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UNEXPECTED RESULT IN THE REACTION OF 3-AMINO-3-THIOXOPROPANAMIDES WITH 2-ANILINOMETHYLENE DERIVATIVES OF 1,3-DICARBONYL COMPOUNDS. SYNTHESIS OF PYRIMIDINE-5-CARBOXAMIDE DERIVATIVES

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The interaction of 3-amino-3-thioxopropanamides with 2-anilinomethylene derivatives of dimedone, 1,3-cyclohexanedione and Meldrum's acid led to the formation of 2-(2-amino-2-oxoethyl)-6-thioxo-1,6-dihydropyrimidine-5-carboxamides. The latter were alkylated in alkaline medium with the formation of 4-(alkylthio)pyrimidine-5-carboxamide derivatives.

Keywords: 3-amino-3-thioxopropanamides, pyrimidine-5-carboxamides, thiomalonamides, alkylation, heterocyclization.

Reactions of activated methylene groups belonging to nitriles and amides with β-enamino ketones and esters are quite widely used in synthetic practice for obtaining pyridine heterocycles (for reviews, see [1-8]). Among the most available enaminocarbonyl substrates are the 2-anilinomethylene derivatives of 1,3-dicarbonyl compounds, which are readily obtained by three-component condensation of activated methylene compound, triethyl orthoformate, and aniline [9-13]. The reaction of 2-anilinomethylene derivatives of 1,3-dicarbonyl compounds with activated methylene nitriles and amides has been used repeatedly and successfully for the synthesis of a range of oxygen- and nitrogen-containing heterocyclic systems [12, 14-20].

We have previously shown [13] that the interaction of compounds **1-3** with cyanothioacetamide (**4**) is a convenient method of preparing azines **5-7**. The practical value of these compounds is explained by the fact that they are starting materials for obtaining a series of biologically active substances, *viz*. modulators of metabotropic glutamate receptors of subtype I ($mGluR_1$) [21], IKKβ enzyme inhibitors [22], ubiquitin C-terminal hydrolase L1 inhibitors [23], HIV-1 integrase inhibitors [24], phosphodiesterase PDE4B inhibitors [25], etc.

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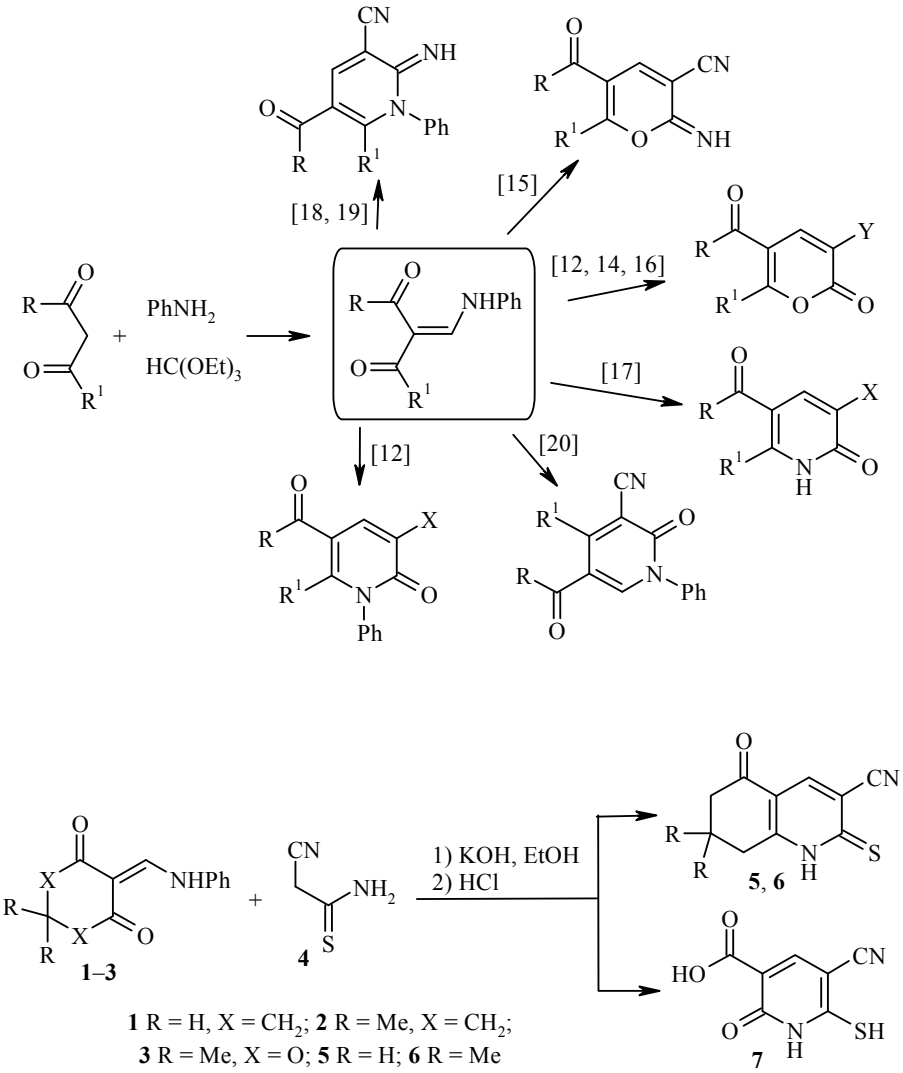
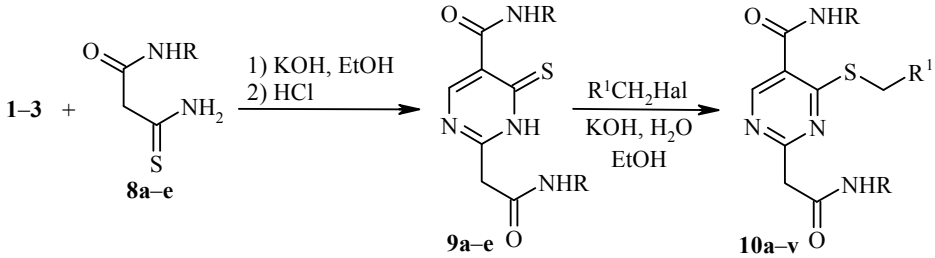


