ACYLATION OF 3-METHYL-2-AZAFLUORENE

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UDC 547.836:542.951

Acylation of 3-methyl-2-azafluorene under various conditions yielded the enol forms of its $(C_{(9)})$ acyl derivatives, whereas the ketol form was also isolated in the case of the p-nitrobenzoyl derivative. The character of the compounds formed in the reaction of 3-methyl-2-azafluorene with benzoyl chloride and acetic anhydride is discussed.

A number of $C_{(9)}$ acyl derivatives of 3-methyl-2-azafluorene (I) were previously obtained [1] in the condensation of I with carboxylic acid esters. In the present research we have accomplished the acylation of azafluorene I with benzoyl and p-nitrobenzoyl chlorides (in the presence or absence of dimethylaniline). The benzoyl derivative is obtained in enol form II. Both the enol (IIIa) and keto (IIIb) forms are isolated from the mixture of reaction products in the preparation of the p-nitrobenzoyl derivative. 3-Methyl-9-[α-hydroxy-(p-aminobenzylidene)]-2-azafluorene (IV) was obtained in the reduction of IIIa and was isolated only in the enol form.

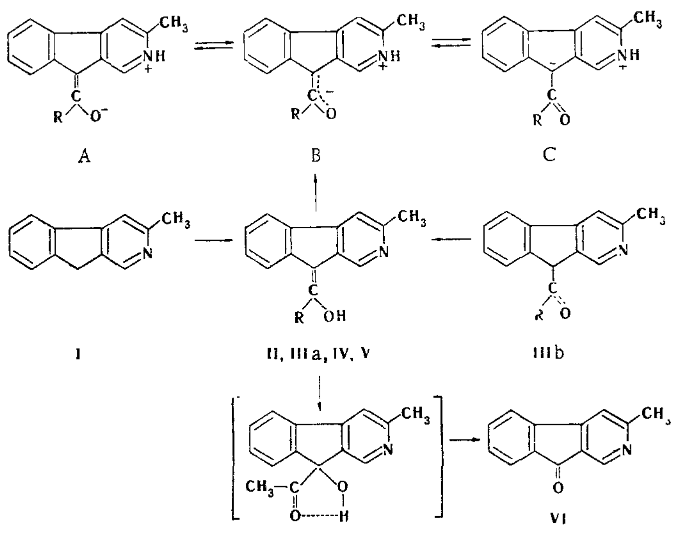
Fluorene does not react with refluxing acetic anhydride. Azafluorene I is acetylated at $C_{(9)}$ under these conditions to give 3-methyl-9-(α-hydroxyethylidene)-2-azafluorene (V), which, like II-IV, has an intense color (red) and melts at a high temperature. It is only slightly soluble in organic solvents. Depending on the pH of the medium, this acetyl derivative undergoes a number of transformations. It is soluble in 18% hydrochloric acid, and the solution takes on a yellow coloration. At pH 7 one observes the formation of dark-green crystals, the nature of which we have not yet been able to establish. On subsequent treatment with a base (at and above pH 7.5) the green crystals are converted to red crystals of V. The molecular ion peak in the mass spectrum of a freshly prepared sample of V is found at m/e 223, which corresponds to its molecular weight. However, peaks with m/e 195 and 239 (the difference of 13 units between the latter and acetyl derivative V corresponds to the oxygen atom) appear in the mass spectrum of a sample that has been in contact with air for some time. This observation must be compared with the following facts. 3-Methyl-2-azafluorenone (VI) is formed in ~16% yield along with V in the reaction of azafluorene I with acetic anhydride. The fact that ketone VI is formed by oxidation of acetyl derivative V was established experimentally by its oxidation by air oxygen in refluxing alcohol; azafluorene is not oxidized under similar conditions. The low yield of ketone VI in the oxidation of V under the indicated conditions is explained by the fact that its solubility in alcohol is negligible.

Considering these observations, it can be assumed that an α-ketol, i.e., 3-methyl-9-hydroxy-9-acetyl-2-azafluorene (molecular weight 239), is formed as an intermediate in the oxidation of V and under the reaction conditions undergoes cleavage to give ketone VI (M-195), identical to a genuine sample [2] with respect to the IR and UV spectral data.

