6,7,8,9-TETRAHYDRODIPYRIMIDO[4,5-b][4',5'-e][1,4]THIAZINE DERIVATIVES. SYNTHESIS AND STRUCTURE

M. P. Nemeryuk, N. I. Traven', T. G. Arutyunyan, E. A. Shatukhina, N. A. Nerseyan, O. S. Anisimova, N. P. Solov'eva, E. M. Peresleni, Yu. N. Sheinker, O. G. Sokol, V. M. Kazakova, and T. S. Safonova

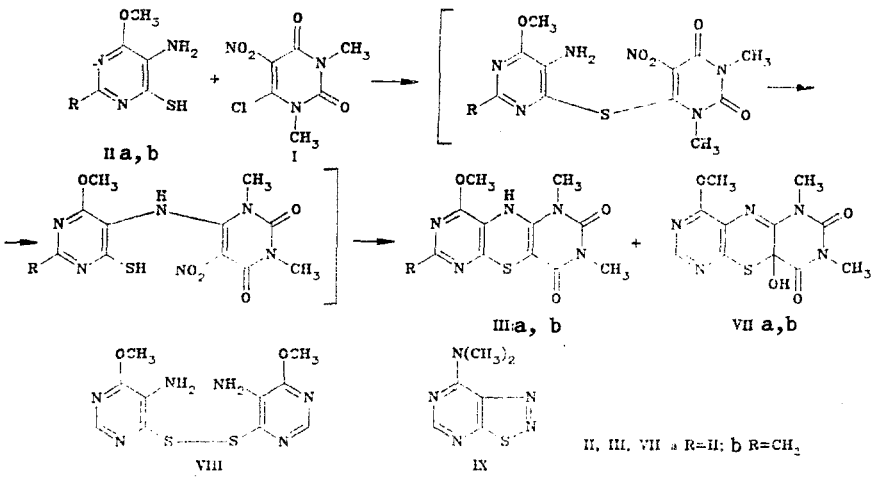
UDC 547.869.6'854'853.7:542.953.5:543.422

The reaction of 5-amino-6-mercaptopyrimidines with 1,3-dimethyl-5-nitro-6-chlorouracil in the presence of bases results in derivatives of 6,7,8,9-tetrahydrodipyrimido[4,5-b][4',5'-e][1,4]-thiazine. If the 5-amino-6-mercaptopyrimdine contains a free or alkyl-substituted amino group at the 4-position, the tetrahydrodipyramidothiazines formed exist in a free radical form. The structure of the compounds formed has been established by spectral methods.

Several publications have recently appeared dealing with the synthesis and examination of properties of derivatives of a series of tricyclic systems,which can be considered as heteroanalogs of isoalloxazine [1-5]. We have earlier reported the synthesis of the azaanalogs of these systems, containing a pyrimidine ring, instead of a benzene ring [6]. In continuation of these investigations we have studied in detail the reaction of 5-amino-6-mercaptopyrimidines IIa-h with 1,3-dimethyl-5-nitro-6-chlorouracil (I).

The reaction of uracil I with pyrimidines IIa-h in the presence of bases does not stop at the formation of the intermediate sulfides, but is accompanied by a rearrangement according to Smiles with simultaneous cyclization into derivatives of a new heterocyclic system — dipyrimido[4,5-b][4',5'-e][1,4]thiazine (IIIa,b or IVc-h). The reaction does not proceed unequivocally, for in all cases not only thiazines III or IV were formed, but also products of their oxidative transformation were isolated (VII), and in some reactions the transformation products of pyrimidines II, dipyrimidyl disulfide VIII and thiadiazolopyrimidine IX, were obtained.

The structure of thiazines III and IV depends on the character of substituents in pyrimidine II. Thus, in the reaction of pyrimidines IIa,b with uracil I in alcohol in the presence of KOH or triethylamine, thiazines IIIa,b and products of their oxidative transformation VIIa,b were obtained, and in the case of the reaction of pyrimidine IIa, silufide VIII was also obtained as a byproduct:



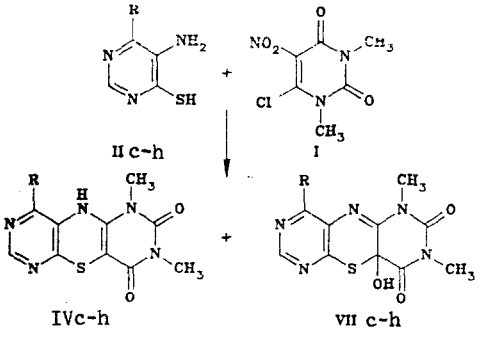
S. Ordzhonikidze All-Union Scientific Research Chemical Pharmaceutical Institute, Moscow 119021. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 258-264, February, 1989. Original article submitted June 24, 1987; revision submitted May 23, 1988.