While continuing investigations in this direction we attempted to prepare analogs of compounds **5-7** from enaminodicarbonyl compounds **1-3** and structural analogs of cyanothioacetamide (**4**), the 3-amino-3-thioxopropanamides (thiomalonamides) **8a-e**. Preliminary results [26] proved to be quite unexpected. Thus, on interacting thiomalonamide **8a** (R = H) with the dimedone 2-anilinomethylene derivative **2** (ratio of **8a**:**2** = 1:1, excess of KOH, EtOH) we obtained 6-thioxo-1,6-dihydropyrimidine-5-carboxamide **9a**. The same product was also formed on introducing the anilinomethylene derivative of Meldrum's acid **3** into the reaction. We established that the analogous thioxopyrimidines **9b-e** could be readily obtained from *N*-substituted 3-thioxopropanamides **8b-e** and electrophilic substrates **1-3**. As expected, the yields and purity of compounds **9a-e** increased on introducing a twofold excess of thioamide component **8a-e** into the reaction with enamines **1-3**. A small library of pyrimidines **10a-v** was obtained by alkylating thioxopyrimidines **9a-e** at the sulfur atom. The low yields of compounds **10a-v** (15-46%) were presumably linked to the unoptimized reaction conditions and the occurrence of side processes in the alkaline medium.

The structures of compounds **9a-e** and **10a-v** were confirmed by data of IR, ^{1}H and ^{13}C NMR spectroscopy, HPLC-MS, and elemental analysis, as well as by NMR experiments for compounds **10a** (^{1}H-^{13}C HMBC, ^{13}C APT) and **10b** (^{13}C APT). In the mass spectra of compounds **9a-e** peaks were detected for molecular ions with *m*/*z* [2M(**8a-e**)-23], in IR spectra absorption bands were observed for amide C=O groups. The ^{1}H NMR spectra of compounds **9a-e** and **10a-v** lacked signals for the fragments of dimedone,

1,3-cyclohexanedione, or the COOH group. Instead, a singlet was detected for the methylene protons at 3.39-4.05 ppm, as well as signals for two CONHR fragments, and also a narrow singlet for the pyrimidine ring proton at 8.71-8.93 ppm. The spectral characteristics of compounds **10a-v** are given in Table 1.



8, **9 a** R = H, **b** R = Bn, **c** R = Ph, **d** R = 4-MeC_6H_4, **e** R = 4-BrC_6H_4;
10 a R = H, R^1 = $CONH_2$; **b** R = H, R^1 = COPh; **c** R = H, R^1 = CONH-4-ClC_6H_4;
d R = Ph, R^1 = COOPr; **e** R = 4-MeC_6H_4, R^1 = CONH-4-BrC_6H_4; **f** R = 4-MeC_6H_4, R^1 = COOEt;
g R = 4-MeC_6H_4, R^1 = CONH(3-EtOOC-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl;);
h R = 4-MeC_6H_4, R^1 = CONH-4-EtC_6H_4; **i** R = 4-MeC_6H_4, R^1 = CONH-2-ClC_6H_4;
j R = 4-MeC_6H_4, R^1 = CONH-3-$MeOC_6H_4$; **k** R = 4-MeC_6H_4, R^1 = CONH-2-$MeOC_6H_4$;
l R = 4-BrC_6H_4, R^1 = CONHPh; **m** R = 4-BrC_6H_4, R^1 = $CONHCH_2Ph$;
n R = 4-BrC_6H_4, R^1 = CONH-2-MeC_6H_4; **o** R = 4-BrC_6H_4, R^1 = CONH-4-MeC_6H_4;
p R = 4-BrC_6H_4, R^1 = CONH-2-EtC_6H_4; **q** R = 4-BrC_6H_4, R^1 = CONH-4-EtC_6H_4;
r R = 4-BrC_6H_4, R^1 = CONH-2,6-$Me_2C_6H_3$; **s** R = 4-BrC_6H_4, R^1 = CONH-2,4-$Me_2C_6H_3$;
t R = 4-BrC_6H_4, R^1 = CONH-2-Me-3-ClC_6H_3; **u** R = 4-BrC_6H_4, R^1 = CO-4-MeC_6H_4;
v R = 4-BrC_6H_4, R^1 = CO-4-ClC_6H_4

