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5-Diazouracils in Azo Coupling Reactions

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Abstract–6-Hydroxy-5-diazo-6*H*-uracil and 6-hydroxy-5-diazo-1,3-dimethyl-6*H*-uracil enter into azo coupling reaction with CH-acids, active phenols, arylamines, and heterocycles. The conditions of reaction depend on the substrate character.

Pyrimidine derivatives, in particular, derivatives of uracil, occupy an important place in the chemistry of heterocyclic compounds. This is caused by the wide spread of such compounds in living matter and by biological activity of many among them. The uracil structure defines that these compounds can act both as unsaturated carbonyl and aromatic compounds thus providing a versatile reactivity.

Although 5-diazouracil and 6-hydroxy-5-diazo-1,3-dimethyl-6*H*-uracil are known for a long time [1, 2], the descriptions of their reactivity with respect to nucleophiles are very limited. It is known that 5-diazouracil and its methyl-substituted derivatives are capable of reversible addition of the simple nucleophiles (water, alcohols, HCN, amines) at *6* position. For instance, by diazotization of 5-aminouracil was obtained a hydrated form, 6-hydroxy-5-diazo-6*H*-uracil [1–4]. Besides recyclizations of 6-hydroxy-5-diazo-6*H*-uracil, 5-diazo-6 methoxy-6H-uracil and 6-hydroxy-5-diazo-1,3-dimethyl-6H-uracil at heating and in the presence of bases were described [4, 5]. As to azo coupling the only communication reported on reaction of 6-hydroxy-5-diazo-6*H*-uracil with Me_2NH in anhydrous medium [1]. The ability of 5-diazouracils to undergo azo coupling with other azo components may be predicted from the essential contribution of betaine frontier structures into their resonance hybrid. The significance of this contribution is demonstrated by the fact that the length of the N=N bond and the position of its absorption band in the IR spectra [1, 6] are intermediate between these parameters in aryldiazonium salts [7, 8] and aliphatic diazo compounds [7, 9]. Recently the most of research connected with 5-diazouracil was directed to its transformations under biochemical conditions or to its biological activity [10]. Therefore it is an urgent task to prepare biologically active uracil derivatives through azo coupling of 5-diazouracil.

The goal of this research was investigation of the ability of 5-diazouracils to azo coupling with active aromatic compounds and CH-acids. We found that 6-hydroxy-5-diazo-6*H*-uracil (**I**) reacted with some substrates without catalyst in boiling methanol where it existed in the form of methoxy derivative **IIa**. This method provided relatively good results when the coupling occurred enough rapidly. Thus strong CH-acids, for instance, acetylacetone, dimedone, 1-phenyl- and 1-(*p*-tolyl)-3-methylpyrazol-5-ones, and also 2-naphthol, under these conditions are readily converted into derivatives **III**–**VII** (Table 1). At the same time in reaction of diazouracil **I** with alkyl cyanoacetate was isolated a product whose structure we failed to establish, and with benzoylacetone, 1-naphthol, and resorcinol the products of azo coupling were strongly contaminated with impurities. The formation of intractable reaction products alongside the azo coupling may be due to diazouracil ability to undergo recyclization (also to photochemical one [11]) and to suffer replacement of diazo group [12]. In water alkali without heating diazo compound **I** readily reacts with 2-naphthol yielding azo dye **VII**. However reaction with CH-acids and less active phenols under these conditions results in complex reaction mixtures.

It turned out that the azo coupling of diazouracil with quite a number of substrates can be more successfully carried out at room temperature in ethanol in the presence of an equimolar amount of NaOH. The best results were obtained when the solution of compound **I** (which in the ethanol transforms apparently into 6-ethoxy derivative **IIb**) was added to a preliminary prepared solution of phenolate or enolate in ethanol. The reaction is fast an in most cases is not complicated by side processes. After neutralization of the reaction mixture with acetic acid the coupling products were isolated in fair yields.

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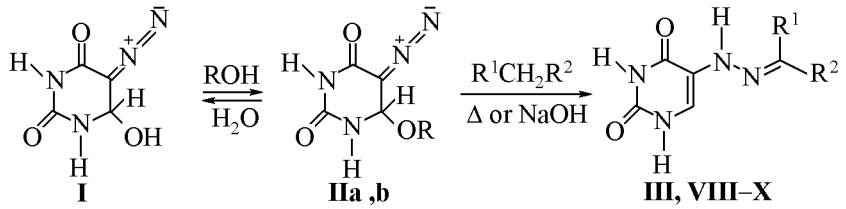
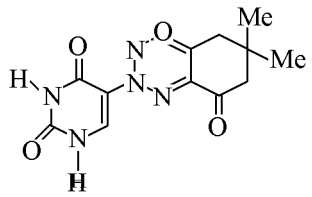
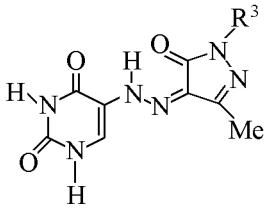


