BENZINDOLES.

XVI.* SYNTHESIS OF 4,5,6,7-DIBENZINDOLE

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Condensation of 9-phenanthrylhydrazine hydrochloride with pyruvic acid and its ethyl ester gave the corresponding hydrazones, Fischer cyclization of which yielded 2-carboxy- and 2-carbethoxy-4,5,6,7-dibenzindoles. 4,5,6,7-Dibenzindole was obtained by decarboxylation of 2-carboxy-4,5,6,7-dibenzindole, and its IR, UR, PMR, mass, and luminescence spectra were studied.

The high physiological activity of compounds of the indole series is stimulating constant interest in the synthesis of substances containing an indole ring. The existence among phenanthrene derivatives of substances having antimalarial [2] and antitumorigenic [3] activity makes it possible to hope that compounds with high biological activity may be found in the 4,5,6,7-dibenzindole series, the molecules of which consist of a combination of indole and phenanthrene rings.

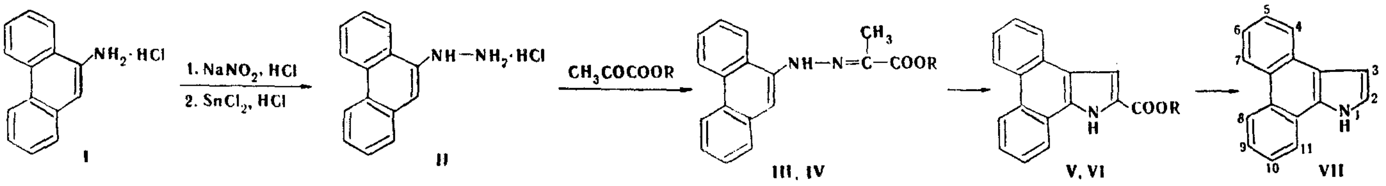
Of the numerous publications devoted to the synthesis of indole derivatives, there is only one in which the preparation of dibenzisoindole derivatives, which were found to be antidepressants [4], is described [4].

The goal of the present research was to develop a preparative method for the synthesis of 4,5,6,7-dibenzindole (VII) and to investigate its physicochemical properties.

Dibenzindole was synthesized by condensation of 9-phenanthrylhydrazine hydrochloride (II) with pyruvic acid and its ethyl ester through the corresponding hydrazones III and IV, which were converted to 2-carboxy-4,5,6,7-dibenzindole (V) and 2-carbethoxy-4,5,6,7-dibenzindole (VI) by Fischer cyclization. Compound VII was obtained by decarboxylation of acid V in a stream of argon at 270-285°C.

Cyclization of hydrazone III with a saturated alcohol solution of hydrogen chloride leads to the formation of ester VI in 37% yield, and cyclization with a solution of sulfuric acid in glacial acetic acid leads to acid V in 22% yield.

Cyclization of hydrazone IV with an alcohol solution of hydrogen chloride (70%) gives the best results.



III, V R = H; IV, VI R = C_2H_5

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*See [1] for communication XV.

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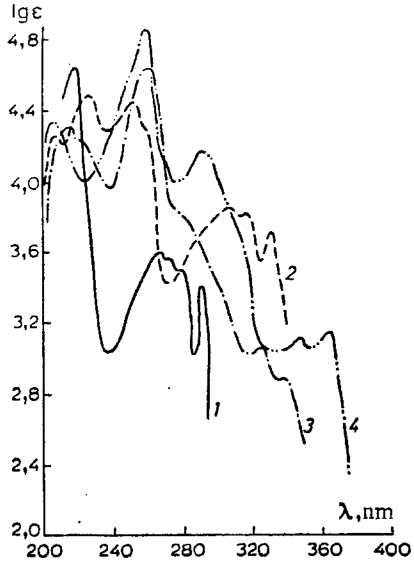


