## SYNTHESIS AND PROPERTIES OF MEROCYANINE FORMS OF INDOLINE SPIROOXOCINES

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The Fischer base with 3-bromo-, 3,5-dibromo-, and 5-nitro-2-hydroxycinnamaldehydes in acetic acid forms merocyanine forms of indoline spirooxocines, of which the first two are readily converted in the presence of water to bis-indoline spirodihydropyrans, while the last one is converted in relatively nonpolar solvents to a cyclic form, which is not a spirooxocine but a chromene derivative.

A number of studies of recent years [1-4] have been devoted to the search for methods of synthesis of indoline spiro-2H-oxocines (I), related to the photochromic spiro-2H-pyrans [5].



a  $X=Y=NO_2$ ; b  $X=NO_2$ , Y=Br; c X=Br, Y=H; d X=Y=Br; e  $X=NO_2$ , Y=H

Only two open forms of spirooxocines (IIa, b), synthesized by the reaction of the Fischer base in alcohol with 3,5-dinitro- and 3-bromo-5-nitro-2-oxocinnamaldehydes, have now been obtained [4]. Compounds IIa and b proved to be stable substances, incapable of intramolecular cyclization on account of the presence of strong electron acceptor substituents in their molecules. An attempt to decrease the influence of the substituents by the use of 5-nitro, 5-bromo-, 3,5-dibromosubstituted and unsubstituted o-hydroxycinnamaldehyde as the starting materials led to the formation of "dicondensed" spirodihydropyrans III, which do not possess photochrome properties [1, 3, 4].



a  $X=NO_2$ , Y=H; b X=Br, Y=H; c X=Y=Br; d X=Y=H

Continuing our search for conditions in which the formation of spirooxocines of type I is possible, we decided to conduct the condensation of the Fischer base with substituted ohydroxycinnamaldehydes in acetic acid rather than in alcohol. It is known that in the synthesis of indoline spirochromenes, an alcohol medium promotes the formation of bis-indoline spirochromanes [6]. At the same time, in acetic acid the "dicondensed" products are never obtained; for example, benzaldehyde and its derivatives form only monoindoline polymethine dyes with a Fischer base in acetic acid [7-9], although in alcohol the products are bisindoline compounds [6, 10-12].

As was shown by our investigation, in the interaction of the Fischer base with 5-bromo-, 3,5-dibromo-, and 5-nitro-2-hydroxycinnamaldehydes in acetic acid, monoindoline compounds are actually formed. In the first two cases, when the reaction solution was poured out into water and the mixture obtained was neutralized with sodium carbonate, deeply colored substances were

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TABLE 1. PMR Spectra of Compounds IIe and II'e

Com pound	Solvent	õ, ppm⁰						J. Hz	
		C(CH₃)	NCH <sub>3</sub>	Hx	Hy, Hm	Hp	Hr	J <sub>xy</sub>	Jpr
lle lle ll'e } <sup>†</sup> lle }	(CD <sub>3</sub> ) <sub>2</sub> SO CDCl <sub>3</sub> (CD <sub>3</sub> ) <sub>2</sub> CO	1,69 1,56 1,56 1,84	3,84 2,98 3,08 4,01	6,75 4,49 4,58 —	~6,0 5,9—6,3	8,14 ~	8,0 8,0	9,7 10,2 10,2 —	2,8 

\*The assignment of certain signals was not made on account of complex overlapping.

<sup>†</sup>Ratio of the isomers [II'e]/[IIe] ~ 5:1.

obtained, which was an indication of their merocyanine structure (IIc, d). However, these merocyanines could not be isolated in pure form, since during subsequent treatment (extraction with ether, purification by reprecipitation and crystallization) they underwent conversions that led to light-colored bis-indoline spirochromanes IIIb and c, which we obtained earlier when the reaction was conducted in alcohol [4]. Conversion of monoindoline compounds II to diindolines III are explainable under the condition that the merocyanines formed in acetic in the presence of water are cleaved to the starting materials (Fischer base and hydroxyaldehyde), which then again react with one another according to the well-known pathway of spirochromane formation [3, 4].

