SYNTHESIS, STRUCTURE, AND SPECTRA OF 6-(2-FURYLPOLYENE) DERIVATIVES OF 5-NITROURACIL

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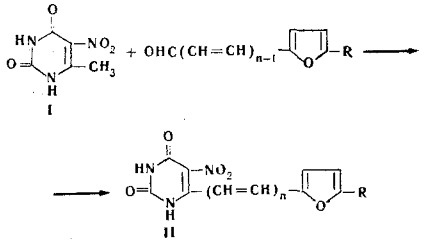
A number of 5-nitro-6-[(5-substituted-2-furyl)polyene]uracils were obtained, and a study was made of the nature of the intramolecular interaction of the functional groups in the above-mentioned compounds on the basis of an investigation of their UV and IR spectra.

In the present work, a study was made of the spectra and structure of 5-nitro-6-[(5-substituted-2-furyl)polyene]uracils (IIa–IIe, obtained by condensation of 5-nitro-6-methyluracil I [1] with aldehydes of the furan series in pyridine in the presence of piperazine as a basic catalyst. It was impossible to achieve condensation with 5-nitrofurfurol under the above-mentioned conditions due to rapid resinification of this compound under the influence of alkaline agents. The conditions of acid catalysis (AcOH, AcOH + + Ac_2O, Ac_2O + H_2SO_4), used by a numer of authors during condensation of 5-nitrofurfurol with other methyl pyrimidines [2,3], were also unsuitable.



a R=H; n=1; c R=H; n=3; e R=Br; n=1;
b R=H; n=2; d R=CH_3; n=1; f R=NO_2; n=1;

In our experiments it was found possible to condense compound I with 5-nitrofurfurol, with a good yield, in a medium of dimethylformamide in the presence of morpholine acetate as a catalyst at a temperature of 60–65° C over a period of 15 hr.

Compounds IIa–IIf are colored crystalline substances, poorly soluble in water and alcohol and readily soluble in dimethylformamide. On heating, they decompose without melting (Table 1).

Spectroscopic characteristics of these compounds are determined by the presence of two conjugated heterocyclic systems, uracil and furan. The UV spectrum of 6-methyluracil III is characterized by a single intensive band in the 260 nm region. In compound I, there is a transition in the 330 nm region, apparently associated with the absorption of the unsaturated system, $-\underset{NO_2}{\underset{|}{C}}=C-C=C-$ [4]. The original compound of the homologous series II, 5-nitro-6-furyluracil, has not yet been obtained, and so the spectrum of 6-furyluracil (IV) [5] was used as a model. In addition to the split band at 260 nm, there is an intensive band at 305 nm. In a previous report [6], this band is interpreted as a bathochromic displacement band of uracil, conjugated with the furyl radical. However, there is sufficient reason to consider that it is the main chromophore in the molecular system of furylacrylic acid, giving an intensive band of absorption with a maximum at 305 nm [7]. Additional weak bands at 260 and 270 nm may be associated with the isolated amide system of the uracil ring.

In compounds **IIa–IIe**, in which the furyl radical is connected to the pyrimidine moiety of the molecule through a system of conjugated ethylene bonds, the absorption of the amide system of uracil produces only a weak shoulder at 270 nm in compound **IIa**, and in the remaining II compounds only one long-wave maximum is found, characterizing the absorption of the conjugated chain.

Table 1

Preparation and Properties of 5-Nitro-6-[(5-substituted-2-furyl)-polyene]uracils

Compound	Conditions of preparation			Empirical formula	Found, %			Calc., %			λ, nm**	$\varepsilon\cdot 10^{-3}$	Yield, %
	method	temp., °C	time, hr		C	H	N	C	H	N			
IIa	A	100	2.5	$C_{10}H_7O_5N_3$	48.70	3.05	16.75	48.20	2.80	16.86	332 270 (melt)	25	84
IIb	A	50–55	2.0*	$C_{12}H_9O_5N_3$	51.78	3.86	14.93	52.37	3.30	15.27	360	32	30
IIc	A	30–40	0.5*	$C_{14}H_{11}O_5N_3$	55.12	3.84	13.72	55.81	3.68	13.95	385	38	24
IId	A	100	1.0	$C_{11}H_9O_5N_3$	50.21	3.56	16.21	50.19	3.45	15 97	344	24.8	90
IIe	A	60	2.0*	$C_{10}H_6O_5N_3$	37.05	2.07	12.69	36.60	1.84	12.81	340	26	30
IIf	B	60–65	15.0	$C_{10}H_6O_7N_4$	40.88	2.02	19.27	40.82	2.06	19.05	365 295 250	23.1 9.6 8.7	45

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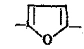
*Reaction under these conditions proceeds incompletely, and under more severe conditions, a strong resinification is found.