Proceeding from the data of HPLC-MS, IR, and NMR spectroscopy, thioxopyrimidines **9a-e** and their *S*-alkyl derivatives **10a-v** may be ascribed the structure of either 2-(carbamoylmethyl) isomer **A**, or 4-(carbamoylmethyl) isomer **B**. An unambiguous choice in favor of structure **A** for the compound **10a** was based on ^1H and ^{13}C heteronuclear correlation experiment through 2-3 bonds. The sole proton of the pyrimidine ring in the HMBC spectrum had four correlation cross peaks (isomer **A**), while in the spectrum of the alternative structure **B** only two cross peaks might be expected (Fig. 1). The observed ^1H-^{13}C HMBC correlations for 2-(2-amino-2-oxoethyl)-4-[(2-amino-2-oxoethyl)thio]pyrimidine-5-carboxamide (**10a**) are given in Figure 2.

Each of the singlets of the methylene groups 2-CH_2CONH_2 and SCH_2 gave two cross peaks: 3.73/165.8 (CH_2/C-2), 3.73/170.4 (CH_2/$CONH_2$) and 3.79/169.2 (SCH_2/C-4), 3.79/170.3 ppm (SCH_2/$CONH_2$), while four correlations were detected for the proton H-6 at 8.73/123.5 (H-6/C-5), 8.73/165.8 (H-6/C-2), 8.73/166.4 (H 6/5-$CONH_2$), and 8.73/169.2 ppm (H-6/C-4). In the ^{13}C APT spectrum of 2-(2-amino-2-oxoethyl)-4-[(2-oxo-

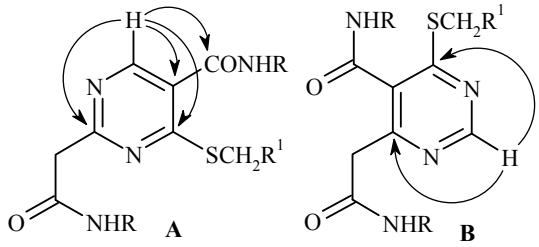


Fig. 1. Alternative structures **A** and **B** for compounds **10a-v.**

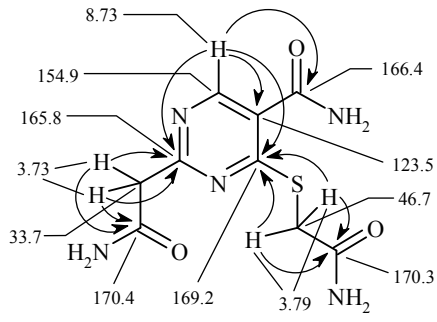
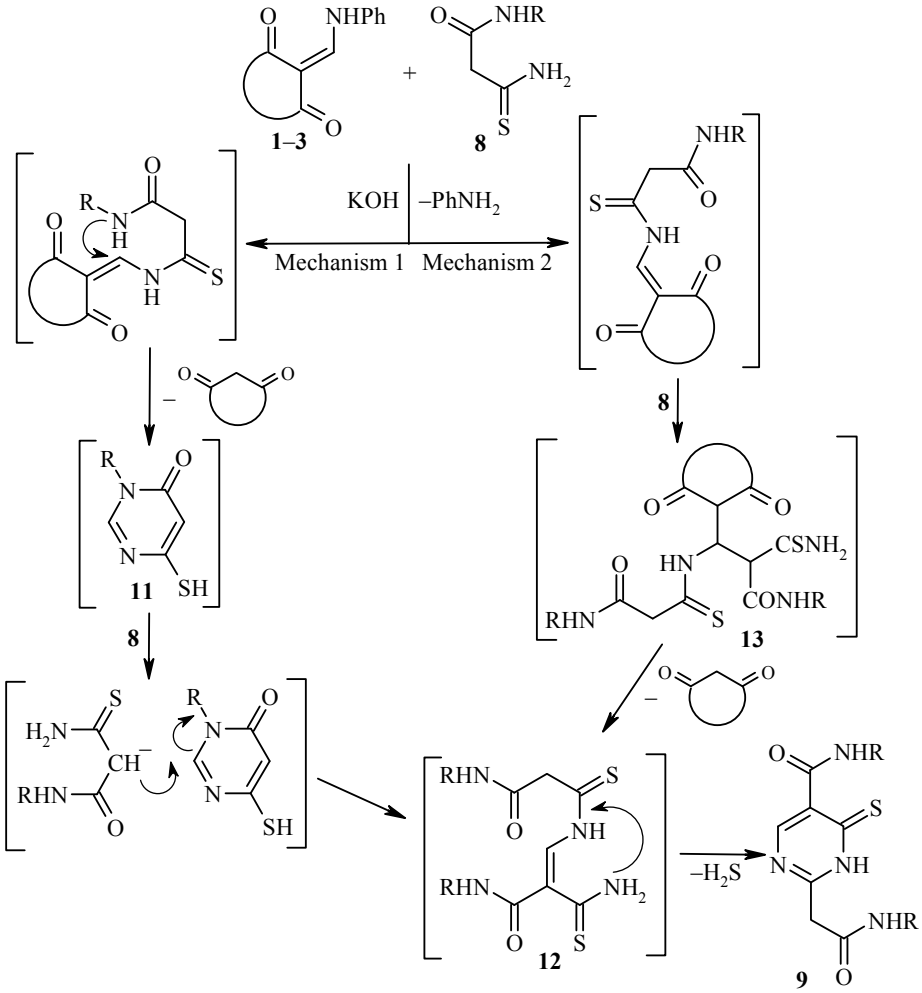