In the case of the interaction of the Fischer base with 5-nitro-2-hydroxycinnamaldehyde, a greenish-black crystalline substance was obtained, which did not change during isolation and purification by crystallization from acetone. According to the data of elementary analysis, the mass spectrum, and considering the deep color, the substance can be considered as the merocyanine IIe. The PMR spectrum recorded in deuterodimethyl sulfoxide (Table 1), in which signals of the equivalent protons of gem-methyl groups ( $\delta$  1.69 ppm) and a very weak-field signal of the N-methyl group (3.84 ppm) were noted, also corresponded to such a bipolar structure. The SSCC of the protons Hx and Hy (J<sub>xy</sub> = 9.7 Hz) was evidence of their cis-arrangement. In dinitrosubstituted merocyanine IIa these same protons were in a trans-position [4]. The ability of merocyanines to exist in cis- and trans-forms has also been noted in a series of indoline spiropyrans [13].

Exceptionally interesting information on the properties of the merocyanine IIe was obtained in an analysis of its PMR spectrum in a less polar solvent — deuterochloroform. This spectrum differed greatly from that obtained in dimethyl sulfoxide. Thus, the signals of the C- and N-methyl groups were in a stronger field (1.56 and 2.98 ppm, respectively). At the same time a new doublet with J = 10.2 Hz appeared in the region of ~4.5 ppm, and a group of signals corresponding to two protons in the region of ~6.0 ppm. These changes in the spectrum are evidence that the merocyanine IIe is converted in chloroform to a closed form, in which there is no positive charge on the nitrogen atom. It should be assumed that this form is the spirooxocine I (X = NO<sub>2</sub>); however, a thorough analysis of the PMR spectrum showed that in chloroform the merocyanine IIe is converted not to a spirooxocine but to a benzopyran derivative II'e.



The presence of a doublet in the region of ~4.5 ppm in the PMR spectrum supports the structure II'e. Such a value of the chemical shift is extremely characteristic of the protons  $H^x$  at the double bond of the methylenindoline fragment. Thus, the value of  $\delta$  of the protons of the methylene group of the Fischer base and its derivatives is ~3.8-4.2 ppm [14, 15], that of the protons at the exocyclic double bond of "dicondensed" chromanes [15-17] is ~4.2 ppm, and that of indoline derivatives of 2H-naphtho[1,8-bc]furan [18] is ~4.4 ppm. At the same time, the signals of the protons at the conjugated double bonds of the oxocine ring are usually observed in a weaker field ( $\delta \sim 5.2-6.2$  ppm) [19-22].

The chemical shift of the N-CH<sub>3</sub> protons (~3.0 ppm) can also serve as a confirmation of the chromene structure of II'e. The signals of the N-methyl groups of the indoline fragments



Fig. 1. Absorption spectra of compound IIe (1-4) and IIa (5): 1) in ethanol; 2-4) in an ethanol-benzene mixture, 3:1 (2), 1:1 (3) and 1:3 (4); 5) in DMFA.

with an exocyclic double bond are usually observed precisely in this region [14-18]. The Nmethyl group of spiro compounds gives a signal in a stronger field, for example, in spiropyrans for N-CH<sub>3</sub>,  $\delta \sim 2.7$ -2.8 ppm [23], and in spirooxepines ~2.0 ppm [18]. The other signals in the spectrum also do not contradict the structure II'e. Thus, the multiplet in the region of ~6.0 ppm evidently belongs to the protons H<sup>y</sup> and H<sup>m</sup>. The signal of the proton H<sup>n</sup> falls in the region of the shifts of the aromatic protons, which is also characteristic of the analogous proton of nitrosubstituted spirobenzopyran [24]. Supplementary investigations showed that the transition of the merocyanine IIe to the chromene II'e occurs not only in chloroform but also in deuteroacetone, as is also indicated by the PMR spectrum. However, in this solvent the conversion does not go to completion, since the signals of the C- and N-methyl groups of the merocyanine IIe (1.84 and 4.01 ppm) are observed in the spectrum together with the signals of the cyclic form. The ratio of the cyclic and merocyanine forms is ~5:1.

