BISINDOLES.

21.* SYNTHESIS AND ALKYLATION OF SOME TETRAMETHYL-SUBSTITUTED BISINDOLES

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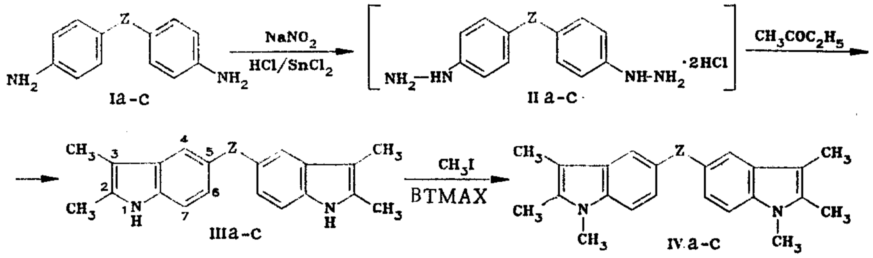
2,3,2',3'-Tetramethyl-substituted bisindoles and their 1,1'-dimethyl derivatives were synthesized. The latter were obtained in high yield by interphase alkylation of the bisindoles. The spectral characteristics of the synthesized bisindoles were studied.

We have accomplished the synthesis and interphase alkylation of 2,3,2',3'-tetramethyl-substituted bisindoles via the scheme



I—IV a Z=—CH$_2$—CH$_2$—; b Z=—CH=CH—; c Z=p-C$_6$H$_4$

As the starting compounds we selected 4,4'-diaminobibenzyl (Ia), trans-4,4'diaminostilbene (Ib), and 4,4'-diamino-p-terphenyl (Ic).

After diazotization and subsequent reduction, diamines Ia-c were converted to the corresponding dihydrazine dihydrochlorides IIa-c, which we did not isolate. The synthesis of a 2,3-substituted indole ring from the corresponding hydrazine by avoiding the step involving the isolation of the hydrazone has been previously described [2]. Using these results, we obtained bisindoles IIIa-c by refluxing dihydrazine dihydrochlorides IIa-c in excess methly ethyl ketone.

An intense absorption band of an NH group (3390, 3400, and 3410 cm^{-1}, respectively), which is characteristic for indole compounds, is present in the IR spectra of IIIa-c (in mineral oil).

A bathochromic shift of the long-wave absorption maximum and an increase in the absorption intensity (Fig. 1) as compared with the UV spectrum of IIIa are observed in the UV spectra of IIIb,c; this is evidently explained by the existence of conjugation between the two indole fragments. The bathochromic shift of the long-wave maximum in the spectrum of IIIb as compared with the spectrum of IIIc can be explained by greater conjugation of the indole fragments with the —C=C— bond.

Compounds IIIa-c have, in their emission spectra (in ethanol), one fluorescence band at λ 352, 402, and 380 nm, respectively (Fig. 2). For IIIa-c, by a relative method, we determined quantum yields of 0.12, 0.24, and 0.19 respectively. In the determination of the fluorescence quantum yields we used specially purified anthracene as the standard.

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*See [1] for Communication 20.

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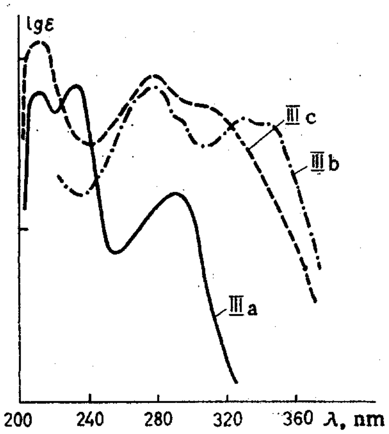


Fig. 1. UV spectra of IIIa-c (in ethanol).

