PYRROLOINDOLES.

13.* PROPERTIES OF 1H,10H-BENZO[e]-PYRROLO[3,2-g]INDOLE

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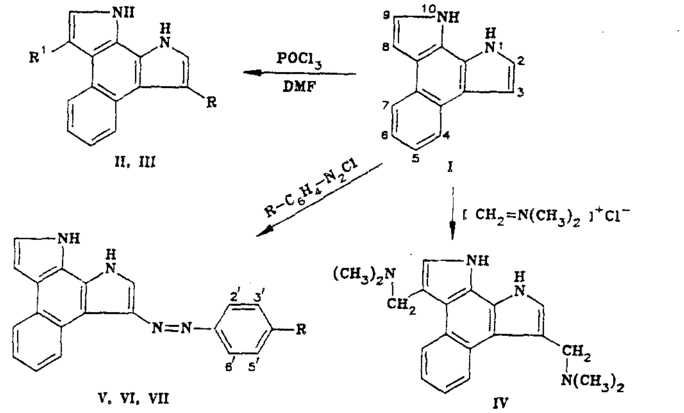
1H,10H-Benzo[e]pyrrolo[3,2-g]indole reacts with the Vilsmeier and Mannich reagents to give disubstituted compounds, whereas monosubstitution products are formed in the case of diazo coupling.

The new unsubstituted heterocycle 1H,10H-benzo[e]pyrrolo[3,2-g]indole (I) obtained by us was described in [1]. The benzopyrroloindole molecule was subjected to quantum-chemical calculation by the SCF MO MINDO/3 method† to establish the character of the electron-density distribution in the molecule of heterocycle I. It is apparent from the molecular diagram (Fig. 1) that the character of the electron-density distribution of the indole ring is retained in the molecule. Consequently, the primary centers of attack in electrophilic substitution reactions are the 3 and 8 positions.

As in the previously studied 1H,6H-indolo[7,6-g]indole [2] and 1H,6H-pyrrolo[2,3-e]indole [3], 1H,10H-benzo[e]pyrrolo[3,2-g]indole forms a monosubstitution product – 3-formyl-1H,10H-benzo[e]pyrrolo[3,2-g]indole (II) – in the formylation reaction (at a benzopyrroloindole–Vilsmeier reagent ratio of 1:3) at 50°C, whereas it forms 3,8-diformyl-1H,10H-benzo[e]pyrrolo[3,2-g]indole (III) when a fivefold excess of the Vilsmeier reagent is used. The formation of 2-formylbenzopyrroloindole is not observed.



II R=CHO, R¹=H; III R=R¹=CHO; V R=Cl; VI R=NO_2; VII R=H

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*See [1] for communication 12.

†The calculations were made by Dzh. A. Kereselidze.

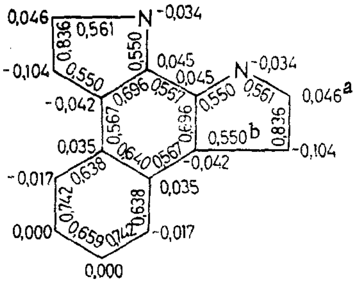

Fig. 1. Molecular diagram of 1H,10H-benzo[e]pyrrolo[3,2-g]indole: a) charge densities on the atoms; b) Wiberg indexes.

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TABLE 1. PMR Spectra of I-IV

