Chemistry of Heterocyclic Compounds, Vol. 40, No. 5, 2004

HALOCYCLIZATION OF SUBSTITUTED 2-(ALKENYLTHIO)PYRIMIDIN-6-ONES

N. Yu. Slivka[1], Yu. I. Gevaza[2], and V. I. Staninets[2]

Bromination and iodation of 2-(alkenylthio)pyrimidin-6-ones occur selectively and lead to formation of the corresponding 7-oxo-2,3-dihydrothiazolopyrimidinium or 8-oxo-3,4-dihydro-2H-pyrimido-thiazinium salts. The selectivity of the reaction is controlled by the nature of the alkenyl substituent on the sulfur atom and the basicity of the $N_{(1)}$ and $N_{(3)}$ atoms of the pyrimidine ring. The iodation reaction rate increases as the basicity of the $N_{(3)}$ atom increases.

Keywords: (allylthio)pyrimidines, pyrimidothiazines, thiazolidine pyrimidines, bromination, heterocyclization, iodation.

Iodation of 2-allylthio-1H-pyrimidin-6-ones leads to formation of 3-iodomethyl-7-oxo-2,3-dihydro-8H-thiazolo[3,2-*a*]pyrimidinium iodides and triiodides [1]. An analogous conversion is also observed in the case of halogenation of 2-(allylthio)thienopyrimidin-6-ones [2, 3].

This work was devoted to determining the selectivity of halocyclization of substituted 2-(alkenylthio)-4-R-pyrimidin-6-ones **1a-g** and studying the effect of the nature of the substituent R on the rate of the indicated reaction.

The starting compounds **1a-d** were synthesized from the sodium salt of 6-methylthiouracil and the corresponding alkenyl halide by the procedure in [3]. Compounds **1e-g** were obtained from 6-amino-4-hydroxy-2-mercaptopyrimidine and the corresponding alkenyl halide by the procedure in [1].

When compounds **1a-g** were reacted with bromine or iodine in chloroform or acetic acid, after treatment of the initially formed trihalo derivatives (see [1]) with acetone we selectively obtained substituted 7-oxo-2,3-dihydrothiazolopyrimidinium salts **2a-d, 3a-d** or 8-oxo-3,4-dihydropyrimidothiazinium salts **4a-c, 5a-c** (Scheme 1).

Obviously the selectivity of cyclization is determined by the nature and position of the substituents on the allyl moiety bonded to the sulfur atom. Thus from compounds **1a,b,e,f**, which have allyl and methallyl substituents, only the salts **2a-d, 3a-d** are formed, while only the salts **4a-c, 5a-c** are formed from compounds **1c,d,g** with a thiocinnamyl or thio-2-methylbutenyl group.

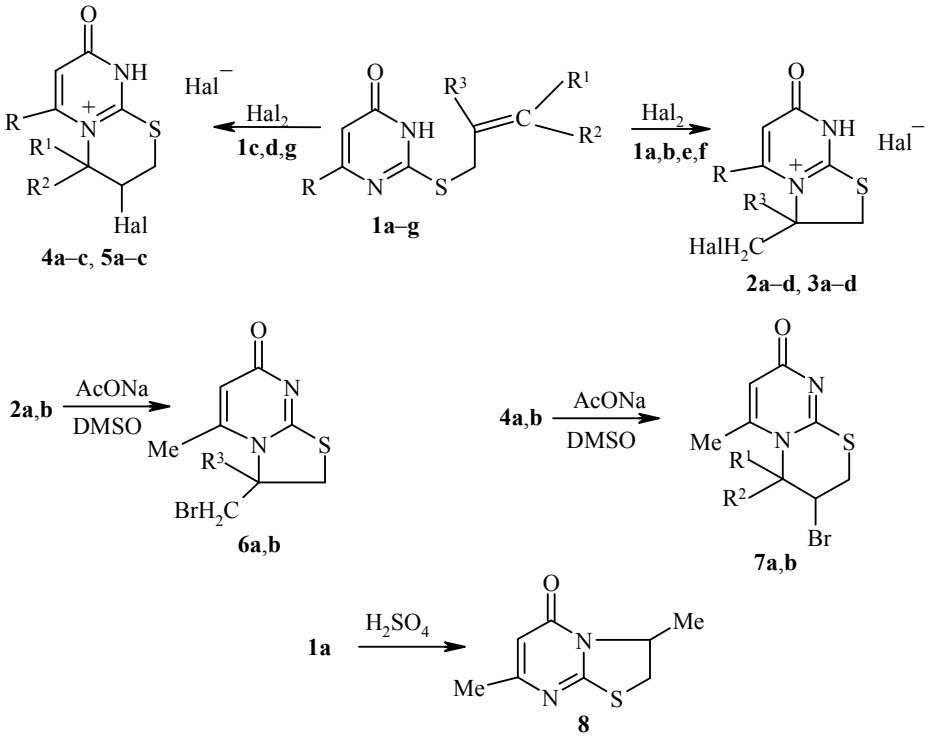
The composition and structure of all the synthesized compounds were confirmed by elemental analysis (Table 1), IR spectra, and ^{1}H NMR (Table 2).