 0009-3122/89/2502-0214$12.50

Compounds IIIa, b are yellow crystalline substances, which are stable on storage and during recrystallization. The IR spectral data show that compounds IIIa,b exist in the form of 5H-derivatives (the presence of the stretching vibrations band of the NH group at 3450 cm^{-1}). The PMR spectra of compounds IIIa,b also do not contradict the proposed structure. Thus, in the spectrum of IIIa in $CDCl_3$ there are signals at 3.49...3.31 (2-NCH_3); 4.02 (OCH_3), 8.12 (2-CH), and 5.76 ppm (NH).

In the IR spectra of VIIa,b, the absorption band of NH group stretching vibrations is absent. In the spectra of these compounds, taken in CCl_4 solutions, an absorption band is observed in the 3510...3250 cm^{-1} region, which is characteristic for the OH group. A shift of the absorption band of one of the CO groups of the uracil ring into a higher frequency region was also noted (1700 → 1740 cm^{-1}). This can be due to the transition of the enamino-ketone fragment NH–C=C–C=O, present in the molecules of III, into an imine form during their transformation into thiazines VII. In the mass spectra of compounds VIIa,b, in addition to the presence of peaks of molecular ions corresponding to the empirical formulas, peaks of $M-O^+$ and $M-OH^+$ ions are also observed. The intensity of the latter reaches 73%. The above data indicate a structure of thiazines VIIa,b as 9α-hydroxy derivatives, the formation of which can be explained by the Pummerer rearrangement of the initially formed sulfoxides [13].

In the reaction of uracil I with pyrimidines IIc-h, containing amino- or alkylamino groups in the 4-position under the conditions of the synthesis of thiazines IIIa,b, thiazines IVc-h, and the products of their oxidative transformation VIIc-h were obtained, and in the reaction of pyrimidine IIc, pyrimidothiadiazole IX was also isolated.



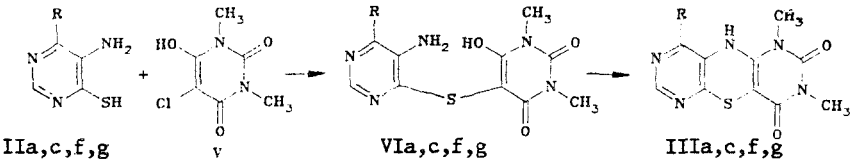
IIc-h I

IVc-h VII c-h

c R=$N(CH_3)_2$, d R=$NHCH_3$, e R=NH_2, f R=NHC_3H_7-*i*, g R=piperidino h R=morpholino

Thiazines IVc-h are dark-blue crystalline substances, which are stable on storage in a solid state, but are unstable in solutions: in chloroform they become decolorized, and during recrystallization undergo partial decomposition. In the IR spectra of thiazines IVc-h, the absorption band of the NH group of the thiazine ring is absent, and the value of the mass numbers of the molecular ions of thiazines IVc-h is 1 a.u. lower than those for thiazines with structure IIIa,b. In the UV spectra of thiazines IVc-h there are absorption bands in the region of 670...735 nm, which are absent in the spectra of thiazines IIIa,b.

To refine the structure of thiazines IVc-h, an alternate synthesis of thiazines IIIa,c, f,g,h was carried out from the corresponding pyrimidines II and 1,3-dimethyl-5-chlorobarbituric acid (V) according to [7].



IIa,c,f,g V VIa,c,f,g IIIa,c,f,g

Comparison of the spectral characteristics of compound IIIa with the previously obtained sample showed that they are identical. At the same time, the spectral data for thiazines IIIc,f,g, obtained according to [7], did not coincide with the characteristics of thiazines IVc,f,g (Fig. 1). In the IR spectra of compounds IIIc,f,g, there is an absorption band characteristic for the stretching vibrations of the NH group (3350 cm^{-1}), and in the mass spectra peaks of molecular ions are observed, the mass value of which corresponds to the 5-NH structure, while in the UV spectra there is no absorption maximum present in the spectra of compounds IVc,f,g in the visible region. Compounds IIIc,f,g are yellow crystalline substances.