**Spectra were determined in a solution of ethyl alcohol containing 4% dimethylformamide.

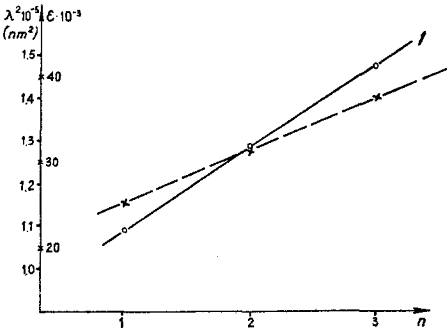
For polymethine derivatives of furan we have previously established [8] the law, $\lambda^2 = a + kn$, where λ = wavelength of the absorption maximum, n = number of conjugated ethylene bonds, and a and k = constants, characteristic for each substitute in position 2 of the furan ring. It is apparent from the figure that an analogous law is found for compounds **II**. Constants a and k in this case are equal to 9.6 and 2.02, respectively. The relationship presented in a previous report [8] between both constants $k = 4.2 - 0.2a$ occurs also for compounds II within the limits of accuracy of the empirical formula.

It is well known that the furan ring is a good conductor of the intramolecular interaction, according to its properties approaching the diene system. Thus, the substitute in position 5 must have a definite effect on the absorption pattern in general. Therefore, the methyl group of compound **IId** or the bromine of compound **IIe** produces a bathochromic displacement of the band in the order of 10 nm. As in the case of numerous other furan derivatives, the 5-nitro group produces a bathochromic displacement of approximately 30 nm. In addition, two weak bands are found in the spectrum of compound **IIf** at 295 and 250 nm, which is apparently the split "forbidden" band of absorption of the nitro group found in the 275 nm region [9].

By combining data concerning UV absorption spectra of furylvinyluracils, it is apparent that the laws presented above are sufficiently characteristic for a wide range of polymethine-substituted heteroaromatic compounds.

The phenomenon of intramolecular interaction of the functional groups ($—NO_2$, $—C{=}O$, ) is also found in the oscillating spectra of compounds II (Table 2).

Two oscillation bands of the β-carbonyl groups of uracil and its derivatives are found in the regions 1745–1710 and 1688–1660 cm^{-1}, respectively. The presence of two bands of carbonyl absorption has been interpreted differently in the literature. The generally accepted point of view is presented in one report [10]. This phenomenon arises from the nonequivalence of both carbonyl groups and the band of higher frequency is associated with the 4-carbonyl, and the band of lower frequency is related to the 2-carbonyl group. However, certain authors [11] consider that in uracil and its derivatives there is a split in the oscillation band of the C=O group as a result of the interaction of two associated resonating oscillators ("coupling-effect"). The possibility of such an interaction has not been disregarded, although its role cannot be significant as both carbonyl groups are conjugated only extremely weakly by means of an unshared electron pair of the amide nitrogen in position 3. In addition, one should note the following characteristics in relation to the behavior of the high frequency oscillation band of the C=O group: 1) increase in ν_{CO} on conjugation of the 4-carbonyl group with the 5-nitro group during transformation from compound III to compound I [12]; 2) decrease of ν_{CO} in the absence of a nitro group and conjugation of the 4-carbonyl group by means of the ethylene bond with the electron donor furyl radical in compound IV; 3) increase in ν_{CO} on incorporation of the nitro group in compound **IIa**; 4) decrease in ν_{CO} during the lengthening of the conjugation chain in compounds **IIb** and **IIc**; 5) presence of the oscillation band of C=O in the region characteristic for saturated carbonyl compounds.

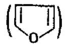


Dependence of the square of the wavelength of the absorption maximum (1) and the coefficient of extinction (2) on the number of ethylene bonds in the molecule.

The position of the second carbonyl absorption band in the 1688–1600 cm^{-1} region is sufficiently close

Table 2

Characteristic Frequencies of Functional Groups in a Number of Uracil Derivatives (cm^{-1})

Compound	$\nu_{C=O}$	$\nu^s_{NO_2}$	$\nu^{as}_{NO_2}$	ν 	δ_{C-H} 		ν^s_{C-O-C}
I	1688, 1725	1327	1511	—	—	—	—
IIa	1665, 1737	1321	1525	1465	857 881	931	1021
IIb	1675, 1715	1315	1513	1478	867 886	925	1021
IIc	1661, 1710	1321	1528	1479	857	925	1017
IId	1669, 1741	1325	1520	—	864	938	1022
IIe	1672, 1745	1316	1525	1460	867	930	1027
IIf	1679, 1726	1327 1347	1518 1526	1475	864	—	1020
III	1665, 1720	—	—	—	—	—	—
IV	1660, 1712	—	—	1480	883	940	—

to the absorption region of the amides of carboxylic acids. The latter confirms the above-mentioned interpretations presented in a previous report [10] and one should consider the point of view of certain authors [11] as insufficiently well-grounded.

