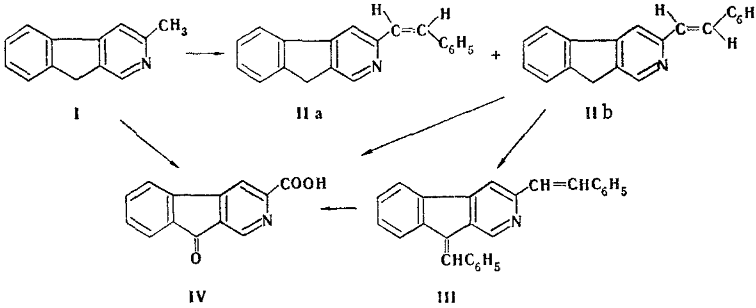
TRANSFORMATIONS OF 3-METHYL-2-AZAFLUORENE INVOLVING THE METHYL AND METHYLENE GROUPS

N. S. Prostakov, L. A. Gaivoronskaya,
G. Alvarado Urbina, L. M. Kirillova,
S. A. Soldatova, A. A. Savina,
and Mauricio Belei dos Santos

UDC 547.836: 542.953: 541.634

The condensation of 3-methyl-2-azafluorene with benzaldehyde at the methyl group, as a result of which the cis and trans forms of 3-styryl-2-azafluorene are formed, proceeds without catalysts. The subsequent condensation with benzaldehyde takes place in the presence of potassium ethoxide and leads to 3-styryl-9-benzylidene-2-azafluorene. Treatment of azafluorene with phenoxyacetyl chloride in the presence of triethylamine yielded 3-methyl-9-(α-hydroxy-β-phenoxyethylidene)-2-azafluorene. On the basis of the spectral data it was concluded that the latter exists in the form of a mixture of the enol form and the zwitterionic form. 3-Methyl-9-(γ-phenyl-α-cinnamoyloxyallylidene)-2-azafluorene was obtained by acylation of azafluorene with cinnamoyl chloride under the same conditions. The PMR and IR spectral data are presented.

The possibilities of transformations of methyl-substituted (in the pyridine ring) azafluorenes are more diverse than in the case of fluorene. In the present communication we describe the condensation of 3-methyl-2-azafluorene (I) with benzaldehyde at both of its reaction centers – the methyl and methylene groups. 3-Styryl-2-azafluorene (II) is obtained in the form of a mixture of cis (IIa) and trans (IIb) isomers when azafluorene I is heated for a long time with benzaldehyde without the catalysts that are normally used in such condensations in the case of α-methyl-substituted pyridines. The geometrical isomers of styryl derivative II differ with respect to their chromatographic mobilities, and this made it possible to isolate each of them.



Condensation of styryl derivative IIb with benzaldehyde in the presence of potassium ethoxide gave 3-styryl-9-benzylidene-2-azafluorene (III), which was previously obtained in [1]. Unsaturated II and III are oxidized under mild conditions to 2-azafluorenone-3-carboxylic acid (IV), which was also obtained by oxidation of azafluorene I with selenium dioxide in pyridine.

In the case of the reaction of azafluorene I with phenoxyacetyl and cinnamoyl chlorides it was established that acylation of I at the methylene group can be accomplished without prior metallation. 3-Methyl-9-(α-hydroxy-β-phenoxyethylidene)-2-azafluorene (V) was obtained by treatment of azafluorene I with phenoxyacetyl chloride in the presence of triethylamine at −10°C. On the basis of the IR spectral data (the absence of a keto group and the presence of a quaternized nitrogen atom) it may be assumed that this compound exists in the crystalline state in the form of a mixture of enol Va and zwitterion Vb. The IR spectrum of 3-methyl-9-(α-hydroxybenzylidene)-2-azafluorene, which was obtained in [2], has similar characteristics.