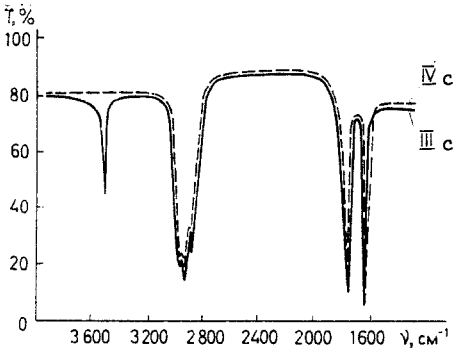


Fig. 1

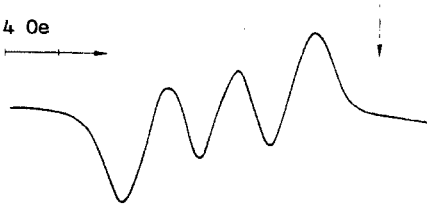


Fig. 2

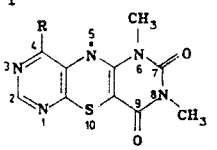
Fig. 1. IR spectra of compounds IIIc and IVc in mineral oil.

Fig. 2. EPR spectrum of thiazine IVc.

The study of the paramagnetic properties of thiazines IVc–h showed that they all have a free radical nature. The EPR spectra of the crystalline samples are in the form of singlet, in which components appear which are related to the anisotropy of the g-factor. The width of the lines is 8 Oe, the g-factor is equal to 2.0049. The concentration of the paramagnetic centers in the solid samples is 2%. When the samples studied are dissolved in chloroform, the concentration of the paramagentic centers increases to 70%. The EPR spectra of the solutions of compounds IVc-h are in the form of a poorly resolved triplet with the distance between the edge components of $\Delta H \approx 13.5$ Oe, and the width of an individual line being 3 Oe, g = 2.0058 (Fig. 2). Computer processing of the EPR spectra of compound IVe showed that the triplet obtained can be due to a reaction of an unpaired electron with three N nuclei with constants $a_1 = 4.60$ Oe; $a_2 = 1.20$ Oe; $a_3 = 1.09$ Oe and a proton with a constant $a_4 = 0.26$ Oe; the corresponding constants for sample IVf are: $a_1 = 4.5$ Oe, $a_2 = 1.2$ Oe; $a_3 = 1.1$ Oe; $a_4 = 0.8$ Oe.

We took the literature data [8-10] into account, and assigned the highest constant to splitting of the N nucleus in the 5-position. The remaining constants are probably related to the splitting of the N nuclei in the 1- and 3-positions and to a splitting of a proton in the 2-position.

It can thus be assumed that the highest density of the unpaired electron in compound IVc-h occurs at the N nucleus in the 5-position.



IV c-h

The formation of radicals IV and the oxidative transformation products of thiazines VII, is possibly explained by the tendency of the dipyrimidothiazines III to undergo one-electron oxidation reactions. On carrying out the reaction of pyrimidine IIa with uracil I in the presence of catalytic amount of the H_2O_2 under the conditions of the preparation of thiazine IIIa, thiazines of IVa and VIIa were isolated. Similar reactions in the presence of oxidizing agents were also noted for pyrimidobenzthiazines [11-13].

The structure of thiazines VIIc-h was confirmed by spectral data, and is analogous to the structure of thiazines VIIa,b discussed above. The structure of thiadiazolopyrimidine IX was confirmed by alternate synthesis by diazotization of pyrimidine IIc. The formation of thiadiazolopyrimidine IX as a by-product in the reaction of 5-aminopyridine IIc with uracil I is explained by the fact that the initial pyrimidine IIc is diazotized by the action of nitrogen oxides liberated during the reaction. The diazotizing action of nitrogen oxides has been described in the literature [14].

Thus, the reaction of ortho-aminomercaptopyrimidines with 1,3-dimethyl-5-nitro-6-chlorouracil in the presence of bases leads to derivatives of tetrahydropyrimidothiazines, the structure of which is determined by the character of the substituent in the ortho-aminomercaptopyrimidine. For dipyrimidothiazines containing amino or alkylamino groups in the 4-position, the free radical form is preferential.

