<u>1,2-(2,2'-Dicarboxy-5,5'-diindoly1)ethane (V).</u> A suspension of 1.5 g (0.003 mole) of ester III, 75 ml of ethanol, and 1.1 g (0.019 mole) of KOH was refluxed with stirring for 5-6 h, after which the solution was evaporated. The solid residue was dissolved in water, and the solution was cooled to 5-10°C and acidified with dilute HC1. Product V was removed by filtration, washed with water, and dried to give 1 g (85%) of a substance with mp 277-278°C and R<sub>f</sub> 0.44 [ethyl acetate - ether (5:1)]. IR spectrum: 3455 (NH) and 1710 cm<sup>-1</sup> (CO). UV spectrum,  $\lambda_{max}$  (log  $\varepsilon$ ): 208 (4.72) and 296 nm (4.42). Found: C 68.6; H 5.0; N 8.0%: C<sub>20</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>. Calculated: C 68.9; H 4.8; N 8.0%.

<u>1,2-(5,5'-Diindolyl)ethane (VI).</u> A 1-g (0.002 mole) sample of acid V was heated at 275-295°C in a stream of argon. Compound VI was purified with a column filled with silica gel by elution with benzene -petroleum ether (5:1). Erlich's solution gave a red coloration with VI. The yield of product with mp 158-159°C and Rf 0.64 [benzene-acetone (5:1)] was 0.18 g (25%). IR spectrum: 3410 cm<sup>-1</sup> (NH). UV spectrum,  $\lambda_{max}$  (log  $\varepsilon$ ): 228 (4.81), 270 (3.52), 280 (3.51), 288 (3.50), and 296 nm (3.36) (Fig. 2). Found: C 83.1; H 6.3; N 10.7%; M<sup>+</sup> 260. C<sub>18</sub>H<sub>16</sub>N<sub>2</sub>. Calculated: C 83.1; H 6.2; N 10.7%; M 260.

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# REACTION OF FISCHER'S BASE

#### WITH O-HYDROXYCINNAMALDEHYDES

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On the basis of a study of the PMR spectra and alternative synthesis it was established that the "dicondensed" products of the reaction of Fischer's base with o-hydroxycinnamaldehydes are not oxocine derivatives, as was previously assumed, but rather are bisindoline spirochromans that are identical to the products of the reaction of vinylogs of Fischer's base with salicylalde-hydes.

We have recently reported [1] an unsuccessful attempt to synthesize indoline spirooxocines from vinylogs of Fischer's base and salicylaldehydes. The products of the reaction of these substances were found to be "dicondensed" spirochromans; in particular, Ia was obtained from 5-nitrosalicylaldehyde and 1,3,3-trimethyl-2-(2-butenyl-1-idene)indoline.



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Fig. 1. PMR spectrum of Ib.

The occurrence of the indicated reaction with the formation of a six-membered ring instead of the expected eight-membered ring cast doubt on the previously drawn conclusion that spiroxocine IIa is formed in the condensation of Fischer's base with 2-hydroxy-5-nitrocinnamaldehyde [2]. To ascertain the truth we carried out the reaction of Fischer's base with  $\alpha$ -methyl-2-hydroxy-5-nitrocinnamaldehyde and obtained a compound that was identical to spirochroman Ia instead of spirooxocine IIb. This result demonstrated that, regardless of the location of the vinyl group (in the heterocyclic base or in the aromatic o-hydroxy aldehyde), the condensation leads to a bisindoline spirochroman rather than to a spiro derivative of an oxocine.