Fig. 2. Scheme of the observed correlations in the ^1H-^{13}C HMBC spectrum of compound **10a**

2-phenylethyl)thio]pyrimidine-5-carboxamide (**10b**) four peaks of opposite phase were observed (154.4 ppm, C-6, 128.1, 128.6, and 133.1 ppm, phenyl CH) and nine peaks in phase (phenyl C-1, three C=O signals, two methylene group peaks, C-2, C-4, C-5). In the ^{13}C APT spectrum of pyrimidine **10a** a sole peak of opposite phase (154.9 ppm, C-6) was observed.

The pyrimidine ring formation mechanism of compound **9** was of interest to us. The enaminodicarbonyl compounds **1-3** had the obvious role of methine C_1-synthons, while one of the thiomalonamide **8** molecules formally reacted as an N-nucleophile, and another as a C-nucleophile. The possible mechanisms of the interaction are shown below.



The mechanism 1 includes vinylic substitution of the aniline fragment with a thioamide fragment and removal of 1,3-dicarbonyl compound followed by cyclization to the pyrimidine derivative **11**. It is suggested that the latter was attacked at the C-2 atom by the carbanion of compound **8** and underwent recyclization through the intermediate **12** with elimination of H_2S and the formation of pyrimidine **9**. The alternative mechanism **2** assumes a sequential formation of the open-chain intermediates **13** and **12**.

The known ability of thioamides to play the role of *N*-nucleophiles in vinylic substitution reactions supports the proposed aniline fragment substitution by thioamide as the first stage of the process [27, 28]. It should also be noted that the competitive C-/N-nucleophilicity of thiomalonamides **8** in S_NVin reactions was noted in a previous work [29]. Presumably the most probable reason for the anomalous reactivity of compounds **8** with enamine substrates **1-3** was the decreased CH-acidity of the methylene fragment of