TABLE 1. Characteristics of Compounds IIIa-c,f,g, IVa,c-h, VIa,c,f,g, VIIa-d,f-h, VIII

Compound	Empirical formula	mp[1]*, °C	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)
IIIa	$C_{11}H_{11}N_5O_3S$	248...250	3450 (NH); 1640, 1700 (CO)	315 (3,78), 280 (3,93), 260 (4,28), 215 (4,26)
IIIb	$C_{12}H_{13}N_5O_3S$	264...266	3450 (NH); 1640, 1700 (CO)	318 (2,48), 282 (3,58), 261 (4,01)
IIIc	$C_{12}H_{14}N_6O_2S$	210...211	3250 (NH); 1640, 1700 (CO)	245 (4,08), 281 (4,04); 312 (3,98), 320 (4,0), 365 (3,58)
IIIf	$C_{13}H_{16}N_6O_2S$	175...176	3300, 3480 (2NH); 1640, 1720 (CO)	—
IIIg	$C_{15}H_{18}N_5O_2S$	224...225	3480 (NH); 1630, 1700 (CO)	—
IVa[2]*	$C_{11}H_{10}N_5O_3S$	190...192	1640, 1700 (CO)	—
IVc	$C_{12}H_{13}N_6O_2S$	222...223	1640, 1700 (CO)	712 (3,64), 372 (11,03), 315 (4,30), 260 (4,10) (пл), 245 (4,28)
IVd	$C_{11}H_{11}N_6O_2S$	224...225	3350 (NH); 1640, 1700 (CO)	—
IVe[3]*	$C_{10}H_9N_6O_2S$	260...262	3250, 3460 (NH_2); 1700 (CO)	670 (—), 354 (—), 296 (—), 245 (—)
IVf	$C_{13}H_{15}N_6O_2S$	195...198	3200 (NH); 1640, 1700 (CO)	247 (4,07), 309 (4,13); 360 (3,86), 695 (3,52)
IVg	$C_{15}H_{17}N_6O_2S$	203...205	1640, 1700 (CO)	247 (4,21), 267 (4,07), 317 (4,1), 375 (3,99), 720 (3,50)
IVh	$C_{14}H_{15}N_6O_3S$	210...211	1640, 1700 (CO)	247 (4,28), 267 (4,12), 322 (4,17), 375 (4,00), 735 (3,49)
VIa	$C_{11}H_{13}N_6O_4S$	194...196	3330 (NH_2); 1640; 1680 (CO)	—
VIc	$C_{12}H_{16}N_6O_3S$	212...214	3330 (NH_2); 1620; 1680 (CO)	—
VIf	$C_{13}H_{18}N_6O_3S$	265...266	3420 (NH_2); 3250 (NH); 1660; 1700 (CO)	—
VIg	$C_{15}H_{20}N_6O_3S$	200...202	3340 (NH_2); 1620; 1680 (CO)	—
VIIa[4]*	$C_{11}H_{11}N_5O_4S$	214...216	1680, 1700 (CO); 3510 (OH)	328 (3,92), 252 (4,32), 309,2, 295 (3,68)
VIIb	$C_{12}H_{13}N_5O_4S$	222...224	1680, 1740 (CO)	—
VIIc	$C_{12}H_{14}N_6O_3S$	212...214	1640, 1740 (CO)	220 (4,35), 235 (4,29), 275 (4,22), 360 (3,88)
VIId	$C_{11}H_{12}N_6O_3S$	253...255	3360 (NH); 1640, 1750 (CO)	—
VIIf	$C_{13}H_{16}N_6O_3S$	219...220	3360 (NH); 1640, 1750 (CO)	—
VIIg	$C_{15}H_{18}N_6O_3S$	220...221	1630, 1750 (CO); 3515 (OH) in CCl_4	—
VIIh	$C_{14}H_{16}N_6O_4S$	217...218	1680, 1730 (CO); 3515 (OH) in CCl_4	360 (3,83), 278 (4,27), 236 (4,32) (пл), 220 (4,41)
VIII	$C_{10}H_{16}N_6O_2S$	159...162	3200, 3280, 3330, 3420 (NH_2)	—

[1]*Compound IIIa-c,f,g, VIg, VIII are crystallized from ethanol, IVc-h, VIIa-d,f-h — from DMFA, VIa,c — from water, VIf — from CH_3COOH, IX — from cyclohexane.

