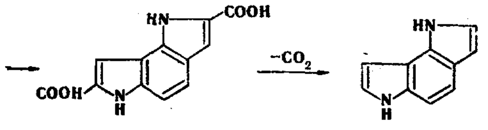


Fig. 1. UV spectra of ethyl pyruvate m-phenylenedihydrazone in heptane: Ia) syn–syn form; Ib) syn–anti form; Ic) anti–anti form.

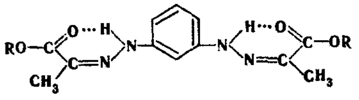


IV V

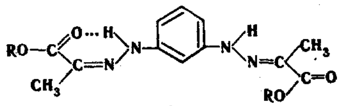
I $R=C_2H_5$; II $R=H$

In the method for the preparation of m-phenylenehydrazine described in [3, 5] hydrogen sulfide was used to remove the tin salts, and the dihydrazine base was isolated with sodium acetate. According to our observations, the presence of tin salts in the reaction mixture does not interfere with the formation of hydrazones I and II, and the reaction can be carried out in acidic media to give the product in quite good yields (40-70%).

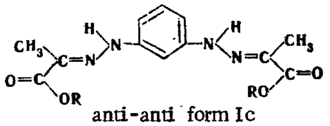
Dihydrazone I has been described as an individual substance with mp 110° [3]. The dihydrazone that we isolated (I) was found to be a mixture of three stereoisomers, which we were able to separate by means of preparative column chromatography to give the syn–syn (Ia), syn–anti (Ib), and anti–anti (Ic) forms:



syn-syn form Ia



syn-anti form Ib



anti-anti form Ic

The study of the geometrical isomerism of dihydrazone I is of great interest, since the formation of a third geometrical isomer – the syn–anti form – is possible in this case.

The physical properties of the syn and anti forms of the hydrazones differ markedly from one another because of the formation of chelate structures with a hydrogen bond [6]; this leads to substantial changes in the UV and IR spectra of the isomers. The presence of a hydrogen bond is manifested in the UF spectra of the syn isomers as a bathochromic shift of the absorption maxima and a sharp increase in the absorption intensity [7]. We observed precisely changes of this type in the spectra of the hydrazones that we isolated. The spectrum of a heptane solution of isomer Ia differs from the spectrum of a heptane solution of isomer Ic with respect to an increase in intensity and a bathochromic shift of the absorption bands (Fig. 1). The long-wave absorption band is shifted particularly markedly (by 50 nm). The spectrum of isomer Ib differs from the spectrum of isomer Ic with respect to the increase in intensity, but the position of the bands undergoes considerably less change: the long-wave band is shifted 10 nm, and a shoulder appears at 360 nm.

The long-wave maximum in the UV spectra of ethanol solutions of Ia-c is observed at 360, 340, and 330 nm, respectively. The absorption maximum of syn–syn isomer Ia is shifted 30 nm to the higher wave-number region relative to anti–anti isomer Ic, and the maximum of syn–anti isomer Ib is shifted 10 nm in the same direction.

A difference in the position of the characteristic absorption bands of the NH group is observed in the IR spectra of Ia-c (in mineral oil). Two absorption bands – a more intense band at 3280 cm^{-1} and a less intense band at 3360 cm^{-1} – are observed in the IR spectrum of anti–anti isomer Ic. Only one absorption band of an NH group at 3270 cm^{-1} is observed in the spectrum of syn–syn form Ia. The spectra of CCl_4 solutions of both

TABLE 1. Chemical Shifts of the Protons of I-V (δ, ppm)

