PREPARATION OF 9-PHENYLETHYNYL-4-AZAFLUOREN-9-OL AND 9-PHENACYLIDENE-4-AZAFLUORENE AND THEIR CONVERSION TO SPIRO COMPOUNDS

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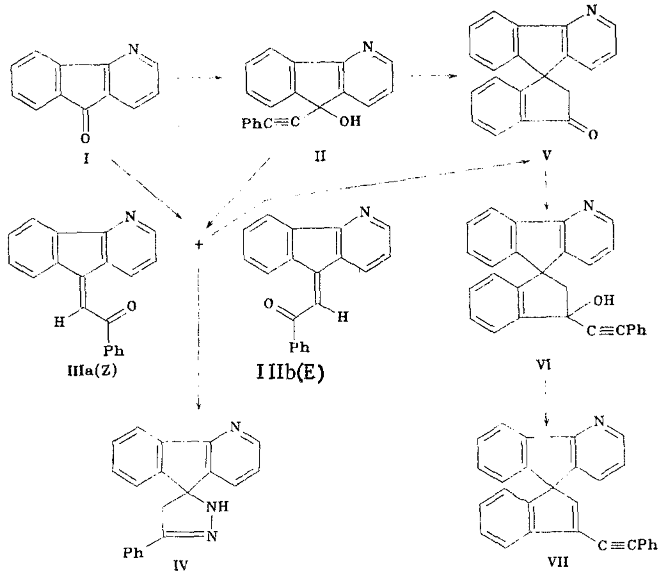
9-Phenylethynyl-4-azafluoren-9-ol, which was obtained from 4-azafluorenone and phenylethynylmagnesium iodide, was used in syntheses of isomeric 9-phenacylidene-4-azafluorenes and spiro compounds with indene, indan, and pyrazoline fragments. It is assumed that the conversion of 9-phenacylidene derivatives to spiro compounds takes place via intramolecular substitution.

Information regarding ethynyl derivatives of azafluorenes is not available. Their synthesis and study are of interest in the search for physiologically active substances among new acetylene derivatives and also for their use in syntheses of new heterocyclic systems. We have carried out the condensation of the accessible 4-azafluorenone (I) [1] with the Iotsich complex obtained from phenylacetylene and methylmagnesium iodide. The first representative of ethynyl derivatives of azafluorenes, viz., 9-phenylethynyl-4-azafluoren-9-ol (II), was isolated in high yield. 9-Phenacylidene-4-azafluorene (III), which was also synthesized by condensation of azafluorenone I with acetophenone, was obtained from alcohol II as a result of an acetylene-allene rearrangement.



According to the PMR spectral data, phenacylidene derivative III is produced in the form of a mixture of Z and E isomers (IIIa, b) in a ratio of 2:1. Their configurations were established from the PMR spectra data. The spectrum of a mixture of the isomeric ketones in C_6D_6 is presented in Fig. 1. The signal at weak field (δ 8.82 ppm) should be assigned to the absorption of the proton in the 1 position of the Z isomer in conformity with the observed spin–spin coupling constants: $J_{12} = 7.8$, $J_{13} = 1.5$, and $J_{1\alpha} = 0.3$ Hz. This large paramagnetic shift is most likely due to the deshielding effect of the magnetically anisotropic benzoyl group in a cis orientation relative to the pyridine ring. In the case of the E isomer the signal of the proton in the 8 position should experience a similar weak-

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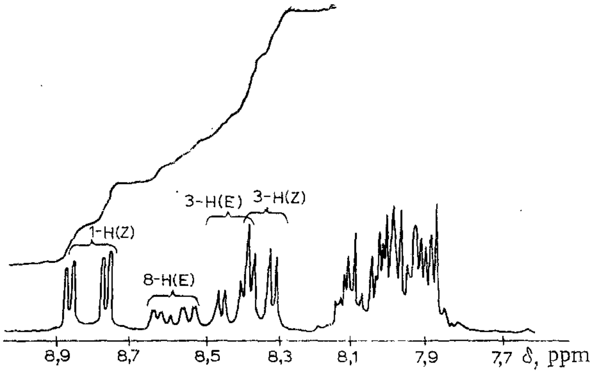

Fig. 1. Weak-field part of the PMR spectrum of Z- and E-9-phenacylidene-4-azafluorenes (IIIa, b) in C_6D_6.

field shift. In fact, a multiplet centered at 8.59 ppm, which has the fine structure characteristic for the 8-H proton in related compounds, is observed at weak field. The overall intensity of the signals of the 1H proton of the Z isomer and the 8-H proton of the E isomer is equal to the overall integral intensity of the adjacent and overlapped signals of the 3-H protons of IIIa (8.35 ppm, q, $J_{13} = 1.5$, $J_{23} = 4.8$ Hz) and IIIb (8.43 ppm, q, $J_{13} = 1.5$, $J_{23} = 4.8$ Hz). The ratio of the integral intensities of the 1-H signal of the Z isomer and the 8-H signal of the E isomer makes it possible to estimate the ratio of the Z and E isomers (Z:E = 2:1).