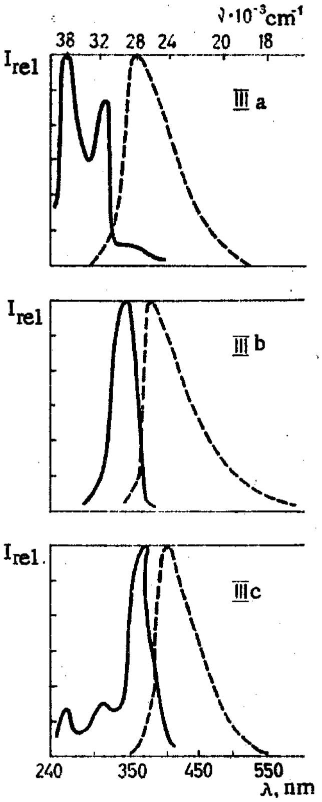


Fig. 2. Excitation (____) and fluorescence (— — —) spectra of IIIa-c (in ethanol).

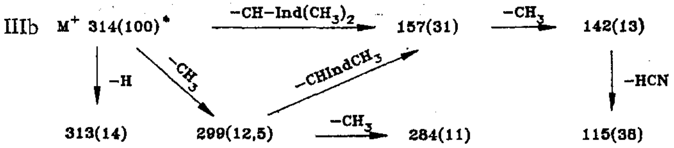
TABLE 1. Parameters of the PMR Spectra of III and IV

Compound	Chemical shifts, δ, ppm							SSCC, J, Hz
	1H(CH$_3$)	2(CH$_3$)	3(CH$_3$)	4H	6H	7H	Z	
IIIa	10,2, br s	2,26, s	2,10, s	7,15, d	6,82, d	7,06, s	2,92, s	$H_{4,6}$=1,1; $H_{6,7}$=8,3
IIIb	10,4, br s	2,28, s	2,16, s	7,45, s	7,18, s		7,09, s	—
IIIc	10,4, br s	2,31, s	2,20, s	7,63, s	7,26, s		7,67, s	
IVa	CH$_3$, 3,35, s	2,28, s	2,13, s	7,18, d	6,87, d	7,12	2,95, d	$H_{4,6}$=1,5; $H_{6,7}$=8,6
IVb	CH$_3$, 3,60, s	2,29, s	2,20, s	7,50, s	7,25, s		7,13	—
IVc	CH$_3$, 3,64, s	2,37, s	2,23, s	7,65, s	7,34—7,35, m		7,67, s	—

The PMR spectra (Table 1) of IIIa-c contain characteristic (for the NH group) signals at, respectively, 10.2, 10.4, and 10.4 ppm.

It follows from Table 1 that the Z bridge grouping has a pronounced effect on the chemical shift of the 4H proton — shielding of the proton decreases in the order Z = $-CH_2-CH_2-$ > $-CH=CH-$ > $-C_6H_4-$. The 6H and 7H protons of IIIa, which form an AB system, have a characteristic spectrum with spin—spin coupling constants (SSCC) $J_{6,7}$ = 8.3 Hz. In the case of IIIb,c the signal from these protons is a singlet (an A_2 system, $\Delta\delta \sim 0$ ppm). This means that the nature of the bridge grouping (in particular, the existence of conjugation in it) affects not only the relative magnitude of the chemical shift but also changes the character of the spectrum of the indole fragment.

The molecular masses of IIIa-c, which were determined by mass spectrometry, are in agreement with the calculated values, and the character of the subsequent fragmentation does not contradict the proposed structures.



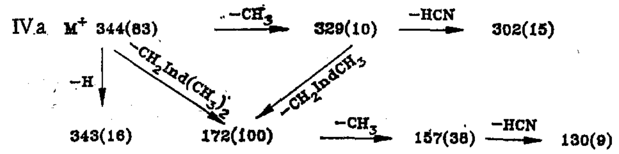
Peaks with m/z 157.5 and 142.5, which correspond to doubly charged 315^{++} and 285^{++} ions, were not detected in the mass spectrum of IIIb.