TABLE 1. Spectral Characteristics of the Synthezised Compounds **10a-v**

Compound	IR spectrum, ν, cm^{-1}		^{1}H NMR spectrum, δ, ppm (*J*, Hz)					
	NH	C=O	R	R^1	CH_2 (2H, s)	SCH_2 (2H, s)	H-6 (1H, s)	NH (1H, br. s)
1	2	3	4		5	6	7	8
10a	3360, 3178	1695, 1665	7.09 (1H, br. s); 7.10 (1H, br. s); 7.52 (1H, br. s); 7.54 (1H, br. s); 7.72 (1H, br. s) and 8.18 (1H, br. s, 3$CONH_2$)		3.73	3.79	8.73	—
10b	—	—	6.96 (1H, br. s); 7.30 (1H, br. s); 7.73 (1H, br. s) and 8.21 (1H, br. s, 2$CONH_2$)	7.56 (2H, dd, ^3J = 7.3, ^3J = 7.8, H-3,5 Ph); 7.68 (1H, dt, ^3J = 7.3, ^4J = 1.0, H-4 Ph); 8.05 (2H, d, ^3J = 7.8, H-2,6 Ph)	3.39	4.67	8.75	—
10c	3380, 3270	1692	7.10 (1H, br. s); 7.51 (1H, br. s); 7.73 (1H, br. s) and 8.21 (1H, br. s, $CONH_2$)	7.35 (2H, d, ^3J = 8.8, H Ar); 7.63 (2H, d, ^3J = 8.8, H Ar); 10.35 (1H, br. s, CONH)	3.69	4.01	8.77	—
10d	3330	1740 (CO_2Pr), 1665	7.05 (1H, t, ^3J = 7.0, H Ar); 7.14 (1H, t, ^3J = 7.0, H Ar); 7.28-7.39 (4H, m, H Ar); 7.60 (2H, d, ^3J = 7.9, H Ar); 7.70 (2H, d, ^3J = 7.7, H Ar)	0.76 (3H, t, ^3J = 7.3, $CH_2CH_2C\underline{H}_3$); 1.44-1.51 (2H, m, $CH_2C\underline{H}_2CH_3$); 3.92 (2H, t, ^3J = 6.7, $C\underline{H}_3CH_2CH_3$)	3.96	3.99	8.88	10.23; 10.60
10e	—	—	2.28 (3H, s, CH_3); 2.32 (3H, s, CH_3); 7.00-7.08 (4H, m, H Ar); 7.29-7.60 (8H, m, H Ar); 10.09 (1H, br. s, NH)		3.46	4.01	8.80	10.23; 10.40
10f	3252, 3175	1729 (CO_2Et), 1659, 1644 (C=O)	2.29 (3H, s, CH_3); 2.32 (3H, s, CH_3); 7.02 (2H, d, ^3J = 8.4, H Ar); 7.08 (2H, d, ^3J = 8.5, H Ar); 7.46 (2H, d, ^3J = 8.4, H Ar); 7.58 (2H, d, ^3J = 8.5, H Ar)	1.18 (3H, t, ^3J = 7.1, $OCH_2C\underline{H}_3$); 4.05 (2H, q, ^3J = 7.1, $OC\underline{H}_2CH_3$)	3.89	3.92	8.81	9.90; 10.33
10g	—	—	2.22 (3H, s, CH_3); 2.27 (3H, s, CH_3); 7.03 (2H, d, ^3J = 7.8, H Ar); 7.17 (2H, d, ^3J = 7.4, H Ar); 7.39 (2H, d, ^3J = 7.8, H Ar); 7.60 (2H, d, ^3J = 7.4, H Ar)	1.19 (3H, t, ^3J = 6.9, $OCH_2C\underline{H}_3$); 1.63-1.69 (4H, m, $2CH_2$); 2.56-2.61 (4H, m, $2CH_2$); 4.12-4.20 (4H, m, signal overlap $OC\underline{H}_2CH_3$ and SCH_2); 11.44 (1H, br. s, CONH)	3.95	(cm. R^1)	8.92	10.08; 10.56
10h	3270	1665	1.12 (3H, t, ^3J = 7.5, $CH_2C\underline{H}_3$); 2.23 (3H, s, CH_3); 2.28 (3H, s, CH_3); 2.49-2.53 (2H, m, $C\underline{H}_2CH_3$); 7.05-7.09 (4H, m, H Ar); 7.17 (2H, d, ^3J = 8.1, H Ar); 7.44-7.46 (4H, m, H Ar); 7.58 (2H, d, ^3J = 8.1, H Ar); 10.11 (1H, br. s, $CON\underline{H}Ar$)		3.97	4.07	8.82	10.13; 10.52
10i	3270	1665	2.23 (3H, s, CH_3); 2.28 (3H, s, CH_3); 7.07 (2H, d, ^3J = 7.9, H Ar); 7.14-7.18 (3H, m, H Ar); 7.24-7.28 (1H, m, H Ar); 7.43-7.45 (3H, m, H Ar); 7.59 (2H, d, ^3J = 7.9, H Ar); 7.67 (1H, d, ^3J = 8.1, H Ar); 9.67 (1H, br. s, $CON\underline{H}Ar$)		4.00	4.15	8.85	10.15; 10.53
10j	3292	1670	2.23 (3H, s, CH_3); 2.28 (3H, s, CH_3); 3.69 (3H, s, OCH_3); 6.61 (1H, d, ^3J = 6.9, H Ar); 7.07-7.11 (3H, m, H Ar); 7.14-7.20 (3H, m, H Ar); 7.27 (1H, s, H Ar); 7.45 (2H, d, ^3J = 7.3, H Ar); 7.59 (2H, d, ^3J = 7.3, H Ar); 10.10 (1H, br. s, $CON\underline{H}Ar$)		3.97	4.08	8.83	10.15; 10.49
10k	3270	1665	2.23 (3H, s, CH_3); 2.27 (3H, s, CH_3); 7.07 (2H, d, ^3J = 7.8, H Ar); 7.17 (2H, d, ^3J = 7.7, H Ar); 7.44 (2H, d, ^3J = 7.8, H Ar); 7.58 (2H, d, ^3J = 7.7, H Ar)	3.75 (3H, s, OCH_3); 6.86 (1H, dd, ^3J = 6.6, ^3J = 6.7, H Ar); 6.99-7.05 (2H, m, H Ar); 7.90 (1H, d, ^3J = 7.6, H Ar); 9.37 (1H, br. s, $CON\underline{H}Ar$)	4.00	4.13	8.87	10.14; 10.53
10l	3255	1665, 1650	6.99 (1H, t, ^3J = 7.2, H-4 Ph); 7.23 (2H, dd, ^3J = 7.2, ^3J = 8.0, H-3,5 Ph); 7.37 (2H, d, ^3J = 8.6, H Ar); 7.47 (2H, d, ^3J = 8.6, H Ar); 7.55-7.59 (4H, m, H Ar); 7.70 (2H, d, ^3J = 8.6, H Ar); 10.19 (1H, br. s, $CON\underline{H}Ph$)		4.00	4.06	8.83	10.45; 10.69