The ^{1}H NMR spectra indicate that the products **2, 3**, and **4, 5** belong to different series of compounds. The signal common to both series, for the SCH_2 moiety, in the case of salts **2, 3** has the shape of two doublets of doublets (for R = Me) or two doublets (for R = NH_2) in the 3.44-3.46 ppm and 3.70-3.89 ppm region. The multiplet signal for the CH_2Hal group is typical of the spectra for compounds **2, 3**, which is found in the

[1] Lesya Ukrainka Volyn State University, Lutsk 43025, Ukraine. [2] Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kiev 02094; e-mail: iochkiev@ukrpack.net. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 776-783, May, 2004. Original article submitted February 15, 2002; revised March 9, 2004.

 0009-3122/04/4005-0660

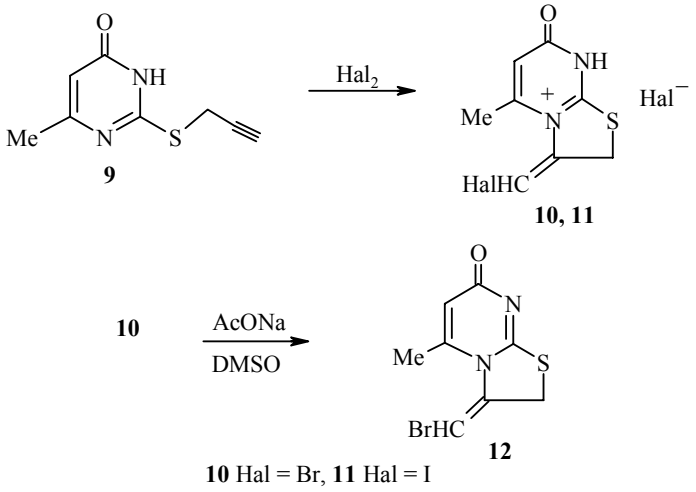
Scheme 1



2, **4** Hal = Br, **3**, **5** Hal = I; **1a–d** R = Me, **e–g** R = NH_2; **a**, **e** $R^1 = R^2 = R^3$ = H, **b**, **f** $R^1 = R^2$ = H, R^3 = Me, **c**, **g** $R^1 = R^2$ = Me, R^3 = H, **d** $R^1 = R^3$ = H, R^3 = Ph; **2**, **3** **a**, **b** R = Me, **c**, **d** R = NH_2; **a, c** R^3 = H, **b**, **d** R^3 = Me; **4**, **5** **a**, **b** R = Me, **c** R = NH_2; **a**, **c** $R^1 = R^2$ = Me, **b** R^1 = H, R^2 = Ph; **6** **a** R^3 = H, **b** R^3 = Me; **7** **a** $R^1 = R^2$ = Me, **b** R^1 = H, R^2 = Ph

4.15-4.18 ppm region for R = Me and in the 3.76-3.89 ppm region for R = NH_2 (compare compounds **2a, 3a** and **2c, 3c, 2b, 3b**, and **2d, 3d**). This difference, and also the different shapes of the signals for the SCH_2 group, may be connected with the effect of the steric factor (closely surrounded by solvent molecules, the basic NH_2 group creates different steric conditions than the neutral methyl substituent). The appearance of the latter is more likely when the substituents R and CH_2Hal are close to each other, i.e., when cyclization occurs at the $N_{(3)}$ atom. Such a direction of the reaction is also confirmed by the conversion of the salts **2a,b** to the bases **6a,b** when treated with AcONa in DMSO. In the IR spectra of the latter, the absorption band for the carbonyl group is found at 1620 cm^{-1}, which indicates they have a *p*-quinoid structure (see [1]).

