B. A misture of 5.00 g (0.06 mole) of compound I and 9.5 g (0.12 mole) of ethyl iodide is added to a solution of 2.5 g (0.09 mole) of potassium hydroxide in 18 ml of absolute ethanol, and the mixture is bioled for 15 min. After the reaction mixture has cooled, the potassium iodide precipitate is filtered out. The solvent is distilled off from the filtrate, and the precipitate formed is washed with 100 ml of diethyl ether and sublimated at a sublimation temperature of 101°C (1.33 hPa). The yield is 4.2 g (85%), and the mp is 70-72°C. Found: C, 78.6, H, 6.6; N, 14.3%. Calculated from $C_{13}H_{12}N_2$: C, 79.6; H, 6.1; N, 14.3%. R_f 0.62.

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3-ARYL- AND 3-(ARYLOXY)PHTHALIC ACIDS IN THE SYNTHESIS OF FLUORENONES AND XANTHONES

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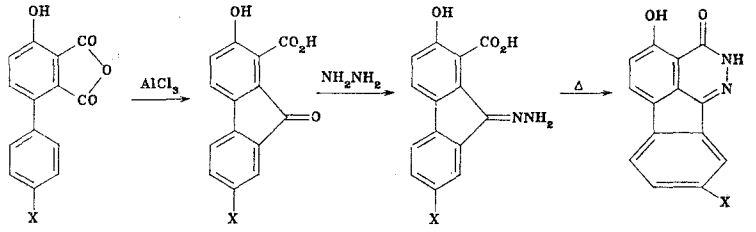
UDC 547.724.7'727.07

Aryl- and aryloxyfurans can serve as the starting compounds in the synthesis of fluorenones, xanthones, and diazafluoranthenes.

3-Aryl(or aryloxy)-6-hydroxyphthalic acids can easily be obtained from aryl and aryloxyfurans with the aid of a Diels–Alder reaction [1]. In the present work the derivatives of diphenyl and diphenyl ether synthesized in this manner (I, V) served as the starting compounds in the synthesis of condensed aromatic and heterocyclic systems, i.e., fluorenones (II) and xanthones (VI).

The presence of antiviral preparations [2, 3] among the derivatives of fluorenone called for a search for new ways of synthesizing the derivatives of this series. We synthesized hitherto unknown 1-carboxy-2-hydroxyfluorenones of type II by cyclization of 3-aryl-6-hydroxyphthalic anhydrides under the action of aluminum chloride (the yield was 87%):



I a, b — II a, b — III a, b — IV a, b

Ia—IVa X=CH_3; Ib X=OCH_3; II—IVb X=OH*

*Under the conditions for cyclization of Ib, demethylation of the latter occurred.

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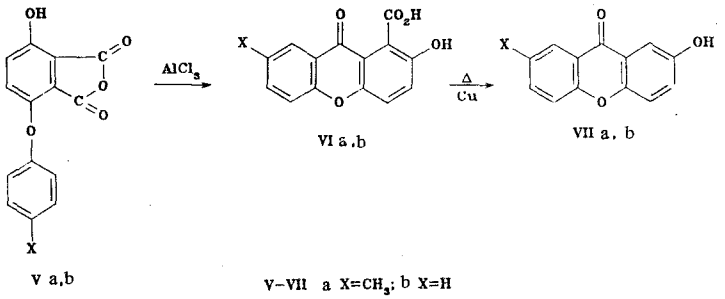
The structure of the compounds obtained was established with the aid of ^{13}C NMR and IR spectroscopy. Confirmation of the structure of the fluorenones of type II was also provided by the formation of the previously described compound 2,7-dihydroxyfluorenone [4] upon the decarboxylation of one of them (IIb).