TABLE 1 (continued)

1	2	3	4		5	6	7	8
					3.94	3.99	8.86	10.55; 10.79
10m	3282	1660	7.47 (2H, d, ^3J = 8.5, H Ar); 7.55 (2H, d, ^3J = 8.5, H Ar); 7.60 (2H, d, ^3J = 8.5, H Ar); 7.69 (2H, d, ^3J = 8.5, H Ar)	4.24 (2H, d, ^3J = 5.1, NHC<u>H</u>$_2$Ph); 7.17-7.21 (3H, m, H Ph); 7.25-7.28 (2H, m, H Ph); 8.62 (1H, t, ^3J = 5.1, N<u>H</u>CH$_2$Ph)				
10n	3270	1650	7.45 (2H, d, ^3J = 8.1, H Ar); 7.54-7.57 (4H, m, H Ar); 7.69 (2H, d, ^3J = 8.0, H Ar)	2.13 (3H, s, CH$_3$); 7.04-7.12 (2H, m, H Ar); 7.17 (1H, d, ^3J = 6.9, H Ar); 7.31 (1H, d, ^3J = 7.4, H Ar); 9.51 (1H, br. s, CON<u>H</u>Ar)		4.03	4.12	8.87	10.40; 10.73
10o	3250, 3186	1680, 1660	2.24 (3H, s, CH$_3$); 7.02 (2H, d, ^3J = 8.5, H Ar); 7.38-7.42 (4H, m, H Ar); 7.49-7.55 (4H, m, H Ar); 7.69 (2H, d, ^3J = 9.0, H Ar); 10.05 (1H, br. s, CON<u>H</u>Ar)		3.98	4.03	8.83	10.34; 10.69
10p	3240	1677, 1658	7.35 (2H, d, ^3J = 8.8, H Ar); 7.46 (2H, d, ^3J = 8.8, H Ar); 7.55 (2H, d, ^3J = 8.8, H Ar); 7.71 (2H, d, ^3J = 8.8, H Ar)	1.08 (3H, t, ^3J = 7.5, CH$_2$C<u>H</u>$_3$); 3.18 (2H, q, ^3J = 7.5, C<u>H</u>$_2$CH$_3$); 7.06-7.14 (3H, m, H Ar); 7.27-7.30 (1H, m, H Ar); 9.41 (1H, br. s, CON<u>H</u>Ar)	4.03	4.08	8.84	10.38; 10.66
10q	3268	1658	1.19 (3H, t, ^3J = 7.5, CH$_2$C<u>H</u>$_3$); 3.27 (2H, q, ^3J = 7.5, C<u>H</u>$_2$CH$_3$); 7.06 (2H, d, ^3J = 8.0, H Ar); 7.42-7.56 (8H, m, H Ar); 7.70 (2H, d, ^3J = 8.6, H Ar); 10.21 (1H, br. s, CON<u>H</u>Ar)		4.01	4.08	8.87	10.52; 10.79
10r	3255	1680, 1659	7.32 (2H, d, ^3J = 8.2, H Ar); 7.44 (2H, d, ^3J = 8.2, H Ar); 7.51 (2H, d, ^3J = 8.2, H Ar); 7.71 (2H, d, ^3J = 8.2, H Ar)	2.09 (6H, s, 2CH$_3$); 6.99-7.10 (3H, m, H Ar); 9.29 (1H, br. s, CON<u>H</u>Ar)	4.04	4.08	8.84	10.35; 10.64
10s	3242	1662	7.44 (2H, d, ^3J = 8.0, H Ar); 7.54-7.58 (4H, m, H Ar); 7.71 (2H, d, ^3J = 8.0, H Ar)	2.08 (3H, s, CH$_3$); 2.21 (3H, s, CH$_3$); 6.87 (1H, d, ^3J = 7.9, H Ar); 6.96 (1H, s, H Ar); 7.14 (1H, d, ^3J = 7.9, H Ar); 9.54 (1H, br. s, CON<u>H</u>Ar)	4.05	4.11	8.88	10.57; 10.81
10t	3310, 3248	1665	7.44 (2H, d, ^3J = 8.4, H Ar); 7.53-7.57 (4H, m, H Ar); 7.69 (2H, d, ^3J = 7.8, H Ar)	2.14 (3H, s, CH$_3$); 7.10-7.14 (1H, m, H Ar); 7.23-7.26 (2H, m, H Ar); 9.80 (1H, br. s, CON<u>H</u>Ar)	4.03	4.12	8.88	10.44; 10.75
10u	3300	1690, 1665	7.42 (2H, d, ^3J = 8.8, H Ar); 7.45 (2H, d, ^3J = 8.8, H Ar); 7.56 (2H, d, ^3J = 8.0, H Ar); 7.70 (2H, d, ^3J = 8.0, H Ar)	2.32 (3H, s, CH$_3$); 7.19 (2H, d, ^3J = 7.6, H Ar); 7.82 (2H, d, ^3J = 7.6, H Ar)	3.74	4.70	8.85	10.21; 10.73
10v	3300, 3170	1700, 1665	7.41-7.45 (6H, m, H Ar); 7.57 (2H, d, ^3J = 8.3, H Ar); 7.70 (2H, d, ^3J = 8.3, H Ar); 7.93 (2H, d, ^3J = 8.3, H Ar)		3.72	4.70	8.86	10.18; 10.74