Fig. 1

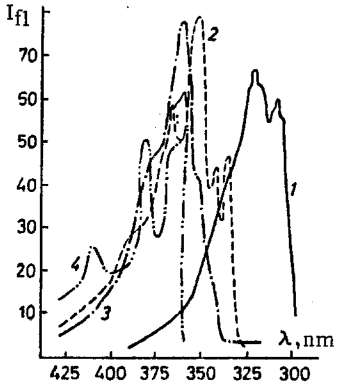


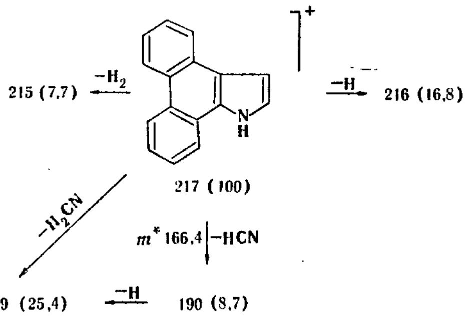
Fig. 2

Fig. 1. UV absorption spectra in alcohol: 1) indole; 2) 4,5-benzindole; 3) 6,7-benzindole; 4) dibenzindole.

Fig. 2. Fluorescence spectra: 1) indole; 2) 4,5-benzindole; 3) 6,7-benzindole; 4) dibenzindole.

The starting 9-aminophenanthrene was obtained by ammonolysis of 9-bromophenanthrene [5]; the latter was obtained by bromination of phenanthrene [6].

The mass spectrum of dibenzindole VII contains an intense molecular-ion [M^+] peak at 217*, and the character of the subsequent fragmentation, which is confirmed by metastable transitions, does not contradict the proposed structure:



The scheme of the fragmentation of dibenzindole VII does not differ fundamentally from the scheme of the fragmentation of indole itself [7].

The UV spectrum of VII in alcohol recalls the spectrum of 6,7-dibenzindole (Fig. 1) but differs with respect to the presence of a maximum at 292 nm, where a shoulder is observed in the spectrum of 6,7-dibenzindole, and two low-intensity maxima at 345 and 362 nm. When the polarity of the solvent is decreased, the spectrum becomes more structured, and the long-wave maxima undergo a small hypsochromic shift, indicating that they are due to a $\pi-\pi^*$ transition.

The fluorescence spectrum of VII (Fig. 2) is shifted markedly to the long-wave region as compared with the spectrum of indole, and the principal maximum coincides with the emission of 6,7-benzindole (∿361 nm); however, there are additional maxima at 383 and 415 nm.

The phosphorescence spectrum of dibenzindole VII (Fig. 3) has three maxima, the location of which corresponds to the location of the maxima in the spectrum of indole (437, 444, and 464 nm, and 438, 448, and 465 nm, respectively).

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*Here and subsequently, the m/e values are presented for the ion peaks.

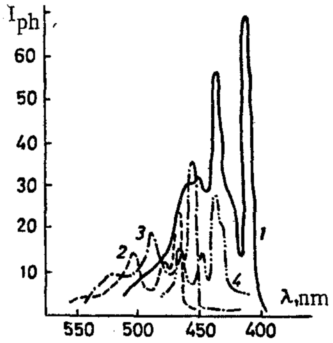

Fig. 3. Phosphorescence spectra: 1) indole; 2) 2) 4,5-benzindole; 3) 6,7-benzindole; 4) dibenzindole.

TABLE 1. Absorption Band of the NH Group of Indole, Angular Benzindoles, and Dibenzindole (ν, cm^{-1}) in the Presence of Some Acceptors*

Acceptor	Indole	4,5-Benzindole	6,7-Benzindole	Dibenzindole
Chloroform	3495free 3405 assoc.	3490free 3420 assoc.	3490free 3430 assoc.	3490free 3440 assoc.
Nujol	3415	3420	3430	3420, 2460
THF	3320	3330	3330	3310
Acetone	3410	3420	3350	3380
Acetonitrile	3385	3390	3380	3390

*The concentrations of indole, the angular benzindoles, and dibenzindole in the solutions ranged from 0.02 to 0.07 mole/liter; this excludes the possibility of the formation of self-associates.

The energies of the first singlet and first triplet states calculated on the basis of the absorption and luminescence spectra are $335.36 \cdot 10^3$ and $254.98 \cdot 10^3$ J/mole (80.1 and 60.9 kcal/mole), respectively; these values are very close to the corresponding values for the angular benzindoles [8].

The position of the absorption band of the NH group in the IR spectrum of VII (in mineral oil) coincides with the position of the corresponding band in the spectrum of 6,7-benzindole and indole. A free NH group is observed in the spectrum (in $CHCl_3$) at 3495 cm^{-1}, i.e., it also coincides with the corresponding band of indole and 6,7-benzindole.