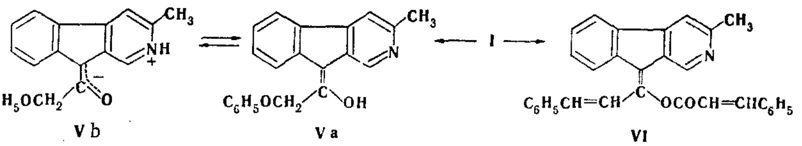
The existence of structures Va and Vb is confirmed by the data from the PMR spectra of solutions in CF_3COOD and CF_3COOH. Two singlets (4.92 and 5.42 ppm) of the methylene group of a phenoxymethyl grouping

---

Patrice Lumumba International-Friendship University, Moscow 117302. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 79–81, January, 1978. Original article submitted December 21, 1976.

and two signals [a doublet at 9.17 ppm and a doublet at 8.63 ppm (CF_3COOH); a singlet at 8.66 ppm and a singlet at 9.20 ppm (CF_3COOD)] of the α proton of the pyridine ring are observed in both cases. A signal providing evidence for protonation of Vb at $C_{(9)}$ (5.67 ppm 1H, 9-H) is present in the spectrum of a solution of Vb in CF_3COOH.

Thus in contrast to $C_{(9)}$-acylated derivatives of fluorene, which exist in keto and enol forms, the analogous 2-azafluorene derivatives have structures of the enol (Va) and zwitterionic (Vb) type.



Vb Va VI

3-Methyl-9-(γ-phenyl-α-cinnamoyloxyallylidene)-2-azafluorene (VI) was obtained under the above-described acylation conditions from azafluorene I and cinnamoyl chloride. The same O-acylated derivatives of the enol forms of the acyl derivatives at $C_{(9)}$ are also formed from fluorene [3].

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were obtained with a BS-487C spectrometer (80 MHz) with tetramethylsilane as the internal standard. The mass spectra were obtained with an MKh-1303 spectrometer. Column chromatography was carried out on activity II aluminum oxide (elution with hexane), and thin-layer chromatography (TLC) was carried out on the same support with ether (for II and III) and on Silufol UV-254 in a chloroform–ethanol system (97: 3) (for V and VI).

3-Styryl-2-azafluorene (II). A mixture of 9 g (50 mmole) of azafluorene I and 16 g (130 mmole) of benzaldehyde was refluxed for 20 h, after which the benzaldehyde was removed by distillation, and the residue was dissolved in ether. The ether solution was shaken with 40% sodium bisulfite and dried with magnesium sulfate. The ether was removed, and the residue (12 g) was separated with a column (h = 53 cm, d = 3.5 cm). Workup of the initial fraction gave 4.3 g (32%) of bright-yellow crystals of IIb with mp 128-130°C (from ligroin) and Rf 0.73. IR spectrum: 1640 (C = C) and 982 cm^{-1} (trans-CH). Found: C 88.9; H 5.7; N 5.0%. $C_{20}H_{15}N$. Calculated: C 89.2; H 5.6; N 5.2%. Workup of the next fraction gave 1.3 g (10%) of yellow crystals of IIa with mp 108-109°C (from ligroin) and Rf 0.53. IR spectrum: 1635 (C = C) and 960 cm^{-1} (cis-CH). Found: C 89.1; H 5.3; N 5.1%. $C_{20}H_{15}N$. Calculated: C 89.2; H 5.6; N 5.2%.

3-Styryl-9-benzylidene-2-azafluorene (III). A mixture of 1 g (3.5 mmole) of IIb, 0.5 g (4 mmole) of benzaldehyde, 10 ml of 10% potassium ethoxide, and 75 ml of ethanol was refluxed for 8 h, after which the alcohol, water, and benzaldehyde were removed by distillation. The residue was extracted with ether, and the extract was dried with sodium sulfate. The ether was removed from the extract, and the residue (1.43 g) was separated with a column to give 0.3 g (22%) of orange crystals of III with mp 148-150°C (from ligroin) and Rf 0.58. No melting-point depression was observed for a mixture of a sample of this product with a genuine sample [1].