The spectra of compounds **4, 5** are considerably different from the spectra considered above. The signal from the SCH_2 group of these compounds has the form of two multiplets, which are found 3.56-3.90 ppm and 3.82-3.89 ppm upfield from the signals of the analogous group of compounds **2,3**. A typical feature of the considered spectra is the presence of signals from the CHHal and $C_{(4)}R^1R^2$ groups. The multiplet signal from the CHHal moiety, compared with the signal from the CH_2Hal moiety of compounds **2,3**, is found downfield in the narrow interval 4.65-4.70 ppm for all salts **4, 5**, which indicates the absence of any appreciable change in its position when the 6-Me substituent is replaced by 6-NH_2. On the other hand, such a replacement causes a 0.19-0.28 ppm upfield shift of the signal from the protons of the methyl group in the 4 position (compare **4a** and **4c, 5a** and **5c**). As in the case of compounds **2,3**, this is possibly connected with the effect of the steric factor, i.e., it is support for the idea that the R and $C_{(4)}R^1R^2$ and R groups are close and consequently that cyclization occurs at the $N_{(3)}$ atom. When the salts **4a,b** are treated with AcONa in DMSO, the corresponding bases **7a,b** are formed, and the absorption band for the C=O of those compounds is found at 1630-1620 cm^{-1}, supporting the idea that they have a *p*-quinoid structure and that the direction of cyclization is at the $N_{(3)}$ atom.



The structure of compounds **2c-5c** is supported by the presence in the IR spectra of a signal from the NH group in the 10.01-10.60 ppm region, which however is missing in the spectra of the rest of the salts **2-5** (also see [3]).

Formation of products **2-5** suggests that halocyclization of compounds **1a-g** occurs, as we might expect [4], with participation of the more basic $N_{(3)}$ atom. However, when the pyrimidinone **1a** is treated with sulfuric acid, cyclization occurs at the $N_{(1)}$ atom to form 3,7-dimethyl-5-oxo-2,3-dihydro-8H-thiazolo[3,2-*a*]pyrimidine (**8**), the structure of which is supported by the ^{1}H NMR data (Table 2) and the IR spectrum (the absorption band for the C=O group is found at 1680 cm^{-1}, which suggests an *o*-quinoid structure for compound **8** (see [1])). In this case, the change in the direction of the reaction is probably connected with the high degree of protonation of the more basic $N_{(3)}$ atom in compound **1a**.

TABLE 1. Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	R_f*	Yield, %
		Hal	N	S			
1	2	3	4	5	6	7	8
1b	$C_9H_{12}N_2OS$		14.03 / 14.28	16.30 / 16.34	146-147	0.84	81
1c	$C_{10}H_{14}N_2OS$		13.19 / 13.33	15.07 / 15.25	166-167	0.79	89
1d	$C_{14}H_{14}N_2OS$		9.97 / 10.55	11.65 / 12.41	160-161	0.74	86
1e	$C_7H_9N_3OS$		22.18 / 22.96	17.74 / 17.50	Oil	0.89	67
1f	$C_8H_{11}N_3OS$		21.11 / 21.33	16.34 / 16.26	Oil	0.88	60
1g	$C_9H_{13}N_3OS$		20.14 / 19.91	15.29 / 15.18	Oil	0.87	64
2a	$C_8H_{10}Br_2N_2OS$	47.11 / 46.70		9.12 / 9.37	155-156	0.46	73
2b	$C_9H_{12}Br_2N_2OS$	45.26 / 44.90		8.98 / 9.11	161-162 (dec.)	0.47	76
2c	$C_7H_9Br_2N_3OS$	46.83 / 46.59		9.18 / 9.34	148-149	0.54	63
2d	$C_8H_{11}Br_2N_3OS$	45.01 / 44.77		8.62 / 8.98	153-155	0.53	60