A comparison of the donor properties of dibenzindole and angular benzindoles during the formation of complexes by means of hydrogen bonds with some acceptors shows that the position of the band of the associated NH group is either very close to the position of the corresponding band for indole (self-associates, acetonitrile) or is shifted to the low-frequency region; this indicates the somewhat more pronounced donor properties of dibenzindole as compared with indole (Table 1).

The assignment of the signals in the PMR spectrum of VII was made by comparison with the PMR spectra of the angular benzindoles. The signal of the 1-H proton attached to the nitrogen atom is found in the low-field region of the spectrum (11.98 ppm); this is in good agreement with the literature data on indoles [9] and angular benzindoles [10]. The signal of the 3-H proton is located in the highest-field region of the spectrum. The multiplet structure of this signal is due to spin–spin coupling with the 1-H and 2-H protons. The signal of the 2-H proton is a triplet. The signals of the 2-H and 3-H protons are virtually identical to the signals of benzindoles [10].

The 4-H, 5-H, 6-H, and 7-H, and 8-H, 9-H, 10-H, and 11-H protons comprise two four-spin signals of the ABCD system, the signals of which are superimposed on one another.

EXPERIMENTAL

The UV spectra of solutions of the compounds in ethanol and heptane were recorded with a Specord spectrophotometer. The IR spectra were recorded with a UR-20 spectrometer with NaCl and LiF prisms (in mineral oil) at a scanning rate of 160 and a spectral slit width of 4 cm^{-1}. The fluorescence spectra of alcohol solutions of the compounds were recorded with a Hitachi apparatus. The phosphorescence spectra were investigated at 77°K with an SDL-1 luminescence spectrophotometer with monochromatic excitation (λ 254 nm) or with a photoelectric apparatus with a spark phosphoroscope (W—Fe electrodes). The mass spectrum was recorded with an MKh-1303 spectrometer with direct introduction of the samples into the ion source at a cathode emission current of 1.5 mA, an accelerating voltage of 50 eV, and a temperature of 100°C. The PMR spectrum of a solution of the compound in DMSO—CCl_4 (1:1) was recorded with a JNM-4H-100 spectrometer with hexamethyldisiloxane as the internal standard. The course of the reaction and the purity of the compounds were monitored on plates with a fixed layer of Silufol UV-254 silica gel. Activity II aluminum oxide was used.

Ethyl Pyruvate 9-Phenanthrylhydrazone (IV). A 4-g (0.017 mole) sample of finely ground I was added with vigorous stirring to a cooled (to 0°C) solution of 11.4 ml of concentrated HCl in 119 ml of water and 11 ml of dioxane, after which a cold solution of 1.4 g (0.02 mole) of sodium nitrite in 6 ml of water was added to the resulting suspension, and the mixture was maintained at −5 to +5°C. Stirring was then continued at 0°C for 1 h. A solution of 16 g (0.08 mole) of $SnCl_2$ in 16 ml of concentrated HCl was added slowly at 0 to −5°C to the suspension of the diazonium salt, and the mixture was stirred for 2 h. The precipitated II was removed by filtration, washed with 50 ml of cold water, and dissolved in 500 ml of hot water. The hot solution was filtered rapidly, a solution of 2 ml (0.018 mole) of ethyl pyruvate in 2 ml of ethanol was added gradually with stirring to the hot aqueous solution of hydrochloride II, and the mixture was maintained under these conditions for 30 min. The yellow precipitate of hydrazone IV was removed by filtration, washed with water, and dried to give 2.73 g (53%) of a product with mp 140-142°C (from aqueous alcohol). IR spectrum: 3390 (NH) and 1715 cm^{-1} (C=O). UV spectrum: λ_{max} (log ε): 211 (4.51), 250 (4.49), 276 (4.29), 315 (4.15), and 573 nm (4.19). Found: C 75.3; H 6.4; N 9.1%. $C_{19}H_{18}N_2O_2$. Calculated: C 75.3; H 5.9; N 9.2%.

