PYRROLOINDOLES.

4.* SPATIAL ISOMERISM OF 3,8-DIFORMYL-1H,6H-PYRROLO[2,3-e]INDOLE DIOXIMES

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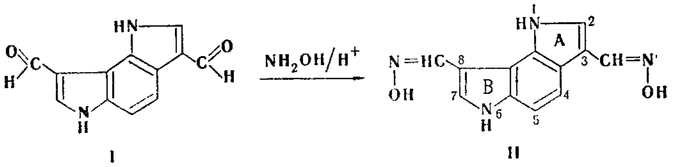
It is shown that 3,8-diformyl-1H,6H-pyrrolo[2,3-e]indole dioxime is produced in the form of a mixture of geometrical isomers, which were separated by column chromatography. It was established by PMR spectroscopy that they have anti,syn and syn,syn configurations with a cisoid—transoid conformation of the side chains.

3,8-Diformyl-1H,6H-pyrrolo[2,3-e]indole (I) [1] readily undergoes condensation with hydroxylamine. In a slightly acidic medium the reaction proceeds with both formyl groups of the dialdehyde. Dioxime II is produced in the form of a mixture of geometrical isomers (a and b with low and high R_f values, respectively), which were separated by means of column chromatography; their structures were established by PMR spectroscopy.



I

II

The dioximes obtained can be distinguished by the conformation and configuration of the side chains.

It is known [3] that in the PMR spectra of isomeric oximes of 3-formyl indole deshielding of the azomethine proton due to the anisotropic effect of the hydroxy group is maximal in the case of the syn configuration, while deshielding of the 2-H proton is maximal for the anti configuration of the azomethine fragment in the case of a close orientation of the 2-H proton and the C=N bond, i.e., for the cisoid conformation of the C=N and C=C bonds of the heteroring.

It follows from the data from the PMR spectra of isomers II (Table 1) that the chemical shifts of the protons for 1-H and pyrrole ring B for the two isomers are identical. We have previously found [1] that the 3,8-diformyl derivative contains an intramolecular hydrogen bond of the 1-H proton with the oxygen atom of the aldehyde group in the 8 position. If the oxygen atom is replaced by an amino group, despite the loss of conjugation of the H-chelate ring, the intramolecular bond in it becomes stronger; this is associated with the favorable overlapping of the orbitals of the atoms that participate in this bond [1]. Consequently, in this case also there should be a rather strong intramolecular hydrogen bond of the NH...N type, which stabilizes the syn configuration and the transoid conformation of the side chain of pyrrole ring B of II for both isomers a and b. It is now apparent that isomers a and b differ only with respect to the geometry of the substituent of pyrrole ring A.

It follows from a comparison of the data for isomers a and b that the chemical shifts of the 2-H and CH=N protons undergo the most pronounced change; the change in them is antibatic: $\Delta\delta_{2\text{-H}} = -0.79$, and $\Delta\delta_{CH=N} = 0.55$ ppm. The magnitudes and signs of these changes indicate that the protons of the OH and CH groups in isomer a have an anti orientation, while those in isomer b have a syn orientation. The signal of the 4-H proton ($\delta\Delta_{4\text{-H}} = 0.31$ ppm) is also sensitive to a change in the configuration; this is in agreement with the data

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*See [1, 2] for Communications 2 and 3.

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TABLE 1. Chemical Shifts (δ, ppm) and Spin–Spin Coupling Constants (J, Hz) for IIa and IIb in d_6-Acetone*

Compound	1-H	2-H	4-H	5-H	6-H	7-H	CH=N at C_3	CH=N at C_8	J, Hz
IIa anti,syn	11,3	8,22	7,69	7,29	10,8	7,64	7,79	8,42	$J_{45}=8{,}6$ $J_{12}=J_{67}\approx 2{,}7$
IIb syn,syn	11,3	7,43	8,00	7,25	10,8	7,62	8,34	8,42	$J_{45}=8{,}6$ $J_{12}=J_{67}\approx 2{,}6$

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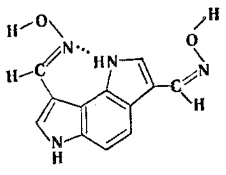
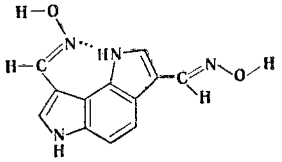
*Insoluble in nonpolar solvents.

in [3], in which by comparison with the data for a 4-methyl-substituted model it is shown that the oximes of 3-acylindoles exist in the cisoid conformation. It is apparently the least sterically strained conformation. Consequently, the side chains of pyrrole rings A in isomers a and b have a cisoid conformation.

Thus the isolated geometrical isomers a and b of 3,8-diformyl-1H,6H-pyrrolo[2,3-e]indole dioximes (II) have, respectively, anti,syn-IIa and syn,syn-IIb configurations with a cisoid-transoid conformation of the side chains. The ratio of isomers IIa-IIb is 3:1, in agreement with the data in [3].



