INVESTIGATIONS IN THE SERIES OF HETEROCYCLES.

55.* SYNTHESIS AND SOME REACTIONS OF 2-ARYL-4-HALO-6-OXO-1,3-THIAZINES

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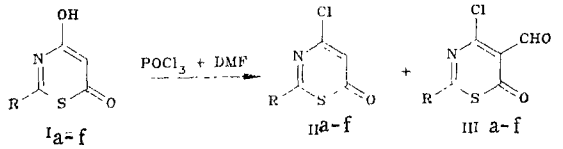
The reaction of 2-aryl-4-hydroxy-6-oxo-1,3-thiazines with Vilsmeier's reagent results in the formation of a mixture of 2-aryl-6-oxo-4-chloro-1,3-thiazines and their 5-formyl analogs. Reactions involving the nucleophilic replacement of the halogen and nucleophilic addition to an aldehydic group have been studied. The intramolecular cyclization of the oxime and phenylhydrazone of 6-oxo-2-phenyl-5-formyl-4-chloro-1,3-thiazine gives new heteroaromatic systems, viz., isoxazolo-[4,5-d]-1,3-thiazine and pyrazolo]4,5-d]-1,3-thiazine, respectively.

The literature offers only fragmentary information on 2- and 6-halo-1,3-thiazinones [2, 3] and absolutely no data on the synthesis of 4-halo-1,3-thiazined. The electrophilic substitution reactions [4] and the splitting of the ring in 2-aryl-4-hydroxy-6-oxo-1,3-thiazines under the action of nucleophilic reactions [5] have mainly been investigated, while nucleophilic substitution has not been investigated in this series of compounds.

It seemed interesting to us to study the replacement of the hydroxyl group in 2-aryl-4-hydroxy-6-oxo-1,3-thiazines (Ia-f) by a chlorine atom and some reactions of the halo-1,3-thiazines obtained. The reaction of thiazines of type I with a mixture of $POCl_3$ and DMFA in benzene gave a mixture of 2-aryl-6-oxo-4-chloro-1,3-thiazines (IIa-f) and their formyl analogs (IIIa-f).



Ia-f IIa-f IIIa-f

I—III a R=*p*-$(CH_3)_2NC_6H_4$; b R=3,4-$(CH_3O)_2C_6H_3$; c R=*p*-$CH_3OC_6H_4$; d R=C_6H_5; e R=*p*-BrC_6H_4; f R=*p*-$NO_2C_6H_4$

The compounds obtained are easily separated. The ratio between the reaction products of types II and III depends on the nature of the substituent in the para position of the benzene ring. Electron-donor substituents increase the yield of 5-formyl-1-3-thiazines III, and substituents with an M effect promote the predominant formation of thiazines of type II (Table 1). For the synthesis of thiazine IIa, which it is difficult to obtain in large amounts by reacting Ia with $POCl_3$ and DMFA, we utilized the reaction of thiazinedione Ia with $POCl_3$ alone. Since thiazines Ia-f are potentially tautomeric, the formation of 4- or 6-halogenated thiazines or their mixtures might have been expected. However, only one isomer of chlorinated thiazine II and its 5-formyl analog of type III always formed in the reaction with Vilsmeier's reagent. It was previously shown that thiazine Id exists in the form of 4-hydroxy-6-oxo-2-phenyl-1,3-thiazine [6]. The compounds synthesized are the 4-chloro derivatives (II), as was demonstrated by the identical nature of the 4-methoxy-6-oxo-2-phenyl-1,3-thiazines obtained by the nucleophilic replacement of the halogen atom (see below) and by alkylation [7] of 4-hydroxy-6-oxo-2-phenyl-1,3-thiazine (Id) with diazomethane.

*For report 54 see [1].