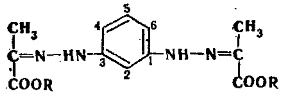
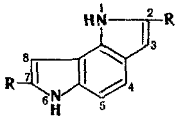
Formula	Compound	R	2H	4H	5H	6H	NH	CH_3	CH_2—Et	CH_3—Et	Solvent
	Ia	C_2H_5	7,07 t	6,69 m	7,13 q	6,69 m	11,95 br.s	2,09 s	4,24 q	1,31 t	d_6-Acetone
	Ib	C_2H_5	7,19 t	6,82 m	7,09 q	6,65 m	9,05 br.s	2,09 s	4,19 q	1,30 t	d_6-Acetone
							11,92 br.s	2,09 s	4,24 q	1,30 t	
	Ic	C_2H_5	7,20 t	6,80 m	7,06 q	6,80 m	9,06 br.s	2,08 s	4,21 q	1,29 t	d_6-Acetone
	II	H	7,34 t	6,93 m	7,14 q	6,93 m	9,73 br.s	2,06 s	—	—	d_6-DMSO

TABLE 1 (continued)

Formula	Compound	R	1H	2H	3H	4H	5H	6H	7H	8H	CH_2—Et	CH_3—Et	Solvent
	III	$COOC_2H_5$	12,24 br.s *	—	7,26 s	7,54 d†	7,28 q	12,04 br.s*	—	7,68 d‡	4,42 q	1,44 t	d_6-DMSO
											4,42 q	1,44 t	
	IV	COOH	12,16 br.s.*	—	7,33 s	7,61 d†	7,35 q	11,88 br.s*	—	7,71 d‡	—	—	d_6-DMSO
	V	H	11,17 br.s *	7,17	6,48 s	7,28 d†	7,14	11,01 br.s*	7,26	6,69 ‡	—	—	d_6-DMSO

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* The reverse assignment of the indicated signals to the 1H and 6H protons is possible.

† $J_{4,5}$ ≈ 8.5-8.8 Hz.

‡ $J_{5,8}$ ≈ 0.8 Hz.

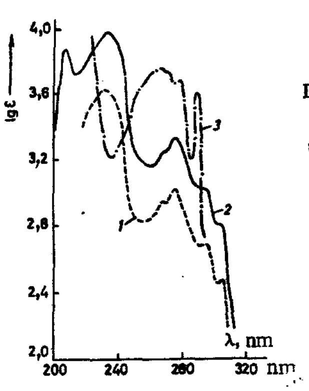


Fig. 2

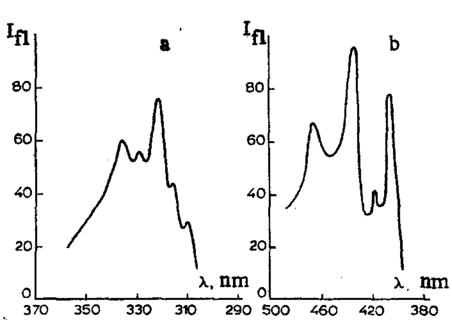


Fig. 3

Fig. 2. UV absorption spectra of 1H,6H-pyrrolo[2,3-e]indole (V) and indole: 1) V in heptane; 2) V in alcohol; 3) indole in heptane.

Fig. 3. Fluorescence (a) and phosphorescence (b) spectra of 1H,6H-pyrrolo[2,3-e]indole (V).

of these isomers contain only one absorption band of an NH group – at 3285 cm^{-1} for syn–syn isomer Ia and at 3385 cm^{-1} for anti–anti isomer Ic. The spectrum of syn–anti isomer Ib (in mineral oil) contains an intense absorption band at 3320 cm^{-1} and a less intense band at 3270 cm^{-1}. Two absorption bands corresponding to the absorption bands of the NH group in the spectra of syn–syn isomer Ia (3290 cm^{-1}) and anti–anti isomer Ic (3380 cm^{-1}) are also observed in the spectrum of a CCl_4 solution of syn–anti isomer Ib.