Compounds II-V have relatively high melting points (> 200°), and this indicates their saltlike character. The benzoyl (II), p-aminobenzoyl (IV), and acetyl (V) derivatives are isolated from the reaction mixtures only in the form of the enols, the stability of which is evidently due to their existence in the form of zwitterions.

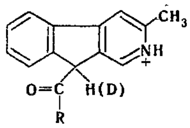
The relative stability of keto form IIIb is due to the electron-acceptor properties of the nitro group, which reduces the ability of the carbonyl group to undergo enolization. However, on heating above 110° keto form IIIb is converted to enol form IIIa, which is also more stable in this case. The hydrochlorides, which decompose to give the starting compounds when they are heated in alcohol, were obtained from IIIa and IV. This is apparently due to the competitive formation of the zwitterion.

Patrice Lumumba International Friendship University, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 963-967, July, 1976. Original article submitted January 14, 1975; revision submitted July 15, 1975.



II $R=C_6H_5$; IIIa, IIIb $R=p\text{-}C_6H_4NO_2$; IV $R=p\text{-}C_6H_4NH_2$; V $R=CH_3$

The IR and PMR spectral data (Table 1) are in agreement with the assumption that enols II and V in the crystalline state and also in neutral solutions apparently have a zwitterion structure with localization of the positive charge on the nitrogen atom, whereas the negative charge may be delocalized on three centers, as shown in the scheme above (structure B). The absorption bands of a carbonyl group are absent in their IR spectra; a broad diffuse band due to the stretching vibrations of the bonded hydroxyl groups at 2300-3000 cm^{-1} and an intense band centered at 2050-2060 cm^{-1} evidently due to vibrations of $>N^{+}-H$ bonds of the pyridine ring are observed in the spectra. The PMR spectra of trifluoroacetic acid solutions contain one-proton singlets at 6.44 (II) and 5.50 ppm (V), which are related to the methylidyne proton attached to $C_{(9)}$. The absence of these signals when CF_3COOD is used as the solvent (Table 1) makes it possible to conclude that the zwitterions are protonated in the 9 position under these conditions to give the cationic form of azafluorene.



EXPERIMENTAL

The UV spectra of alcohol solutions were obtained with a Hitachi spectrophotometer. The IR spectra of KBr pellets were recorded with a UR-20 spectrometer. The PMR spectra of CCl_4 (VI) and CF_3COOH and CF_3COOD (V) solutions were recorded with T-60 and HA-100D spectrometers with tetramethylsilane as the internal standard. The mass spectra were obtained with an MKh-1303 spectrometer at an ionizing-electron energy of 70 eV. Thin-layer chromatography (TLC) was carried on activity II Al_2O_3 in a $CHCl_3-C_2H_5OH$ system (15 : 1).

3-Methyl-9-(α-hydroxybenzylidene)-2-azafluorene (II). A 1.55-g (0.011 mole) sample of benzoyl chloride was added gradually with vigorous stirring to a solution of 2 g (0.011 mole) of I and 1.33 g (0.011 mole) of dimethylaniline in 5 ml of benzene, during which the mixture warmed up and initially turned blue and then brown. It was stirred at 20° for 2 h, after which ammonium hydroxide was added. The reaction products were extracted with benzene, and the residue from the benzene extract was passed through a column filled with activity II aluminum oxide with elution by alcohol to give 1 g of starting I and 0.6 g (38% based on converted azafluorene I) of fine-grained red crystals of II with mp 204.5-205° (from benzene) and R_f 0.78. Found: N 5.0%. $C_{20}H_{15}NO$. Calculated: N 4.9%.