TABLE 1 (continued)

1	2	3	4	5	6	7	8
3a	$C_8H_{10}I_2N_2OS$	58.50 / 58.21		7.13 / 7.35	184 (dec.)	0.43	79
3b	$C_9H_{12}I_2N_2OS$	56.82 / 56.41		7.01 / 7.12	189-190 (dec.)	0.45	63
3c	$C_7H_9I_2N_3OS$	58.43 / 58.10	9.31 / 9.62		177-178	0.56	61
3d	$C_8H_{11}I_2N_3OS$	56.61 / 56.30	9.20 / 9.32		182-183	0.54	57
4a	$C_{10}H_{14}Br_2N_2OS$	43.47 / 43.19		8.34 / 8.66	182-183 (dec.)	0.44	78
4b	$C_{14}H_{14}Br_2N_2OS$	37.98 / 38.20		7.51 / 7.67	169-176*[2]	0.44, 0.62	77
4c	$C_9H_{13}Br_2N_3OS$	43.28 / 43.08		8.34 / 8.16	158-159	0.55	69
5a	$C_{10}H_{14}I_2N_2OS$	55.03 / 54.71		6.88 / 6.90	222 (dec.)	0.42	61
5b	$C_{14}H_{14}I_2N_2OS$	49.83 / 49.58	5.21 / 5.47		200-209*[2] (dec.)	0.43, 0.60	64
5c	$C_9H_{13}I_2N_3OS$	54.78 / 54.62	9.16 / 9.04		185-186	0.57	58
6a	$C_8H_9Br_2N_2OS$	30.62 / 30.59		12.04 / 12.27	139-140	0.81	80
6b	$C_9H_{11}BrN_2OS$	29.32 / 29.04		11.83 / 11.65	148-149	0.80	75
7a	$C_{10}H_{13}BrN_2OS$	27.51 / 27.63	9.83 / 9.69		165-166	0.85	78
7b	$C_{14}H_{13}BrN_2OS$	24.02 / 23.69	8.56 / 8.31		148-160*[2]	0.83, 0.92	79
8	$C_8H_{10}N_2OS$		15.65 / 15.38	17.82 / 17.60	101-103	0.90	62
9	$C_8H_8N_2OS$		15.65 / 15.55	17.81 / 17.79	162-163	0.70	81
10	$C_8H_8Br_2N_2OS$	47.37 / 47.00		9.28 / 9.43	177-178	0.48	73
11	$C_8H_8I_2N_2OS$	58.83 / 58.53	6.28 / 6.46		212-213 (dec.)	0.46	82
12	$C_8H_7BrN_2OS$	31.11 / 30.84		12.58 / 12.31	157-158	0.81	72

* Eluent for TLC: chloroform–acetone–diethylamine, 10:2:1 (compounds **1b-d, 6a,b, 7a,b, 8, 9,** and **12**), ethyl acetate–methanol–acetone, 15:4:2 (compounds **2a,b-5a,b, 10, 11**), methanol–acetone–diethylamine, 10:10:2 (compounds **1e-g, 2c,d, 3c,d, 4c, 5c**).
*[2] mp of the mixture of diastereomers.

Halocyclization also occurs selectively in the case of 6-methyl-2-(propynylthio)pyrimidin-6-one (**9**): when it is halogenated with bromine or iodine in chloroform, only substituted thiazolidinopyrimidinium salts **10, 11** are formed (Scheme 2). The structure of the latter is supported by ^{1}H NMR spectra (the presence of singlet signals from the SCH_2 and CHHal groups in the 4.25-4.34 ppm and 7.07-7.18 ppm respectively), and also by the conversion of product **10** to base **12** when treated with AcONa in DMSO. In the IR spectrum of compound **12**, the absorption band for the C=O group is found at 1640 cm^{-1}, which indicates that it has a *p*-quinoid structure. The starting compound **9** was obtained by the procedure in [3].

