REACTION OF 4-AMINOURACIL WITH 2-(ARYLMETHYLENE)INDAN-1, 3-DIONES

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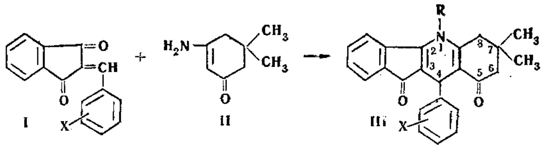
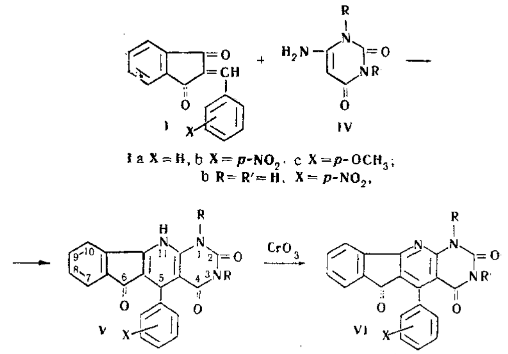
The reaction of the arylmethyleneindanones (I) with 4-aminouracil or its N-methyl derivative (IV) gives new multinuclear nitrogen-containing systems—5-aryl-2, 4, 6-trioxo-1-R-3-R'-1, 2, 3, 4, 5, 11-hexahydro-11-azafluoreno[3, 2-d]pyrimidines (V), which are oxidized by chromic anhydride to 5-aryl-2, 4, 6-trioxo-1-R-3-R'-1, 2, 3, 4-tetrahydro-11-azafluoreno[3, 2-d]pyrimidines (VI). The UV and IR spectra of the compounds synthesized are given.

In preceding papers [1, 2], one of us has shown that the cyclic β-aminovinylcarbonyl compound 3-amino-5, 5-dimethylcyclohex-2-enone (II) readily reacts with arylmethyleneindandiones (I) to form a multinuclear system—11-aryl-1, 10-dioxo-3, 3-dimethyl-1, 2, 3, 4, 5, 11-hexahydroindeno [1, 2-b]quinoline (III).



On the basis of these results, we assumed that the 4-aminouracils IVa–IVc should react similarly, since formally they also have a β-aminovinylcarbonyl grouping. In actual fact, the reaction of IVa–IVc with the arylmethyleneindandiones Ia–IVc gave the new multinuclear nitrogen-containing systems 5-aryl-2, 4, 6-trioxo-1-R-3-R'-1, 2, 3, 4, 5, 11-hexahydro-11-azafluoreno[3, 2-d]pyrimidines (Va–Ve).

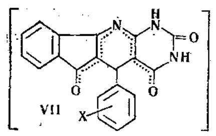


I a X = H, b X = p-NO_2, c X = p-OCH_3;
b R = R' = H, X = p-NO_2,

IV a R = R' = H, b R = CH_3, R' = H, c R = R' = CH_3; V, VI a R = R' = X = H,
c R = R' = H, X = p-OCH_3, d R = CH_3, R' = X = H, e R = R' = CH_3, X = H

Probably the 4-aminouracil first adds to the double bond of the arylmethyleneindandione, and only then does cyclization take place. We did not isolate the intermediate compounds. The condensation reaction takes place with good yields in acetic acid. The reactants Ia–Ic and IVa–IVc were previously dissolved separately in acetic acid, and then these solutions were mixed and heated.

From 4-amino-3-methyluracil (IVb) and 4-amino-1, 3-dimethyluracil (IVc) we obtained the N-substituted hexahydroazofluorenopyrimidines Vd and Ve. Compounds Va–Ve are stable red crystalline substances which readily form dark red monosodium salts. We assume that the salts are formed through the N—H group in the dihydropyridine ring and the anions have the structure VII:



This is indicated by the similar UV absorption curves of compounds Va and Ve in an alkaline medium (Fig. 1). Compound Ve can dissociate only the N—H bond of the dihydropyridine ring and therefore its anion corresponds accurately to structure VII. It is not excluded that in a more alkaline medium compounds Va–Vd may also dissociate at the other N—H bonds.