3-Methyl-9-(p-nitrobenzoyl)-2-azafluorene (IIIb) and 3-Methyl-9-[α-hydroxy-(p-nitrobenzylidene)]-2-azafluorene (IIIa). A) A solution of 5.6 g (0.03 mole) of p-nitrobenzoyl chloride in 30 ml of benzene was added with stirring in the course of 20 min to 5 g (0.028 mole) of I and 5.5 g (0.045 mole) of dimethylaniline in 5 ml of benzene, during which the color of the solution turned to red-brown. It was then refluxed for 3 h, after which it was treated with ammonium hydroxide. The reaction products were extracted with benzene, and the residue from the benzene extract was washed with three 30-ml portions of ether. Workup of the ether extract

TABLE 1. Data from the PMR Spectra of 9-Acyl-3-methyl-2-azafluorenes

Compound	Solvent	Parameters* and assignments of the signals				
		CH_3 (ethylidene), s, 3 H	α-CH_3, s, 3H	9-H s, 1H(2H)	1-H	other aromatic protons
II	CF_3COOH	—	2,96	6,44	8,61 d, J=6,0Hz, 1H	7.20—8.30m,10H
V	CF_3COOH	2,37	2,98 (2,87;2,93) †	5,50	8.81 d, J=6.1Hz, 1H	7.50—8,43m,5H
	CF_3COOD	2,37	3,00 (2,87;2,93) †	—	8,80 s,1H	7,60—8.37m,5H
VI	CF_3COOH	—	2,95	—	8,75 s,1H	7.69—8.02m,5H
	CCl_4	—	2,56	—	8,59 s,1H	7,10—7,77m,5H
I‡	CF_3COOH	—	3.25	(4,55)	8.93 d, J=6,0 Hz,1H	7.76—8,65m,5H

*Chemical shifts (δ, ppm), multiplicity, and integral intensity.

†These are the chemical shift of the impurities in V, the possible formation of which (and the structure) is discussed in the paper.

‡ The measurements were made with a BS-487C spectrometer at 80 MHz.

yielded 1.9 g of azafluorene I. The ether-insoluble residue was passed through a column filled with aluminum oxide with elution by chloroform—alcohol (5 : 1) to give 2.07 g (36.6% based on converted azafluorene I) of brown crystals, which, according to TLC data, contained two substances with R_f 0.9 and 0.23. A 1-g sample of the crystals was heated in 10 ml of chloroform—benzene (10 : 1), and the insoluble yellow residue was removed by filtration, washed with chloroform, and dried to give 0.2 g of fine-grained light-yellow crystals of IIIb, which turned red at 110° and had R_f 0.9. The split bands in the IR spectrum at 1720 and 1753 cm^{-1} correspond to a carbonyl group. Found: N 8.8%. $C_{20}H_{14}N_2O_3$. Calculated: N 8.5%. Cooling of the chloroform solution yielded 0.53 g (53%) of dark-red crystals of IIIa with mp 253-254° and R_f 0.23. The two absorption bands at 2100-3200 and 1800-2100 cm^{-1} in the IR spectrum correspond to a strongly associated enol hydroxyl group; the absorption bands at 1535, 1343, and 860 cm^{-1} are due to an aromatic ring nitro group. The bands at 1500, 1315, and 1183 cm^{-1} characterize the skeletal vibrations of the azafluorenylidene system with an exocyclic C=C bond [1]. UV spectrum, λ_{max}, nm (log ε): 274 (4.30); 350 (4.10); 490 (3.75).

The solvate of the hydrochloride of IIIa decomposes at 260°. Found: Cl 18.4%. $C_{20}H_{14}N_2O_3 \cdot HCl \times C_2H_5OH$. Calculated: Cl 8.5%. This solvate decomposes on heating in alcohol to give enol IIIa.

B) A solution of 3.1 g (0.017 mole) of p-nitrobenzoyl chloride in 75 ml of benzene was added to 3 g (0.017 mole) of I in 30 ml of benzene, during which the mixture turned brown. It was then refluxed for 3 h and treated with an aqueous sodium carbonate solution. The reaction products were extracted repeatedly with benzene, and the residue from the benzene extract was washed with three 20-ml portions of ether. The ether extract was worked up to give 0.9 g of starting I. The ether-insoluble residue was crystallized from benzene to give 1.2 g (31% based on converted azafluorene I) IIIb with R_f 0.9.