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TABLE 1. Ratio of the Yields of 2-Aryl-6-oxo-4-chloro-1,3-thiazines (IIa-f) and Their 5-Formyl Analogs (IIIa-f) in the Reaction of 2-Aryl-4-hydroxy-6-oxo-1,3-thiazines (Ia-f) with Vilsmeier's Reagent

Compound	R	Yield, %		Compound	R	Yield, %	
		thiazine II	5-formylthiazine III			thiazine II	5-formylthiazine III
Ia	p-$(CH_3)_2NC_6H_4$	2	85	Ia	C_6H_5	56	32
Ib	3,4-$(CH_3O)_2C_6H_3$	10	73	Ib	p-BrC_6H_4	62	16
Ic	p-$CH_3OC_6H_4$	21	59	Ic	p-$NO_2C_6H_4$	64	5

TABLE 2. Spectral Characteristics of Compounds II-VII

Compound	UV spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-4}$)	PMR spectrum, δ, ppm			IR spectrum (suspension in liquid petrolatum) ν C=O, cm^{-1}
		Ar	HC[5]	C(=O)H	
IIa	230 (1,68), 262 (0,45), 295 (0,50), 460 (3,40)	7,75 m (4H)	6,4 s (1H)	—	1665
IIb	219 (1,72), 247 (0,78), 257 (0,55), 390 (1,20)	7,19 m(3H)	6,31s (1H)	—	1667
IIc	230 (1,37), 237 (1,05), 370 (1,40)	7,44 m(4H)	6,3 s (1H)	—	1670
IId	228 (1,40), 290 (0,68), 340 (0,62)	7,77 m(5H)	6,4 s (1H)	—	1660
IIe	228 (1,68), 303 (0,70), 347 (0,86)	7,68 m(4H)	6,3 s (1H)	—	1670
IIf	230 (0,88), 260 (0,59), 285 (0,75), 346 (0,55)	8,29 m(4H)	6,48 s (1H)	—	1665
IIIa	230 (0,87), 317 (0,21), 506 (1,90)	7,29 m(4H)	—	10,27 s (1H)	1700, 1620
IIIb	218 (1,45), 246 (0,95), 320 (0,32), 395 (1,02)	7,29 m(3H)	—	10,24 s (1H)	1710, 1660
IIIc	231 (1,10), 241 (0,88), 380 (1,65)	7,51 m(4H)	—	10,29 s (1H)	1720, 1675
IIId	228 (0,95), 290 (0,53), 340 (0,62)	7,85 m(5H)	—	10,38 s (1H)	1730, 1680
IIIe	230 (1,40), 290 (0,62), 350 (0,90)	7,68 m(4H)	—	10,38 s (1H)	1725, 1665
IIIf	212 (1,52), 270 (1,42), 285 (1,52), 345 (0,40)	8,36 m (4H)	—	10,41 s (1H)	1720, 1660
IV*	220 (1,70), 285 (1,10), 340 (0,92)	7,90 m (5H)	6,42 s (1H)	—	1685, 1660
V	218 (0,65), 265 (2,54)	7,65 m(5H)	5,23 s (1H)	—	1630
VI*	222 (1,05), 227 (1,00), 237 (0,70), 285 (0,62), 350 (0,40)	7,92 m(5H)	5,40 s (1H)	—	1640
VII*	225 (1,88), 240 (1,75), 270 (1,60), 350 (0,62)	8,02 m (5H)	5,78 s (1H)	—	1655

*The PMR spectrum was recorded in DMSO-d_6.

In the PMR spectra (Table 2) of solutions of compounds II in $CDCl_3$ there are signals of the protons in the benzene ring and a signal of the "olefinic" 5-H proton. The PMR spectra (Table 2) of compounds III also contain signals of the protons in the benzene ring and a singlet signal of the proton in the aldehyde group (δ 10.2-10.4), whose position depends on the electron-donor properties of the substituents in the para position of the benzene ring. In the ^{13}C NMR spectrum of a solution of 1,3-thiazine IId in $CDCl_3$ recorded with complete suppression of the ^{13}C–^{1}H spin–spin coupling, there are three low-field signals at 182.9, 179.1, and 164.0 ppm, which are assigned to $C_{(6)}$, $C_{(2)}$, and $C_{(4)}$, respectively. The signals of the carbon atoms of the bezene ring are observed at 139.8-131.5 pp, and the signal at 115.2 pp, is assigned to $C_{(5)}$ of the thiazine ring. The IR spectra (Table 2) of crystalline samples of 4-chloro-1,3-thiazines II and their 4-formyl analogs III show an intense band at 1650-1675 cm^{-1}, which corresponds to the stretching vibrations of the C=O bonds. In addition, in the spectra of compounds II and III there are less intense bands at 1500-1600 cm^{-1}, which are assigned to vibrations of the C=C and C=N bonds. The bands associated with the stretching vibrations of the C–Cl bonds are relatively uncharacteristic and lie in the 460-480-cm^{-1} region. Similar lowering of the vibrational frequencies of the C–Cl bonds was noted for 4,6-dichloropyrimidines [8]. The IR spectra of compounds III contain an intense band in the 1700-1730-cm^{-1} region, which is characteristic of the stretching vibrations of the C=O bond