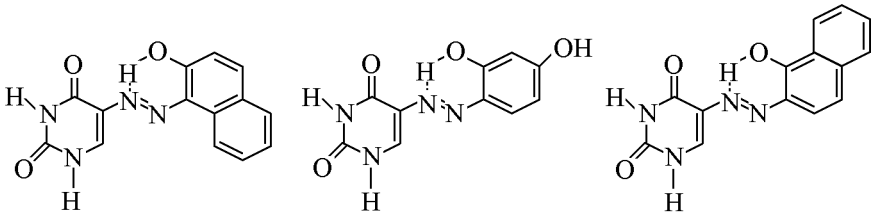
I **IIa ,b** **III, VIII–X**



IV



V, VI



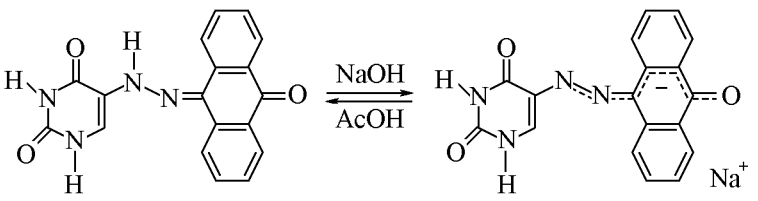
VII **XI** **XII**

II, R = Me (**a**), Et (**b**); **III**, R^1 = R^2 = C(O)Me; **VIII**, R^1 = C(O)Ph, R^2 = C(O)Me; **IX**, R^1 = CN, R^2 = CO_2Et; **X**, R^1 = R^2 = CN; **V**, R^3 = Ph; **VI**, R^3 = 4-MeC_6H_4.

Under these conditions compound **I** cleanly reacted with acetylacetone, benzoylacetone, alkyl cyanoacetate, malononitrile, resorcinol, 1- and 2-naphthols, and anthrone furnishing the corresponding azo coupling products (**III, VII–XIII**) (Table 1); compounds **III** and **VII** were identical to those obtained by the corresponding reactions in methanol without alkali.

In the reaction of diazo compound **I** with anthrone in alkaline reaction mixture arose a sodium salt **XIV** that was isolated as dark-blue crystalline substance. The free acid **XIII** of light-yellow color was obtained by neutralization of the reaction mixture. Compounds **XIII** and **XIV** are always isolated with anthraquinone impurity due apparently to the ease of their hydrolysis. This assumption is confirmed by the fact that at heating hydrazone **XIII** in water-ethanol solution of hydrochloric acid anthraquinone forms in high yield. We failed to clear the transformation of the uracil fragment of molecule **XIII** in the course of this process.

The structure of compounds **III–VI, VIII–X, XIII** was confirmed by ^1H NMR spectra (Table 2). In the spectrum of compound **III** the methyl, and in the spectrum of compound **IV** the methylene groups appear as couples of singlets, and in the spectra of compounds **VIII** and **IX** the signals of all protons appear in double set including the protons of heterocycles. All eight anthracene protons of anthrone derivative **XIII** appear as separate signals, and in the presence of oxygen traces they coalesce by pairs into four peaks. Therefore to the compounds mentioned may be assigned the structure of 2-(uracil-5-yl)hydrazones of 1,2,3-tricarbonyl compounds **III, IV, VIII–X**, of 4-(uracil-5-yl)hydrazones of pyrazole-4,5-diones **V, VI**, and uracil-5-yl)hydrazone of anthraquinone **XIII**. Just the hydrazone structure in the



XIII **XIV**

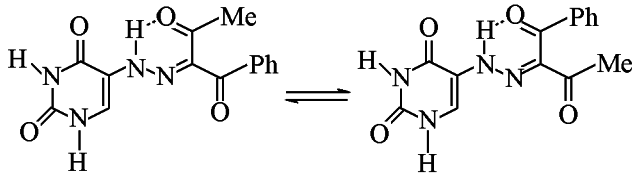
Table 1. Reaction conditions and characteristics of compounds **III**–**XV, XVII, XVIII**