In order to determine the effect of the nature of the substituent R on the $C_{(4)}$ atom of (alkenylthio)pyrimidin-6-ones **1a-g**, we estimated the relative rate of iodation of compounds **1a,d,e**. We found that under identical conditions, after 5 h this reaction proceeds to 57.6% (**1a**), 51.0% d (**1d**), 81.6% (**1e**)

TABLE 2. ^{1}H NMR and IR Spectra of Synthesized Compounds

Compound	Chemical shifts, δ, ppm (*J*, Hz)	ν (C=O), cm^{-1}
1b	1.76 (3H, s, CH_3); 2.12 (3H, s, 4-CH_3); 3.81 (2H, s, SCH_2); 5.02 (2H, m, =CH_2); 5.97 (1H, s, H-5); 12.50 (1H, s, NH)	1670
1c	1.69 (6H, s, two CH_3); 2.16 (3H, s, 4-CH_3); 3.77 (2H, d, ^3J = 6.9, SCH_2); 5.38 (1H, m, =CH); 5.96 (1H, s, H-5); 12.46 (1H, s, NH)	1670
1d	2.21 (3H, s, 4-CH_3); 3.97 (2H, d, ^3J = 7.2, SCH_2); 6.39 (1H, m, =CH); 6.66 (1H, d, ^3J = 10.5, =CHC_6H_5,); 7.23-7.39 (5H, m, C_6H_5); 12.52 (1H, s, NH)	1670
2a	2.31 (3H, s, 5-CH_3); 3.51 and 3.70 (2H, two dd, $^2J_1 = {}^2J_2$ = 12.0, ^3J = 5.9, SCH_2); 4.12 (2H, m, CH_2Br); 5.18 (1H, m, H-3); 6.20 (1H, s, H-6)	1680
2b	1.83 (3H, s, 3-CH_3); 2.16 (3H, s, 5-CH_3); 3.58 and 3.75 (2H, two dd, $^2J_1 = {}^2J_2$ = 12.3, ^4J = 2.2, SCH_2); 4.15 (2H, m, CH_2Br); 6.22 (1H, s, H-6)	1700
2c	3.46 and 3.76 (2H, two d, $^2J_1 = {}^2J_2$ = 12.4, SCH_2); 3.81 (2H, m, CH_2Br); 5.17 (1H, m, H-3); 6.97 (1H, s, H-6); 9.17 (2H, br. s, NH_2); 10.59 (1H, s, NH)	1690
2d	1.88 (3H, s, 3-CH_3); 3.46 and 3.72 (2H, two d, $^2J_1 = {}^2J_2$ = 12.1, SCH_2); 3.89 (2H, m, CH_2Br); 6.09 (1H, s, H-6); 8.73 (2H, br. s, NH_2)	1695
3a	2.31 (3H, s, 5-CH_3); 3.53 and 3.78 (2H, two dd, $^2J_1 = {}^2J_2$ = 12.3, ^3J = 5.8, SCH_2,); 4.13 (2H, m, CH_2I); 5.21 (1H, m, H-3); 6.23 (1H, s, H-6)	1685
3b	1.84 (3H, s, 3-CH_3); 2.15 (3H, s, 5-CH_3); 3.66 and 3.76 (2H, two dd, $^2J_1 = {}^2J_2$ = 12.3, ^4J = 1.8, SCH_2); 4.18 (2H, m, CH_2I); 6.11 (1H, s, H-6)	1700
3c	3.48 and 3.77 (2H, two d, $^2J_1 = {}^2J_2$ = 12.0, SCH_2); 3.85 (2H, m, CH_2I); 5.03 (1H, m, H-3); 6.99 (1H, s, H-6); 9.14 (2H, br. s, NH_2); 10.60 (1H, s, NH)	1700
3d	1.83 (3H, s, 3-CH_3); 3.44 and 3.78 (2H, two d, $^2J_1 = J_2$ = 12.3, SCH_2); 3.88 (2H, m, CH_2I); 6.16 (1H, s, H-6); 8.82 (2H, br. s, NH_2)	1700
4a	2.06 (3H, s, 4-CH_3); 2.15 (3H, s, 4-CH_3); 2.65 (3H, s, 6-CH_3); 3.56 and 3.82 (2H, two m, SCH_2); 4.66 (1H, m, H-3); 6.21 (1H, s, H-7)	1700
4b	2.34 (3H, s, 6-CH_3); 3.90 and 4.02 (2H, two m, SCH_2); 4.65 (1H, m, H-3); 5.76 (1H, d, ^3J = 10.2, H-4); 6.21 (1H, s, H-7); 6.42–7.67 (5H, m, C_6H_5)	1690
4c	1.87 (3H, s, 4-CH_3); 1.94 (3H, s, 4-CH_3); 3.67 and 4.09 (2H, two m, SCH_2); 4.65 (1H, m, H-3); 6.19 (1H, s, H-7); 9.13 (2H, br. s, NH_2); 10.01 (1H, s, NH)	1685
5a	2.11 (3H, s, 4-CH_3); 2.23 (3H, s, 4-CH_3); 2.49 (3H, s, 6-CH_3); 3.60 and 3.87 (2H, two m, SCH_2); 4.67 (1H, m, H-3); 6.15 (1H, s, H-7)	1680
5b	2.31 (3H, s, 6-CH_3); 3.85 and 4.00 (2H, two m, SCH_2); 4.70 (1H, m, H-3); 5.79 (1H, d, ^3J = 10.1, H-4); 6.22 (1H, s, H-7); 7.54–7.72 (5H, m, C_6H_5)	1700
5c	1.89 (3H, s, 4-CH_3); 1.95 (3H, s, 4-CH_3); 3.70, 4.12 (2H, two m, SCH_2); 4.67 (1H, m, H-3); 6.17 (1H, s, H-7); 9.12 (2H, br. s, NH_2); 10.08 (1H, s, NH)	1690
6a	2.11 (3H, s, 5-CH_3); 3.48 and 3.66 (2H, two d, $^2J_1 = {}^2J_2$ = 6.6, SCH_2); 3.99 (2H, m, CH_2Br); 5.06 (1H, m, H-3); 6.01 (1H, s, H-6)	1620
8	2.19 (3H, d, ^3J = 6.9, 3-CH_3); 2.21 (3H, s, 7-CH_3); 3.83 (2H, d, ^3J = 6.9, SCH_2); 5.11 (1H, m, H-3); 6.21 (1H, s, H-6)	1680
9	2.11 (3H, s, 4-CH_3); 3.19 (1H, t, ^4J = 2.2, ≡CH,); 3.99 (2H, d, ^4J = 2.2, SCH_2); 6.07 (1H, s, H-5); 12.49 (1H, s, NH)	1670
10	2.31 (3H, s, 5-CH_3); 4.25 (2H, s, SCH_2); 6.26 (1H, s, H-6); 7.18 (1H, s, =CHBr)	1700
11	2.21 (3H, s, 5-CH_3); 4.34 (2H, s, SCH_2); 6.06 (1H, s, H-6); 7.07 (1H, s, =CHI)	1700