3-Methyl-9-[α-hydroxy-(p-aminobenzylidene)]-2-azafluorene (IV). A solution of 0.5 g of calcium chloride in 5 ml of water and 20 g of zinc dust were added to a solution of 1 g (0.003 mole) of IIIa in 60 ml of alcohol, and the mixture was refluxed for 3 h. The hot mixture was filtered, and the solid material was washed with 50 ml of hot alcohol. Water (500 ml) was added to the filtrate, and the resulting precipitate was removed by filtration, washed with water, and dried to give 0.77 g (85%) of the solvated form of IV as a fine-grained red—orange powder with mp 224-226° (from alcohol—benzene) and R_f 0.46. The IR spectrum contained bands at 2800-3200 and 1175 cm^{-1} (enol hydroxyl group). The bands at 3380 and 1265 cm^{-1}, which are absent in the IR spectrum of enol IIIa, and the considerable broadening of the band at 1610 cm^{-1} constitute evidence for reduction of the NO_2 group to an NH_2 group. The presence of intense absorption bands at 1440-1505, 1320, and 1175 cm^{-1} is due to the skeletal vibrations of the azafluorenylidene system. Found: N 8.2%. $C_{20}H_{16}N_2O \cdot C_2H_5OH$. Calculated: N 8.1%. The solvate of hydrochloride IV decomposed on heating in alcohol. Found: Cl 18.1%. $C_{20}H_{16}N_2O \cdot 2HCl \cdot 1/2C_2H_5OH$. Calculated: Cl 17.9%.

3-Methyl-9-(α-hydroxyethylidene)-2-azafluorene (V) and 3-Methyl-2-azafluorenone (VI). A) A solution of 5 g (0.028 mole) of I in 50 ml of acetic anhydride was heated at 140° for 14 h, after which 50 ml of water was added to the black reaction mixture, and it was made alkaline with 10% sodium carbonate solution and treated with 300 ml of chloroform. The mixture was then shaken vigorously, and the resulting precipitate was removed by filtration and washed with acetone to give 0.31 g of red crystals of V with mp 215-216° (from alcohol). IR spectrum, cm^{-1}: 3097, 3047, 2995, 2932; a broad intense band at 2200-2900 (associated OH); 2097 and 2037 ($>N{-}H$) ; 1647, 1617, 1490 (broad s); 1317, 1240, 1174, 1112, 962, 872, 752, and 722. Found: C 80.7; H 6.1; N 6.0%; M 223. $C_{15}H_{13}NO$. Calculated: C 80.7; H 5.8; N 6.3%; M 223. Workup of the chloroform solution gave a solid dark residue (5.7 g) with an inclusion of red crystals, which was partially dissolved in 60 ml of 10% hydrochloric acid. The acid solution was washed with ether and treated with 10% sodium carbonate solution to pH 7.5. The orange bases were extracted with ether and chloroform. A total of 1.93 g of the residue of these extracts was separated with a column filled with activity II Al_2O_3 with elution with ether–hexane (1 : 20) to give 0.95 (15.7%) of ketone VI with mp 141-146° (no melting-point depression was observed for a mixture of this product with a genuine sample [2]). The hydrochloric acid-insoluble residue (~2 g) was shaken with 15 ml of 10% sodium carbonate solution and 30 ml of ether to give an additional 1.34 g of V, the overall yield of which was 26%.

B) A mixture of 1.8 g (0.01 mole) of I, 2.6 g (0.03 mole) of ethyl acetate, and 0.5 g (0.02 g-atom) of finely cut sodium was refluxed for 10 h, during which it turned green. Alcohol (5 ml) was added, and the mixture was poured into a solution of 2 ml of acetic acid in 15 ml of water. The mixture was shaken, and the resulting red crystals were removed by filtration, washed successively with water, alcohol, and ether, and dried to give 0.44 g (19.9%) of V with mp 224-225° (from alcohol) (mp 209-212° [1]). Found: C 80.7; H 6.3; N 6.5%; M 223. $C_{15}H_{13}NO$. Calculated: C 80.7; H 5.8; N 6.3%; M 223.

C) A 0.35-g (1.5 mmole) sample of freshly prepared (and successively washed with ether, benzene, cold and hot chloroform, and alcohol) enol V was refluxed for 14 h in 40 ml of alcohol with continuous bubbling of air into the mixture. The resulting precipitate was removed by filtration, dissolved in alcohol, and chromatographed to give 0.02 g (6.6%) of ketone VI with mp 144-146° [2]. Found: M 195. $C_{13}H_9NO$. Calculated: M 195.

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