Compound*	Chemical shifts, δ, ppm								SSCC, J, Hz
	1-H (br.s)	2-H	3-H	4-H; 7-H	5-H; 6-H	8-H	9-H	10-H (br.s)	
I	10,3	7,17 dd	7,02 dd	8,18 dd	7,33 dd	7,02 dd	7,17 dd	10,3	$J_{12}=2{,}6$; $J_{13}=2{,}4$; $J_{23}=3{,}0$; $J_{45}=6{,}3$; $J_{46}=3{,}2$ $J_{89}=3{,}0$; $J_{810}=2{,}4$
II	11,8	7,86 br. s	9,69 s CHO	8,1—8,3	7,3—7,4	7,0 dd	~7,4	10,8	
III	11,8	7,93 br.s	9,78s CHO	8,25 dd	7,48 dd	9,78 s CHO	7,93 br.s	11,8	$J_{45}=6{,}3$; $J_{46}=3{,}4$
IV	10,5	6,86 d	3,65s CH_2; 2,26s CH_3	8,15 dd	7,34 dd.	3,65 s CH_2; 2,26 s CH_3	6,86 d	10,5	$J_{12}=2{,}93$; $J_{45}=5{,}9$; $J_{46}=2{,}9$

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*d_6-Acetone was used as the solvent in obtaining the PMR spectra of I and IV, while d_6-DMSO was used for II and III.

The IR spectra of II and III contain two absorption bands of NH groups at 3270 and 3320 cm^{-1} and 3290 and 3390 cm^{-1}, respectively, which are shifted to the low-frequency region as compared with the spectrum of the unsubstituted heterocycle (3400, 3450 cm^{-1}) because of the formation of a CO...NH intermolecular hydrogen bond. The absorption of the carbonyl groups in the spectra of II and III is observed in the form of characteristic bands at 1630, 1650, and 1700 cm^{-1}. In the UV spectra of II and III the introduction of a formyl group into the unsubstituted benzopyrroloindole molecule gives rise to an increase in the intensities of the bands and a bathochromic shift of the absorption maxima.

The molecular masses of II and III found by mass spectrometry correspond to the calculated values, and the schemes of the fragmentation of the molecules do not contradict the proposed structures. The scheme of the fragmentation is as follows from dialdehyde III*:

$$M^{+}\ 262\ (100) \xrightarrow{-CO} 234\ (6) \xrightarrow{-CO} 206\ (21) \xrightarrow{-H} 205\ (96) \xrightarrow{-HCN} 178\ (12) \xrightarrow{-HCN} 151$$

The dimethylaminomethylation of the benzopyrroloindole using dimethylmethyleneimmonium chloride in dry DMF proceeds at 20°C with the formation of 3,8-bis(dimethylaminomethyl)-1H,-10H-benzo[e]pyrrolo[3,2-g]indole (IV). Two absorption bands of an indole NH group at 3485 and 3250 cm^{-1} appear in the IR spectrum of IV.

The mass spectrum of IV contains a low-intensity molecular-ion peak (M^+) at 320 (3.3). The loss of two dimethylamine residues $N(CH_3)_2$ leads to the ion at 232 (10). The rather high intensity of the peak at 231 (20) is explained by rearrangement of the ion at 232, which proceeds with the detachment of hydrogen and expansion of one pyrrole ring to a quinoline ring [4]. The fragment ion with the maximum intensity in the spectrum at 214 (100) is probably formed through the successive loss by the ion at 231 of two hydrogen atoms and a CH_3 group.

As in the case of 1H,6H-indolo[7,6-g]indole [2], only monosubstituted derivatives — 3-(p-chlorophenylazo)-, 3-(p-nitrophenylazo)-, and 3-phenylazo-1H,10H-benzo[e]pyrrolo[3,2-g]-indole (V-VII) — were isolated from the reaction products as a result of the diazo coupling of benzopyrroloindole with p-chloro-, p-nitro-, and benzenediazonium chlorides. We were unable to obtain disubstituted derivatives using a large excess of the diazo component, evidently because of the weak electrophilicity of the ArN_2^+ ion.

In the IR spectra of V-VII stretching vibrations of NH groups appear at 3415 (sh), 3385, 3380, and 3430 (sh) and at 3380 and 3410 cm^{-1}, respectively. Intense absorption bands corresponding to the symmetrical (at 1260-1320 cm^{-1}) and asymmetrical (at 1560-1630 cm^{-1}) vibrations of a nitro group are also observed in the spectrum of VI. Absorption bands in the visible region of the spectrum at 510, 568, and 540 nm, respectively, which are due to lengthening of the conjugated chain, appear in the electronic spectra of V-VII.