[2]*Compound IVa decomposes during crystallization.

[3]*The data of the UV spectrum characterize the overall form of the curve.

[4]*The IR spectrum was run in CCl_4.

The properties and the reactivity of thiazines III, IV, and VII will be discussed in a subsequent publication.

EXPERIMENTAL

The IR spectra of the compounds synthesized were run in mineral oil and in carbon tetrachloride on a Perkin-Elmer 457 spectrophotometer and the UV spectra (in ethanol) on a Perkin-Elmer 575 spectrophotometer. The NMR spectra were recorded on a Varian XL-100 spectrometer, using TMS as internal standard. The mass spectra were obtained on an MX-1303 mass-spectrometer with direct introduction of the sample into the ion source. The EPR spectra were recorded on RE-1306 and E-109 spectrometers, fitted with an E-232 double resonator. The α,α-diphenyl-β-picrylhydrazyl (DPPH) radical with a g-factor 2.0036 served as standard.

All the reactions were carried out in argon atmosphere. 4-Methoxy-, 4-amino-, 4-dimethylamino, 4-methylamino-5-amino-6-mercaptopyrimidines (IIa, c, d, e) were obtained according to [15, 17]. 4-Isopropylamino-, 4-piperidino-, 4-morpholino-5-amino-6-mercaptopyrimidines (IIf-h) were obtained from the corresponding 4-substituted 5-nitro-6-chloropyrimidines [16] under the conditions of the synthesis of IId [17].

Compounds: IIf, $C_7H_{12}N_4S$, yield 46%, mp 205°C (from alcohol); IIg, $C_9H_{14}N_4S$, yield 48%, mp 186°C (from benzene) IIh, $C_8H_{13}N_4OS$, yield 49%, mp 174°C (from alcohol). The physical constants and characteristics of the synthesized compounds are given in Table 1. The data of the elemental analysis for C, H, N, S correspond to the calculated values.

2-Methyl-4-methoxy-5-amino-6-mercaptopyrimidine (IIb, $C_6H_9N_3OS$). From 10 g (49.3 mmoles) of 2-methyl-4-methoxy-6-chloro-5-nitropyrimidine [19], under the conditions described in the procedure in [15], 6 g (75%) of pyrimidine IIb were obtained, mp 188...190°C (from alcohol).

4-Methoxy-6,8-dimethyl-7,9-dioxo-5H-6,7,8,9-tetrahydrodipyrimido[4,5-b][4'5'-e][1,4]thiazine (IIIa), 4-Methoxy-6,8-dimethyl-7,9 dioxo-9a-hydroxytetrahydrodipyrimido[4,5-b][4',5'-e][1,4]thiazone (VIIa), and Bis(4-methoxy-5-aminopyrimid-6-yl] disulfide (VIII). A solution of 1.4 g (6.4 mmoles) of uracil I [18] in 20 ml of methanol is added to a solution of 1 g (6.4 mmoles) of pyrimidine IIa in 30 ml of methanol containing 0.38 g (6.4 mmoles) of KOH. The mixture is stirred for 30 min at 20°C and 0.7 g (40%) of thiazine IIIa is filtered off. Yellow crystalline substance. Mass spectrum: M^+ 293. Calculated M 293. The filtrate is evaporated, the residue is ground with water and 0.57 g (30%) of thiazine VIIa are filtered. Colorless crystals. Mass spectrum: M^+ 309. Calculated M 309.

When the reaction is carried out in the presence of triethylamine, from 1 G (4.5 mmoles) of uracil I and 0.7 g (4.5 mmoles) of pyrimidine IIa, 0.4 g (31%) of thiazine IIa and 0.4 g (25%) of disulfide VIII are obtained. Yellow crystalline substance. Mass spectrum: M^+ 312. Calculated: M 312.

2-Methyl-4-methoxy-6,8-dimethyl-7,9-dioxa-5H-6,7,8,9-tetrahydrodipyrimido[4,5-b][4',5'-e][1,4]thiazine (IIIb) and 2-Methyl-4-methoxy-6,8-dimethyl-7,9-dioxo-9a-hydroxy-6,7,8,9-tetrahydrodipyrimido[4,5-b][4'5'-e][1,4]thiazone (VIIb). Under the conditions of the preparation of thiazine IIIa, from 1.3 g (5.9 mmoles) uracil and 1.0 g (5.9 mmoles) of pyrimidine IIb in the presence of 1.2 g (12 mmoles) of triethylamine in 30 ml of methanol, 0.3 g (17%) of thiazine IIIb are obtained. Yellow crystals. Mass spectrum: M^+ 307. Calculated M 307. From the filtrate 0.5 g (30%) of thiazine (VIIb) is obtained. Colorless crystals. Mass spectrum: M^+ 323. Calculated: M 323.