thioamides **8** (estimated pK_a = 14-15, assessed by analogy with structurally related compounds [30]), in comparison with the CH acidity of cyanothioacetamide **4** (pK_a ~ 9.5 [31] and the overall NH acidity of primary thioamides (pK_a 12-13 [32]). Compounds **11** have been described in the work [29] among other products of the thiomalonamide **8** reaction with ethoxymethylenemalonic ester. The conversion **11** → **12** → **9** is formally a variant of the Kost–Sagitullin rearrangement. The possibility of nucleophilic attack at C-2 position of the pyrimidine ring is in agreement with literature data for this type of reactions [33].

Compounds **9a-e** were yellow powders, insoluble in EtOH, poorly soluble in acetone and AcOH, moderately soluble in DMF and DMSO. Pyrimidines **10a-v** were colorless crystals or white/beige powders, insoluble in EtOH, moderately soluble in acetone, and soluble in hot AcOH and DMF.

In conclusion it should be mentioned that the reaction discovered by us opened a principally new approach to the construction of the pyrimidine ring and enabled the creation of new fuctionally substituted derivatives of pyrimidine. Currently the work continues on the method optimization for obtaining these compounds, characterization of their properties and investigating the mechanism of their formation.

EXPERIMENTAL

The IR spectra were recorded on Thermo Nicolet Avatar 370 DTGS (in KBr pellets, compound **9a**) and on IKS-29 spectrophotometers (in nujol, remaining compounds). The ^{1}H NMR spectra were recorded on Bruker DRX-500 (500 MHz for compounds **9a**, **10a-c**), Varian Gemini 200 (200 MHz for compounds **8a**, **9c-e**, **10e**,**f**,**l**,**o**,**p**,**r**),Varian Unity Plus (400 MHz for compounds **9b, 10d,g-k**,**m**,**n**,**q**,**s-v**) instruments. The ^{13}C NMR, ^{13}C APT, and two-dimensional ^{1}H–^{13}C HMBC spectra were recorded on a Bruker DRX-500 (500 and 125 MHz for ^{1}H and ^{13}C nuclei, respectively). The solvent for all NMR spectra was DMSO-d_6, internal standard was TMS. The HPLC-MS analysis of compounds **10d**,**j** was carried out on an Agilent 1100 chromatograph with a diode matrix (215, 254, and 264 nm) and mass selective (Agilent LC/MSD SL) detectors, ionization type APCI. HPLC-MS analysis of the remaining compounds was performed on a Shimadzu LC-10AD liquid chromatograph with Shimadzu SP D-10A UV-Vis (254 nm) and Sedex 75 ELSD detectors, linked with a PE SCIEX API 150EX mass detector, ionization by electrospray at atmospheric pressure. Elemental analysis was performed on a Carlo-Erba 1106 Elemental Analyzer. Melting points were determined on a Kofler hot stage apparatus and were not corrected. The purity of the obtained compounds was checked by TLC on Silufol UV-254 plates, eluent was acetone–hexane, 1:1, visualization with iodine vapor, UV detector.

2-Anilinomethylene-1,3-cyclohexanedione (**1**), 2-anilinomethylene-5,5-dimethyl-1,3-cyclohexanedione (**2**) and 5-anilinomethylene-2,2-dimethyl-1,3-dioxane-4,6-dione (**3**) were obtained by known procedures [13, 17]. 3-Amino-3-thioxopropanamides **8a-e** were obtained by passing H_2S through a solution of the corresponding cyanoacetamide in a pyridine–Et_3N mixture [34, 35].