conversion. The high percentage conversion of compound **1e** is probably connected with the presence in that compound of an NH_2 group, the electronic effect of which on the $N_{(3)}$ atom increases the basicity of the latter and consequently increases the reactivity.

Thus the direction of halocyclization of 2-alkyenylthiopyrimidin-6-ones is substantially affected by the structure of the S-alkeynyl substituent, which leads to regioselective formation of thiazolidinopyrimidinium or pyrimidothiazinium derivatives. An electron-donor substituent on the heterocycle (R = NH_2) accelerates the heterocyclization of 2-(alkyenylthio)pyrimidin-6-ones.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 in KBr disks. The ^{1}H NMR spectra of solutions of the substances in DMSO-d_6 were obtained on a Varian VXR-300 spectrometer (300 MHz), internal standard TMS. The course of the reaction was monitored by TLC on Silufol UV-254 plates.

2-Allylthio- (1a), 2-Methallylthio- (1b), and 2-Propargylthio-4-methyl-1H-pyrimidin-6-one (9) (General Procedure). A solution of allyl bromide, methallyl chloride, or propargyl chloride (45 mmol) in alcohol (20 ml) was added with heating (~90°C) to sodium salt of 6-methyl-2-thiouracil (5.0 g, 30 mmol) in water (150 ml). The mixture was vigorously shaken and held for 4-5 h at 18-20°C. The precipitate of product **1a,b** or **1c** formed was filtered out and washed with alcohol, then crystallized from a 1:2 alcohol–water mixture and dried at 80-90°C. For compound **1a**: mp 134°C (mp 133°C [1]). According to the data in [5], the mp of compound **9** is 162°C.