4-Methoxy-6,8-dimethyl-7,9-dioxo-6,7,8,9-tetrahydrodipyrimido-[4,5-b][4',5'-e][1,4]thiazinyl (IVa) and Thiazine (VIIa). Under the conditions of the preparation of thiazine IIIa, from 1 g (6.4 mmoles) of KOH, and 1.4 g (6.4 mmoles) of uracil I in the presence of a few drops a 30% H_2O_2 solution, 0.2 g (11%) thiazinyl IVa is obtained. Dark-blue crystals. Mass spectrum: M^+ 292. Calculated: M 292. From the filtrate 0.5 g (17%) of thiazine VIIa is isolated.

4-Dimethylamino-6,8-dimethyl-7,9-dioxo-6,7,8,9-tetrahydrodipyrimido [4,5-b][4',5-e][1,4]thiazinyl (IVc) and 4-Dimethylamino-6,8-dimethyl-7,9-dioxo-9a-hydroxy-6,7,8,9-tetrahydrodipyrimido-[4,5-b][4',5'-e][1,4]thiazine (VIIc). Under the conditions of the preparation of thiazines IIIa,b, from 1 g (5.9 mmoles) of pyrimidine IIc and 1.3 g (5.9 mmoles) of uracil I, 0.61 g (32%) of thiazinyl IVc are obtained. Dark-blue crystals. Mass spectrum: M^+ 292. Calculated M 292. From the filtrate, 0.6 g (26.5%) of thiazine VIIc are isolated. Colorless crystals. Mass spectrum: M^+ 309. Calculated: M 309. After the separation of

thiazine VIIc, the filtrate is chromatographed on a column (2 × 40 cm) with activity grade II aluminum oxide, carrying out the elution with ether. The ether eluates are evaporated to yield 0.4 g (36%) of thiadiazole IX.

7-Dimethylamino[1,2,3]thiadiazolo[5,4-d]pyrimidine (IX, $C_6H_7N_5S$). A solution of 1 g of $NaNO_2$ in 10 ml of water is added at 0°C to a solution of 1.5 g (8.4 mmoles) of pyrimidine IIc in a mixture of 6 ml of concentrated HCl and 20 ml of water. The solution obtained is stirred at 0°C for 30 min and then is neutralized with an aqueous solution of sodium acetate. The precipitate that separates is filtered and dried. Yield 1 g (66%) of thiadiazole IX, mp 132...134°C. Comparison of spectral characteristics and melting points of the thiadiazole IX samples obtained showed that they are identical.

4-Methylamino-6,8-dimethyl-7,9-dioxo-6,7,8,9-tetrahydrodipyrimido[4,5-b][4',5'-e][1,4]thiazinyl (IVd) and 4-Methylamino-6,8-dimethyl-7,9-dioxo-9a-hydroxy-6,7,8,9-tetrahydrodipyrimido-[4,5-b][4',5'-e][1,4]thiazine (VIId). Under the conditions of the preparation of thiazines IVc and VIIc, form 1 g (6.4 mmoles) of pyrimidine IId, 1.1 g (6.4 mmoles) of uracil I, and 3 ml of triethylamine in 20 ml of methanol, 0.45 g (25%) of thiazinyl IVd are obtained. Dark-blue crystals. Mass spectrum: M^+ 291. Calculated: M 291. From the filtrate, 0.65 g (46%) of thiazine VIId is isolated. Colorless crystals. Mass spectrum: M^+ 307. Calculated: M 307.