The PMR spectra of III and IV correspond to symmetrical structures (Table 1). One signal of protons of an NH group and one signal of protons of the α positions of the pyrrole ring are observed in the spectra; in the case of III the latter signal shows up in the form

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*Here and subsequently, the m/z values are presented, and the I_{rel} values are given in parentheses.

TABLE 2. PMR Spectra of V-VII

Compound*	Chemical shifts, δ, ppm										SSCC, J, Hz
	1-H (br.s)	2-H (br.s)	4-H	5-H, 6-H	7-H	8-H (dd)	9-H	10-H (br.s)	2'-H, 6'-H	3'-H, 5'-H	
V	11,3	7,97	8,38 m	7,4—7,5	8,27 m	7,15	7,45 dd	10,79	7,86 d	7,55 d	$J_{89}=2{,}93$; $J_{810}=2{,}20$; $J_{910}=2{,}56$; $J_{2'3'}=J_{5'6'}=8{,}77$
VI	11,3	7,99	8,3 m	7,4—7,5	7,9 m	7,09	~7,4	10,8	7,86 d	8,27 d	$J_{89}\approx 3$; $J_{810}=2{,}5$; $J_{2'3'}=J_{5'6'}=9{,}2$
VII	11,6	7,86	8,1—8,3	7,3—7,5	8,1—8,3	7,03	~7,4 m	11,0	7,8	3'-H, 4'-H, 5'-H 7,3—7,5	$J_{89}=J_{810}=2{,}7$

*d_6-Acetone was used as the solvent in obtaining the PMR spectra of V and VI, while d_6-DMSO was used for VII.

of a broad singlet because of rapid NH → ND exchange, while in the case of IV it appears in the form of a doublet at 6.86 ppm with J = 2.93 Hz shifted to strong field as compared with the analogous signal of unsubstituted I as a consequence of the electron-donor effect of the dimethylaminomethyl group. Signals of protons of the β positions of the pyrrole rings are absent in the spectra. The protons of the naphthalene ring give two signals in the form of a doublet of doublets with ortho and meta spin-spin coupling constants.

Because of the unsymmetrical character of the molecules, two sets of signals are observed in the PMR spectra of II and V-VII (Tables 1 and 2): two signals of NH groups of substituted and unsubstituted pyrrole rings appear; the protons of the naphthalene ring (4-H, 5-H, 6-H, 7-H) give complex multiplets as a consequence of superimposition of their signals. The presence of aldehyde and azo groups in the 3 position of benzopyrroloindole in II and V-VII is confirmed by the absence of the signal of a 3-H proton and the shift of the signal of the 2-H proton to weak field as compared with the analogous signal of the unsubstituted ring. This signal shows up in the form of a broad singlet as a consequence of rapid NH → ND exchange, in contrast to the signal of the 9-H proton of the unsubstituted pyrrole ring.

EXPERIMENTAL

The course of the reactions and the purity of the compounds were monitored on Silufol UV-254. Preparative chromatography of the compounds was carried out on SiO_2 (100/250 μm). The IR spectra of suspensions of the compounds in mineral oil were recorded with a UR-20 spectrometer. The UV spectra of solutions in ethanol were recorded with a Specord spectrophotometer. The PMR spectra were recorded with Varian CFT-20 (80 MHz) and WP-20SI (200 MHz) spectrometers with tetramethylsilane (TMS) as the internal standard. The mass spectra of II and IV were recorded with an R-10-10B quadrupole chromatographic mass spectrometer connected to a Sidar system for data processing* at an ionizing voltage of 70 eV and an emission current of 200 mA; the mass spectrum of III was recorded with an MKh-1303 spectrometer at an ionizing voltage of 70 eV. The calculations were made by means of the program developed in the NMR Laboratory of Moscow State University [5] with a BÉSM-6 computer at the Institute of Applied Mathematics of Tbilisi State University.