Compounds Va–Ve are readily oxidized under the action of CrO_3 to the corresponding 5-aryl-2, 4, 5-trioxo-1-R-3-R'-1, 2, 3, 4-tetrahydro-11-azafluoreno[3, 2-d]pyrimidines (VIa–VIe). In contrast to Va–Ve, these are yellow crystalline substances forming bright yellow monosodium salts, except for VId and VIe. In these cases the monosodium salt is formed at the expense of the N—H bond of the uracil ring, since there is no N—H bond in the dihydropyridine ring. The UV absorption spectra of the dihydropyridine and pyridine derivatives differ markedly. Fig. 2 gives the absorption curves of Va and VIa in ethanol and in ethanolic alkali.

To define the structure, the IR spectra of the substances Va–Ve and VIa–VIe that we had synthesized were also recorded. The identification of the individual absorption bands presents difficulties (Table 1). However, it can be seen that compounds Va–Ve have spectra similar to one another, and the same applies to compounds VIa–VIe. In the spectra of compounds Va–Ve the three high frequencies in the 6μ region (for example, in the spectrum of Va—1640, 1673, and 1710 cm^{-1}) must be ascribed to the vibrations of the carbonyl groups of both the five-membered and six-membered rings. In the spectra of VIa–VIe (with the exception of VIc) only two such vibrations are observed since, obviously, the bands overlap. The remaining bands of compounds VIa–VIe must be ascribed to $\nu_{C=C}$ and $\nu_{C=N}$. These features are in harmony with those of the IR absorption spectra of the 1, 10-dioxo-1, 2, 3, 4, 5, 11-hexahydroindeno[1, 2-b]quinolines [3] and the 5-aryl-8, 8-dimethyl-2, 4, 6-trioxoocta- (and -deca-)-hydropyrimido[4, 5-b]quinolines [4] that we synthesized previously.

Table 1
Frequencies of the IR Absorption Spectra of Compounds Synthesized*

Compound	ν, cm^{-1} in the region of											
	6 μ									3 μ		
Va	1494 w		1542 w		1606 s	1640 w		1673 sh	1710 s	3068 m	3175 m	3260 m
Vb	1513 s		1524 sh		1600 sh	1640 s		1679 sh	1732 m	3074 m	3191 s	3220 s
Vc	1508 m		1532 s		1603 s	1638 m		1664 s	1691 s, 1738 s	3062 sh	3112 w	3219 s
Vd	1491 s		1501 sh		1604 w	1638 s		1688 m	1720 s	3093 m	3184 s	3266 s
Ve	1500 s				1607 w	1638 s		1684 w	1721 m	3089 m	3195 s	3265 s
VIa		1526 sh		1565 s	1590 w		1703 sh		1723 s	3096 s		3162 sh
VIb		1521 s		1565 s	1604 sh		1697 sh		1722 s	3021 m		3261 s
VIc	1508 m			1554 s	1589 m	1606 w		1699 sh	1715 s 1731 w	3024 s		3126 sh
VId	1498 s			1561 s	1604 w			1694 m	1731 s	3043 s	3148 s	3170 s
VIe	1495 s			1566 s				1669 s	1721 s			

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* All the spectra in the 6μ region were taken in paraffin oil and those in the 3μ region in hexachlorobutadiene.

Table 2
Characteristics of Compounds Synthesized

Compound	Mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %
			C	H	N	C	H	N	
Vb	275	$C_{20}H_{12}N_4O_5$	—	—	14.24	—	—	14.43	42.0
Vc	305	$C_{21}H_{15}N_3O_4$	—	—	11.14	—	—	11.26	78.0
Vd	301—302	$C_{21}H_{15}N_3O_3$	70.91	4.52	11.77	70.55	4.23	11.77	73.0
Ve	335	$C_{22}H_{17}N_3O_3$	71.09	4.29	11.98	71.12	4.61	11.31	65.0
VIb	326	$C_{20}H_{10}N_4O_5$	—	—	14.27	—	—	14.51	71.0
VIc	306—307	$C_{21}H_{13}N_3O_4$	—	—	11.27	—	—	11.31	60.5
VId	300	$C_{21}H_{13}N_3O_3$	70.96	4.00	11.92	70.96	3.68	11.82	35.0
VIe	342—345	$C_{22}H_{15}N_3O_3$	71.33	4.40	11.69	71.57	4.10	11.38	58.0

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* All the substances melted with decomposition.