The 1-carboxyfluorenones of type II, in turn, served as the starting compounds in the synthesis of 9-substituted 3-oxo-4-hydroxy-1,2-diazadihydrofluoranthenes (IV). For this purpose we obtained the hydrazones of type III, which were converted under thermal treatment in a vacuum into the corresponding diazadihydrofluoranthenes of type IV.*

Aryloxyphthalic anhydrides (V), which we obtained precisely as anhydrides I by thermal treatment of the corresponding acids, were the starting compounds in the synthesis of xanthones of type VI:



The compounds of type V underwent cyclization under the action of aluminum chloride and formed the hitherto undescribed 2-hydroxyxanthonecarboxylic acids of type VI with an 80-86% yield. The structure of the xanthonecarboxylic acids of type VI was confirmed by converting them upon decarboxylation into the known hydroxyxanthones of type VII [6, 7]. Hydroxyxanthone VIIa was also obtained by cyclization of an ester of 3-tolyloxy-6-hydroxyphthalic acid in polyphosphoric acid.

EXPERIMENTAL

The TLC was carried out on Silufol UV-254 planes with a 95:25:4 benzene–dioxane–acetic acid solvent system and development in UV light. The ^{13}C NMR spectra were recorded on a Varian XL-100 spectrometer with DMSO-d_6 as the solvent and TMS as an internal reference. The IR spectra were recorded on a Perkin–Elmer 457 instrument in liquid petrolatum.

3-(p-Tolyl)-6-hydroxyphthalic Anhydride (Ia). A 2.7 g portion (10 mmole) of 3-(p-tolyl)-6-hydroxyphthalic acid [8] is heated at 180-200°C in a vacuum with a residual pressure of 20 mm Hg for 30 min. This yields 1.8 g (70%) of anhydride Ia, mp 225-227°C (from acetic acid) (see [9]), R_f 0.85.

3-(p-Anisyl)-6-hydroxyphthalic anhydride (Ib) is obtained in a similar manner, 66% yield, mp 275-277°C (from acetic acid) (see [9]), R_f 0.81.

2-Hydroxy-9-oxo-7-methylfluorene-1-carboxylic Acid (IIa). A suspension of 1 g (4 mmole) of anhydride Ia in 65 ml of dry benzene is given an addition of 2.6 g (20 mmole) of anhydrous aluminum chloride in 15 ml of dry benzene. The reaction mixture is boiled for 2 h, cooled, and poured into 200 ml of 5% hydrochloric acid. The precipitate is filtered out and reprecipitated from a 5% solution of sodium hydroxide. This gives 0.9 g (87%) of acid IIa, mp 207-209°C (from benzene). ^{13}C NMR spectrum, δ: 191.6 (CO), 166.2 ppm (COOH). IR spectrum: 1700-1650 cm^{-1} (CO). Found: C, 70.9; H, 3.8%. Calculated from $C_{15}H_{10}O_4$: C, 70.9; H, 3.9%.

2,7-Dihydroxy-9-oxo-fluorene-1-carboxylic acid (IIb) was obtained in a similar manner, 87% yield, mp 285-288°C (from a 1:1 DMFA–water mixture), R_f 0.58 (chloroform). IR spectrum: 1700, 1650 cm^{-1} (CO). Found: C, 65.8; H, 3.2%. Calculated for $C_{14}H_8O_5$: C, 65.8; H, 3.1%.

2,7-Dihydroxyfluoren-9-one was obtained by melting 0.1 g of IIb with 0.1 g of calcium oxide. Dark red crystals with mp 230°C [4] were sublimed.

9-Hydrazono-2-hydroxy-7-methylfluorene-carboxylic Acid (IIIa). A suspension of 1.0 g (4 mmole) of oxo acid IIa in 30 ml of methanol is given an addition of 0.3 ml (6 mmole) of hydrazine hydrate. The reaction mixture is boiled for 2 h, and the precipitate formed upon

*The synthesis of 3-oxo-1,2-diazadihydrofluoranthene not containing substituents in the ring is described in [5].

cooling is filtered out. This gives 0.8 g (76%) of hydrazone IIIa, mp 245-247°C (from DMFA), R_f 0.86. IR spectrum: 1670, 1620 cm^{-1} (C=N, CO_2H). Found: C, 67.1; H, 4.6; N, 10.3%. Calculated for $C_{15}H_{12}N_2O_3$: C, 67.2; N, 4.5; N. 10.4%.