Thus, a study of the PMR spectra of the merocyanine IIe showed that this compound is capable of partial or complete conversion to an indoline derivative of benzopyran (II'e) in relatively nonpolar solvents as a result of intramolecular cyclization. This property of the merocyanine was also detected with the aid of the absorption spectra (Fig. 1). A solution of the merocyanine in ethanol has a bright blue color, while in mixtures containing various ratios of benzene and ethanol it has a blue color, the intensity of which is lower the larger the amount of benzene contained in the solvent mixture. The absorption spectra of these solutions represent a family of curves with isobestic point in the region of ~350 nm (Fig. 1, curves 1-4); the absorption spectrum of dinitrosubstituted merocyanine IIa (curve 5), which, like photomerocyanines of indoline spiropyrans [25], possesses two absorption bands in the visible region, an intense long-wave band with  $\lambda_{max}$  562 nm and extinction coefficient on the order of  $5 \cdot 10^4$  (corresponds to the oscillation of the charge along the chromophore chain of the merocyanine) and a less intense band with  $\lambda_{max}$  422 nm (corresponds to the oscillation of the charge in the quinone allide fragment of the molecule), is cited for comparison. A comparison of curves 1-4 and the extinction coefficients of the maxima of the absorption bands with the spectrum of dinitrosubstituted merocyanine permits us to conclude that in the solutions studied compound IIe exists in the form of a mixture of two forms at equilibrium merocyanine and chromene; the latter does not adsorb in the visible region of the spectrum. Taking into consideration the values of the apparent extinction coefficients at the absorption maxima of curves 1-4 in comparison with curve 5, it can be assumed that the concentrations of the merocyanine and chromene forms are comparable in order of magnitude.

Compound IIe does not possess photochrome properties, since the merocyanine-chromene equilibrium is unchanged under the action of light.

The results of our investigation show that condensation of a Fischer base with 5-nitro-2-hydroxycinnamaldehyde in acetic acid leads to the formation of a merocyanine, which can be converted to a closed form in relatively nonpolar solvents. However, cyclization forms not the spirooxacine I but an indolinylidenemethyl derivative of benzopyran (IIe), as a result of the great thermodynamic stability of the latter. These results and the data obtained earlier [3] permit us to conclude that spirooxocines of type I cannot exist. In connection with this, let us note that the production of the spirooxocine IV in the reaction of 2,3-trimethyleno-1-benzopyrylium perchlorate with o-hydroxycinnamaldehyde was reported in [1]. Evidently in this case too a benzopyran structure V corresponds to the reaction product.



## EXPERIMENTAL

The PMR spectra of compound IIe were recorded on Varian CFT-20 (80 MHz) [in  $CDCl_3$  and  $(CD_3)_2SO$ ] and Varian XL-100A-12 (100 MHz) [in  $(CD_3)_2CO$ ] instruments. The chemical shifts were measured relative to tetramethylsilane as an internal standard. The IR spectrum was recorded on a UR-20 instrument, the absorption spectra on a Specord spectrophotometer.

1,3,3-Trimethyl-4'-[3-(1,3,3,trimethylindolin-2-ylidene)-1-propenyl-1]-6'-bromoindoline-2-spiro-2'-chroman (IIIb). To a solution of 1.0 g (4.40 mmoles) 5-bromo-2-hydroxycinnamaldehyde in 17 ml of acetic acid we added 0.76 g (4.38 mmoles) of Fischer base in 4 ml of acetic acid and left at room temperature for seven days. Then the mixture was poured out onto ice and neutralized with a saturated solution of sodium carbonate. The blue-black precipitate formed was extracted with ether. The ether solution was washed with water, dried in magnesium sulfate, and the ether evaporated. The residue was dissolved in alcohol and poured out into water. The precipitate formed was removed. Yield 0.97 g (79%, calculated for the Fischer base). It was crystallized from a benzene ethanol mixture. The crystals were light yellow. Mp 172-174°C. Gives no depression of the melting point with a known sample, produced according to the method of [4].