Compd. no.	Time, h (method)	Yield, g (%)	mp, °C	Found, %		Formula	Calculated, %	
				C	H		C	H
III	5 (*a*)	0.25 (52)	268-270	45.15	4.36	$C_9H_{10}N_4O_4$	45.38	4.20
III	0.25 (*b*)	0.32 (67)	269-271	45.62	4.41	$C_9H_{10}N_4O_4$	45.38	4.20
IV	10 (*a*)	0.36 (67)	298-300	51.57	5.16	$C_{12}H_{14}N_4O_4$	51.80	5.04
V	0.25 (*a*)	0.33 (54)	330-335	54.05	3.68	$C_{14}H_{12}N_6O_3$	53.85	3.85
VI	0.25 (*a*)	0.36 (56)	335-340	55.40	4.36	$C_{15}H_{14}N_6O_3$	55.21	4.29
VII	0.25 (*b*)	0.45 (75)	319-321	59.29	3.67	$C_{14}H_{10}N_4O_3$	59.57	3.55
VIII	0.3 (*b*)	0.42 (67)	286-288	56.48	4.36	$C_{14}H_{12}N_4O_4$	56.00	4.00
IX	1 (*b*)	0.24 (47)	260-261	43.69	3.05	$C_9H_9N_5O_4$	43.03	3.59
X	0.25 (*b*)	0.17 (42)	249-252	41.52	2.20	$C_7H_4N_6O_2$	41.18	1.96
XI	0.5 (*b*)	0.40 (75)	360-362	48.90	3.44	$C_{10}H_7N_4O_4$	48.39	3.23
XII	0.25 (*b*)	0.27 (50)	320-322	59.35	3.80	$C_{14}H_{10}N_4O_3$	59.57	3.55
XIII	0.1 (*b*)	0.27 (42)	290-295	65.37	3.74	$C_{18}H_{12}N_4O_3$	65.06	3.61
XIV	0.1 (*b*)	0.24 (35)	[a]	60.52	3.21	$C_{18}H_{11}N_4O_4Na$	61.02	3.10
				Na: 6.15			Na: 6.50	
XV	20 (*a*)	0.25 (64)	301-304	61.65	4.71	$C_{16}H_{14}N_4O_3$	61.94	4.52
XVII	7 (*a*)	0.25 (69)	243-245	62.24	4.45	$C_{16}H_{14}N_4O_3$	61.94	4.52
XVIII	5 (*a*)	0.31 (76)	272-275	58.64	4.16	$C_{16}H_{14}N_4O_4$	58.90	4.29

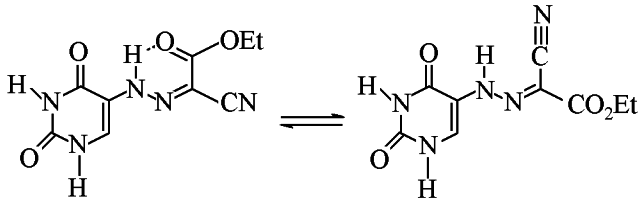
[a] Compound decomposed at 250–300°C without melting.

molecules of these compounds results in nonequivalence of methyl (methylene) groups in the azo coupling products **III** and **IV**, and in existence of a mixture of *E*- and *Z*-isomers in asymmetrical derivatives **VIII** and **IX**. That the C=N bond possesses nearly double character is testified by the fact, that coalescence of signals in the spectrum of compound **VIII** in DMSO-d_6 starts to appear only at 130°C, and in the spectrum of compound **III** it is not observed. The interconversion of *syn*- and *anti*-isomers is also hampered by the intramolecular hydrogen bond between hydrazone NH proton and carbonyl groups of the fragment of CH-acid; this hydrogen bond is indicated by downfield shift of this proton in the spectra: 14.0 (**III**), 14.75 (**IV**), 13.95 (**VIII**), 12.65 ppm (**IX**).

Intramolecular hydrogen bond stabilizes the stereoisomeric derivatives of unsymmetrical CH-acids to unequal extent. For instance, in compound **VIII** where an efficient intramolecular hydrogen bond may arise with any of two carbonyls, the ratio of A and B isomers equals to 72 : 28; in the derivative of cyanoacetate **IX** where the cyano group cannot form a hydrogen bond the ratio of A and B isomers is 87 : 13 (in DMSO-d_6). An evidence of the strong influence of the hydrazone fragment structure on the electron density distribution in heterocycle is the splitting of proton signals from the uracil ring in the spectra of compounds **VIII** and **IX**. In the spectra of hydrazones **V, VI** appears a single set of signals; it means that the interconversion *E*- and *Z*-isomers occurs relatively easily, or that in solution exists a single isomer. Intramolecular hydrogen bond in these molecules apparently does not exist for the C=O group in a five-membered ring is strongly deviated from the hydrazone NH proton. It is confirmed by the lack in their ^{1}H NMR spectra of a characteristic downfield signal.



VIIIA **VIIIB**



IXA **IXB**

The coupling products with phenols: 5-(2-hydroxy-1-naphthylazo)uracil (**VII**), 5-(2,4-dihydroxyphenylazo)uracil (**XI**), and 5-(1-hydroxy-2-naphthylazo)-

uracil (**XII**) unlike hydrazones **III–VI, VIII–X** have deeper color. The proton C^6H of the uracil ring gives a signal in their ^1H NMR spectra in weaker field (8–8.5 ppm) (Table 2). On this basis a structure of azo compounds and not hydrazones was assigned to these compounds. In the molecules of compounds in question the azo group with OH group of the aromatic fragment form an intramolecular hydrogen bond as shows the downfield position of the signal from this proton (**X**, 12.45; **XI**, 15.2; **XII**, 13.7 ppm).

Dye **XII** was separated with an impurity hard to isolate. According to ^1H NMR spectrum the latter is an isomeric product substituted in *para*-position. The aromatic signals of this impurity had the chemical shifts similar to those in the spectrum of *para*-substituted product **XV** that we obtained by heating 1,3-dimethyl-5-diazouracil (**XVI**) with 1-naphthol in methanol.