4-Methyl-2-(3-methyl-2-butenylthio)- (1c) and 4-Methyl-2-cinnamylthio-1H-pyrimidin-6-one (1d) (General Procedure). 1-Chloro-3-methyl-2-butene or cinnamyl chloride (45 mmol) was added with stirring to a solution of sodium salt of 6-methyl-2-thiouracil (5 g, 30 mmol) in DMF (70 ml). The mixture was held for 2 h at 50-60°C and then cooled down and diluted with water (100 ml). The colorless precipitate of product **1c** or **1d** formed was filtered out and washed with ether, then crystallized from an alcohol–water mixture and dried at 80-90°C.

2-Allylthio- (1e), 2-Methallylthio- (1f), and 2-(3-Methyl-2-butenylthio)-4-amino-1H-pyrimidin-6-one (1g) (General Procedure). 6-Amino-4-hydroxy-2-mercaptopyrimidine (5.0 g, 35 mmol) and allyl bromide, methallyl chloride, or 1-chloro-3-methyl-2-butene (35 mmol) were added to a solution of KOH (1.95 g, 35 mmol) in alcohol (90 ml). The mixture was boiled for 2 h under reflux and then cooled down; the colorless precipitate was filtered out and then the filtrate was evaporated down. The product **1e,f** or **1g** was obtained as a dark yellow oil that dissolved well in water.

3-Bromomethyl-5-methyl- (2a) and 3-Bromomethyl-3,5-dimethyl-7-oxo-2,3-dihydro-8H-thiazolo[3,2-*a*]pyrimidinium (2b), 3-Bromo-4,4,6-trimethyl- (4a), and 3-Bromo-6-methyl-8-oxo-4-phenyl-3,4-dihydro-9H-pyrimido[3,2-*a*]thiazinium (4b), 3-Bromomethylidene-5-methyl-7-oxo-2,3-dihydro-8H-thiazolo[3,2-*a*]pyrimidinium (10) Bromides (General Procedure). A solution of bromine (1.44 g, 9.0 mmol) in glacial acetic acid (15 ml) was added with stirring to a solution of compound **1a-d** (4.5 mmol) or **9** in glacial acetic acid (40 ml). After 2 h, the yellow precipitate of the corresponding tribromide (see [1]) was filtered out and then washed with hot glacial acetic acid. The tribromide obtained (3.0 mmol) was added in several portions to acetone (15 ml); the reaction mixture was stirred for 30 min at 25°C. The precipitate was filtered out, washed with acetone, crystallized from alcohol, and dried at 90-100°C. The product **2a,b, 4a,b**, or **10** was obtained respectively.

3-Iodomethyl-5-methyl- (3a) and 3-Iodomethyl-3,5-dimethyl-7-oxo-2,3-dihydro-8H-thiazolo-[3,2-*a*]pyrimidinium (3b), 3-Iodo-4,4,5-trimethyl- (5a), and 3-Iodo-6-methyl-8-oxo-4-phenyl-3,4-dihydro-9H-pyrimido[3,2-*a*]thiazinium (5b), and 3-Iodomethylidene-5-methyl-7-oxo-2,3-dihydro-8H-thiazolo-[3,2-*a*]pyrimidinium (11) Iodides (General Procedure). A solution of iodine (1.01 g, 4.0 mmol) in alcohol or chloroform (30 ml) was added to a suspension of compound **1a-d** or **9** (0.4 g, 2.0 mmol) in alcohol or chloroform (30 ml). The mixture was stirred for 3 h, and then it was held at room temperature for 10-12 h. The brown precipitate of the corresponding triiodide formed (see [1]) was filtered out and washed with alcohol. A solution of $NaI \cdot 2H_2O$ (0.74 g, 4.0 mmol) in acetone (10 ml) was added with stirring to a solution of the triiodide obtained (1.66 g, 2.0 mmol) in acetone (5 ml). After 1 h, the yellow precipitate was filtered out, washed with acetone, crystallized from alcohol, and dried at 90°C; the product **3a,b, 5a,b**, or **11** was obtained respectively. For compound **3a**, the literature mp was 182°C [1].