A comparison of the PMR spectra (Table 1) of hydrazones Ia-c shows the isomer Ib, in contrast to isomers Ia and Ic, is unsymmetrical, i.e., it is the syn–anti isomer. The disparity in the chemical shifts of the C_4H and C_6H protons of the benzene ring of isomer Ib and in the chemical shifts of the protons of identical groups of substituents in the 1 and 3 positions attests to this. The shift of the signal of the protons of one of the amino groups of the isomer to considerably weaker field (11.97 ppm) as compared with the other (9.03 ppm) is evidently associated with participation of this proton in the strong intramolecular hydrogen bond that is possible in the case of a syn orientation of the substituent. The same difference is observed between the chemical shifts of the protons of the groups of the syn–syn isomer (11.89 ppm) that participate in an intramolecular hydrogen bond and those of the anti–anti isomer (9.07 ppm), in which this sort of bond is impossible.

The IR and PMR spectroscopic data confirm the conclusions drawn on the basis of the absorption spectra and make it possible to definitively assign a syn–syn configuration to Ia, an anti–anti configuration to Ic, and a syn–anti configuration to Ib.

We were able to accomplish the cyclization of hydrazones I and II with dry HCl in absolute alcohol.

Compound V was obtained by thermal decarboxylation of 1H,6H-pyrrolo[2,3-e]indole-2,7-dicarboxylic acid (IV). The angular structure of this heterocycle is confirmed by a study of the PMR spectra of both pyrroloindole V itself and its 2,7-dicarbethoxy (III) and 2,7-dicarboxy (IV) derivatives (Table 1). Two singlets belong to the pyrrole ring NH and β-CH protons in the PMR spectra of III and IV; this constitutes evidence for nonequivalence of the two NH protons and the β-CH protons in the molecules of the indicated compounds. The assumption of the symmetrical linear structure of the pyrroloindole ring in III and IV can be repudiated on the basis of this. The angular structure of these compounds also follows from the large constant of spin–spin coupling with the protons of the benzene ring ($J \sim 8.8$ Hz), which constitutes evidence for their ortho orientation.

The presence in the spectra of III and IV of long-range spin–spin coupling of one of the protons of the phenyl ring with the proton of the CH group of one of the pyrrole rings ($J \sim 0.8$ Hz) makes it possible to assign the corresponding signals to the 5H and 8H protons on the basis of the known stereospecificity of the J constant in unsaturated polycyclic compounds ("double trans–trans zigzag") [8]. This assignment is also in agreement with the weak-field shift of the signal of the 8H proton, which is drawn together with the adjacent pyrrole ring and is subject to the effect of its ring current, relative to the signal of the 3H proton, for which the effect should be weaker.

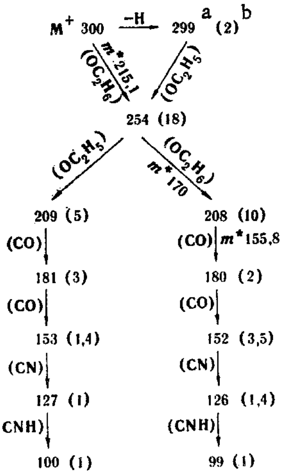
The same peculiarities are also characteristic for the PMR spectrum of V, in which the ratio of the sig-

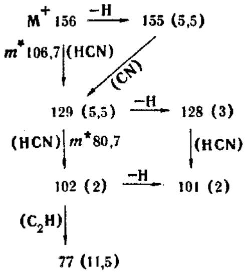
TABLE 2. Absorption Bands of the NH Groups of Indole and Pyrroloindole in the Presence of Some Acceptors

Acceptor	Indole, ν, cm^{-1}	1H,6H-Pyrrolo[2,3-e]indole, ν, cm^{-1}
$CHCl_3$	3495 (NH bond), 3410	3495 (NH bond), 3400
KBr	3405	3385, 3420
$H_5C_2OC_2H_5$	3320	3330
CH_3Cl	3384	3400
Pyridine	3240	3250

nals to the 2H and 7H protons is realized by the double-resonance method by suppression of the 2H-3H and 7H-8H spin–spin couplings.

