9-ACYL- AND 9-AROYL-3-METHYL-2-AZAFLUORENES

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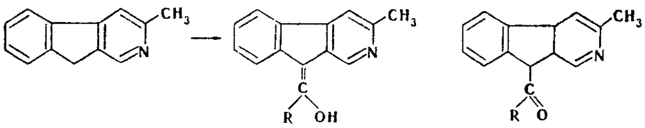
The condensation of 3-methyl-2-azafluorene with esters of aromatic and aliphatic acids has given 9-aroyl and 9-acyl derivatives of 2-azafluorene. They are stable in the enolic form. The 9-benzoyl derivative (II) has also been isolated in the oxo form. The transition from (II) to the cis-trans isomers of 9-benzylidene-3-methyl-2-azafluorene has been effected.

The condensation of fluorene with esters has been studied for many cases. This is due to the absence of suitable methods of synthesizing azafluorenes. We decided to fill this gap by using for this purpose 3-methyl-2-azafluorene (I) which is obtained in satisfactory yield by a comparatively simple method which we have developed [1].

Esters of aromatic and aliphatic acids were condensed with (I). The condensation was performed in the presence of potassium or sodium. Compound (I) and esters of benzoic, thiophene-α-carboxylic, 5-methyl-4-phenylpicolinic, acetic, and formic acids yielded, respectively, 9-benzoyl-, 9-α-thienoyl-, 9-(5-methyl-4-phenylpicolinoyl)-, 9-acetyl-, and 9-formyl-3-methyl-2-azafluorenes (II, III, IV, V, and VI, respectively).



I

II-VI a

II-VI b

II R=C_6H_5, III R=α-thienyl; IV R=5-methyl-4-phenylpicolinoyl; V R=CH_3; VI R=H.

These azafluorene derivatives differ from the analogous fluorene derivatives. They are bright red (the analogous compounds of the fluorene series are yellow), and are insoluble in ether and benzene and only slightly soluble in ethanol and acetone. They all melt at comparatively high temperatures. The IR spectrum of (II) has the band of an associated hydroxy group (3240 cm^{-1}) and lacks the band corresponding to a carbonyl group, which shows the enolic (IIa) structure of this compound. Similar information follows from the IR spectra of compounds (III-VI), in which there are no absorption bands in the 1700-1660-cm^{-1} region that are characteristic for diaryl and alkyl aryl ketones.

The presence of a hydroxy group at the double bond of the 2-azafluoren-9-ylidene derivatives causes the appearance of two strong bands in the high-frequency region of the spectrum in the 3400-2400- and 2200-1800-cm^{-1} regions, which are due to the formation of strong intramolecular bonds between the basic nitrogen and the acidic hydroxyl of the enol. The first of the bands mentioned is due to the stretching vibrations of an associated hydroxy group. According to the literature [2, 3], the second band is characteristic for the $C{=}\overset{+}{N}H$ grouping, which corresponds to the formation of the bipolar ions $\geqslant\overset{+}{N}H\ldots\overset{-}{O}{-}C{=}$ in the limiting case. It follows from these facts that in the crystalline state compounds (II-VI) exist in the enolic form as polyassociates. The salt-like nature of the latter is responsible for their physicochemical properties and also apparently, for the color of these compounds. Their deep color disappears when the nitrogen of the ring is blocked, which is connected with the destruction of the associates. The picrate and

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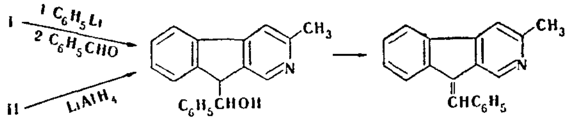
the hydrochloride of (II) form yellow crystals, but when they are stored in ethanol they decompose and the solution gradually acquires the red color characteristic for the free base. When the hydrochloride of (II) is heated, its color gradually changes, and the melt, like the melt of the free base, is bright red.