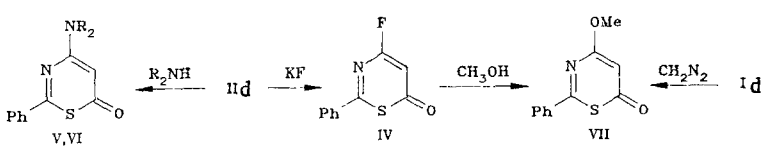
TABLE 3. Spectral Characteristics of Compounds VIII-XII

Compound	UV spectrum, λmax, nm (ε)	PMR spectrum, δ, ppm					IR spectrum (suspension in liquid petrolatum), ν, cm^{-1}		
		C_6H_5	HC=N	>NH	OH	CHO	C=O	NH	OH
VIII	228 (21500), 289 (13700), 345 (14400)	7,64 m (5H)	—	—	—	9,84 s (1H)	1660, 1620	—	—
IX*	212 (12100), 227 (12800), 292 (5200), 378 (7800)	7,6—8,0 M (7H)	—	—	8,05 c (1H)	—	1650	—	3225
X	233 (21200), 300 (16300), 315 (15400), 508 (21700)	7,42 m (5H); 7,90 m (5H)	8,17 s (1H)	7,07 s (1H)	—	—	1620	3270	—
XI	225 (13000), 285 (7900), 334 (7900), 363 (4000)	7,84 m (5H)	8,75 s (1H)	—	—	—	1685	—	—
XII	227 (45100), 243 (38300), 268 (34600), 322 (26300)	7,38 m (5H); 7,91 m (5H)	8,16 s (1H)	—	—	—	1695	—	—

*The PMR spectrum was recorded in DMSO-d_6.

of an aldehydic group. In the UV spectra of compounds II and III (Table 2) in ethanol there are three principal absorption maxima at 220-230, 285-303, and 340-508 nm. The position of the long-wavelength maximum varies as a function of the electron-donor properties of the substituents in the benzene ring and is scarcely subject to the influence of electron-acceptor substituents.

The nucleophilic replacement of a halogen atom in the 1,3-thiazine ring has been studied only in the case of the reaction of 4-oxo-2-chloro-1,3-thiazines with amines [2]. Therefore, it seemed to be of interest to investigate the chemical properties of 4-chloro-1,3-thiazine IId in reactions with various nucleophiles. We should at once mention the very low reactivity of the halogen at $C_{(4)}$, despite the presence of the activating carbonyl group. For example, even after prolonged (> 20 h) boiling of thiazine IId in methanol, ethanol, or 1-butanol, only the original compound was recovered. Chlorothiazine IId did not react with sodium iodide or potassium iodide in acetone, acetonitrile, or acetic acid even in the presence of a crown ether (dibenzo-18-crown-6). 2-Oxo-2-phenyl-4-fluoro-1,3-thiazine (IV) forms with a 40% yield only after the prolonged heating of chloride IId with a fivefold excess of KF and when the crown ether is added. The reactions with dimethylamine and diisobutylamine took place under relatively mild conditions (dioxane, 20-90°C) with the formation of 4-dialkylamino-1,3-thiazines V and VI with high yields. 6-Oxo-4-chloro-1,3-thiazines II have two nucleophilic centers, viz., $C_{(4)}$ and $C_{(6)}$; therefore, reactions with nucleophiles could result in the formation of cyclic products of the nucleophilic replacement of the chlorine atom or products of ring opening with cleavage of the $C_{(6)}$—S bond and maintenance or replacement of the halogen atom. The products of the reaction of thiazine IId with sodium methoxide or sodium ethoxide in alcohols or toluene could not be identified owing to the formation of a complex difficult to separate mixture (at least 3 or four compounds, according to the TLC data), obviously as a consequence of the splitting of the thiazine ring. 4-Methoxy-6-oxo-2-phenyl-1,3-thiazine (VII) could be synthesized only by the prolonged boiling of 4-fluoro-1,3-thiazine IV in methanol. Compound VII obtained in this manner is identical, according to the data from elemental analysis, TLC, UV, and the IR, and PMR spectra, to the product of the alkylation of 4-hydroxy-6-oxo-1,3-thiazine Id with diazomethane [7].