The structures of III and V are also confirmed by a study of their mass spectra. The molecular weights of III and V determined by mass spectrometry correspond to the calculated values, and the character of the subsequent fragmentation, which is confirmed by the metastable transition, does not contradict the proposed structures. The schemes of fragmentation of III and V are as follows:





The fragmentation of 1H,6H-pyrrolo[2,3-e]indole under the influence of electron impact does not differ fundamentally from the fragmentation of indole itself [9, 10].

Two intense absorption bands at 208 and 233 nm and a band of low intensity at 265–307 nm are observed in the absorption spectrum of 1H,6H-pyrrolo[2,3-e]indole (V) in ethanol. Replacement of the polar solvent by a nonpolar solvent does not affect the position of the absorption bands (Fig. 2).

The position of the principal emission band in the fluorescence spectrum of V coincides with the emission band in the spectrum of indole (322 and 320 nm, respectively), but the spectrum of V has several additional bands that are not present in the spectrum of indole (310, 316, 329, and 336 cm) (Fig. 3, spectrum a).

The phosphorescence spectrum of 1H,6H-pyrrolo[2,3-e]indole also resembles the spectrum of indole [11], except that the longest-wave band displays a bathochromic shift of 20 nm (Fig. 3, spectrum b).

Absorption bands belonging to the NH group are observed at 3385 and 3420 cm^{-1} in the IR spectrum of KBr pellets of V. The absorption band of the NH group appears in the IR spectrum of a $CHCl_3$ solution of V at 3495 cm^{-1}, i.e., it coincides with the absorption band of the indole NH group (Table 2).

A comparison of the donor properties of the angular pyrroloindole and indole during the formation of complexes by means of hydrogen bonds with some acceptors shows that in most cases the absorption band of the associated NH group of the pyrroloindole is shifted to the higher-frequency region as compared with indole. This shift amounts to 10–15 cm^{-1} and demonstrates the somewhat weaker donor properties of pyrroloindole as compared with indole during the formation of complexes by means of hydrogen bonds (Table 2).

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[a] Here and subsequently, the m/e values are presented.

[b] Here and subsequently, the relative intensities with respect to the total ion current are presented.

EXPERIMENTAL

The course of the reactions and the purity of the compounds were monitored on Silufol UV-254. The UV spectra of the compounds were recorded with a Specord spectrophotometer. The IR spectra were recorded with a UR-20 spectrometer with NaCl and LiF prisms. The mass spectra were recorded with an MKh-1303 mass spectrometer with a modified system for introduction of the samples (direct introduction into the ion source) and a system for recording at an ionizing-electron energy of 50 eV. The PMR spectra were recorded with a JNM-MH-100 spectrometer (100 MHz) with hexamethyldisiloxane as the internal standard. The luminescence spectra were recorded with an SDL-1 spectrophotometer with monochromatic excitation (λ = 274 nm) of the slit (inlet 0.22 mm, middle 1.8 mm, and outlet 0.23 mm) and with a photoelectric apparatus with a spark phosphoroscope (with W–Fe electrodes) with an amplification of 0.3/1000 V; third degree 0.2/0.4.

m-Phenylenehydrazine, A solution of 11.5 g (0.167 mole) of sodium nitrite in 40 ml of water was added dropwise with vigorous stirring at −5° to a suspension of 14.48 g (0.08 mole) of m-phenylenediamine dihydrochloride in 300 ml of concentrated HCl. Chunks of pure ice (a total of no more than 120 g) were added periodically to the reaction mixture. After the addition of the nitrite solution was completed, the mixture was stirred for another 5-10 min. It was then added in a fine stream with vigorous stirring to a cooled (to −5°) solution of the reducing agent (obtained from 70 g of $SnCl_2$ and five to six granules of tin metal, which were dissolved in 160 ml of concentrated HCl by heating on a water bath. The resulting solution was cooled and treated with 180 ml of HCl). The resulting white precipitate of m-phenylenedihydrazine was separated, washed with isopropyl alcohol and ether, and dissolved at 40° in a small amount of water.