The benzoyl derivative of (II) was also isolated in the oxo form (IIb). In acetone solution in the presence of caustic soda, (IIa) gradually changes into the colorless oxo form (IIb), the IR spectrum of which lacks a band corresponding to a hydroxy group but has a strong carbonyl band at 1678 cm^{-1}. On being heated above 110°C, compound (IIb) is converted into (IIa).

As a proof of the structure of (II) may be considered its reduction with lithium tetrahydroaluminate to 3-methyl-2-azafluoren-9-yl phenyl carbinol (VII), which was also obtained from the lithium derivative of (I) and benzaldehyde. From (VII), the isomeric cis- and trans-9-benzylidene-3-methyl-2-azafluorenes (VIIIa, b) [4] have been obtained by two methods – the replacement of the hydroxy group in (VII) by chlorine with subsequent dehydrochlorination, and by the thermal decomposition of (VII) [5]. In the latter case, in addition to the isomers of (VIII), compound (I) was isolated and the formation of benzaldehyde was detected.



VII VIII

The formyl derivative (VI) has an intense red coloration, while its oxime forms colorless crystals. Compound (VI) was reduced with lithium tetrahydroaluminate to 9-(hydroxymethyl)-3-methyl-2-azafluorene (IX), which was also detected by means of its mass spectrum in the products of the thermal rearrangement of (VI). It is represented by a peak with a mass of 211. In addition to (IX), the products of the thermolysis of (VI) contained (I) (peak with a mass of 181) and 3-methyl-2-azafluorenone (peak with a mass of 196). These substances are probably formed as a result of redox reactions of the formyl derivative (VI).

The 9-acyl and 9-aroyl derivatives of 2-azafluorene crystallize in the form of solvates. Their derivatives at the nitrogen atom do not form solvates, and their color differs sharply from the color of the free bases. The IR spectra of all the compounds containing the azafluorenylidene grouping are characterized by the presence of a series of three bands in the ranges 1316-1326, 1236-1242, and 1185-1192 cm^{-1}. This group of bands retains its form and the ratio of the intensities (the first being the strongest and the third the weakest) in the spectra of all the compounds. Apparently, this group of bands is connected with the skeletal vibrations of the azafluorenylidene system itself, since these vibrations are absent from the spectra of compounds containing no exocyclic C=C bond in position 9.

The presence of three strong bands is characteristic for the UV spectra of the azafluorenylidene derivatives: at 280, 360, and 480 nm. The strongest maximum is found in the 260-300-nm region. In (IIa) it is shifted in the long-wave direction as compared with the absorption maximum of (I) by 22 nm, which is apparently due to the existence of strong intramolecular hydrogen bonds in (IIa).

EXPERIMENTAL

9-Benzoyl-3-methyl-2-azafluorene (II). To 3.62 g (0.02 mole) of (I) and 9 g (0.06 mole) of ethyl benzoate was added 1.56 g (0.04 g-atom) of finely cut potassium, and the mixture was stirred at 20°C for 12 h and at 70°C for 2 h. Then 10 ml of ethanol, 30 ml of water, and 5 ml of acetic acid were added successively. The resulting bright-red solution was treated with 100 ml of ether and shaken vigorously. The orange precipitate was filtered off, washed with water, ethanol, and ether, and crystallized from ethanol. This gave 3.9 g (68.5%) of (IIa) in the form of red crystals with mp 196.5-201°C. Found, %: C 81.5; H 6.5; N 4.8. $C_{20}H_{15}NO \cdot {}^1/_2C_2H_5OH$. Calculated, %: C 81.8; H 5.8; N 4.5. To a solution (bright red) of 0.3 g of (IIa) in 200 ml of acetone was added 0.1 g of caustic potash in 5 ml of methanol. The mixture was stirred until the solid matter had dissolved and was left to stand. The intensity of the coloration gradually decreased, and after 20 days the solution was colorless. It was filtered, and the solvent was distilled off. The residue was crystallized from hexane, the solution being heated with activated carbon. This gave 0.1 g of (IIb) as colorless crystals which melted in the interval from 111 to 199°C. At 111°C the substance began to acquire a color, and at 140°C it became bright red. Found, %: N 5.1. $C_{20}H_{15}NO$. Calculated, %: N 4.9. Picrate of (II). Bright-yellow crystals with mp 114-116°C. Found, %: N 11.2. $C_{20}H_{15}NO \cdot C_6H_3N_3O_7$. Calculated, %: N 10.9. On being boiled in ethanol, the picrate decomposed with the formation of red crystals of (IIa). Hydrochloride of (II). Bright-yellow crystals; at 154°C they became red, and they melted between 171 and 182°C.