4-Amino-6,8-dimethyl-7,9-dioxo-6,7,8,9-tetrahydrodipyrimido-[4,5-b][4',5'-e][1,4]thiazinyl (IVe) and 4-Amino-6,8-dimethyl-7,9-dioxo-9a-hydroxy-6,7,8,9-tetrahydrodipyrimido[4,5-b][4',5,-e]-[1,4]thiazine (VIIe). Under the conditions of the preparation of compounds IVd and VIId, from 1 g (7 mmoles) of pyrimidine IIe, 1.5 g (6.9 mmoles) of uracil I, and 3 ml of triethylamine in 20 ml of methanol, 0.8 g (42%) of radical IVe are obtained. Dark-violet crystals. Mass spectrum: M^+ 277. Calculated: M 277. From the filtrate, 0.6 g (30%) of thiazine VIIe are isolated. Colorless crystals. Mass spectrum: M^+ 294. Calculated: M 294.

4-Isopropylamino-6,8-dimethyl-7,9-dioxo-6,7,8,9-tetrahydrodipyrimido[4,5-b][4',5'-e][1,4]thiazinyl (IVf) and 4-Isopropylamino 6,8-dimethyl-7,9-dioxo-9a-hydroxy-6,7,8,9-tetrahydrodipyrimido-[4,5-b][4',5'-e][1,4]thiazine (VIIf). Under the conditions of the preparation of compounds IVd and VIId, from 1 g (5.5 mmoles) of pyrimidine IIf and 1.2 g (5.5 mmoles) of uracil I, 0.6 g (35%) of radical IVf is obtained. Violet crystals. Mass spectrum: M^+ 319. Calculated: M 319. From the filtrate 0.17 g (10%) of thiazine VIIf is isolated. Colorless crystals. Mass spectrum: M^+ 366. Calculated: M 336.

4-Piperidino-6,8-dimethyl-7,9-dioxo-6,7,8,9-tetrahydrodipyrimido[4,5-e][4',5'-e][1,4]thiazinyl (IVg) and 4-Piperidino-6,8 dimethyl-7,9-dioxo-9a-hydroxy-6,7,8,9-tetrahydrodipyrimido-[4,5-b][4],5'-e][1,4]thiazine (VIIg). Under the conditions of the preparation of compounds IVf and VIIf, from 0.5 g (2.4 mmoles) of pyrimidine IIg, 0.53 g (2.4 mmoles) of uracil I and 2.6 g (25 mmoles) of triethylamine in 30 ml of methanol, 0.42 g (48%) of thiazinyl IVg is obtained. Dark-blue crystals. Mass spectrum: M^+ 345. Calculated: M 345. From the filtrate, 0.27 g (31%) of thiazine VIIg is isolated. Colorless crystals. Mass spectrum: M^+ 362. Calculated: M 362.

4-Morpholino-6,8-dimethyl-7,9-dioxo-6,7,8,9-tetrahydrodipyrimido[4,5-b][4',5'-e][1,4]thiazinyl (IVh) and 4-Morpholine-6,8-dimethyl-7,9-dioxo-9a-hydroxy-6,7,8,9-tetrahydrodipyrimido-[4,5-b][4',5'-e][1,4]thiazine (VIIh). Under the conditions of the preparation of compounds IVg and VIIg, from 1 g (4.7 mmoles) of pyrimidine IIh, 1 g (4.6 mmoles) of uracil I, 0.91 g (58%) of thiazinyl IVg is obtained. Mass specrum: M^+ 347. Calculated: M 347. From the filtrate, 0.2 g (12%) of thiazine VIIg is isolated. Colorless crystals. Mass spectrum: M^+ 364. Calculated: M 364.

4-Methoxy-5-amino-6-(1,3-dimethyl-2,4,6-trioxohexahydropyrimid-5-yl)thiopyrimidine (VIa). A solution of 0.5 g (3.2 mmoles) of pyrimidine IIa in 10 ml of methanol containing 2.3 g (20 mmoles) of triethylamine is added at 40...50°C to a solution of 0.61 g (3.2 mmoles) of 1,3-dimethyl-5-chlorobarbituric acid (V) in 20 ml of methanol. The mixture is stirred at the boiling point for 6 h, the solution is evaporated in vacuo, the residue is ground with 15 ml of water, and acidified by acetic acid to pH 5...6. The precipitate that separates is filtered to yield 0.9 g (90%) of thiopyrimidine VIa. Colorless crystals. Mass spectrum: M^+ 311. Calculated: M 311.

4-Dimethylamino-5-amino-6-(1,3-dimethyl-2,4,6-trioxohexahydropyramid-5-yl)thiopyrimidine (VIc). Under the conditions of the preparation of compound VIa, from 1.1 g (6 mmoles) of V and 1 g (6 mmoles) of pyrimidine IIc, 1.6 g (80%) of pyrimidine VIc is obtained. Colorless crystals. Mass spectrum: M^+ 324. Calculated M 324.