V R=Me; VI R=i-Bu

TABLE 4. Characteristics of Compounds II-XII

Compound	mp, °C	R_f	Found, %					Empirical formula	Calculated, %				
			C	H	Cl	N	S		C	H	Cl	N	S
IIa	178—180	0,54	51,2	4,0	12,2	9,9	12,6	$C_{12}H_{11}ClN_2OS$	54,0	4,1	13,3	10,5	12,0
IIb	156—158	0,42	50,0	3,1	12,9	4,6	10,3	$C_{12}H_{10}ClNO_3S$	50,1	3,5	12,5	4,9	11,3
IIc	126—128	0,72	51,2	3,4	—	5,4	—	$C_{11}H_8ClNO_2S$	52,1	3,15	14,0	5,5	12,6
IId	122—124	0,85	53,8	4,0	15,9	6,1	14,5	$C_{10}H_6ClNOS$	53,7	2,7	15,9	6,3	14,3
IIe	165—166	0,82	38,0	1,9	—	4,9	10,9	$C_{10}H_5BrClNOS$	39,7	1,7	11,7	4,6	10,6
IIf	176—178	0,64	44,7	2,0	11,5	10,3	11,8	$C_{10}H_5ClN_2O_3S$	44,7	1,9	13,2	10,4	11,9
IIIa	200 (decomp.)	0,16	53,4	3,8	12,2	—	—	$C_{13}H_{11}ClN_2O_2S$	53,0	3,7	12,1	9,5	10,9
IIIb	94—95	0,20	50,0	3,4	11,4	4,6	—	$C_{13}H_{10}ClNO_4S$	50,6	2,3	11,5	4,5	10,4
IIIc	126—128	0,39	51,5	2,9	13,6	4,9	11,1	$C_{12}H_8ClNO_3S$	51,2	2,9	12,6	4,9	11,4
IIId	123—125	0,43	52,7	2,4	13,8	6,1	11,7	$C_{11}H_6ClNO_2S$	52,5	2,6	14,1	5,6	12,7
IIIe	135—137	0,59	40,8	1,7	—	4,5	9,7	$C_{11}H_5BrClNO_2S$	39,9	1,5	10,7	4,2	9,7
IIIf	99—101	0,26	44,6	1,9	—	9,4	10,7	$C_{11}H_5ClN_2O_4S$	44,5	1,7	12,0	9,4	10,8
IV	115—116	0,78	58,0	3,0	—	6,8	15,7	$C_{10}H_6FNOS$	58,0	2,9	—	6,8	15,5
V	164—166	0,93[a]	61,0	4,8	—	12,3	13,8	$C_{12}H_{12}N_2OS$	62,1	5,2	—	12,1	13,8
VI	101—103	0,37	67,6	6,6	—	8,8	10,9	$C_{18}H_{24}N_2OS$	68,3	7,6	—	8,9	10,1
VII	91—92	0,57	60,1	4,1	—	6,5	14,2	$C_{11}H_9NO_2S$	60,3	4,1	—	6,4	14,6
VIII	108—110	0,43	66,0	3,0	—	8,1	8,8	$C_{19}H_{25}N_2O_2S$	65,1	3,0	—	8,1	9,6
IX	154—155	0,79[b]	49,7	2,2	—	—	—	$C_{11}H_7ClN_2O_2S$	49,7	2,3	13,4	10,5	12,1
X	123—124	0,41	58,8	3,4	9,8	13,9	9,2	$C_{17}H_{12}ClN_3OS$	59,9	3,51	10,4	12,3	9,4
XI	215—217	0,59	58,0	2,7	—	12,4	14,1	$C_{11}H_6N_2O_2S$	57,4	2,6	—	12,2	13,9
XII	163—164	0,67	65,4	4,0	—	14,0	11,3	$C_{17}H_{11}N_3OS$	66,8	3,6	—	13,8	10,5