IIa



IIb

EXPERIMENTAL

The course of the reaction and the purity of the compounds were monitored on Silufol UV-254. Silica gel with a particle size of 100/160 μ was used for preparative column chromatography. The IR spectrum was recorded with a UR-20 spectrometer. The UV spectra of solutions of the compounds in ethanol were recorded with a Specord spectrometer. The PMR spectra were obtained with a Varian CFT-20 spectrometer (80 MHz) with tetramethylsilane as the internal standard. The accuracy in the measurement of the chemical shifts was ±0.01 ppm, and the spin–spin coupling constant was ±0.1 Hz.

3,8-Diformyl-1H,6H-pyrrolo[2,3-e]indole Dioximes (IIa, b). A 0.15-g (2.1 mmole) sample of hydroxylamine hydrochloride and a solution of sodium bicarbonate at pH 4-5 were added to a hot solution of 0.2 g (1 mmole) of 3,8-diformyl-1H,6H-pyrrolo[2,3-e]indole (I) in 100 ml of ethanol, and the reaction mixture was refluxed for 1 h. The solvent was removed by evaporation *in vacuo*, the residue was treated with water up to 50 ml, and the pH of the solution was brought up to pH 6-7. The resulting precipitate was removed by filtration, washed with water, and dried. The yield of the mixture of the two geometrical isomers was 0.19 g (80%). IR spectrum (in mineral oil): 3370 (NH), 3250-3320 (broad band, OH), and 1635 cm^{-1} (C=N). The isomers were separated by column chromatography by elution with petroleum ether–ether (5:4). Work-up of the eluate with R_f 0.53 [ethyl acetate–benzene (6:5)] yielded 0.03 g (12%) of syn,syn isomer IIb as colorless crystals with mp 155-156°C. UV spectrum, λ_{max} (log ε): 211 (4.52) and 282 nm (4.50). Found: C 59.2; H 4.3; N 23.2%. $C_{12}H_{10}N_4O_2$. Calculated: C 59.5; H 4.1; N 23.1%.

Elution was continued with petroleum ether–ether (1:1). Work-up of the eluate with R_f 0.34 [ethyl acetate–benzene (6:5)] yielded 0.09 g (38%) of anti,syn isomer IIa as colorless crystals that darkened at 190°C but melted at 210-211°C. UV spectrum, λ_{max} (log ε): 216 (4.56) and 282 nm (4.51). Found: C 59.3; H 4.5; N 23.0%. $C_{12}H_{10}N_4O_2$. Calculated: C 59.5; H 4.1; N 23.1%.

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REACTION OF VINYLOGS OF A FISCHER BASE WITH SALICYLALDEHYDES

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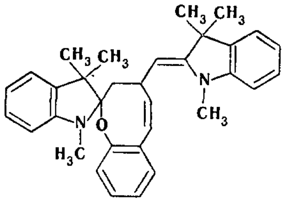
The reaction of vinylogs of the Fischer base, viz., 1,3,3-trimethyl-2-(3-methyl-2-buten-1-ylidene)indoline, 1,3,3-trimethyl-2-(2-penten-1-ylidene)indoline, 1,3,3-trimethyl-2-(3-phenyl-2-propen-1-ylidene)indoline, and 1,3,3-trimethyl-2-(2-buten-1-ylidene)indoline, with salicylaldehydes commences with displacement by the aromatic o-hydroxy aldehyde of the vinyl part of the dienamine molecule, as a result of which the usual spirobenzopyran is formed. In the case of the first two dienamines the reaction stops at this stage, whereas in the latter two a second molecule of dienamine adds to the initially formed spirobenzopyran at the double bond of the pyran ring to give "dicondensed" spirochromans.

At the present time a rather good deal of study has been devoted to spiropyrans of the indoline series, numerous representatives of which have valuable thermo- and photochromic properties [1]. It was recently reported [2] that fundamentally new indoline spirans that contain an eight-membered oxocin ring, viz., spirooxocins, had been synthesized. Babeshko and co-workers studied the condensation of a Fischer base with o-hydroxycinnamaldehydes and arrived at the conclusion that the products of this reaction are "dicondensed" spirooxocins with general formula I. Nothing regarding the photochromic properties of the compounds obtained was stated in the paper, although it is known that such "dicondensed" products in series of indoline spirobenzopyrans do not have these properties [1, p. 254].



I

We made an attempt to achieve the synthesis of "monocondensed" spirooxocins starting from vinylogs of a Fischer base (I), which were recently obtained by French chemists by condensation of a Fischer base with saturated aliphatic aldehydes [3]. It was assumed that the reaction of dienamines IIa-c with salicylaldehydes would proceed with the formation of indoline spirans that contain an eight-membered oxocin ring. However, our study showed that "dicondensed" spirochromans V rather than spirooxocins are formed in this case (Scheme and Table 1)

The reaction of vinylogs of the Fischer base with salicylaldehydes evidently commences with displacement by the aromatic o-hydroxy aldehyde of the vinyl part of the dieneamine molecule in the form of the corresponding saturated aliphatic aldehyde; the usual spirobenzopyran (III) is formed in this case. Similar reactions involving replacement of one aldehyde by another have been described in the literature. For example, it is known that 3,5-dinitrosalicylaldehyde displaces salicylaldehyde from the molecule of the corresponding spiropyran [1, p. 257].

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