LITERATURE CITED

1. V. E. Kirichenko and O. N. Chupakhin, Khim. Geterotsikl. Soedin., No. 5, 675 (1974).
2. K. Ziegler and H. Zeisel, Ber., 64, 1848 (1930).
3. M. Khamana, Khim. Geterotsikl. Soedin., No. 9, 1155 (1973).
4. A. K. Sheinkman, Khim. Geterotsikl. Soedin., No. 1, 3 (1974).
5. S. M. Shein and T. M. Ivanova, Zh. Org. Khim., 5, 1816 (1969).
6. V. L. Rusinov, O. N. Chupakhin, V. A. Trofimov, M. I. Kollegova, and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., No. 2, 216 (1973).
7. V. A. Trofimov, O. N. Chupakhin, and Z. V. Pushkareva, Khim. Geterotsikl. Soedin., No. 5, 653 (1971).
8. V. L. Rusinov, Author's Abstract of Candidate's Dissertation, Sverdlovsk (1973).
9. A. M. Émanuél and D. G. Knorre, Course in Chemical Kinetics [in Russian], Moscow (1974).
10. P. Ris, P. Skrabal, and H. Zollinger, Angew. Chem., 84, 921 (1972).
11. I. Heilbron and G. M. Bunbury (editors), Dictionary of Organic Compounds, Vols.1-3, Eyre and Spottiswoode, London (1953).
12. General Laboratory Manual of Organic Chemistry [in Russian], Mir, Moscow (1965), p. 613.

FORMATION OF A SPIRAN STRUCTURE IN THE CONDENSATION OF 2-AZAFLUORENE WITH ESTERS OF α, β-UNSATURATED ACIDS

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4'-Hydroxy-3-methyl-2',6'-diphenyl-3'ethoxycarbonylspiro(2-azafluorene-9,1'-cyclohex-3'-ene) was obtained by condensation of 3-methyl-2-azafluorene with ethyl cinnamate in the presence of potassium. The chemical mechanism of its formation and its three-dimensional structure are discussed.

Fluorene undergoes the Michael reaction with nitriles of α,β-unsaturated acids (for example, see [1]), but it does not react with their esters in the presence of alkaline catalysts [2]. We have established that the reaction of 3-methyl-2-azafluorene (I) with ethyl cinnamate in the presence of potassium leads to 4'-hydroxy-3-methyl-2',6'-diphenyl-3'-ethoxycarbonylspiro(2-azafluorene-9,1'-cyclohex-3'-ene) (II), the chelate structure of which is confirmed by the IR spectral data and also by the presence in the PMR spectrum of a singlet of an OH group at 12.65 ppm.

Keto ester II was converted to oxospiran V by hydrolysis and decarboxylation. Azafluorrene I evidently initially undergoes Michael condensation with ethyl cinnamate, and the resulting 3-methyl-9-bis(1-phenyl-2-ethoxycarbonylethyl)-2-azafluorene undergoes subsequent Dieckmann cyclization to give spiro compound II.

Ethyl acrylate and ethyl crotonate were subjected to a similar condensation with azafluorene I. Spirans III (previously obtained by a different method [3]) and IV were obtained. (See scheme on following page.)

It was shown by the double-resonance and INDOR methods that the signal at 5.62 ppm in the PMR spectrum of II (Table 1) is due to an aromatic proton that couples with two other protons with spin–spin coupling constants (SSCC) J = 8.0 and 1.5 Hz. Consequently, the

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TABLE 1. PMR Spectrum of II in $CDCl_3$

Assignment of the signals	δ, ppm (J, Hz)
CH_3—CH_2	0,80t (7,0)
CH_3—CH_2	3,71—4,03 m
5-H_e	2,98 q (13,0; 2,0)
5-H_a	3,17 q (13,0; 3,5)
2-H	3,64 s
3-CH_3	2.62s
1-H	8,76 s
8-H	5,62 q (8,0; 1,5)
7-H	6,78 q (8,0; 6,0)*
6-H	6,98sex (6,0; 1,0)
Other aromatic protons	6,27—7,43
4-OH	12,65s

*The J values were found by the INDOR method.