[a] 1:9 ethanol—chloroform. [b] 8:2:1 dichloroethane—diethyl ether—acetone.

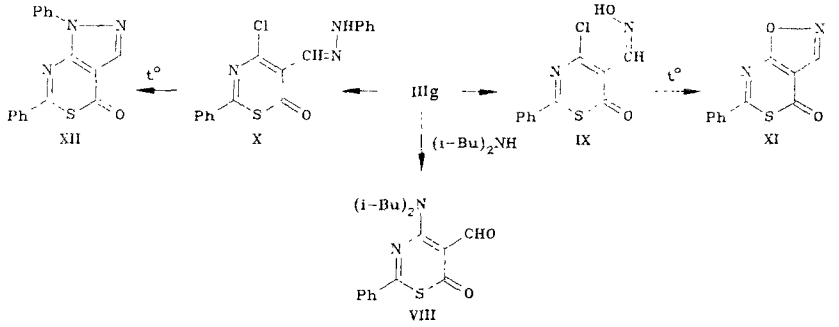
The PMR spectra of solutions of compounds IV-VII in $CDCl_3$ or DMSO-d_6 show signals of the protons of the benzene ring, the 5-H proton, and the protons of the alkyl groups in the substituent at $C_{(4)}$ (see Table 2). The signal of the 5-H proton in the spectrum of fluorothiazine IV is split due to spin—spin coupling (J = 15 Hz). The IR spectra of crystalline samples of compounds IV-VII are characterized by the disappearance of the bands of the stretching vibrations of the C—Cl bonds. The increase in the frequency of the stretching vibrations of the C=C bond in the spectra of compounds V and VI is caused by the electron-donor properties of the dialkylamino group, the UV spectra of compounds IV, VI, and VII (Table 2) are similar to the spectrum of 6-oxo-2-phenyl-4-chloro-1,3-thiazine (IId), and only the spectrum of 4-dimethylamino-1,3-thiazine V is characterized by intense absorption at 265 nm. This is possibly due to the most effective interaction of the lone pair of the nitrogen atom with the π electrons of the thiazine ring.

It was natural to expect that 6-oxo-2-phenyl-5-formyl-4-chloro-1,3-thiazine (IIId) would react with nucleophiles more readily than thiazine IId. The choice of the reactant was limited by the presence in the molecule of an aldehydic group capable of being involved in a nucleophilic addition reaction. The most convenient nucleophile was diisobutylamine, under whose action compound IIId is converted in dioxane into 4-diidobutylamino-6-oxo-2-phenyl-5-formyl-1,3-thiazine (VIII). The resistance of thiazine IIId to nucleophilic ring splitting should be noted: No acyclic products were discovered in the reaction with diisobutylamine, while 4-hydroxy-6-oxo-2-phenyl-1,3-thiazine, when reacted with diisobutylamine, is converted into the corresponding thioaroylmalonic diamide [5].

Hydroxylamine and phenylhydrazine react with 6-oxo-2-phenyl-5-formyl-4-chloro-1,3-thiazine (IIId) to form oxime IX and phenylhydrazone X, respectively. The IR spectra of crystalline samples of compounds IX and X (Table 3) are characterized by the disappearance of the band of the stretching vibrations of the C=O bond in the aldehydic group at 1730 cm^{-1}, an increase in the intensity of the bands assigned to the vibrations of the C=N bonds, and the appearance of bands of the stretching vibrations of the OH or NH groups at 3225-3270 cm^{-1}. The PMR spectra of compounds IX and X (Table 3) also show the disappearance of the signal of the proton of the aldehydic group and the appearance of a signal for NH or OH. Unfortunately, the signal of the proton at the C=N multiple bond in the PMR spectrum of a solution of oxime IX in DMSO-d_6 is superimposed on the signals of the protons in the benzene rings.