3-Formyl-1H,10H-benzo[e]pyrrolo[3,2-g]indole (II). A 0.39 ml (4.2 mmole) sample of freshly distilled $POCl_3$ was added dropwise at 0°C to 1.16 ml (15 mmole) of DMF, and the mixture was stirred at room temperature for 30 min. It was then cooled again to 0°C, and a solution of 0.3 g (1.4 mmole) of I in 2 ml of DMF was added relatively rapidly. The mixture was stirred for 1 h at 50°C, after which it was cooled and poured into water. The aqueous mixture was made alkaline to pH 10 with 10% NaOH solution, and the precipitate was removed by filtration and washed with water until the wash water was neutral. This procedure gave

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*The spectra were recorded in the Republican Mass Spectrometry Center at Tbilisi State University.

a mixture of aldehydes of benzopyrroloindole, which was separated with a column by elution in benzene to give 0.17 g (50%) of II with mp 293-294°C and R_f 0.62 [benzene–acetone (1:1)]. IR spectrum: 3270 sh, 3320 (NH), 1630 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 224 (3.58), 254 (3.78), 296 (3.13), 307 (3.21), 326 nm (3.47). Found: C 76.7; H 4.2; N 12.1%; M^+ 234. Fragmentation scheme:

$$M^+\ 234\ (100) \xrightarrow{-CO} 206\ (15) \xrightarrow{-H} 205\ (18) \xrightarrow{-HCN} 178\ (10) \xrightarrow{-HCN} 151\ (7)$$

$C_{15}H_{10}N_2O$. Calculated: C 76.9; H 4.3; N 12.0%; M 234. The product gave a yellow coloration with Erlich's reagent. Dialdehyde III was not eluted from the column.

3,8-Diformyl-1H,10H-benzo[e]pyrrolo[3,2-g]indole (III). A 1.36 ml (18 mmole) sample of distilled DMF was cooled to –5°C, 0.47 ml (5 mmole) of freshly distilled $POCl_3$ was added dropwise, and the mixture was stirred at room temperature for 30 min. It was then cooled again to –5°C, a solution of 0.2 g (1 mmole) of I in 1.4 ml of DMF was added slowly, and the mixture was stirred at 40-45°C for 1 h. A yellow precipitate formed. The reaction mass was poured into ice water, and the aqueous mixture was made alkaline to pH 10 with 10% NaOH solution and allowed to stand overnight. The precipitate was removed by filtration, washed with water until the wash water was neutral, dried, and recrystallized from DMF to give 0.16 g (64%) of a product with mp 337°C (dec.) and R_f 0.52 (ether). IR spectrum: 3290, 3390 (NH), 1650, 1700 cm^{-1} (C=O). UV spectrum, λ_{max}: 208, 217, 236, 250, 257, 278, 289, 322, 342, 353 nm. Found: C 73.5; H 3.8; N 10.2%; M^+ 262. $C_{16}H_{10}N_2O_2$. Calculated: C 73.3; N 3.8; N 10.7%; M 262.

3,8-Bis(dimethylaminomethyl)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (IV). A solution of 0.2 g (1 mmole) of I in 10 ml of DMF was added dropwise at 0°C to a suspension of 1 g of the crystalline Mannich reagent in 10 ml of distilled DMF, and the mixture was stirred at room temperature for 1 h. It was then diluted with water, made alkaline to pH 10 with dilute NaOH solution, and extracted with ether. The ether extract was dried with Na_2SO_4, the solution was evaporated, and the residue was crystallized by trituration with benzene to give 0.1 g (33%) of colorless crystals with mp 109-110°C and R_f 0.4 [ethanol–ammonia (3:1.5)]. IR spectrum: 3485, 3250 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 217 (4.63), 229 (4.73), 251 (5.07), 273 (4.85), 286 (4.51), 317 (4.23), 329 nm (4.11). Found: C 74.8; H 8.0; N 17.1%; M^+ 320. $C_{20}H_{24}N_4$. Calculated: C 75.0; H 7.5; N 17.5%; M 320.