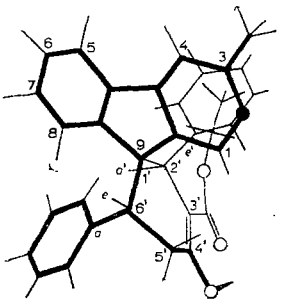
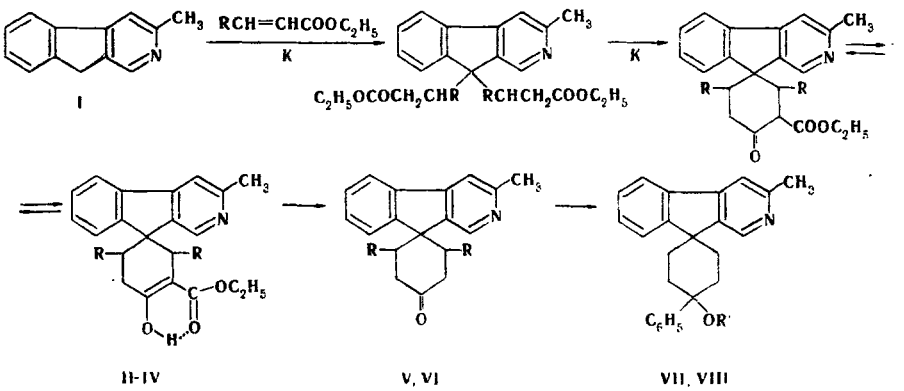


Fig. 1. Three-dimensional structure of II: ●) nitrogen atom; O) oxygen atom. The fine lines designate the C—C bonds situated behind the plane of the azafluorene system.



II, V R = C_6H_5; III, VI, VII R = H; IV R = CH_3, VIII R = COC_2H_5

ortho and meta positions with respect to this proton are free. This proton may be either the 5-H or 8-H proton. The 5-H proton is excluded from consideration because of the impossibility of additional shielding for it, whereas a fixed orientation above the plane of the benzene ring at C_6 is possible for 8-H, a consequence of which is a diamagnetic shift of its signal. It follows from the SSCC constants of the 5-6-H protons (2.0 and 3.5 Hz, respectively) that the the 6-H hydrogen is equatorially oriented and the phenyl ring is axially oriented. It follows from an analysis of a Stuart—Briegleb molecular model of II that the phenyl group attached to C_2 can only be equatorially oriented, since a model cannot be constructed at all in the case of its axial orientation because of the steric interaction of the two axial phenyl groups attached to C_2 and C_6. A distorted chair form is the most preferable conformation for the cyclohexene ring. The $J_{5,6}$ values determined by the magnitudes of the corresponding dihedral angles are in best agreement with this conformation. The C_3—C_5 fragment is oriented on the side of the nitrogen-containing ring; if this fragment had the opposite orientation, the conditions of simultaneous shielding of the 8-H proton by one of the benzene rings of the spiro ring and the axial orientation of the phenyl ring attached to C_6 would not be observed.

On the basis of these data it may be assumed that in spiro compound II in the indicated conformation and orientation of the cyclohexene ring the phenyl groups attached to C_2 and C_6 are trans oriented, the phenyl group attached to C_2 is pseudoequatorially oriented, and the phenyl ring attached to C_6 is pseudoaxially oriented (Fig. 1).

Yet another fact attests to the correctness of the selected structure of II. In the chelate structure the hydroxyl group attached to C_4 and the ester carbonyl group are fixed, as a result of which steric interaction arises between the phenyl group attached to C_2 and

the ethoxy group leading to restricted rotation about the O—acyl and O—alkyl bonds. It follows from an examination of the molecular model that in the case of free rotation about the C—C bond the methyl group of the ethoxy group should be situated in the region of shielding by the phenyl ring attached to C_2; in fact, the signal of the methyl group in the PMR spectrum is found at δ 0.80 ppm rather than at 1.20 ppm [4].

EXPERIMENTAL

The molecular weights were determined with an MKh-1303 mass spectrometer. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of $CDCl_3$ (II) and CF_3COOH (VII) solutions were obtained with an HA-100D spectrometer with hexamethyldisiloxane (II) and tetramethylsilane (VII) as the internal standards.