With dilute solutions of oxime IX and phenylhydrazone X in dioxane are heated, they are converted as a result of an intramolecular nucleophilic attack at $C_{(4)}$ into 7-oxo-2-phenylisoxazolo[4,5-d]-1,3-thiazine (XI) and 7-oxo-2,4-diphenylpyrazolo[4,5-d]-1,3-thiazine (XII). The IR spectra of crystalline samples of compounds XI and XII are characterized by an increase in the frequency of the stretching vibrations of the C=O bond and the disappearance of the

bands of the stretching vibrations of the OH and NH groups in the high-frequency region of the spectrum (Table 3). The PMR spectrum of compound XII reveals the disappearance of the signal of the proton of the NH group, which is also an indication of the formation of a bicyclic system.



Thus, the reaction of 1,3-thiazinediones I with Vilsmeier's reagent makes it possible to obtain 2-aryl-6-oxo-4-chloro-1,3-thiazines and their 5-formyl analogs; the ratio between the yields of the reaction products is determined by the electronic nature of the substituent in the para position of the benzene ring. The nucleophilic replacement of the halogen atom in 4-halo-1,3-thiazinones takes place under severe conditions. The intramolecular cyclization of the oxime and phenyl-hydrazone of 6-oxo-2-phenyl-5-formyl-4-chloro-1,3-thiazine makes it possible to obtain new heteroaromatic systems which have not previously been described in the literature.

EXPERIMENTAL

The UV spectra of solutions of the compounds investigated in ethanol ($c \approx 10^{-4}$ to 10^{-5} M) were recorded on an SF-20 spectrophotometer, and the PMR spectra of solutions in $CDCl_3$ were recorded on a Tesla BS-487 (80 MHz) spectrometer with HMDS as an internal reference. The IR spectra of suspensions of compounds II-XII in liquid petrolatum were recorded on an IKS-29 spectrometer. The individuality of all the compounds was demonstrated by TLC on silufol UV-254 plates (10:1 CCl_4—acetone) with detection in UV light. The data from the elemental analysis of compounds II-XII are given in Table 4.

2-(p-Dimethylaminophenyl)-4-hydroxy-6-oxo-1,3-thiazine (Ia). A solution of 1.5 g (8.3 mmole) of p-dimethylaminothiobenzamide [9] in 1200 ml of ethylacetate was given a portionwise addition of a 0.5% solution of 0.83 g (12.4 mmole) of carbon suboxide [10] in ethyl acetate with stirring. The mixture was stirred for 2 h at 20-25°C and left to stand for 12 h at 20-25°C. The precipitate was filtered out, recrystallized from acetonitrile, and dried. The yield was 73%, mp 212-214°C, R_f 0.52 (1:9 ethanol—chloroform). IR spectrum: 1618 (C=O), 1497 (C=N), 1570 cm^{-1} (C=C). UV spectrum (in ethanol), λ_{max}, nm ($\varepsilon \cdot 10^{-4}$): 232 (1.88), 280 (0.45), 328 (0.67), 410 (2.25). PMR spectrum (DMSO-d_6): 12.15 (1H, s, OH), 7.38 (4H, m, Ar), 5.46 ppm (1H, s, 5-H). Found: N, 10.8; S, 12.4%; M 248. Calculated from $C_{12}H_{12}N_2O_2S$: N, 11.3; S, 12.9%.