The position of azo group in compounds **XII** and **XV** was deduced from the following observations: The chemical shifts of naphthalene protons in these compounds are very different; therewith th coupling constant in the doublets in the spectrum of compound **XII** is larger (9.1 HZ) than in the spectrum of azo compound **XV** (8.4 Hz). Taking into account the known fact that in similar naphthalene derivatives the coupling constant for C^1H and C^2H protons is usually larger than for C^2H and C^3H protons [13] to compound **XII** was assigned an *ortho*-substituted structure, and substance **XV** was regarded as *para*-hydroxyazo compound. It is not yet clear how two methyl groups in diazouracil affect the orientation of the substituents. At the same time the reaction conditions apparently did not significantly influence the orientation, for the main component of the mixture obtained at heating diazouracil **I** with 1-naphthol in methanol was azo compound **XII**.

Methylated diazouracil **XVI** possesses reactivity similar to that of diazouracil **I**; however its coupling with naphthols at heating in ethanol or methanol occurs more cleanly. By this procedure we prepared

Table 2. IR, UV, and ^1H NMR spectra of compounds **III**–**XV, XVII**–**XIX, XXI, XXII, XXIV**

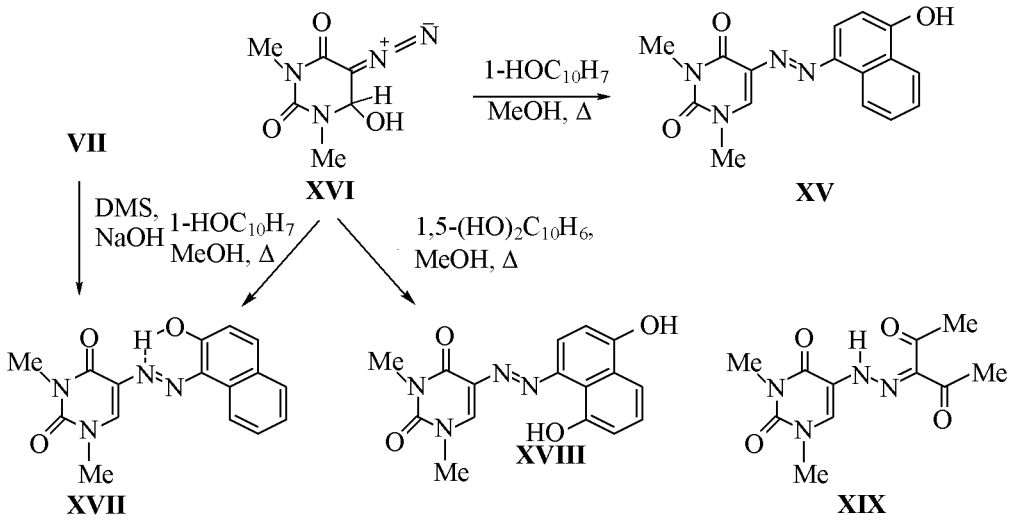
Compd. no.	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)	^1H NMR spectrum, δ, ppm, *J*, Hz[a]
III	905, 1290, 1510, 1620, 1665, 1700, 3070, 3570	251 (3.86), 394 (4.12)	2.35 s (3H, $COCH_3$) 2.45 s (3H, $COCH_3$), 7.7 d (1H, H^6, *J* 6.1), 11.15 d (1H, H^1, *J* 5.3), 11.7 s (1H, H^3), 14.0 s (1H, NH)
IV	1600, 1665, 1710, 3245, 3515	262 (3.79), 424 (4.27)	1.0 s (6H, $3CH_3$), 2.5 s (2H, CH_2 and DMSO), 2.6 s (2H, CH_2), 7.6 s (1H, H^6), 11.3 s (1H, H^1), 11.8 s (1H, H^3), 14.75 s (1H, NH)
V	1380, 1630, 1690, 1705, 3240	245, 424	2.3 s (3H, CH_3), 7.2 t.t (1H, $H^{4'}$, ^3J 7.4), 7.45 t.d (2H, $H^{3'}$, $H^{5'}$, ^3J 7.1), 7.65 s (1H, H^6), 7.9 d.d (2H, $H^{2'}$, $H^{6'}$, ^3J 8.2), 10.7 br.s (1H, H^1), 11.25 br.s (1H, H^3)
VI	1380, 1515, 1640, 1675, 1705, 3090, 3215	246, 434	2.25 s (3H, Me in pyrazole), 2.35 s (3H, C_6H_4Me), 7.25 d (2H, $H^{3'}$, $H^{5'}$, *J* 8.7), 7.6 s (1H, H^6), 7.75 d (2H, $H^{2'}$, $H^{6'}$, *J* 8.5), 10.5–11.5 br.s (2H, H^1, H^3)
VII	810, 830, 1650, 1690, 3380	321 (4.13), 483 (4.55)	7.05 d (1H, $H^{3'}$, *J* 9.2), 7.45 t (1H, $H^{6'}$, *J* 7.4), 7.6 t (1H, $H^{7'}$ *J* 7.7), 7.85 d (1H, $H^{8'}$, *J* 7.8), 7.95 d (1H, $H^{4'}$, *J* 9.3); 8.3 s (1H, H^6), 8.7 d (1H, $H^{8'}$, *J* 8.2), 11.8 s (2H, H^1, H^3); 15.2 s (1H, OH)
VIII	950, 1560, 1595, 1660, 1700, 3190, 3570	275 (3.91), 402 (4.16)	Form (A): 2.5 s (3H, Me and DMSO), 7.0 d (1H, H^6, *J* 5.9), 7.8 d (2H, $H^{2'}$, $H^{6'}$, *J* 7.2), 10.95 d (1H, H^1, *J* 5.2), 13.95 s (1H, NH); Form (B): 2.45 s (3H, Me), 11.1 d (1H, H^1, *J* 5.4). Common: 7.4–7.7 m [Ph and H^6 of form (B)], 11.6 m (NH)
IX	760, 870, 1105, 1650, 1665, 1685, 2220, 3095, 3140, 3200	283 (3.76), 379 (4.36)	Form (A): 7.6 s (1H, H^6), 11.8 s (1H, H^3), 12.65 s (1H, NH); Form (B): 7.5 s (1H, H^6), 10.8 br.s (1H, H^1), 11.6 s (1H, NH); Common: 1.3 m (CH_2Me), 4.3 m (CH_2CH_3), 11.2 d.s (NH)
X	770, 1635, 1680, 2190, 2210, 3125	308 (3.84), 395 (4.27)	7.6 s (1H, H^6), 11.15 s (1H, H^1), 11.6 s (1H, H^3), 12.0 s (1H, NH)
XI	1200, 1330, 1605, 1670, 3170, 3440	258 (3.52), 400 (3.61), 432 (3.62)	6.3 d (1H, $H^{3'}$, *J* 2.12), 6.45 d.d (1H, $H^{5'}$, ^3J 8.8, ^4J 2.2), 7.55 d (1H, $H^{6'}$, *J* 8.8), 8.0 s (1H, H^6), 10–12 br (1H, $OH^{4'}$), 11.5 s (2H, H^1, H^3), 12.45 s (1H, $OH^{2'}$)
XII	1685, 1715, 3150,	426 (3.73),	7.3 d (1H, $H^{3'}$, *J* 9.1), 7.5 s (2H, $H^{4'}$, $H^{7'}$), 7.65 t (1H, $H^{6'}$, *J* 7.3), 7.8 d