Phenacylidene derivative III was used in syntheses of two types of spiro compounds that contain an azafluorene fragment. 3'-Phenylspiro[4-azafluorene-9,5'-pyrazol-2'-ine] (IV) was obtained in quantitative yield in the reaction of III with hydrazine hydrate. A spiro compound with a different structure, viz., 3'-oxospiro[4-azafluorene-9,1'-indan] (V), is formed both in the treatment of phenacylidene derivative III with sulfuric acid and from azafluorenol II under the same conditions. In the latter case ethynylazafluorenol II evidently undergoes rearrangement to a phenacylidene derivative, which is converted to spiro compound V via intramolecular electrophilic substitution. The structures of the spiro compounds were confirmed by spectral and analytical data.

Several transformations of ketone V were studied in order to synthesize new ethynyl derivatives. 3'-Hydroxy-3'-phenylethynylspiro[4-azafluorene-9,1'-indan] (VI) was obtained from V and phenylethynylmagnesium iodide. When VI was treated with 25% sulfuric acid, it underwent dehydration rather than an acetylene-allene rearrangement, and 3'-phenylethynylspiro-[4-azafluorene-9,1'-indene] (VII) was formed in high yield.

EXPERIMENTAL

The PMR spectra of the compounds (III and VII in C_6D_6 and the remaining compounds in d_6-DMSO) were investigated with a Brucker WP-80 spectrometer (80 MHz) with tetramethylsilane as the internal standard. When necessary, $Eu(dpm)_3$ was added for the assignment of the signals. The multiplets were analyzed within the first-order approximation. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The mass spectra were obtained with an MKh-1303 mass spectrometer (70 eV) by direct introduction of the samples into the ion source.

9-Phenylethynyl-4-azafluoren-9-ol (II). An Iotsich reagent was obtained from 1.6 g (66 mmole) of magnesium, 9.3 g (66 mmole) of methyl iodide, and 18 g (180 mmole) of phenylacetylene in 15 ml of ether (activation with iodine), a solution of 1.5 g (8.2 mmole) of azafluorenone I in 50 ml of benzene was added gradually with heating, and the mixture was refluxed for 3 h. Water (50 ml) and 130 ml of a saturated solution of ammonium chloride were added successively, the benzene—ether layer was separated, and the reaction products were extracted from the aqueous layer with ether. The solvents were removed by distillation, the residue was triturated in heptane—ehtyl acetate (4:1), and the precipitate was washed with heptane to give 2 g (87%) of alcohol II with mp 179-180°C [from heptane—ethyl acetate (1:1)]. PMR spectrum: 8.07 (1H, q, 1-H), 7.37 (q, 2-H), 8.55 (1H, q, 3-H), 7.7-7.9 (2H, m, 5-H and 8-H), 7.4-7.6 (m, 6-H and 7-H), 7.35 (narrow m, C_6H_5), and 6.9 ppm (1H, s, OH); the overall intensity of the signals at 7.0-7.9 ppm was 8H; J_{12} = 7.5, J_{23} = 5.1, and J_{13} = 1.5 Hz. IR spectrum: 3190 (OH) and 2240 cm^{-1} (C≡C). Found: C 84.8; H 4.9; N 4.9%; M^+ 283. $C_{20}H_{13}NO$. Calculated: C 84.8; H 4.6; N 4.6%; M 283.

9-Phenacylidene-4-azafluorene (III). A) A solution of 1.5 g (5.3 mmole) of azafluorenol II in 50 ml of 25% sulfuric acid was heated at 100°C for 4 h, after which it was cooled and made alkaline with sodium carbonate. The reaction products were extracted with chloroform, and the extract was dried with magnesium sulfate and worked up to give 1.2 g (80%) of a mixture of isomers of III with mp 149-154°C (from heptane). IR spectrum: 1655 cm^{-1} (C=O). Found: C 84.3; H 4.5; N 4.8%; M^+ 283. $C_{20}H_{13}NO$. Calculated: C 84.8; H 4.6; N 4.6%; M 283.