Mixture of Isomers of Ethyl Pyruvate m-Phenylenedihydrazone (I). The aqueous solution of the dihydrazine was alkalized with sodium acetate to pH 4, and the mixture was added with stirring and cooling to a solution of 18.56 g (0.16 mole based on the starting m-phenylenediamine dihydrochloride) of ethyl pyruvate in ethanol, and the mixture was stirred for another hour. It was then extracted with ether, and the extract was washed successively with sodium bicarbonate solution and water. It was then dried over anhydrous sodium sulfate and filtered, and the solvent was evaporated from the filtrate to give an oily residue, which was found to be a mixture of isomeric ethyl pyruvate m-phenylenedihydrazones. The yield was 10.68 g (40% based on the m-phenylenediamine dihydrochloride). This mixture was separated into its individual components by column chromatography (see below).

anti–anti Form (Ic) of Ethyl Pyruvate m-Phenylenedihydrazone. The mixture of isomers I was dissolved in benzene, and the light-yellow precipitate that formed after a certain time was removed by filtration, washed, and vacuum dried at 60° and a residual pressure of 2 mm (mercury column) to give 5 g (47% based on the mixture of isomeric dihydrazones I) with mp 125-126° and R_f 0.41 [benzene–acetone (5:1)]. Found: C 57.3; H 6.8; N 17.0%. $C_{16}H_{22}N_4O_4$. Calculated: C 57.5; H 6.6; N 16.8%. UV spectrum (in ethanol), λ_{max} (log ε): 253 (3.8) and 330 nm (4.33).

syn–anti Form (Ib) and syn–syn Form (Ia) of Ethyl Pyruvate m-Phenylenedihydrazone. A benzene solution of a mixture of isomers Ia and Ib containing a certain amount of isomer Ic was vacuum evaporated, and the residue was chromatographed with a 60-cm long column with a diameter of 3 cm filled with silica gel (particle size 100-250 μm). Elution with benzene gave 0.3 g (3% based on the mixture of isomeric dihydrazones I) with mp 101-102° and R_f 0.63 ($CHCl_3$). Found: C 58.2; H 7.1; N 16.4%. $C_{16}H_{22}N_4O_4$. Calculated: C 57.5; H 6.6; N 16.8%. UV spectrum (in ethanol), λ_{max} (log ε): 263 (3.85) and 360 nm (4.34). Also obtained was 3.2 g (30% based on the mixture of isomeric hydrazones I) of isomer Ib with mp 103-104° and R_f 0.65 [benzene–acetone (5:1)]. Found: C 57.4; H 6.6; N 16.8%. $C_{16}H_{22}N_4O_4$. Calculated: C 57.5; H 6.6; N 16.8%. UV spectrum (in ethanol), λ_{max} (log ε): 258 (3.68) and 340 nm (4.20). Isomer Ic [1.6 g (15%)] eluted with benzene–acetone (5:1).

Pyruvic Acid m-Phenylenedihydrazone (II). An aqueous solution of the dihydrazine obtained from 72.4 g (0.4 mole) of m-phenylenediamine dihydrochloride was alkalized to pH 3 with sodium acetate, and the solution was added with stirring to an aqueous solution of 70.4 g of freshly distilled pyruvic acid (0.8 mole based on the starting m-phenylenediamine dihydrochloride). After 1 h, the solid material was removed by filtration, washed with hot water, and dried to give 78 g (70% based on the starting diamine dihydrochloride) of light-yellow crystals with mp 195-196° and R_f 0.58 (acetone). Found: C 52.0; H 5.8; N 19.6%. $C_{12}H_{14}N_4O_4$. Calculated: C 5.18; H 5.1; N 20.1%. IR spectrum (in mineral oil): 3310 and 3380 (NH); 1720 cm^{-1} (C=O). UV spectrum (in ethanol), λ_{max} (log ε): 212 (3.34), 244 (2.92), and 310 nm (3.49).