Table 2. (Contd.)

Compd. no.	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)	^{1}H NMR spectrum, δ, ppm, *J*, Hz[a]
	3430	473 (3.72)	(1H, $H^{5'}$, *J* 8.0), 8.2 s (1H, H^6), 8.3 d (1H, $H^{8'}$, *J* 7.9), 11.6 br.s (1H, H^1), 11.7 s (1H, H^3), 13.7 s (1H, OH)
XIII	1300, 1590, 1660, 1725, 3150, 3310, 3440	443 (4.02)	7.55 m (2H, H^6 and H arom); other H arom: 7.75 m (2H), 8.1 d (1H, *J* 7.9), 8.35 d (1H, *J* 8.0), 8.4 d (1H, *J* 7.7), 8.5 d (1H, *J* 7.9), 7.95 m (H arom and anthraquinone); 9.35 s (1H, NH), 10.85 s (1H, H^1), 11.55 s (1H, H^3), anthraquinone: 7.95 d.d, 8.2 d.d
XIV	1500, 1585, 1620, 1650, 3400-3500	249 (3.64), 287 (3.45), 469 (3.02), 600 sh	7.15 t (2H, H arom, *J* 7.4), 7.3 s (1H, H^6), 7.5 t (2H, H arom, *J* 7.6), 8.3 d (2H, H arom, *J* 8.0), 9.45 t (2H, H arom, *J* 8.0); anthraquinone: 7.95 d.d, 8.2 d.d
XV	845, 1580, 1615, 1640, 1720, 3300	243, 282, 450, 650	3.3 s (3H, N^1Me), 3.5 s (3H, N^3Me), 7.0 d (1H, $H^{3'}$, *J* 8.4), 7.6 t (1H, $H^{6'}$, *J* 9.0), 7.7 m (2H, $H^{2'}$, $H^{7'}$), 8.2 d (1H, $H^{5'}$, *J* 7.7), 8.4 s (1H, H^6), 8.9 d (1H, $H^{8'}$, *J* 8.1)
XVII	1075, 1615, 1660, 705, 3400	240, 360, 520	3.4 s (3H, N^1Me), 3.6 s (3H, N^3Me), 6.9 d (1H, $H^{3'}$, *J* 9.4), 7.4 t.d (1H, $H^{6'}$, ^3J 7.5, ^4J 1.3), 7.5 t.d (1H, $H^{7'}$, ^3J 7.7, ^4J 1.4), 7.6 d.d (1H, $H^{5'}$, ^3J 7.93), 7.7 d (1H, $H^{4'}$, *J* 9.4), 7.9 s (1H, H^6), 8.45 d (1H, $H^{8'}$, *J* 8.0), 15.4 s (1H, OH)
XVIII	1535, 1585, 1630, 1660, 1705, 1220	221, 295, 338, 490	3.25 s (3H, N^1Me), 3.5 s (3H, N^3Me), 6.95 m (2H, $H^{3'}$, $H^{7'}$), 7.35 t (1H, $H^{6'}$, *J* 7.9), 7.65 d.d (1H, $H^{5'}$, ^3J 8.3, ^4J 1.1), 7.85 d (1H, $H^{2'}$, *J* 8.5), 8.8 s (1H, H^6), 12.0 s (1H, $C^{8'}$OH)
XIX	1300, 1630, 1660, 1705	255 (3.88), 400 (4.28)	2.4 s (3H, $COCH_3$), 2.45 s (3H, $COCH_3$), 3.2 s (3H, N^1Me), 3.4 s (3H, N^3Me), 8.1 s (1H, H^6), 14.1 s (1H, NH)
XXI	1440, 1600, 1730, 1770, 3180	439 (3.47)	3.3 s (6H, NMe_2), 7.85 d (2H, $H^{3'}$, $H^{5'}$), 8.0 (2H, $H^{2'}$, $H^{6'}$), 9.1 s (1H, H^6)
XXII	1595, 1640, 1705	220, 275, 482	3.1 s (6H, NMe_2), 3.45 s (3H, N^1Me), 3.5 s (3H, N^3Me), 6.7 d (2H, $H^{3'}$, $H^{5'}$, *J* 9.2), 7.7 s (1H, H^6), 7.8 d (2H, $H^{2'}$, $H^{6'}$, *J* 9.2)
XXIV	1580, 1610, 1665, 1705, 3070, 3215	252, 296, 404, 439 sh	1.1 t (3H, CH_2CH_3, *J* 7.2), 3.15 s (3H, N^3Me), 3.8 s (3H, N^1Me), 4.2 q (2H, CH_2CH_3, *J* 6.4), 7.5 m (5H, Ph), 7.7 s (1H, $H^{6'}$), 11.0–11.6 br. (2H, NH)