4'-Hydroxy-3-methyl-2',6'-diphenyl-3'-ethoxycarbonylspiro(2-azafluorene-9,1'-cyclohex-3-ene) (II). A 0.88-g (0.022 g-atom) sample of finely cut potassium was added to a solution of 2 g (11 mmole) of I in 30 ml of benzene, and a solution of 5.6 g (32 mmole) of ethyl cinnamate in 10 ml of benzene was added gradually with stirring to the red reaction mixture. It was then stirred at 60° for 2 h, after which it was cooled to room temperature, treated with 30 ml of water, and extracted with 500 ml of ether. The ether—benzene extract was dried with magnesium sulfate, the solvents were removed, and the residue was purified with a chromatographic column filled with silica gel (elution with chloroform) to give, after crystallization from hexane) 1.08 g (20%) of colorless crystals of spiran II with mp 203-204° and R_f 0.7 [Silufol, chloroform—ethanol (97:3)]. IR spectrum: 1660 (C=O group participating in a chelate bond), 1615, 1570, 1500, 760, 740, and 702 cm^{-1}. Found: C 81.6; H 5.8; N 3.1%; M 487 (mass spectrometrically). $C_{33}H_{29}NO_3$: Calculated: C 81.3; H 6.0; N 2.9%. The picrate had mp 198-202° (dec., from alcohol). Found: N 7.6%. $C_{33}H_{29}NO_3 \cdot C_6H_3N_3O_7$. Calculated: N 7.8%.

4'-Hydroxy-3-methyl-3'-ethoxycarbonylspiro(2-azafluorene-9,1'-cyclohex-3'-ene) (III). A 0.88-g (0.022 g-atom) sample of finely cut potassium was added to a solution of 2 g (11 mmole) of I and 3 g (30 mmole) of ethyl acrylate in 25 ml of absolute benzene, and the mixture was refluxed for 4 h. Ethanol (5 ml) was added, and the mixture was treated successively with 20 ml of water and 500 ml of ether. The benzene—ether extract was dried with magnesium sulfate, the solvents were removed, and the residue was separated with a chromatographic column filled with silica gel (elution with chloroform) to give 2 g (54%) of oily spiral III. IR spectrum: 1657, 1623, 767, 750, and 715 cm^{-1}. The product had an R_f value of 0.6 (same system as above) and a molecular weight of 335 (by mass spectrometry). The picrate had mp 199-200° (from alcohol) [3].

4'-Hydroxy-2',3,6'-trimethyl-3'ethoxycarbonylspiro(2-azafluorene-9,1'-cyclohex-3'-ene) (IV). This compound was obtained as above by reaction of 2 g (11 mmole) of I, 3.4 g (30 mmole) of ethyl crotonate, and 0.88 g (0.022 g-atom) of potassium in 30 ml of benzene. Chromatography of the crude product yielded 1.2 g (36%) of oily spiran IV with R_f 0.6 (same system as above). The picrate had mp 194-196° (from alcohol). Found: N 9.4%. $C_{23}H_{25}NO_3 \cdot C_6H_3N_3O_7$. Calculated: N 9.5%.

4'-Oxo-3-methyl-2',6'-diphenylspiro(2-azafluorene-9,1'-cyclohexane) (V). A mixture of 0.22 g (0.45 mmole) of keto ester II, 3.5 ml of acetic acid, 3.5 ml of concentrated hydrochloric acid, and 0.7 ml of water was refluxed for 13 h, after which it was neutralized with 20% sodium hydroxide and extracted with benzene. Workup of the extract gave 0.09 g (40%) of colorless crystals of ketone V with mp 199.5-200.5° (from hexane—ethyl acetate). IR spectrum: 1723, 1623, 1565, 1502, 758, 738, and 702 cm^{-1}. The product had a molecular weight of 415 (by mass spectrometry). Found: C 86.4; H 6.0; N 3.4%. $C_{30}H_{25}NO$. Calculated: C 86.7; H 6.07; N 3.37%.

4'-Oxo-3-methylspiro(2-azafluorene-9,1'-cyclohexane) (VI). This compound was similarly obtained from spiran III. The residue remaining from the extract after removal of the benzene by distillation was converted to the hydrochloride, from which the free base was isolated with a column filled with activity II Al_2O_3 (elution with chloroform) to give the product, with mp 210-212° (from heptane—ethyl acetate), in 54% yield. IR spectrum: 1730 cm^{-1}. PMR spectrum, δ, ppm: 2.85 (3H), 2.37 (4H), and 3.01 (4H). Found: C 81.7; H 6.9; N 5.9%. $C_{18}H_{17}NO$. Calculated: C 82.0; H 6.5; N 5.4%.