Oscillations of the nitro group are of interest from the point of view of the nature of the uracil ring. The frequency of the symmetrical oscillations of the nitro group in uracil derivatives is found in the 1327–1315 cm^{-1} region, (i. e., in the region closer to the values ν_{NO_2}, symmetrical in saturated aliphatic compounds than in aromatic compounds, which is in agreement with the existing concepts concerning the weak aromatic nature of the uracil ring). One should note the condition in the spectrum of compound **IIf** in which, in addition to the 1327 cm^{-1} band of the 5-nitro group in the uracil ring, there is a 1347 cm^{-1} band associated with the 5-nitro group of the furan ring [12].

Antisymmetrical oscillations of the nitro group in compound I appear in the form of a narrow band at 1511 cm^{-1}. This value is relatively low in comparison with data in the literature [13], especially considering the conjugation of the nitro group with the electron acceptor 4-carbonyl group. In furyl derivatives of uracil, this band is slightly displaced although it does not exceed the limits of 1528–1513 cm^{-1}. During conjugation of the 5-nitro group of uracil with the polyene system of bonds in compounds **IIa–IIc**, the position of the band does not markedly alter. When two nitro groups are present in compound **IIf** the band splits into two closely situated peaks at 1526 and 1518 cm^{-1}.

It was difficult to study the interaction between the uracil and furan rings in compounds **IIa–IIf**, in relation to the displacement of the characteristic bands of these rings, because of the strong overlapping of oscillation bands of both rings. Only certain bands of the furan ring are free from overlapping. Thus, the following characteristics of the oscillation bands of furan are apparent: oscillations of the ring in the 1480–1460 cm^{-1} region, deformation oscillations of C—H in the 886–857 and 940–925 cm^{-1} regions [14], and the band of symmetrical oscillations of the —C—O—C— bonds in the 1027–1017 cm^{-1} region (the latter disappears in compound IV, apparently because of a decrease in intensity).

The slight change in position of the band of the furan ring indicates the insignificant interaction between the furan and uracil rings forming an additive system.

EXPERIMENTAL

G. Volynkina participated in the experimental part of this work.

5-Nitro-6-[(2-furyl)vinyl]uracil (IIa). Method A. A 42.8 g quantity (0.25 mole) of compound I was dissolved in 320 ml of dry pyridine by heating in a water bath, 0.8 g piperazine was added, and a solution of 26 g (22.4 ml, 0.27 mole) of freshly distilled furfurol in 80 ml pyridine was added. The reaction mixture was heated to boiling during which it darkened and within 30 min a greenish-yellow precipitate began to form. Heating was continued for a further 2 hr after which the reaction mixture was cooled to room temperature and the precipitate was filtered by suction. The mother liquor was poured onto ice and neutralized with HCl (1 : 1) to pH 5. The precipitate was filtered by suction. The precipitates were washed on a filter with hot water, alcohol, and ether. A 52 g quantity of compound IIa was obtained (84% of theoretical calculating for compound I). The compound was recrystallized from dimethylformamide.

Compounds IIb–IIe were synthesized in an analogous manner (Table 1).

5-Nitro-6-[(5-Nitro-2-furyl)vinyl]uracil (IIf). Method B. 7.78 g of quantity (0.045 mole) of compound I was dissolved in 50 ml dimethylformamide, a catalyst (1 ml acetic acid, 0.1 ml morpholine, and 3 ml dimethylformamide) and then a solution of 7.1 g (0.05 mole) of 5-nitrofurfurol in 15 ml dimethylformamide were added, and the mixture was heated for 15 hr at a temperature of 60–65° C. On cooling, a crystalline precipitate was formed which was filtered by suction. The mother liquor was poured onto ice and the resulting precipitate was also filtered by suction. The precipitates were washed on a filter with alcohol and ether. A 6.0 g quantity of the substance was obtained (45% of the theoretical calculating from compound I). It was recrystallized from a mixture of ethanol and dimethylformamide (1 : 2).

The UV spectra were determined in an SF-4 spectrophotometer. IR spectra were determined in a double beam IKS-14 spectrophotometer from a suspension of the analytical samples of the substances in vaseline oil for the frequency interval of 700–1800 cm^{-1} and in hexachlorobutadiene for the frequency interval of 1300–1500 cm^{-1}.

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