[a] ^{1}H NMR spectrum of compound **XXI** was recorded in CF_3COOH, of compound **XXII** in $CDCl_3$, the rest spectra were registered in DMSO-d_6.

already mentioned azo compound **XV**, and also coupling products with 2-naphthol and 1,5-dihydroxynaphthalene: 1,3-dimethyl-5-(2-hydroxy-1-naphthylazo)uracil (**XVII**), and 1,3-dimethyl-5-(4,8-dihydroxy-1-naphthylazo)uracil (**XVIII**) (Table 1). Reaction of compound **XVI** under these conditions with resorcinol

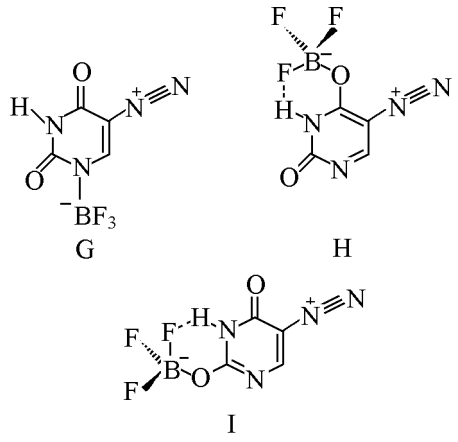


and phloroglucinol, as in the case of its NH-analog **I**, results in intractable mixture of reaction products. Compound **XVII** was also prepared by independent synthesis: by treating the coupling product of diazouracil **I** with 2-naphthol (**VII**) with dimethyl sulfate under standard conditions used for uracils methylation [14]. Hydrazone **III** also was successfully subjected to this reaction yielding dimethylderivative **XIX**.

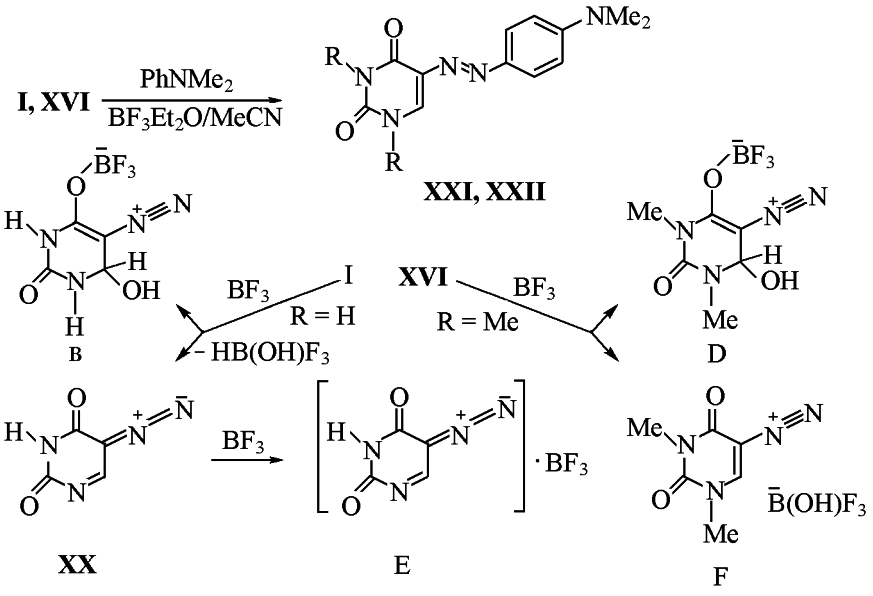
Reaction of diazouracil **I** with ethanol solution of sodium phenolate in the cold did not result in azo coupling, and from the reaction mixture was isolated only uracil apparently generated by reduction of compound **I** with phenol.