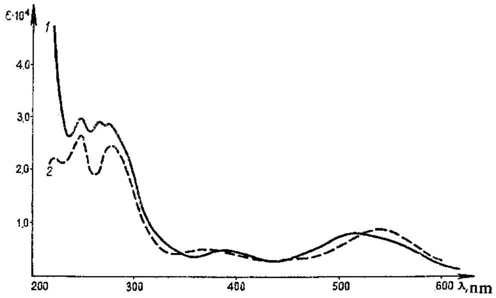

Fig. 1. UV spectra of compounds Va and Ve in solutions (0.1 ml of 40% KOH to 10 ml of 1 × 10^{-4}M solution of Va or Ve in ethanol): 1) Va; 2) Ve.

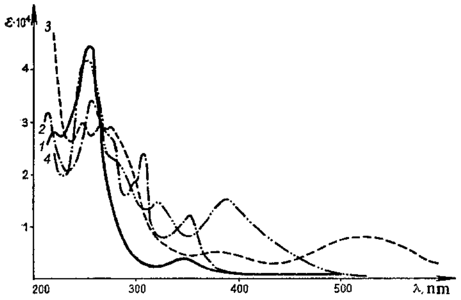

Fig. 2. UV spectra of compounds: 1) Va; 2) VIa (in ethanolic solution); 3) Va; 4) VIa (in alkaline ethanolic solutions).

EXPERIMENTAL

2,4,6-Trioxo-5-phenyl-1,2,3,4,5,11-hexahydro-11-azafluoreno[3,2-d]pyrimidine (Va). A solution of 1.26 g (8.5 mM) of 4-aminouracil in 200 ml of glacial acetic acid was added to a solution of 2 g (8.5 mM) of benzylideneindandione in 50 ml of glacial acetic acid, and the mixture was boiled for 1 hr. After cooling, a microcrystalline orange substance deposited. Yield 2.49 g (82.8%), mp 352° C (decomp., from acetic acid). The substance dissolves in alcoholic alkali with a violet coloration. Found, %: C 69.55; H 3.97; N 12.54. Calculated for $C_{20}H_{13}N_3O_3$, %: C 69.97; H 3.82; N 12.24.

2,4,6-Trioxo-5-phenyl-1,2,3,4-tetrahydro-11-azafluoreno[3,2-d]pyrimidine (VIa). With heating, 2 g (5.8 mM) of **Va** was dissolved in 120 ml of acetic acid, and a solution of CrO_3 in distilled water was added to the cooled solution until the orange coloration disappeared. Then more water was added until a light yellow precipitate appeared. Yield 0.44 g (22%), mp 334° C (decomp., from acetic acid). The substance dissolves in ethanolic alkali with dark yellow coloration. Found, %: C 70.81; H 3.50; N 12.28. Calculated for $C_{20}H_{11}N_3O_3$, %: C 70.37; H 3.23; N 12.31.

The characteristics of the other compounds synthesized are given in Table 2.

Na salt of 2,4,6-trioxo-5-phenyl-1,2,3,4,5,11-hexahydro-11-azafluoreno[3,2-d]pyrimidine. A solution of 0.23 g (0.01 mole) of Na in 50 ml of absolute methanol was prepared, and 3.45 g (0.01 mole) of **Va** was dissolved in it. After the solution had stood for one day at 0° C, a dark red substance deposited. Yield 3.0 g (82%).

After recrystallization from ethanol, found, %: N 11.27. Calculated for $C_{20}H_{18}N_3NaO_3$, %: N 11.50.

Na salt of 2,4,6-trioxo-5-phenyl-1,2,3,4-tetrahydro-11-azafluoreno[3,2-d]pyrimidine. To a solution of 0.27 g (7.9 mM) of **VIa** in 10 ml of absolute methanol was added 9.1 ml of the sodium methoxide solution prepared from 0.2 g of sodium and 50 ml of absolute methanol. A bright yellow substance deposited immediately. Yield 0.21 g (73%). It was crystallized from water. Found, %: N 11.48. Calculated for $C_{20}H_{10}N_3NaO_3$, %: N 11.57.

The UV spectra were taken in ethanol solution on an SF-4 spectrophotometer.

The IR spectra were taken on an IKS-14 double-beam infrared spectrophotometer with a sodium chloride prism in the 1400–1800 mμ region and with a lithium fluoride prism in the 3000–3500 mμ region.

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