4-Isopropylamino-5-amino-6-(1,3-dimethyl-2,4,6-trioxohexahydropyramid-5-yl)thiopyrimidine (VIf). Under the conditions of the synthesis of thiopyrimidine VIa, from 2 g (10.6 mmoles) of V and 2 g (10.6 mmoles) of pyrimidine IIf, 3.6 g (99%) of thiopyrimidine VIf is obtained. Mass spectrum: M^+ 338. Calculated: M 338.

4-Piperidino-5-amino-6-(1,3-dimethyl-2,4,6-triozohexahydropyrimid-5-yl)thiopyrimidine (VIg). Under the conditions of the synthesis of thiopyrimidine VIa, from 1 g (4.5 mmoles) of V and 0.95 g (4.5 mmoles) of pyrimidine IIg, 1.6 g (97%) of thiopyrimidine VIg is obtained. Mass spectrum: M^+ 364. Calculated: M 364.

4-Methoxy-6,8-dimethyl-7,9-dioxo-5H-6,7,8,9-tetrahydrodipyrimido-[4,5-b][4',5'-e][1,4]thiazine (IIIa). A 0.75 g portion (2.4 mmole) of thiopyrimidine VIa in 40 ml of a 13% alcoholic solution of HCl is boiled for 3 h. The solvent is distilled off in vacuo, and the residue is ground with 10 ml of water and filtered to yield 0.1 g (15%) of thiazine IIIa. Mass spectrum M^+ 293.

Compounds IIIc (yield 89% Mass spectrum M^+ 306. Calculated M 306); IIIf (yield 66%. Mass spectrum M^+ 320. Calculated M 320); IIIg (Yield 47%. Mass spectrum M^+ 346. Calculated: 346) were obtained in a similar way.

LITERATURE CITED

1. Yan Lung-Chi and T. C. Bruice, J. Am. Chem. Soc., 106, 1530 (1984).
2. Y. Yano, M. Ohshine, I. Yatsu, and S. Suton, J. Chem. Soc., Perkin 2, No. 6, 753 (1985).
3. Y. Maki, M. Tanabe, Y. Kojima, M. Sako, Heterocycles, 22, 12 (1984).
4. H. Fenner, R. W. Grauert, and L. Tessendorf, Arch. Pharm. (Weinheim), 314, 1015 (1981).
5. Y. Maki, T. Hiramitsu, and M. Suzuki, Chem. Pharm. Bull, 22, 1265 (1974).
6. M. P. Nemeryuk, N. I. Traven', N. A. Nersesyan, and T. S. Safonova, Khim. Geterotsikl. Soedin., No. 1, 131 (1985).
7. H. Fenner, R. Grauert, and P. Hemerich, Annalen No. 2, 193 (1978).
8. F. Ciminale, G. Liso, and G. Trapani, Tetrahedron Lett., 22, 1455 (1981).
9. A. L. Buchachenko and A. M. Vasserman, Stable Radicals [in Russian], Khimiya, Moscow (1973).
10. M.F. Chiu, B. C. Gilbert, and P. Hanson, J. Chem. Soc. B, No. 9, 1700 (1970).
11. J. M. Goldman, French Patent 1565368; Chem. Abstr., 72, 79067 (1970).
12. H. Fenner, Tetrahedron Lett., 11, 617 (1970).
13. Y. Maki and T. Hiramitsu, Chem. Pharm. Bull., 24, No. 12, 3135 (1976).
14. B. Huston and T. B. Johnson, J. Am. Chem. Soc., 47, 3011 (1925).
15. M. P. Nemeryuk, L. A. Tolokontseva, V. A. Yadrovskaya, and T. S. Safonova, Khim.-farm. Zh., No. 7, 810 (1985).
16. J. Clark, I. Gelling, I. W. Souton, and M. S. Morton, J. Chem. Soc., C, No. 3, 494 (1970).
17. R. K. Robins and Hsi Hufin, J. Am. Chem. Soc., 79, 492 (1957).
18. W. R. Boon and W. G. M. Jones, J. Chem. Soc. No. 2, 591 (1951).
19. E. Bühler and W. W. Pfteiderer, Chem. Ber., 99, 2997 (1966).