3-Methyl-9-(α-thienoyl)-2-azafluorene (III). The reaction was performed with 1.81 g (0.01 mole) of (I), 4.68 g (0.03 mole) of ethyl thiophene-2-carboxylate, and 0.78 g (0.02 g-atom) of potassium. The reaction conditions and the working-up process were the same as in the preparation of (II). This gave 1.73 g (59.5%) of (III) in the form of bright-red crystals with mp 128-131°C (ethanol) (according to analysis, this was one of the solvated forms). Found, %: C 68.9; H 6.1; N 4.0. $C_{18}H_{13}NOS \cdot 2C_2H_5OH$. Calculated, %: C 69.0; H 6.5; N 3.7. Picrate of (III). Yellow-brown crystals with mp 170-172°C (ethanol). Found, %: N 10.4. $C_{18}H_{13}NOS \cdot C_6H_3N_3O_7$. Calculated, %: N 10.8.

3-Methyl-9-(5-methyl-4-phenylpicolinoyl)-2-azafluorene (IV). A mixture of 1.8 g (0.01 mole) of (I), 2.4 g (0.01 mole) of ethyl 5-methyl-4-phenylpicolinate, and 0.7 g (0.02 g-atom) of finely cut potassium was heated in a current of nitrogen at a temperature to melt the potassium for 2 h and was then heated at 80°C for 2 h. After this, 30 ml of acetone and 5 ml of acetic acid in 20 ml of water were added. The resulting precipitate was washed successively with water, acetone, ethanol, and ether. This gave 2.16 g (57.5%) of (IV), which was crystallized from ethanol. Compound (IV) formed red-orange crystals with mp 204-206°C. Found, %: C 79.5; H 6.4; N 6.8. $C_{26}H_{20}N_2O \cdot C_2H_5OH$. Calculated, %: C 79.6; H 6.2; N 6.6.

9-Acetyl-3-methyl-2-azafluorene (V). A mixture of 1.8 g (0.01 mole) of (I), 2.6 g (0.03 mole) of ethyl acetate, and 0.2 g (0.01 g-atom) of finely cut sodium was stirred at 90-100°C for 10 h. The mixture was treated with 2 ml of ethanol, and then 2 ml of acetic acid and 15 ml of water were added to the solution and it was shaken with ether. This gave (after washing with water, ethanol, and ether and drying) 0.33 g (14%) of (V) as red crystals with mp 209-212°C (three crystallizations from ethanol). Found, %: C 80.3; H 6.1; N 6.2. $C_{15}H_{13}NO$. Calculated, %: C 80.7; H 5.8; N 6.3. Picrate of (V). Mp 190-193°C (ethanol). Found, %: N 12.3. $C_{15}H_{13}NO \cdot C_6H_3N_3O_7$. Calculated, %: N 12.7.