Diazouracils **I** and **XVI** under suitable conditions enter into azo coupling with aromatic amines. For instance, at dissolution of compound **I** in anhydrous pyridine it suffers dehydration and transforms into the more electrophilic 5-diazouracil (**XX**). At heating this solution with N-substituted arylamines occurs azo coupling affording dyes containing impurities. More efficient activation of diazouracils **I** and **XVI** provides addition of boron trifluoride etherate to their solutions in acetonitrile. Under these conditions the azo coupling with amines occurs fast at room temperature. This procedure furnished sufficiently pure 5-(4-dimethylaminophenylazo)uracil (**XXI**) and 1,3-dimethyl-5-(4-dimethylaminophenylazo)uracil (**XXII**). Under these conditions into reaction with compound **I** enter also 1-diphenylaminonaphthalene and diphenylamine; however the azo compounds obtained in these processes are not individual. The catalytic effect of Lewis acids in reactions of heterocyclic diazo compounds is known. In our case the boron trifluoride may on the one hand operate as a dehydrating agent transforming the hydrated diazouracil **I** into more active form **XX**; on the other hand BF_3 may coordinate with the nucleophilic sites of the molecules of diazouracils **I, XVI, XX** undoubtedly increasing the electrophilicity of the diazo group [complexes (C, D, E)]. With substituted diazouracil **II** is not also excluded the rupture of the 6-hydroxy group providing highly active diazonium salt (**F**).

According to ab initio calculations in the orbital basis 3-21G with the use of software [15] among all possible complexes of E type the most feasible are the complexes with participation of the unshared electron pairs of pyridine nitrogen and oxygen atoms



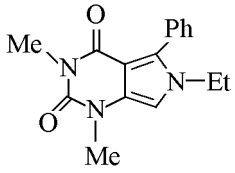
G H I



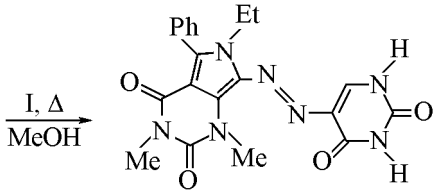
R = H (**XXI**), Me (**XXII**).

(the latter are additionally stabilized by attractive interaction H···F). Their stabilization energies (kJ mol^{-1}) equal to 164.6 for (G), 153.2 for (H), and 151.2 for **I**.

Besides reactions with amines we found that diazouracil **I** reacted with a heterocyclic substrate that did not show either CH or OH acidity, namely with 1,3-dimethyl-5-phenyl-6-ethylpyrrolo[3,4-d]pyrimidine-2,4(1H,3H)-dione (**XXIII**). After a short heating in ethanol an orange 1,3-dimethyl-5-phenyl-6-ethyl-7-(5-uracilylazo)pyrrolo[3,4-d]pyrimidine-2,4-dione (**XXIV**) was obtained. Interestingly, in this case sufficient activation of diazouracil is achieved by adding HCl traces; the reaction proceeds also without catalyst, but more slowly.



XXIII



XXIV

Thus the research performed demonstrated that 5-diazouracils are capable of entering into azo coupling with some active substrates. This ability is due to a significant contribution of the betaine frontier forms into their electronic structure.

EXPERIMENTAL

IR spectra were recorded on spectrometer Specord 75IR from mulls in mineral oil. ^{1}H NMR spectra were registered on spectrometers Varian XL-100 (compound **XXI**) and Bruker DPX-250 (all other compounds) at operating frequencies 100 and 250 MHz respectively, as reference served the signals from residual protons of solvent. Electron absorption spectra were measured on Specord M-40 instrument from solvents in ethanol or methanol. Elemental analyses were carried out in the microanalysis laboratory of the Chair of Organic Chemistry of Rostov State University. Melting point were measured by common method and are listed without correction.

5-Diazouracils **I** and **XVI** were prepared along procedures previously described [1, 2].

Azo coupling of 5-diazouracils with CH-acids and phenols. (a). 2 mmol of diazouracil **I, XVI** was dissolved at heating in methanol (60 ml in reaction with phenols, 20 ml in reaction with CH-acids), 2.1 mmol of CH-acid or phenol was added, and the mixture was heated to boiling. On cooling the separated precipitate was washed and purified. (b) 2 mmol of diazouracil **I** was dissolved at heating and stirring in 35 ml of ethanol, and on cooling to 30–40°C, avoiding formation of ethoxy derivative **IIb** precipitate the solution was mixed with a solution containing 2 mmol of CH-acid or phenol and 2.5 mmol of NaOH in 10 ml of ethanol. The reaction mixture was kept until the solution sample no more gave crimson color at heating with water solution of R-salt. Then the reaction mixture was neutralized with glacial acetic acid and was stirred to the end of formation of the crystalline reaction product. The separated precipitate was filtered off (if necessary the main part of solvent was distilled off), washed with ethanol, with water, and again with ethanol. In the synthesis of salt **XIV** the reaction mixture was not neutralized, and fast crystallization was initiated by cooling, the separated blue-black precipitate was filtered off and washed on filter with anhydrous methanol and then with benzene. Compounds **III, IV, VIII–X** were recrystallized from alcohol, compounds **V, VI, XV, XVII, XVIII, XXIV** were recrystallized from DMF. Compounds **VII, XI, XII** were purified by precipitation from DMF solution with water. Compounds **XIII, XIV** are not efficiently purified by recrystallization; the anthraquinone impurity may be partially removed by extraction in a Soxhlet apparatus.