9-Hydrazono-2,7-dihydroxyfluorene-1-carboxylic acid (IIIb) was obtained in a similar manner, 76% yield, mp >300°C, R_f 0.90. IR spectrum: 1670, 1600 cm^{-1} (C=N, $-CO_2H$). Found: C, 61.9; H, 3.7; N, 10.0%. Calculated for $C_{14}H_{10}N_2O_4$: C, 62.2; H, 3.7; N, 10.4%.

3-Oxo-4-hydroxy-9-methyl-1,2-diazadihydrofluoranthene (IVa). A 0.5-g portion (2 mmole) of hydrazone IIIa is heated at 180-200°C in a vacuum with a residual pressure of 20 mm Hg in a sublimation apparatus. This gives 0.2 g (42%) of IVa, mp >300°C, R_f 0.98. IR spectrum: 1680 cm^{-1} (CO). Found: C, 71.7; H, 3.9; N, 11.6%. Calculated for $C_{15}H_{10}N_2O_2$: C, 72.0; H, 4.0; N, 11.2%.

3-Oxo-4,9-dihydroxy-1,2-diazadihydrofluoranthene (IVb) is obtained in a similar manner, 42% yield, mp >300°C, R_f 0.90. IR spectrum: 1690 cm^{-1} (CO). Found: C, 67.05; H, 3.4; N, 10.8%. Calculated for $C_{14}H_8H_2O_2$: C, 66.7; H, 3.2; N, 11.1%.

3-(p-Tolyloxy)-6-hydroxyphthalic Anhydride (Va). A 2.9-g portion (10 mmole) of 3-(p-tolyloxy)-6-hydroxyphthalic acid [8] is heated for 20 min at 180-200°C in a vacuum with a residual pressure of 20 mm Hg. The residue is recrystallized for acetic acid. This gives 1.7 g (63%) of anhydride Va, mp 175-177°C, R_f 0.61. Found: C, 66.7; H, 3.8%. Calculated for $C_{15}H_{10}O_5$: C, 66.7; H, 3.7%.

3-Phenoxy-6-hydroxyphthalic anhydride (Vb) is obtained in a similar manner, 71%, mp 161-162°C (from acetic acid), R_f 0.90. Found: C, 65.9; H, 2.8%. Calculated for $C_{14}H_8O_5$: C, 65.5; H 3.1%.

2-Hydroxy-9-oxo-7-methylxanthene-1-carboxylic Acid (VIa). A suspension of 1.4 g (5 mmole) of anhydride Va in 50 ml of dry benzene is given an addition of 2.3 g (17 mmole) of anhydrous aluminum chloride in 25 ml of dry benzene. The reaction mixture is boiled for 1 h, cooled, and poured into 100 ml of 5% hydrochloric acid. The precipitate is filtered out and reprecipitated from a 5% solution of sodium hydroxide. This gives 1.2 g (86%) of acid VIa, mp 223-225°C (from 50% aqueous DMFA), R_f 0.80. Found: C, 66.7; H, 3.8%. Calculated from $C_{15}H_{10}O_5$: C, 66.7; H, 3.7%.

2-Hydroxy-9-oxoxanthene-1-carboxylic acid (VIb) is obtained in a similar manner, 80% yield, mp 186-188°C (from 50% aqueous methanol). Found: C, 65.7; H, 3.2%. Calculated for $C_{14}H_8O_5$: C, 65.6; H, 3.1%.

2-Hydroxy-9-oxo-7-methylxanthene (VIIa). A. A 0.6-g portion (2 mmole) of acid VIa and 0.1 g of copper powder are heated in an apparatus for sublimation at 180-200°C for 15 min. This gives 0.4 g (80%) of hydroxyxanthene VIIa, mp 240-241°C (from ethanol) (see [7]).