For the synthesis of IVa-c we chose alkylation under interphase-catalysis conditions [3], which has been used for the preparation of 1-alkyl-substituted indoles [4]. By the action of methyl iodide on bisindoles IIIa-c in the presence of sodium hydroxide and catalytic amounts of trimethylbenzylammonium chloride we were able to synthesize IVa-c in high yields. The absorption band that is characteristic for the NH group is absent in the IR spectra of IVa-c.

The UV spectra of IVa-c contain intense absorption maxima in the long-wave region at, respectively, 294, 366, and 333 nm. The PMR spectra of these compounds (Table 1) do not contain signals that correspond to NH groups, but one does observe signals of NCH_3 groups with chemical shifts at 3.55, 3.60, and 3.64 ppm, respectively. It follows from Table 1 that the above-noted peculiarities of the spectral characteristics of IIIa-c are also retained for IVa-c.

Like the starting diamine Ib, the bisindoles IIIb and IVb that we synthesized have an energically more stable trans configuration) this is in agreement with the data from the PMR spectra of these compounds (Table 1).

The molecular masses of IVa-c were found by mass spectrometry and were in agreement with the calculated values. Let us present the fragmentation of one of them:



EXPERIMENTAL

Monitoring of the course of the reaction and the purity of the compounds and the determination of the R_f values were carried out in Silufol UV-254. The IR spectra of suspensions in mineral oil were obtained with a UR-20 spectrometer. The mass spectra of all the compounds were recorded with an MKh-1303 mass spectrometer with direct introduction of the samples into the ion source at an ionizing-electron energy of 50 eV. The UV spectra of solutions in ethanol were recorded with a Specord M-40 spectrophotometer. The fluorescence spectra were recorded with an SLM-4800 spectrofluorometer. The PMR spectra of solutions in d_6-DMSO were obtained with a Varian CFT-20 spectrometer (f_0 = 80 MHz). The accuracy in the measurement of the chemical shifts was no lower than ±0.01 ppm, and the accuracy in the measurement of the SSCC was ±0.1 Hz. The internal standard was tetramethylsilane (TMS).

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*Here and subsequently, the m/z values are presented, and the relative intensities of the ion peaks in percent relative to the maximum peak are given in parentheses.

1,2-Bis(2,3-dimethyl-5-indolyl)ethane (IIIa). A solution of 3.45 g (50 mmoles) of $NaNO_2$ in 10 ml of water was added dropwise at –5°C to 0°C in the course of 20 min to a mixture of 4.24 g (20 mmole) of 4,4'-diaminobibenzyl (Ia), 20 ml of water, and 20 ml of concentrated HCl after which the mixture was maintained at –5°C to 0°C, and stirring at 0°C was continued for 20 min. A solution of 20.8 g (110 mmoles) of stannous chloride in 30 ml of concentrated HCl was added slowly at –5°C to 2°C to the resulting solution of the diazonium salt, and the mixture was stirred for 4 h. The resulting precipitate of dihydrazine dihydrochloride IIa was removed by filtration and squeezed dry. The precipitate was refluxed in 150 ml of methyl ethyl ketone for 3-4 h, after which the suspension was filtered. The solution was evaporated to 50 ml, and the white crystalline substance that precipitated from the solution was removed by filtration and washed with small portions of methyl ethyl ketone, ethanol, and ether to give 1.8 g (28%) (based on starting diamine Ia) of a product with mp 242-243°C and R_f 0.64 [benzene—acetone (5:1)]. IR spectrum: 3390 cm^{-1} (NH). UV spectrum, λ_{max} (log ε), nm: 210 (4.8), 238 (4.85), 280 (4.20), and 300 shoulder (4.10). Found: C 83.5; H 7.6; N 8.9%; M^+ 316. $C_{22}H_{24}N_2$. Calculated: C 83.6; H 7.6; N 8.8%; M 316.