We subjected the compound to which the IIa structure had been previously assigned [2] to a more thorough investigation. An analysis of the PMR spectrum (360 MHz, Fig. 1) showed that the investigated substance, like Ia, is a bisindoline spirochroman and that structure Ib corresponds to it. The signal of the aliphatic H<sup>m</sup> proton is a multiplet that contains constants of spin-spin coupling with the two protons of the methylenc group (H<sup>a</sup>, H<sup>b</sup>), which in this case are equivalent, and the closest vinyl proton  $(H^Z)$ . In principle, this could also be the case for the Ha structure for that orientation of the protons adjacent to H<sup>m</sup> in which one of the dihedral angles is close to 90°. However, the multiplicity of the signals in the region of the shifts of the vinyl protons demonstrates the presence of a diene fragment in the compound, which completely confirms the Ib structure. Thus the spectrum contains signals of two vinyl protons ( $H^{Z}$  and  $H^{Y}$ ), each containing constants of spin-spin coupling with two adjacent protons, whereas in the IIa structure only one vinyl proton  $(H^Z)$  could have such multiplicity. The existence of spin-spin coupling through the 4-7 bonds is interesting. In particular, the additional small splitting (0.8 Hz) of the quartet of the 7'-H proton is evidently due to its coupling with  $H^{Z}$  in the case of a primarily transoid zigzag orientation of these protons [3]. The signals of the gem-methyl groups of the A ring are observed in the form of two singlets, and the signals of the gem-methyl groups of the B ring are also noted in the form of two singlets but in the weaker-field region; this is explained by the deshielding effect of the exocyclic double bond [4].

The formation of bisindoline spirochromans with structure I in the reaction of o-hydroxycinnamaldehydes with the Fischer base (III) can be explained by nucleophilic attack by one molecule of the methylene base on the carbonyl group of the aldehyde with subsequent splitting out of water and the addition of a second molecule of base III to the  $C_5 = C_6$  bond via a reaction of the Michael type.



The proposed reaction scheme is in good agreement with [5-8] and other studies in which the direct synthesis of bis products from chromenes and methylene bases was realized [1, 9-12, 13, p. 256]. A second indoline fragment does not add to the  $C_3 = C_4$  bond to give products with structure II, evidently because of the lower thermodynamic stability of spirooxocines as compared with spirochromans.

"Dicondensed" product Ib (R = H), like the other bis products [13, p. 245], does not have photochromic properties. However, when an alcohol solution of this product is heated, it turns bright blue. This coloration slowly vanishes upon standing but not completely; it develops again when the solution is reheated. Let us note that the thermochromic properties of "dicondensed" compounds were also pointed out in [14]. The color of an alcohol solution of Ia ( $R = CH_3$ ) does not change when it is heated.

## EXPERIMENTAL

The PMR spectrum of a solution of lb in  $(CD_3)_2CO$  was recorded with a Bruker WH-360 high-resolution spectrometer with a superconducting magnet (360 MHz); the chemical shifts were measured relative to tetramethylsilane as the internal standard. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer.

<u> $\alpha$ -Methyl-2-hydroxy-5-nitrocinnamaldehyde</u>. A 6.49-g (39 mmole) sample of 5-nitrosalicylaldehyde was dissolved by heating in 300 ml of distilled water containing 2.7 g (68 mmole) of NaOH, after which the mixture was cooled, treated with 6.08 g (105 mmole) of propionaldehyde, and allowed to stand at 20°C for 21 h. It was then neutralized with 20% hydrochloric acid, and the resulting precipitate was recrystallized from aqueous ethanol to give 4.2 g (52%) of yellowish needles with mp 189°C. IR spectrum: 1650 (C = O); 1520, 1350 cm<sup>-1</sup> (NO<sub>2</sub>). Found: N 6.8%; M 207 (from the mass spectrum obtained with an MKh-1303 spectrometer). C<sub>10</sub>H<sub>9</sub>NO<sub>4</sub>. Calculated: N 6.8%; M 207.

1,3,3-Trimethyl-4'-[4-(1,3,3-trimethylindolin-2-ylidene)-2-buten-2-yl]-6'-nitroindoline-2-spiro-2'chroman (Ia). A 0.66-g (3.8 mmole) sample of Fischer's base was added to a solution of 0.78 g (3.8 mmole) of  $\alpha$ -methyl-2-hydroxy-5-nitrocinnamaldehyde in 20 ml of absolute alcohol, and the mixture was allowed to stand at room temperature for 24 h. The resulting precipitate was removed by filtration to give 0.65 g (64% based on Fischer's base) of chroman Ia. The product was recrystallized from benzene-ethanol to give light-yellow needles with mp 181-182°C. No melting-point depression was observed for a mixture of this product with a genuine sample obtained by the method in [1]. IR spectrum: 1640 (C=C); 1255 (=C-O); 970 (C<sub>spiro</sub>-O); 1518, 1360 cm<sup>-1</sup> (NO<sub>2</sub>). See [1] for the PMR spectrum.