B) A 0.5-ml (1.34 mmole) sample of a 15% alcohol solution of potassium hydroxide and 0.2 g (1.6 mmole) of acetophenone were added successively to a solution of 0.1 g (0.55 mmole) of azafluorenone I in 20 ml of ethanol, and the mixture was heated at 50°C for 3 h. It was then passed through a column (h = 10 cm, d = 2 cm) packed with aluminum oxide by elution with ether. The solvents were removed by distillation. According to TLC and mass-spectral data, the residue (0.095 g) contained a mixture of isomers of III. Crystallization of the residue from heptane gave 0.015 g (15%) of a mixture of IIIa and IIIb with mp 148-153°C.

3'-Phenylspiro[4-azafluorene-9,5'-pyrazol-2'-ine] (IV). A solution of 0.1 g (0.35 mmole) of a mixture of the isomers of III and 0.5 g (15 mmole) of hydrazine hydrate in 20 ml of ethanol was maintained at 70°C for 1.5 h, during which the initially yellowish reaction mixture became colorless. The mixture was cooled, and the precipitated crystals were removed by filtration and washed with ether to give 0.1 g (96%) of spiro compound IV with mp 149-152°C (dec.). PMR spectrum: 7.85 (1H, q, 1-H), 7.26 (1H, q, 2-H), 8.52 (1H, q, 3-H), 3.56 (2H, s, 4'-H_2), and 3.1-3.5 ppm (broad signal, N—H, underwent exchange with the residual water in the DMSO); J_{12} = 7.5, J_{23} = 4.8, and J_{13} = 15 Hz; the remaining protons were found at 7.3-7.8 ppm (9H, m). IR spectrum: 2180 cm^{-1} (N—H). Found: C 80.5; H 5.1; N 13.8%; M^+ 297. $C_{20}H_{15}N_3$. Calculated: C 80.8; H 5.1; N 14.1%; M 297.

3'-Oxospiro[4-azafluorene-9,1'-indan] (V). A) A 0.15-g (0.53 mmole) sample of a mixture of isomers of III was heated at 100°C for 3 h in 20 ml of sulfuric acid (monohydrate), during which the initially red mixture became pale yellow. The mixture was poured into 100 ml of ice water, and the aqueous mixture was neutralized with sodium carbonate. The reaction products were extracted with chloroform, the extract was dried with magnesium sulfate, the chloroform was removed by distillation, and the residue (0.12 g) was crystallized from heptane—ethyl acetate (3:1) to give 0.08 g (53%) of spiro compound V with mp 189-190°C.

B) A 1-g (3.5 mmole) sample of alcohol II was heated at 70-90°C for 1 h in 20 ml of sulfuric acid (monohydrate), after which the mixture was poured into 100 ml of ice water, and the aqueous mixture was neutralized with sodium carbonate. The reaction products were extracted with chloroform, the extract was dried with magnesium sulfate, the solvent was removed by distillation, and the residue (0.62 g of an oily substance) was applied to a column packed with aluminum oxide. Chromatography [elution with heptane—ether (1:4)] gave 0.15 g (15%) of a mixture of isomers IIIa and IIIb, 0.15 g (15%) of spiroindanone V, and 0.20 g (20%) of a mixture of III and V. PMR spectrum of indanone V: 7.71 (1H, q, 1-H), 7.34 (1H, q, 2-H), 8.70 (1H, q, 3-H), 7.95 (1H, m, 5-H), 6.71 (1H, m, 8-H), and 8.13 ppm (1H, m, 7'-H); J_{12} = 7.5, J_{23} = 4.9, and J_{13} = 1.5 Hz; 2'-H_2 spectrum of the AB type: δ_A = 3.16, δ_B = 3.42 ppm, J_{AB} = 19.9 Hz; remaining protons at 7.2-7.7 ppm (5H, m). PMR spectrum of V: 1715 cm^{-1} (C=O). Found: C 84.7; H 4.7; N 5.0%; M^+ 283. $C_{20}H_{13}NO$. Calculated: C 84.8; H 4.6; N 4.6%; M 283.