<u>1,3,3-Trimethyl-4'-[3-(1,3,3-trimethylindolin-2-ylidene)-1-propenyl-1]-6',8'-dibromoin-</u> <u>doline-2-spiro-2'-chroman (IIIc).</u> Produced analogously to compound IIIb by condensation of <u>1.0 g (3.26 mmoles) of 3,5-dibromo-2-hydroxycinnamaldehyde with 0.57 g (3.26 mmoles) Fischer</u> base in 22 ml of acetic acid. Yield 0.69 g (66%, calculated for the Fischer base). Crystallized from a benzene-ethanol mixture. Light yellow crystals. Mp 161-163°C. Gives no depression of the melting point with a known sample, produced according to the method of [4].

<u>1,3,3-Trimethyl-2-[4-(2-oxido-5-nitrophenyl)-1,3-butadienyl-1]-3H-indoleninium (IIe).</u> Produced by condensation of 0.97 g (5.02 mmoles) 5-nitro-2-hydroxycinnamaldehyde with 0.87 g (5.02 mmoles) of Fischer base in 39 ml of acetic acid at room temperature for a period of 10 days. The precipitate formed after the reaction mass was poured out onto ice and neutralized with sodium carbonate was filtered off and washed with water. Yield 1.60 g (91%). For additional purification the product was dissolved in acetone, filtered, and the acetone solution partially evaporated. A greenish-black powder was formed. Mp 204-206°C. IR spectrum (liquid petrolatum): 1520, 1345 cm<sup>-1</sup> (NO<sub>2</sub>). Found: N 7.7%; M 348 (mass spectrometrically on a Varian MAT-311A instrument.  $C_{21}H_{20}N_2O_6$ . Calculated: N 8.0%; M 348.

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INDOLE DERIVATIVES.

125.\* SYNTHESIS OF DISUBSTITUTED TRYPTAMINES

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Disubstituted tryptamines, containing methyl, methoxy, nitro, and amino groups, chlorine, and bromine in the benzene ring, were synthesized. The influence of substituents on the course of individual stages of synthesis was noted.

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The radioprotective activity chiefly of monosubstituted tryptamines has been studied heretofore [2]. The number of disubstituted tryptamines produced and studied is small. We synthesized disubstituted tryptamines<sup>†</sup> according to the scheme of Abramovich and Shapiro:



a  $R^2 = CH_3O$ ,  $R^4 = CH_3$ ; b  $R^2 = R^4 = CH_3$ ; c  $R^1 = R^4 = CH_3$ ; d  $R^1 = R^4 = CI$ ; e  $R^2 = R^4 = CI$ ; f  $R^1 = R^2 = CI$ ; g  $R^2 = R^3 = CI$ ; h  $R^2 = CH_3$ ,  $R^4 = Br$ ; i  $R^1 = NO_2$ ,  $R^4 = CH_3$ ; j  $R^2 = CH_3$ ,  $R^4 = NO_2$ ; k  $R^2 = CH_3O$ ,  $R^4 = NO_2$ ; l  $R^1 = NO_2$ ,  $R^4 = CH_3O$ ; m  $R^2 = R^4 = CH_3O$ ; n  $R^2 = R^3 = CH_3O$ ; o  $R^1 = R^4 = CH_3O$ ; p  $R^1 = R^3 = CH_3O$ ; q  $R^2 = CH_3O$ ,  $R^4 = CH_3O$ . Here and henceforth, unless superscripts are indicated, R = H

\*For communication 124, see [1]. <sup>†</sup>The radioprotective activity of the compounds obtained was reported earlier [3].

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