Pyruvic acid 9-phenanthrylhydrazone (III) was similarly obtained. Compound III was purified with a column filled with aluminum oxide [elution with ether—CCl_4 (1:1)] to give a product with mp 185-186°C in 83% yield. IR spectrum: 3180 (NH) and 2500-3060 cm^{-1} (OH band of a dimeric acid). UV spectrum, λ_{max} (log ε): 211 (2.45), 225 (2.36), 252 (2.62), 317 nm (1.90). Found: C 73.3; H 5.4; N 10.2%. $C_{17}H_{14}N_2O_2$. Calculated: C 73.4; H 5.0; N 10.1%.

2-Carbethoxy-4,5,6,7-dibenzindole (VI). A 0.75-g (0.002 mole) sample of hydrazone IV was suspended in 30 ml of a saturated alcohol solution of hydrogen chloride, and the suspension was refluxed with stirring for 4 h. It was then cooled to room temperature and poured over ice. The resulting precipitate was removed by filtration and dissolved in 15 ml of acetone. The acetone solution was passed through a column filled with Al_2O_3 (1:30) with elution of the product with ether—petroleum ether (1:1) (the elution process was monitored with Erlich's reagent) to give 0.49 g (71%) of a product with mp 249-250°C. IR spectrum: 3285 (NH), 1685 (C=O), and 735-770 cm^{-1} (CH). UV spectrum, λ_{max} (log ε): 203 (4.24), 244 (4.41), 254 (4.61), 262 (4.82), 269 (4.61), 320 (4.27), 339 (3.99), 355 nm (4.06). Found: C 78.3; H 5.5; N 4.7%. $C_{19}H_{15}NO_2$. Calculated: C 78.9; H 5.2; N 4.8%.

Compound VI, with mp 249-250°C, was similarly obtained from hydrazone III in 38% yield.

2-Carboxy-4,5,6,7-dibenzindole (V). A) 0.81-g (0.003 mole) sample of ester VI was refluxed for 1 h in 50 ml of 10% alcoholic KOH, after which the mixture was poured into 200 ml of cold water. The aqueous mixture was acidified to pH 7 with HCl, and the precipitate was removed by filtration, washed with water, and dried to give 0.58 g (79%) of a product with mp 283-285°C (dec.). IR spectrum: 3480 (NH), 2500-3000 (OH group of a dimeric acid), 1680 (C=O), and 735-770 cm^{-1} (benzene ring CH). UV spectrum, λ_{max} (log ε): 206 (4.31), 244 (4.40), 254 (4.64), 262 (4.82), 268 (4.71), 229 (4.25), 318 (4.22), 399 (3.62), 354 nm (3.67). Found: C 77.1; H 4.7; N 5.1%. $C_{17}H_{11}NO_2$. Calculated: C 78.2; H 4.2; N 5.4%.

B) A 2.25-g (0.008 mole) sample of III was suspended in 23 ml of glacial acetic acid, the suspension was heated to the boiling point, 1 ml of concentrated H_2SO_4 was added, and the mixture was refluxed for 10 min. It was then cooled to room temperature and poured over ice. The precipitated V was removed by filtration and dissolved in 250 ml of a hot saturated aqueous solution of $NaHCO_3$. The solution was filtered rapidly, and the filtrate was acidified to pH 7 with HCl. The precipitate was removed by filtration, washed with water, and dried to give 0.47 g (22%) of a product with mp 283-285°C (dec.). Acid V was identical to the sample obtained from experiment A with respect to its IR and UV spectra. The results of elementary analysis were in agreement with the calculated values.

4,5,6,7-Dibenzindole (VII). A 0.5-g (0.002 mole) sample of acid V was heated in a stream of argon at 270-285°C for 10 min, and the decarboxylation product was mixed with 5 g of aluminum oxide and 15 ml of acetone. The solvent was removed by vacuum distillation, and the residue was transferred to a column filled with aluminum oxide and eluted with ether–hexane (1:1) (the elution process was monitored with Erlich's reagent) to give 0.3 g (72%) of a product with mp 163-165°C. IR spectrum: 3360 and 3425 (NH); 735-770 cm^{-1} (benzene ring CH). UV spectrum, λ_{max} (log ε): 207 (4.38), 252 (4.71), 258 (4.93), 290 nm (4.24). PMR spectrum, δ: 11.93 (s, 1-H), 6.93 (q, 3-H), and 7.26 ppm (t, 2-H). Found: C 88.2; H 5.3; N 6.2%. $C_{16}H_{11}N$. Calculated: C 88.5; H 5.1; N 6.4%.

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