5-Amino-3-bromomethyl- (2c) and 5-Amino-3-bromomethyl-3-methyl-7-oxo-2,3-dihydro-8H-thiazolo[3,2-*a*]pyrimidinium (2d), 6-Amino-3-bromo-4,4-dimethyl-8-oxo-3,4-dihydro-9H-pyrimido[3,2-*a*]-thiazinium (4c) Bromides (General Procedure). A solution of bromine (0.79 g, 5.0 mmol) in acetic acid

(15 ml) was added dropwise with stirring over a 20 min period to a solution of compound **1e-g** (2.5 mmol) in glacial acetic acid (15 ml). The reaction mixture was held for 4 h at 20°C and then held for 4 h at -4°C. The yellow precipitate of the corresponding tribromide was filtered out and washed with ether. The products **2c,d, 4c** were isolated as for compound **2a**.

5-Amino-3-iodomethyl- (3c) and 5-Amino-3-iodomethyl-3-methyl-7-oxo-2,3-dihydro[3,2-*a*]-pyrimidinium (3d), 6-Amino-3-iodo-4,4-dimethyl-8-oxo-3,4-dihydro-9H-pyrimido[3,2-*a*]thiazinium (5c) Iodides (General Procedure). A solution of iodine (1.01 g, 4.0 mmol) in ethanol (40 ml) was added over a 30 min period to a suspension of compound **1e-g** (2.0 mmol) in ethanol (30 ml). The alcoholic solution was decanted from the oil formed, the oil was dissolved in acetone (10 ml), and a solution of $NaI \cdot 2H_2O$ (0.74 g, 4.0 mmol) in acetone (10 ml) was added with stirring to the solution obtained. The precipitate was filtered out and washed with acetone, dried at 100°C and crystallized from alcohol. The product **3c,d** or **5c** respectively was obtained.

3-Bromomethyl-5-methyl- (6a) and 3-Bromomethyl-3,5-dimethyl-7-oxo-2,3-dihydrothiazolo-[3,2-*a*]pyrimidine (6b), 3-Bromo-4,4,6-trimethyl- (7a), and 3-Bromo-6-methyl-8-oxo-4-phenyl-3,4-dihydropyrimido[3,2-*a*]thiazine (7b), 3-Bromomethylidene-5-methyl-7-oxo-2,3-dihydrothiazolo[3,2-*a*]-pyrimidine (12) (General Procedure). A 15% solution of AcONa (30 ml) in water was added with stirring to a solution of bromide **2a,b**, **4a,b,** or **10** (2.0 mmol) in DMSO (50 ml) and the mixture was held at room temperature for 2 h. The white precipitate of the corresponding product **6a,b, 7a,b, 12** was filtered out and dried at 80°C.

3,7-Dimethyl-5-oxo-2,3-dihydrothiazolo[3,2-*a*]pyrimidine (8). A solution of compound **1a** (0.18 g, 1.0 mmol) in conc. H_2SO_4 (2 ml) was held for 10 min in a water bath at 50°C, and then was held for 25 h at 15-25°C. The reaction mixture was poured into ice water (10 ml) and held for 24 h at 0°C. The precipitate of product **8** was filtered out and recrystallized from chloroform.

REFERENCES

1. D. G. Kim and V. I. Shmygarev, *Khim. Geterotsikl. Soedin.*, 211 (1995).
2. P. Wippich, H. Guetschow, and S. Leistner, *Synthesis*, 714 (2000).
3. R. I. Vas'kevich, S. M. Kripak, V. I. Staninets, Yu. L. Zborovskii, and A. N. Chernega, *Zh. Org. Khim.*, **36**, 1091 (2000).
4. V. I. Staninets and E. A. Shilov, *Usp. Khim.*, **40**, 491 (1971).
5. M. M. Heravi, K. Aghapoor, and M. A. Nooshabadi, *Synth. Commun.*, **28**, 233 (1998).