Diethyl 1H,6H-Pyrrolo[2,3-e]indole-2,7-dicarboxylate (III). A 10.6-g (0.03 mole) sample of dihydrazone I was added to a three-necked flask equipped with a stirrer and reflux condenser, and the solid was dissolved with stirring in 30 ml of a 20% solution of HCl in absolute alcohol, after which the solution was refluxed gently for 4 h. It was then cooled and poured into water, and the precipitated crystals were removed by filtration, washed with water, and dried to give 2 g (20%) of crude product. The same product can be obtained from dihydrazone II. The reaction was carried out under similar conditions, except that a twofold amount of the catalyst (20% HCl in absolute alcohol) was used. The yield of crude product, with mp 266-267° [from alcohol or by chromatography with a column filled with silica gel (particle size 100-250 μm) (elution with diethyl ether)] and R_f 0.52 [benzene–acetone (5 : 1)], was obtained in 20% yield. Found: C 63.8; H 5.5; N 9.2%. $C_{16}H_{16}N_2O_4$. Calculated: C 64.0; H 5.4; N 9.3%. IR spectrum (in $CHCl_3$): 3480 (NH) and 1700 cm^{-1} (C=O). UV spectrum (in ethanol), λ_{max} (log ε): 208 (4.07) and 294 (4.40). Compound III was obtained as yellow crystals and gave a crimson coloration when it was heated with Erlich's reagent.

1H,6H-Pyrrolo[2,3-e]indole-2,7-dicarboxylic Acid (IV). A 1.5-g (0.005 mole) sample of III and 70 ml of absolute alcohol were placed in a three-necked flask equipped with a stirrer and a reflux condenser, and a solution of 1.2 g (0.03 mole) of NaOH in 30 ml of absolute ethanol was added in portions to the heated suspension. The mixture was then refluxed for another 2 h, and the precipitated sodium salt of acid IV was removed by filtration, washed with alcohol and ether, and dried on the filter. The filtrate was acidified to pH 1 and extracted with ethyl acetate. The extract was washed to neutrality with water, and the solvent was evaporated to give 0.07 g of IV. The salt of acid IV was dissolved in 200 ml of water, the solution was filtered, and the filtrate was acidified to pH 1. The resulting precipitate was removed by filtration, washed with water, and dried to give 0.87 g of the acid for an overall yield of 0.94 g (77%). For analysis, an ethyl acetate solution was passed through a layer of silica gel (5/40 μm) to give a product with mp 230-236° (dec.) and R_f 0.44 (ethyl acetate). Found: C 59.2; H 4.0; N 11.0%. $C_{12}H_8N_2O_4$. Calculated: C 59.0; H 3.3; N 11.5%. IR spectrum (in mineral oil): 3450 (NH) and 1690 cm^{-1} (C=O). UV spectrum (in ethanol), λ_{max} (log ε): 208 (4.07), 250 (3.68), and 285 (4.43). Compound IV was obtained as a yellowish-grayish powder that gave a blue-violet coloration when it was heated with Erlich's reagent.

1H,6H-Pyrrolo[2,3-e]indole (V). A 1.2-g (0.005 mole) sample of IV was placed in a two-necked flask equipped with a gas-inlet tube, and the contents were heated under argon at 230-240° for 20 min until CO_2 evolution ceased. The mixture was then cooled to room temperature and extracted with acetone. The extract was evaporated, and the product was dried and dissolved in ~10 ml of benzene. The benzene solution was chromatographed on silica gel (100-250 μm) (elution with benzene). The benzene was removed from the eluate by distillation, and the residue was recrystallized from petroleum ether–benzene (10 : 1) to give 0.23 g (30%) of a product with mp 134.5-135° and R_f 0.42 [benzene–acetone (5 : 1)]. Found: C 77.0; H 5.4; N 17.8%. $C_{10}H_8N_2$. Calculated: C 76.9; H 5.1; N 17.9%. The product was obtained as colorless flocculent crystals that gave a blue coloration when they were treated with Erlich's reagent at room temperature.

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