9-Formyl-3-methyl-2-azafluorene (VI). With stirring, 9.7 g (0.12 mole) of ethyl formate was gradually added to a mixture of 7.8 g (0.04 mole) of (I) and 3 g (0.08 g-atom of potassium). To the solidified mass was added 20 ml of absolute ether, and the mixture was stirred at the boiling point of the ether for 1 h. Then 15 ml of ethanol was added, followed by a solution of 4.5 ml of acetic acid in 30 ml of water. The precipitate was washed successively with water, acetone, and ether and was dried. This gave 6 g (74%) of (VI) in the form of dark-red crystals with mp 226-227°C (two crystallizations from ethanol). Found, %: C 79.7; H 6.2; N 6.6. $C_{14}H_{11}NO$. Calculated, %: C 80.0; H 5.3; N 6.7. Picrate of (VI). Green crystals, mp 183-185°C (ethanol). Found, %: N 12.5. $C_{14}H_{11}NO \cdot C_6H_3N_3O_7$. Calculated, %: N 12.7. Oxime of (VI). A mixture of 0.5 g (1.7 mmoles) of (VI), 0.3 g of hydroxylamine hydrochloride, 17 ml of pyridine, and 3 ml of ethanol was boiled for 1 h 30 min. The ethanol and the pyridine were distilled off. Then the mixture was poured into 10 ml of water and was neutralized with sodium carbonate. The precipitate was washed with water and dried, giving 0.4 g (78%) of the oxime of (VI) in the form of colorless crystals with mp 215-217°C (dioxane). Found, %: C 75.5; H 5.1; N 12.3. $C_{14}H_{12}N_2O$. Calculated, %: C 75.0; H 5.4; N 12.5.

The dark-red crystals of (VI) were gradually heated in a current of nitrogen to 245°C. On melting, the color changed to bright blue, and then to dark blue. According to the mass spectrum, in this process compounds (I) and (IX) and 3-methyl-2-azafluorenone were formed.

3-Methyl-2-azafluoren-9-yl Phenyl Carbinol (VII). a) To the phenyllithium obtained from 0.4 g of lithium and 9.7 g of bromobenzene in 100 ml of ether at −8°C was added a solution of 5.6 g (0.03 mole) of (I) in 100 ml of ether. The dark cherry-red solution was stirred at −5°C for 1 h and at 20°C for 1 h. Then it was cooled to −10°C, and 13 g (0.12 mole) of freshly distilled benzaldehyde was added. The resulting mixture was stirred at 20°C for 1 h and at the boil for 1 h. Then it was cooled and, with vigorous stirring, 50 ml of water was added. The precipitate of (VII) (3 g) was separated off. The aqueous layer was extracted with ether. The ethereal extract was dried with magnesium sulfate and was then saturated with hydrogen chloride. The resulting hydrochloride was washed with a mixture of ethanol and ether, and was then converted into the free base. An additional 0.83 g of (VII) was isolated. Total yield 63%. Compound (VII) formed colorless crystals with mp 162-170°C (four crystallizations from ethanol). Found, %: C 83.3; H 6.2; N 4.9. $C_{20}H_{17}NO$. Calculated, %: C 83.6; H 5.9; N 4.9. Picrate of (VII). Mp 213-215°C (ethanol). Found, %: N 10.8. $C_{20}H_{17}NO \cdot C_6H_3N_3O_7$. Calculated, %: N 10.9. Hydrochloride of (VII). Mp 199-201°C (ethanol).

b) To a solution (crimson) of 0.5 g (175 mmoles) of (IIa) in 30 ml of freshly distilled tetrahydrofuran was gradually added 0.38 g (0.01 mole) of lithium tetrahydroaluminate. The mixture was stirred at

20°C for 20 min and was then boiled for 10 h. The color of the reaction mixture changed in the following sequence: yellow, brown, green, dark cherry-red, violet. Then 5 ml of ethyl acetate was added and the solvent was distilled off. The dry residue was treated with 20 ml of water and repeatedly extracted with ether; the extract was dried with magnesium sulfate. This yielded 0.2 g (40%) (after two crystallizations from gasoline) of (VII) in the form of colorless crystals with mp 163-171°C. The picrate of this sample of (VII) (mp 212-214°C) melted without a temperature depression in admixture with that described above.

c) The reduction of 0.12 g (0.42 mmole) of (IIb) (0.2 g of lithium tetrahydroaluminate and 15 ml of tetrahydrofuran) gave 0.02 g (16.7%) of (VII) with mp 161-169°C (from gasoline).