2-(3,4-Dimethoxyphenyl)-4-hydroxy-6-oxo-1,3-thiazine (Ib). A solution of 1.0 g (5.0 mmole) of 3,4-dimethoxythiobenzamide [9] in 100 ml of acetonitrile was supplied with 0.69 g (10 mmole) of gaseous carbon suboxide. The precipitate formed was filtered out, recrystallized from acetonitrile, and dried. The yield was 65%, mp 193-193°C, R_f 0.61 (1:9 ethanol—chloroform). IR spectrum: 1640 (C=O), 1525 (C=N), 1600 cm^{-1} (C=C). UV spectrum (in ethanol), λ_{max}, nm ($\varepsilon \cdot 10^{-4}$): 240 (1.90), 250 (0.90), 310 (0.40). PMR spectrum (DMSO-d_6): 12.18 (1H, s, OH), 7.38 (3H, m, Ar), 5.54 ppm (1H, s, 5-H). Found: N, 5.5; S, 11.8%; M 265. Calculated for $C_{12}H_{11}NO_4S$: N, 5.3; S, 12.1%.

2-(p-Bromophenyl)-4-hydroxy-6-oxo-1,3-thiazine (Ie). A solution of 2.0 g (9.2 mmole) of p-bromothiobenzamide [9] in 60 ml of ethyl acetate was supplied with 1.26 g (18.4 mmole) of gaseous carbon suboxide. The precipitate formed was filtered out, recrystallized from acetonitrile, and dried. The yield was 70%, mp 194-196°C, R_f 0.49 (1:9 ethanol—chloroform). IR spectrum: 1600 (C=O), 1500 (C=N), 1570 cm^{-1} (C=C). UV spectrum (in ethanol), λ_{max}, nm ($\varepsilon \cdot 10^{-4}$): 250 (1.98), 268 (1.80), 350 (0.67). PMR spectrum (DMSO-d_6): 12.22 (1H, s, OH), 7.92 (4H, m, Ar), 5.62 ppm (1H, s, 5-H). Found: N, 4.9; S, 11.0%, M 284. Calculated for $C_{10}H_6BrNOS$: N, 4.9; S, 11.3%.

2-(p-Nitrophenyl)-4-hydroxy-6-oxo-1,3-thiazine (If). A solution of 1.0 g (5.5 mole) of p-nitrobenzamide [9] in 75 ml of dichloroethane was given a portionwise addition of a 5% solution of 0.93 g (6.6 mmole) of malonyl chloride in dichloroethane with stirring. The reaction was conducted at 60° for 2 h. The precipitate was filtered out recrystallized from acetonitrile, and dried. The yield was 65%, mp 196-197.5, R_f 0.48 (1:9 ethanol—chloroform). IR spectrum: 1620 (C=O), 1534 (C=N), 1570 cm^{-1} (C=C). UV spectrum (in ethanol), λ_{max}, nm ($\varepsilon \cdot 10^{-4}$): 233 (1.42), 267 (2.00), 370 (0.42). PMR spectrum (DMSO-d_6): 12.50 (1H, s, OH), 8.30 (4H, m, Ar), 5.56 ppm (1H, s, 5-H). Found: N, 11.1; S, 12.5%; M 250. Calculated for $C_{10}H_6N_2O_4S$: N, 11.2; S, 12.8%.

6-Oxo-2-phenyl-4-chloro-1,3-thiazine (IId) and 6-Oxo-2-phenyl-5-formyl-4-chloro-1,3-thiazine (IIId). A suspension of 1.0 g (4.9 mmole) of 4-hydroxy-6-oxo-2-phenyl-1,3-thiazine (Id) [11] in 15 ml of benzene was given an addition of a mixture of phosphorous oxychloride [1.0 ml (6.4 mmole] and DMFA [1.0 ml (17 mmole)] with continual stirring. The reaction mass was heated for 40 min at 60°C until the thiazine dissolved completely and was cooled. The benzene layer was separated, and the residue remaining after evaporation of the solvent was treated with ice water, filtered out, dried, and recrystallized from hexane. Thiazine IId was obtained.

The solvent was distilled off from the lower oily layer, the residue was treated with ice water, the precipitate was filtered out, dried, and recrystallized from hexane, and formyl-1,3-thiazine IIId was obtained.

Compounds IIa-c, e, f, IIIa-c, e, and f were obtained in a similar manner.