trans-2,2-Bis(2,3-dimethyl-5-indolyl)ethene (IIIb). This compound was obtained in the same manner as IIIa from 4.2 g (20 mmole) of diamine IIb. Workup gave 1.1 g (17.5%) of a compound with mp 325-326°C and R_f 0.54 [benzene—acetone (5:1)]. IR spectrum: 3400 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 220 (4.30), 280 (4.85), 296 (4.65), 330 (4.65), 335 (4.70), and 345 nm (4.60). Found: C 84.1; H 7.0; N 8.9%; M^+ 314. $C_{22}H_{22}N_2$. Calculated: C 84.2; H 7.0; N 8.8%; M 314.

1,4-Bis(2,3-dimethyl-5-indolyl)benzene (IIIc). A 5.2-g (20 mmoles) sample of 4,4'-diamino-p-terphenyl (Ic) was dissolved by refluxing in 100 ml of acetic acid, 20 ml of concentrated HCl was added, and a solution of 3.45 g (50 mmoles) of $NaNO_2$ in 10 ml of water was added at 0-5°C dropwise in the course of 20 min while maintaining the temperature of the mixture at –5°C to 0°C. Stirring was then continued at 0°C for 30 min. The mixture was then worked up as in the case of IIIa. The yield based on starting diamine Ic was 1.5 g (20%); the product had mp 329-330°C and R_f 0.60 [benzene—acetone (5:1)]. IR spectrum: 3400 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 210 (5.11), 276 (4.90), and 314 nm (4.68). Found: C 85.7; H 6.6; N 7.7%; M^+ 364. $C_{26}H_{24}N_2$. Calculated: C 85.8; H 6.6; N 7.6%; M 364.

1,2-Bis(1,2,3-trimethyl-5-indolyl)ethane (IVa). A 0.32-g (10 mmoles) sample of IIIa and 40 ml of 50% NaOH solution were added to a mixture of 10 ml of methyl iodide and 0.05 g of trimethylbenzylammonium chloride, after which the mixture was stirred at 35-40°C for 5-6 h. It was then evaporated to remove the CH_3I, and the resulting suspension was diluted with water and filtered. The filtrate was washed with water until the washings had pH 7 and then dried. The solid product was recrystallized from ethanol to give 0.3 g (88%) of a product with mp 165-166°C and R_f 0.8 (benzene). UV spectrum, λ (log ε): 204 (4.26), 248 (4.47), and 294 nm (3.87). Found: C 83.7; H 8.15; N 8.15%; M^+ 344. $C_{24}H_{28}N_2$. Calculated: C 83.6; H 8.2; N 8.2%; M 344.

trans-1,2-Bis(1,2,3-trimethyl-5-indolyl)ethene (IVb). This compound was obtained in a manner similar to that used to synthesis IVa from 0.31 g (10 mmole) of IIIb. It was recrystallized from methyl ethyl ketone to give 0.28 g (82%) of a product with mp 195-196°C and R_f 0.8 (benzene). UV spectrum, λ_{max} (log ε): 208 (3.74), 217 (3.81), 287 (3.72), and 366 nm (3.66). Found: C 85.7; H 6.6; N 7.7%; M^+ 342. $C_{28}H_{28}N_2$. Calculated: C 85.6; H 6.6; N 7.9%; M 342.

1,4-Bis(1,2,3-trimethyl-5-indolyl)benzene (IVc). This compound was obtained in a manner similar to that used to prepare IVa from 0.39 g (10 mmole) of IIIc and was recrystallized from methyl ethyl ketone to give 0.35 g (89%) of a product with mp 310-311°C and R_f 0.75 (benzene). UV spectrum, λ_{max}: 208, 285, 333 nm. Found: C 85.8; H 7.15; N 7.15%; M^+ 392. $C_{28}H_{28}N_2$. Calculated: C 85.8; H 7.1; N 7.1%; M 392.

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