3'-Hydroxy-3'-phenylethynylspiro[4-azafluorene-9,1'-indan] (VI). A solution of 0.3 g (1.06 mmole) of spiro ketone V in 25 ml of benzene was added to phenylethynylmagnesium iodide obtained from 4.6 g (45 mmole) of phenylacetylene, 3.2 g (20 mmole) of methyl iodide, and 0.5 g (20 mmole) of magnesium in 30 ml of ether, and the mixture was refluxed for 1-1.5 h. Water (40 ml) and 80 ml of a saturated solution of ammonium chloride were added successively, and the resulting precipitate was removed by filtration, washed with water, and dried to give 0.3 g (73.5%) of colorless crystals of VI with mp 163-165°C [from ethyl acetate—benzene (1:1)]. PMR spectrum: 7.74 (1H, q, 1-H), 7.22 (1H, q, 2-H), 8.58 (1H, q, 3-H), 7.78 (1H, 3 d, 5-H), 6.30 (1H, 3 d, 8-H), 8.0 ppm (1H, m, 7'-H or 4'-H); J_{12} = 7.7, J_{23} = 4.8, J_{13} = 1.5, J_{56} = 7.4, J_{57} = 1.6, J_{58} = 0.7, J_{78} = 7.5, J_{68} = 1.3 Hz; 2'-H_2 spectrum of the AB type: $\delta_A = 2.98$, $\delta_B = 3.26$ ppm; $J_{AB} = 14.0$ Hz; remaining protons at 7.2-7.7 ppm (10H, m). IR spectrum: 3160 cm^{-1} (OH). Found: N 3.7%; M$^+$ 385. $C_{28}H_{19}NO$. Calculated: N 3.7%; M 385.

3'-Phenylethynylspiro[4-azafluorene-9,1'-indene] (VII). A 1.4-g (3.6 mmole) sample of acetylenic alcohol VI was heated in 80 ml of 25% sulfuric acid on a boiling-water bath for 4 h, after which the mixture was cooled and neutralized with sodium carbonate, and the reaction products were extracted with ether. The extract was dried with magnesium sulfate, and the ether was removed by distillation to give 0.78 g of an oily reddish-yellowish substance that solidified upon trituration in heptane to give 0.7 g (53.8%) of spiran VII with the same color and mp 160-161°C. PMR spectrum: 8.5 (1H, q, 3-H), 8.33 (1H, 3 d, 5-H), 6.45 (1H, 3 d 8-H), 6.3 ppm (1H, s, 2'-H); $J_{23} = 4.9$, $J_{13} = 1.6$, $J_{56} = 7.6$, $J_{57} = 1.2$, $J_{58} = 0.7$, $J_{78} = 7.5$, $J_{68} = 1.1$ Hz; the remaining protons were found at 6.5-7.8 ppm (3H, m). Found: C 91.5; H 4.4; N 4.0%; M$^+$ 367. $C_{28}H_{17}N$. Calculated: C 91.5; H 4.6; N 3.8%; M 367.

LITERATURE CITED

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DIAZO CARBONYL DERIVATIVES OF HETEROCYCLES.

3.* ALTERNATIVE 1,3-DIPOLAR ADDITION TO AZIDOALKYL α-DIAZO KETONES AND SYNTHESIS OF FIVE-MEMBERED HETEROCYCLES BASED ON THEM

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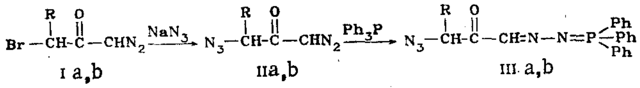
It is shown that the cycloaddition of dimethylacetylenedicarboxylate and N-phenylmaleinimide to azidoalkyl diazomethyl ketones leads to the corresponding 1,2,3-triazole and 2-pyrazoline derivatives. The electronic structure of one of the bisdipoles was determined.

Both diazo ketones [2, 3] and azides [4-6] react readily with various dipolarophiles to give five-membered heterocycles. When an azido grouping is present in the diazo ketone molecule, one cannot a priori predict the direction of 1,3-dipolar addition of dipolarophiles.

It is known that 2-furyl diazomethyl ketone reacts with acetylenedicarboxylic acid ester only at the diazomethine fragment to give pyrazoles and pyrazolines; the diene system of furan does not participate in cycloaddition [7]. In the case of azidoalkyl diazomethyl ketones, which contain two 1,3-dipoles, the reaction may take place at both the azido group and at the diazomethine fragment. A triazole system (VIa, b) or a triazoline system (Xa, b) should be formed in the first case, whereas a pyrazole system (VIIIa, b) or a pyrazoline system (XIIa, b) should be formed in the second case.

To study competitive 1,3-dipolar cycloaddition we synthesized azidoalkyl diazomethyl ketones IIa, b by the reaction of the corresponding bromoalkyl diazomethyl ketones Ia, b with sodium azide:



I—III a R=H, b R=CH$_3$

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*See [1] for communication 2.

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