2-(p-Dimethylaminophenyl)-6-oxo-4-chloro-1,3-thiazine (IIa). A suspension of 0.5 g (2.0 mmole) of thiazine Ia in 5 ml of phosphorus oxychloride was heated with continual stirring for 3 h at 40-50°C. The solvent was driven off in a vacuum, the residue was treated with ice water, filtered out, dried, and recrystallized from petroleum ether (70-100°C fraction). The yield was 28%.

6-Oxo-2-phenyl-4-fluoro-1,3-thiazine (IV). A solution of 1.0 g (4.4 mmole) of thiazine IId and 0.03 g of dibenzo-18-crown-6 in 15 ml of dry acetonitrile was added to 1.3 g (20 mmole) of thoroughly dried potassium fluoride. The reaction mass was heated for 24 h at 80°C with continual stirring. The mixture was cooled, and the precipitate was filtered out. After the solvent was removed from the filtrate, the product was recrystallized twice from hexane. The yield was 36%.

4-Dimethylamino-6-oxo-2-phenyl-1.3-thiazine (V). A solution of 0.5 g (2.2 mole) of thiazine IId in 20 ml of absolute dioxane was given an addition of 1.6 ml (8.8 mmole) of a 25% ethanolic solution of dimethylamine, and the mixture was left to stand for 48 h at 20°C. The precipitate was filtered out. The solvent was removed from the filtrate, and the residue was recrystallized from ethanol. The yield was 86%

4-Diisobutylamino-6-oxo-2-phenyl-1,3-thiazine (VI). A solution of 1.0 g (4.4 mmole) of thiazine IId in 15 ml of absolute dioxane was given an addition of 1.56 ml (8.8 mmole) of diisobutylamine. The reaction mass was heated for 7 h at 90°C and cooled, and the precipitate formed was filtered out. The solvent was removed from the filtrate, and the residue was recrystallized from hexane. The yield was 68%.

4-Methoxy-6-oxo-2-phenyl-1,3-thiazine (VII). A solution of 2.0 g (10 mmole) of thiazine IV in 20 ml of methanol was boiled for 60 h. The solvent was removed, and the residue was recrystallized from hexane. The yield was 50%.

4-Diisobutylamino-6-oxo-2-phenyl-5-formyl-1,3-thiazine (VIII). A solution of 0.5 g (2.0 mmole) of chloro-1,3-thiazine IIId in 15 ml of absolute dioxane was given an addition of 0.7 ml (4.0 mmole) of diisobutylamine. The reaction mass was heated for 1 h at 60°C and cooled, and the precipitate was filtered out. The solvent was removed from the filtrate, and the residue was recrystallized from petroleum ether (the 70-100°C fraction). The yield was 70%.

6-Oxo-2-phenyl-5-formyl-4-chloro-1,3-thiazine Oxime (IX). A solution of 1.0 g (4.0 mmole) of IIId in 50 ml of ethanol was given an addition of a solution of 0.27 g (4 mmole) of hydroxylamine hydrochloride and 0.27 g (3.3 mmole) of sodium acetate in 4 ml of water. The mixture was cooled, and the precipitate was filtered out and recrysatallized from absolute dioxane. The yield was 42%.

6-Oxo-2-phenyl-5-formyl-4-chloro-1,3-thiazine Phenylhydrazone (X). A 1.0-g portion (4 mmole) of thiazine IIId was dissolved in 50 ml of methanol with heating, and a solution of 0.67 g (4.6 mmole) of phenylhydrazine hydrochloride in 3 ml of water was added. The mixture was cooled, and the precipitate was filtered out. The yield was 62%.

7-Oxo-2-phenylisoxazolo[4,5-d]-1,3-thiazine (XI). A solution of 1.0 g (3.8 mmole) of oxime IX in 50 ml of absolute dioxane was heated for 10 h at 100°C. The residue remaining after the removal of the solvent was triturated with water, filtered out, and recrystallized twice from aqueous ethanol. The yield was 22%.

7-Oxo-2,4-diphenylpyrazolo[4,5-d]-1,3-thiazine (XII). A solution of 1.0 g (2.9 mmole) of phenylhydrazone X in 20 ml of absolute dioxane was heated for 6 h at 90°C. The residue remaining after the removal of the solvent was recrystallized from a 1:3 benzene–hexane mixture. The yield was 34%.

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