3-(p-Chlorophenylazo)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (V). A solution of 3 mmole of p-chlorobenzenediazonium chloride was added dropwise at –5°C to a solution of 0.2 g (1 mmole) of I in 10 ml of dioxane and 10 ml of water while maintaining the pH at 6-7 by the addition of sodium acetate, after which the mixture was stirred for 30 min. It was then extracted with ether, and the extract was dried with Na_2SO_4 and evaporated. The residue was dried and purified by column chromatography [benzene–ether (10:1)] to give 0.1 g (30%) of a product with mp 216-217°C and R_f 0.35 (benzene). IR spectrum: 3415 sh, 3385 (NH), 1420 cm^{-1} (N=N). UV spectrum, λ_{max} (log ε): 206 (4.22), 231 (4.55), 274 (4.37), 270 (4.42), 510 nm (4.54). Found: Cl 10.1; N 15.7%. $C_{20}H_{13}ClN_4$. Calculated: Cl 10.3; N 16.3%; M 344.5.

3-(p-Nitrophenylazo)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (VI). This compound was obtained from 0.41 g (2 mmole) of I and 6 mmole of diazotized p-nitroaniline by a procedure similar to that used to prepare V. Chromatography with a column by elution with benzene gave 0.21 g (30%) of VI with mp 300°C (dec.) and R_f 0.55 [benzene–acetone (10:1)]. IR spectrum: 3380, 3430 sh (NH), 1260-1320, 1560-1630 cm^{-1} (NO_2). UV spectrum, λ_{max} (log ε): 208 (4.13), 229 (4.38), 267 (4.19), 568 nm (4.44). Found: N 19.5%. $C_{20}H_{13}N_5O_2$. Calculated: N 19.8%.

3-Phenylazo-1H,10H-benzo[e]pyrrolo[3,2-g]indole (VII). This compound was obtained from 0.32 g (1.5 mmole) of I and 6 mmole of benzenediazonium chloride by a procedure similar to that used to prepare V. Chromatography with a column by elution with hexane–ether (5:1) gave 0.26 g (54%) of VII with mp 203°C (dec.) and R_f 0.58 [benzene–acetone (10:1)]. IR spectrum: 3380, 3410 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 202 (4.45), 229 (4.59), 264 sh (4.47), 269 (4.50), 315 (4.08), 540 nm (4.56). Found: N 18.4%. $C_{20}H_{14}N_4$. Calculated: N 18.0%; M 355.

LITERATURE CITED

1. Sh. A. Samsoniya, M. V. Trapaidze, N. A. Kuprashvili, A. M. Kolesnikov, and N. N. Suvorov, Khim. Geterotsikl. Soedin., No. 8, 1222 (1985).

2. Sh. A. Samsoniya, M. V. Trapaidze, L. N. Kurkovskaya, L. G. Tret'yakova, T. K. Efimova, and N. N. Suvorov, Khim. Geterotsikl. Soedin., No. 9, 1221 (1979).
3. Sh. A. Samsoniya, Zh. Sh. Lomtatidze, S. V. Dolidze, and N. N. Suvorov, Khim.-Farm. Zh., No. 12, 1452 (1984).
4. P. B. Terent'ev, Mass Spectrometry in Organic Chemistry [in Russian], Vyssh. Shkola, Moscow (1979), p. 124.
5. Yu. A. Ustynyuk (ed.), Quantum-Chemical Methods of Calculation of Molecules [in Russian], Khimiya, Moscow (1985).