1,3-Dimethyl-5-(2-hydroxy-1-naphthylazo)uracil (XVII). To a suspension of 0.2 g (0.67 mmol) of dye **VII** in 1 ml of water containing 0.1 g (1.5 mmol) of KOH was added 0.255 ml (2.68 mmol) of dimethyl sulfate. The mixture was heated to 40–45°C till the start of reaction, and in the course of dimethyl sulfate consumption was added 4 N solution of KOH maintaining the pH of the reaction mixture within 9–12 range. After the pH measuring was finished the mixture was acidified with glacial acetic acid, the reaction product was extracted into chloroform and purified by column chromatography on alumina, eluent chloroform. Yield of red crystalline compound **XVII** 0.075 g (34%), mp 298–300°C (reprecipitation from DMF with water). Spectral characteristics were identical to those of the product obtained by coupling diazouracil **XVI** with 2-naphthol.

3-(1,3-Dimethyl-5-uracilyl)hydrazone of pentane-2,3,4-trione (XIX) was synthesized in a similar way as compound **XVII** from dye **VII** with the use of 0.2 g (2.1 mmol) of hydrazone **III** in 1 ml of 2 N NaOH solution, 0.5 ml (4 mmol) of dimethyl sulfate, and 4 N solution of NaOH. The precipitate formed after neutralization of the reaction mixture was separated and thrice recrystallized from benzene (if the precipitate did not form, the reaction product was extracted into ethyl acetate). Yield of yellow crystalline compound **XIX** 0.14 g (26%), mp 180–182°C. Found, %: C 50.03; H 5.38. $C_{11}H_{14}N_4O_4$. Calculated, %: C 49.62; H 5.26.

Uracil. Along procedure b was carried a reaction between 0.3 g (2 mmol) of diazouracil **I** with 0.2 g (2.1 mmol) of phenol. After neutralization of the reaction mixture the solvent was evaporated to dryness, the residue was heated for 30 min in 2 ml of ethanol, and on cooling the residue was separated and recrystallized from water. Yield 0.1 g (45%), light-gray crystalline compound, mp>305°C (decomp). IR and ^{1}H NMR spectra identic to those of uracil registered under the same conditions.

5-(4-Dimethylaminophenylazo)uracil (XXI). In 100 ml of anhydrous acetonitrile was dissolved 1.6 g (10 mmol) of diazouracil **I** in the presence of 1.3 ml (10 mmol) of boron trifluoride etherate. Then 1.22 ml (10 mmol) of *N*,*N*-dimethylaniline was added. In 1 h the separated precipitate was filtered off, boiled for 1.5 h in 150 ml of ethanol, again filtered off, and recrystallized from DMF. Yield of brown crystalline compound **XXI** 2.2 g (79%), mp 284–286°C. Found, %: C 55.77; H 4.93; N 26.83. $C_{12}H_{13}N_5O_2$. Calculated, %: C 55.60; H 5.02; N 27.03.

1,3-Dimethyl-5-(4-dimethylaminophenylazo)-uracil (XXII) was prepared in a similar way from 0.18 g (1 mmol) of diazouracil **II**, 0.13 ml (1 mmol) of boron trifluoride etherate, and 0.13 ml (1.1 mmol) of *N*,*N*-dimethylaniline in 10 ml of anhydrous acetonitrile. The product was purified by boiling in 15 ml of ethanol for 1.5 h. Yield of orange crystalline compound **XII** 0.22 g (77%), mp 257–259°C (from DMF). Found, %: C 58.87; H 5.83. $C_{14}H_{17}N_5O_2$. Calculated, %: C 58.54; H 5.92.

1,3-Dimethyl-7-(5-uracilylazo)-5-phenyl-6-ethylpyrrolo[3,4-d]pyrimidine-2,4-dione (XXIV). A solution of 0.3 g (2 mmol) of diazouracil **Ib** in 10 ml of ethanol was added to a hot solution of o.53 g (2 mmol) of 1,3-dimethyl-5-phenyl-6-ethylpyrrolo-[3,4-d]pyrimidine-2,4-dione (**XXIII**) in 20 ml of ethanol containing a catalytic amount of HCl, and the mixture was heated for 1 h. The separated precipitate was filtered off and recrystallized from DMF. Yield of orange powder of compound **XXIV** 0.37 g (46%), mp >310°C. Found, %: C 57.36; H 4.39. C20H19N7O4. Calculated, %: C 57.01; H 4.51.

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