B. A 10-ml protion of 83% orthophosphoric acid is given an addition of 21 g of phosphorus pentoxide with stirring and then an addition of 1.5 g (5 mmole) of dimethyl 3-(p-tolyloxy)-6-hydroxyphthalate [1], the mixture is heated for 1 h at 140-160°C, poured into water, and neutralized by a 30% solution of sodium hydroxide to pH 6, and the precipitate formed is filtered out. This gives 0.5 g (47%) of VIIa, mp 240-241°C. A mixed sample with a specimen obtained by method A did not show any melting-point depression.

2-Hydroxy-9-oxoxanthene (VIIb) is obtained in a similar manner (Method A), 73% yield, mp 237-238°C (from acetic acid) (see [6]). Found: C, 73.6; H, 3.0%. Calculated: C, 73.6; H, 3.8%.

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SYNTHESIS OF N-(1-URACILYLALKYL)POLYMETHYLENEDIAMINES

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The alkylation of polymethylenediamines with 2-(1-uracilyl)ethyl bromide and 3-(1-uracilyl)propyl bromide yields the corresponding N-(1-uracilylalkyl)polymethylenediamines.

Biogenic polyamines, such as putrescine, cadaverine, spermidine, and spermine, take direct part in biophysical and biochemical processes taking place both in microorganisms and in plants and animals [1]. It is noteworthy that putrescine modified by a nucleic-acid nitrogenous base, viz., 5-(4-aminobutylaminomethyl)uracil, which appears in DNA, has been successfully isolated from bacteriophage FW-14 and characterized [2]. The antitumor properties of N,N'-bis(6-purinyl)ethylenediamine are known [3]. N-Alkylputrescines have hypotensive properties [4].

The present work was devoted to the synthesis of derivatives of diamines containing bases of nucleic acids. In order to preserve the basic properties inherent in biogenic polyamines, our purpose was to synthesize monosubstituted diamines, i.e., N-(1-uracilylalkyl)polymethylenediamines. 2-(1-Uracilyl)ethyl bromide and 3-(1-uracilyl)propyl bromide were selected as the reagents for alkylating the diamines [5, 6]. It was found that in the case of the reaction of the bromides with diamines (putrescine, cadaverine, trimethylenediamine, and hexamethylenediamine) in dimethylformamide, a mixture of mono- and diaklylated diamines which is difficult to separate forms even with a large excess of the diamine. In other words, in order to obtain only monoalkyldiamines, it is necessary to protect one amino group in the diamine. We selected the benzyloxycarbonyl grouping for the protection of the amino group. When the diamines are reacted with carbobenzoxy chloride in 0.1 N NaOH, the corresponding N,N'-biscarbobenzoxy derivatives form. The elimination of one carbobenzoxy group was carried out in glacial acetic acid with an equimolar amount of hydrochloric acid. It was not possible to rid the monocarbobenzoxypolymethylenediamine hydrochlorides obtained from the admixtures of the polymethylenediamine dihydrochlorides by recrystallization, as was proposed in [7]. Chromatographically pure products could be obtained only with the aid of column chromatography. The purified monocarbobenzoxypolymethylenediamines are converted into the corresponding hydrochlorides by treating them with a 1:1 mixture of absolute ethanol and concentrated hydrochloric acid. The physicochemical characteristics of the monocarbobenzoxypolymethylenediamine hydrochlorides obtained correspond to the data in [7].

The reaction of 2(or 3)-(1-uracilyl)ethyl(or propyl) bromide (I, II) with monocarbobenzoxypolymethylenediamines readily takes place in dimethylformamide at room temperature and gives the corresponding N-[2(or 3)-(1-uracilyl)ethyl)or propyl)]-N'-carbobenzoxypolymethylenediamine hydrobromides (IIIa-d, IVa-d) with good yields.

After the elimination of the carbobenzoxy group by a 33% solution of hydrogen bromide in glacial acetic acid, the N-[2(or 3)-(1-uracilyl)ethyl(or propyl)]polymethylenediamine dihydrobromides (Va-d, VIa-d) were obtained.

The structures of compounds III-VI were confirmed by data from the PMR, IR, and UV spectra. The UV spectra recorded at pH 1, 7, and 10 show an absorption maximum at 265-267 nm, which is characteristic of N_1-substituted uracils with a lactam structure.

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