9-Benzylidene-3-methyl-2-azafluorene (VIII). a) At −5°C, 10 ml of thionyl chloride was added to 0.65 g (3.6 mmoles) of (VII). The mixture was stirred at room temperature for 1 h and then at the boil for 1 h. The thionyl chloride was distilled off and the residue was cooled and treated with a solution of 1 g of caustic potash in 5 ml of ethanol. The mixture was stirred at 20°C for 30 min and at the boil for 2 h. Then the ethanol was distilled off, 10 ml of water was added, and the reaction products were extracted with ether. The ethereal extract was dried with magnesium sulfate and the residue after distillation was heated in hexane. The hexane-insoluble residue yielded 0.13 g (20%) of (VII). A seed of the trans isomer (VIIIb) was added to the hot hexane solution; after 3 h, 0.22 g (36.2%) of (VIIIb) was isolated in the form of yellow plates with mp 128-129.5°C. A seed of the cis isomer (VIIIa) was added to the decanted hexane solution, giving 0.08 g (13.1%) of (VIIIa) in the form of light-yellow acicular crystals with mp 117-118°C. In admixtures with authentic samples, both isomers melted without temperature depression.

b) Compound (VII) (1 g) was kept in an atmosphere of helium at 170-180°C for 1 h. According to chromatography, the reaction products that condensed in the condenser contained benzaldehyde. The reaction mixture was dissolved in ether, and air was passed through the solution for 5 min, after which it was shaken with a solution of 0.5 g of sodium carbonate in 10 ml of water. After treatment with hydrochloric acid, the aqueous layer yielded 0.01 g of benzoic acid (mp 120-121.5°C). By column chromatography (Al_2O_3 of activity grade II, ether) the ethereal extract yielded 0.12 g (13%) of (VIIIb) (mp 128-129°C; R_f 0.84), 0.02 g (2.2%) of (VIIIa) (mp 115-116.5°C; R_f 0.67) and, at the end of chromatography, 0.16 g (16.5%) of (I) (mp 90-91°C; R_f 0.54).

9-(Hydroxymethyl)-3-methyl-2-azafluorene (IX). To 0.5 g (2.4 mmoles) of (VI) in 40 ml of tetrahydrofuran was added 0.5 g of lithium tetrahydroaluminate, and the mixture was boiled for 10 h. Then 4 ml of ethyl acetate was added. The solvent was distilled off and the residue was treated with 20 ml of water. The reaction products were extracted with ether (3 × 20 ml), and the extract was dried with magnesium sulfate. The organic bases were isolated from the ethereal extract and converted into the picrates which, after crystallization from ethanol, were decomposed with sodium carbonate. This gave 0.3 g (60%) of (IX) in the form of colorless crystals with mp 160-162°C (gasoline). Found, %: N 7.0. $C_{14}H_{13}NO$. Calculated, %: N 6.6. Picrate of (IX). Mp 221-223'C (ethanol). Found, %: N 12.8. $C_{14}H_{13}NO \cdot C_6H_3N_3O_7$. Calculated, %: N 12.7.

The molecular weights of (IIa, IIb, III, IV, VI, and IX) were determined on an MKh-1303 mass spectrometer. The IR spectra were measured in the 3800-400-cm^{-1} region on a UR-20 spectrophotometer in KBr tablets, and the UV spectra were recorded on a Hitachi spectrophotometer using ethanol as solvent.

LITERATURE CITED

1. N. S. Prostakov, C. J. Matthew, and V. A. Kurichev, Khim. Geterotsikl. Soedin., 876 (1967).
2. L. Bellamy, Infra-red Spectra of Complex Molecules, 2nd ed., Methuen (1958).
3. K. Nakanishi, Infrared Spectroscopy. Practical, Holden-Day, San Francisco (1962).
4. N. S. Prostakov, S. S. Moiz, A. T. Soldatenkov, V. P. Zvolinskii, and G. I. Cherenkova, Khim. Geterotsikl. Soedin., 1398 (1971).
5. E. J. Greenhow, D. McNeil, and E. N. White, J. Chem. Soc., 986 (1952).