 $\begin{array}{l} 1,3,3-\text{Trimethyl}-4'-[3-(1,3,3-\text{trimethylindolin}-2-ylidene)-1-\text{propen}-1-yl]-6'-\text{nitroindolin}-2-\text{spiro}-2'-\\ \underline{\text{chroman (Ib).}} & \text{A mixture of 0.22 g (1.26 mmole) of Fischer's base and 0.24 g (1.24 mmole) of 2-hydroxy-5-\\ \underline{\text{nitrocinnamaldehyde [15] in 30 ml of absolute alcohol was allowed to stand at 20°C for 24 h, after which the precipitate was removed by filtration to give 0.26 g (78% based on Fischer's base) of chroman Ib as orange crystals with mp 162°C (from benzene -ethanol). IR spectrum: 1650 (C=C); 1260 (=C-O); 970 (C_{\text{spiro}}-O); 1520, 1345 cm^{-1} (NO_2). PMR spectrum: 1.22 and 1.26 (both 3H, s, 3-CH_3); 1.54 and 1.59 (both 3H, s, 3"-CH_3); 2.34 (2H, d, J_{am} = J_{bm} = 9.0 Hz, H^a, H^b); 2.84 (3H, s, 1-CH_3); 3.07 ppm (3H, s, 1"-CH_3); J_{mz} = 8.7, J_{my} = 0.5, J_{m5}' = 1.3, J_{ZY} = 14.5, J_{ZX} \approx J_{Z7}' \approx 0.8, J_{XY} = 11.5, J_{76} = _7 "_6" = 7.8, J_{75} = J_7 "_5" = 1.0, J_{74} = J_7 "_4" = 0.6, J_{54} = J_5 "_4" = 7.4, J_{56} = J_5 '_6' = 7.7, J_8' '_7 ' = 9.0, J_{46} = J_4 "_6" = 1.3, J_7' := 2.8 Hz (also see Fig. 1). Found: C 75.9; H 6.8; N 8.0%. C_{33}H_{35} - N_2O_3. Calculated: C 76.0; H 6.8; N 8.1%. \end{array}$ 

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AZAINDOLE DERIVATIVES.

61.\* ELECTROPHILIC SUBSTITUTION REACTIONS

IN 1-BENZYL-6-METHOXY-7-CYANO-5-AZAINDOLE

AND 6-OXO-5-AZAINDOLINE

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The electrophilic substitution reactions (nitration, bromination, acylation, and the Mannich and Vilsmeier reactions) of 1-benzyl-6-methoxy-7-cyano-5-azaindole and the nitration and Vilsmeier reaction of 6-hydroxy-5-azaindoline were studied.

Some of the efficient methods for the synthesis of polysubstituted 5-azaindoles, which are of interest for biological study, are the conversion of N-benzyl-2-pyrrolidone to 1,6,7-tri- or 1,4,6,7-tetrasubstituted 5-azaindolines [2, 3], their oxidation to the corresponding azaindoles [3], and the introduction of additional groups in the 3 position by means of electrophilic substitution reactions. We have previously shown [4] that despite the literature data [5], electrophilic substitution in the 3 position of 5-azaindoles is realized readily; however, the presence of electron-acceptor substituents may hinder these reactions.

In the present communication we examine the peculiarities of electrophilic substitution processes in 1benzyl-6-methoxy-7-cyano-5-azaindole (I).



x1a  $\mathbf{R}' \neq \mathbf{NO}_2$ ; b  $\mathbf{R}' = \mathbf{CHO}$ ; VII  $\mathbf{R} = \mathbf{CH}_2\mathbf{C}_6\mathbf{H}_4\mathbf{NO}_2 \cdot \mathbf{p}$ ; VIII  $\mathbf{R} = \mathbf{CH}_2\mathbf{C}_6\mathbf{H}_4\mathbf{NO}_2$ 

The process takes place most smoothly with a strong electrophilic reagent such as bromine. Azaindole I reacts with bromine in chloroform at 0°C to give 1-benzyl-3-bromo-6-methoxy-7-cyano-5-azaindole (II) in

\*See [1] for Communication 60.

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