3-Methyl-4'-hydroxy-4'-phenylspiro)2-azafluorene-9,1'-cyclohexane) (VII). A solution of 1 g (3.8 mmole) of ketone VI in 30 ml of dry toluene was added gradually at 0° to phenyl-

lithium, obtained from 0.1 g (0.014 g-atom) of lithium and 1.45 g (9.2 mmole) of bromobenzene in 10 ml of ether, after which the mixture was stirred at room temperature for 1 h. The ether was removed by distillation, and the residual mixture was refluxed for 2 h. It was then treated with 50 ml of water, and the reaction products were extracted with benzene. The benzene extract was dried with sodium sulfate and worked up to give 1.1 g (85%) of colorless crystals of alcohol VII with mp 231-235° (from benzene–ligroin). IR spectrum: 3556 (associated OH group) and 703 cm^{-1} (monosubstituted benzene ring). Found: C 84.9; H 6.7; N 4.0%. $C_{24}H_{23}NO$. Calculated: C 84.4; H 6.8; N 4.1%.

A mixture of 0.52 g (1.5 mmole) of alcohol VII, 2 g (15 mmole) of propionic anhydride, and 15 ml of pyridine was refluxed for 12 h, after which the pyridine and excess propionic anhydride were removed by vacuum distillation. The residual mixture was treated with 50 ml of water and made alkaline with sodium carbonate solution. The reaction products were extracted with ether. The ether extract was passed through a column filled with aluminum oxide (elution with ether) to give 0.32 g (53%) of colorless crystals of ester VIII with mp 175-181.5° (from heptane). Found: N 3.7%. $C_{27}H_{27}NO_2$. Calculated: N 3.5%.

LITERATURE CITED

1. N. Campbell and A. E. S. Fairfull, J. Chem. Soc., 1239 (1949).
2. R. S. Taylor and R. Connor, J. Org. Chem., 6, 696 (1941).
3. N. S. Prostakov, V. P. Shalimov, and V. P. Zvolinskii, Khim. Geterotsikl. Soedin., No. 11, 1668 (1972).
4. High-Resolution Nuclear Magnetic Resonance Spectra Catalog, Varian Associates, No. 79 (1962).

SYNTHESIS AND PROPERTIES OF CHROMONO[2,3-b]PYRIDINES

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Chromono[2,3-b]pyridines were synthesized by cyclization of 2-phenoxynicotinic acids. Their UV spectra are due to π–π^* transitions and, in contrast to the spectrum of xanthone, are of high intensity. In concentrated sulfuric acid the chromono[2,3-b]pyridines form a doubly charged pyridinium–pyrylium ion, and the reaction is accompanied by an increase in the intensity of the long-wave bands (330-340 nm) in the UV spectrum. The spectrophotometrically determined pK_a values of 8-R-chromono[2,3-b]pyridines range from –8.62 to –9.81, depending on the substituent in the 8 position, and correlate with Hammett σ_p constants.

Practically no study has been devoted to chromono[2,3-b]pyridines. In the present research in order to ascertain the effect of the pyridine ring on the properties of the benzopyran fragment of these compounds and compare them with the properties of xanthones, we synthesized 8-R-chromono[2,3-b]pyridines (VI-X, Table 1) by cyclization of substituted 2-phenoxynicotinic acids (I-V, Table 1) by means of phosphorus oxychloride or polyphosphoric acid (PPA). (See scheme on following page.)

In the case of VI it was shown that replacement of the carbonyl oxygen atom by a sulfur atom to give thiochromono[2,3-b]pyridine (XI) occurs in the reaction with phosphorus pentasulfide. Heating the same compound with an alcoholic potassium hydroxide solution is accompanied by cleavage of the pyran ring to give 3-(o-hydroxybenzoyl)-2-pyridone (XII). Cyclization to give chromono[2,3-b]pyridine in 73% yield is observed in turn when XII is

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