2-Azafluorenone-3-carboxylic Acid (IV). A) A 5-g (30 mmole) sample of potassium permanganate was added in portions with vigorous stirring and cooling to 0°C to a solution of 1.5 g (5.3 mmole) of a mixture of isomers of II in 200 ml of acetone, and the mixture was then stirred at 20°C until it was completely decolorized. The manganese dioxide was removed by filtration and washed repeatedly with hot water, and the aqueous solution was evaporated to 20 ml. The concentrated solution was acidified to pH 5 with sulfuric acid and worked up to give 0.6 g (51%) of yellow crystals of acid IV with mp 211-213°C (from alcohol). IR spectrum: 2400-2900 (COOH) and 1700 cm^{-1} (CO). Found: C 69.5; H 3.3; N 6.2%. $C_{13}H_7NO_3$. Calculated: C 69.3; H 3.1; N 6.2%. The ethyl ester of acid IV was obtained as yellow crystals with mp 118-120°C (from ligroin). IR spectrum: overlapped bands at 1725 and 1720 cm^{-1} ($-COOC_2H_5$ and $>CO$). Found: C 71.3; H 4.6; N 5.9%. $C_{15}H_{11}NO_3$. Calculated: C 71.1; H 4.3; N 5.6%.

Acid IV was similarly obtained by oxidation of III.

B) A mixture of 2 g (11 mmole) of azafluorene I, 2.85 g (25 mmole) of selenium dioxide, and 150 ml of pyridine was refluxed gently with vigorous stirring for 4 h, after which the pyridine was partially removed by distillation (to a residual volume of 30 ml), and the supernatant liquid was decanted and poured into 10% potassium hydroxide solution. The alkaline mixture was extracted with ether. The aqueous solution was acidified with respect to Congo red with 50% sulfuric acid and worked up to give 1.6 g (64%) of acid IV with mp 211-213°C.

3-Methyl-9-(α-hydroxy-β-phenoxyethylidene)-2-azafluorene (V). A solution of 3.96 g (23 mmole) of phenoxyacetyl chloride in 20 ml of ether was added gradually at −10°C to a solution of 4 g (22 mmole) of azafluorene I and 2.22 g (22 mmole) of triethylamine in 150 ml of absolute ether, and the mixture was stirred at 20°C for 1 h. It was then made alkaline to pH 10 with sodium carbonate, and the resulting dark-brown precipitate was refluxed in 20 ml of chloroform. Workup gave 1.47 g (21.4%) of orange crystals of V with mp 197-198°C and R_f 0.32. IR spectrum: 3400, 3200 (OH); 2000 cm^{-1} $(=\overset{+}{N}H-)$. Found: C 80.1; H 5.32; N 4.4%; M 315 (by mass spectrometry). $C_{21}H_{17}NO_2$. Calculated: C 80.0; H 5.4; N 4.4%; M 315.

3-Methyl-9-(α-cinnamoyloxyallylidene)-2-azafluorene (VI). This compound was obtained from 1.8 g (10 mmole) of azafluorene I, 1.3 g (13 mmole) of triethylamine, 1.7 g (10 mmole) of cinnamoyl chloride, and 115 ml of ether, as in the synthesis of V. The residue from the ether layer was treated with hexane (extraction of azafluorene I) and was then crystallized from ethyl acetate to give 0.6 g (13%) of yellow crystals of VI with mp 222-224°C (dec.) and R_f 0.76. IR spectrum: 1735 (ester C=O); 1635, 1622 (C=C); 980 cm^{-1} (trans-CH). Found: C 84.1; H 5.2; N 3.0%; M 441 (by mass spectrometry). $C_{31}H_{23}NO_2$. Calculated: C 84.3; H 5.3; N 3.2%; M 441. The picrate had mp 214°C (dec., from alcohol). Found: N 8.1%. $C_{31}H_{23}NO_2 \cdot C_6H_3N_3O_7$. Calculated: N 8.4%.

LITERATURE CITED

1. N. S. Prostakov, S. Sipeu Moiz, A. T. Soldatenkov, V. P. Zvolinskii, and G. I. Cherenkova, Khim. Geterotsikl. Soedin., No. 10, 1398 (1971).
2. N. S. Prostakov, A. Ya. Ismailov, and V. P. Zvolinskii, Khim. Geterotsikl. Soedin., No. 7, 986 (1973).
3. G. W. H. Scherf and R. F. Brown, Can. J. Chem., 39, 1613 (1961).