3-Amino-3-thioxopropanamide (8a) was obtained by a modification of published procedure [34] in the following way. Cyanoacetamide (25 g, 0.297 mol) was placed in an 150-ml Erlenmeyer flask, then pyridine (25 ml) and Et_3N (21 ml, 0.151 mol) were added. H_2S was passed through the obtained suspension with heating (40-50°C) and stirring for 6 h. The reaction mixture was maintained overnight in a freezer (-10°C), the precipitated solid was filtered off and washed with cold EtOH and Et_2O. The filtrate was kept in the freezer for 72 h and a further quantity of pure product was obtained. The overall yield was 23.65 g (67%), beige powder, mp 105-107°C (EtOH) (mp 103-105°C [35], mp 110-112ºC [36]). The product dissolved readily in water, hot EtOH, and was not soluble in Et_2O. ^{1}H NMR spectrum, δ, ppm: 3.42 (2H, s, CH_2); 6.96 (1H, br. s) and 7.41 (1H, br. s, $CONH_2$); 9.29 (1H, br. s) and 9.43 (1H, br. s, $CSNH_2$). Found, %: C 30.66; H 5.18; N 23.59. $C_3H_6N_2OS$. Calculated, %: C 30.49; H 5.12; N 23.71.

2-(2-Amino-2-oxoethyl)-6-thioxo-1,6-dihydropyrimidine-5-carboxamides 9a-e (General Method). Thioamide **8a-e** with activated methylene group (0.030 mol) and the corresponding enamino-1,3-dicarbonyl compound **1-3** (0.015 mol) were placed in a 100-ml beaker, and 96% EtOH (40 ml) was added. KOH (3.4 g, 0.061 mol) was added to the obtained suspension with vigorous stirring and mild heating (~40°C). In this way the starting compounds gradually dissolved (in the case of thioamides **8a**,**e**, the solid potassium salt of the product precipitated after 10-20 min). The reaction mixture was stirred for 6 h at 25°C, maintained for 48 h at room temperature, and then an excess (10 ml) of conc. HCl was added dropwise with stirring. The precipitated yellow product was filtered off, washed with EtOH, water, and acetone. The obtained substances were refluxed in AcOH or acetone to obtain analytically pure samples. Thioxopyrimidines **9a-e** were also formed by reacting compounds **8a-e** and **1-3** at a ratio of 1:1, but in reduced yield and significantly contaminated with the starting enamines **1-3**.

2-(2-Amino-2-oxoethyl)-4-[(2-amino-2-oxoethyl)thio]pyrimidine-5-carboxamide (9a). Yield 2.13 g (67%) (from thiomalonamide **8a** and enamino diketone **2**, 2:1), 2.04 g (64%) (from thiomalonamide **8a** and Meldrum's acid derivative **3**, 2:1), 0.81 g (51% calculated compound **8a**, from thiomalonamide **8a** and compound **3**, 1:1). The preparation of compound **9a** from compounds **8a** and **2** (1:1) was described in the work [26]. Yellow powder; mp 245-250°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 3.74 (2H, s, 2-CH_2); 7.08 (1H, br. s) and 7.54 (1H, br. s, CH_2CONH_2); 7.72 (1H, br. s) and 9.28 (1H, br. s, 5-$CONH_2$); 8.71 (1H, s, H-4); 14.03 (1H, br. s, NH). The results of HPLC-MS, elemental analysis, and spectral investigations (IR and ^{13}C NMR spectra) were in agreement with those given in study [26].

***N*-Benzyl-2-[2-(benzylamino)-2-oxoethyl]-6-thioxo-1,6-dihydropyrimidine-5-carboxamide (9b)**. Yield 4.36 g (74%) (from thioamide **8b** and enaminoketone **2**, 2:1). Pale-yellow powder; mp >250°C (decomp.). R_f 0.45. IR spectrum, ν, cm^{-1}: 3275 (N–H), 1650 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.83 (2H, s, C$\underline{H}_2$CONH); 4.30 (2H, d, ^3J = 5.9, C$\underline{H}_2$NH); 4.55 (2H, d, ^3J = 5.7, C$\underline{H}_2$NH); 7.24-7.37 (10H, m, H Ph); 8.72 (1H, s, H-4); 8.33 (1H, t, ^3J = 5.7, $CH_2N\underline{H}$); 10.36-10.42* (1H, m, $CH_2N\underline{H}$); 14.57 (1H, br. s, CONH). Mass spectrum, *m*/*z*: 393.6 $[M+H]^+$, 786.0 $[2M+H]^+$. Found, %: C 64.40; H 5.27; N 14.12. $C_{21}H_{20}N_4O_2S$. Calculated, %: C 64.27; H 5.14; N 14.28.

2-(2-Anilino-2-oxoethyl)-*N*-phenyl-6-thioxo-1,6-dihydropyrimidine-5-carboxamide (9c). Yield 4.15 g (76%, from thiomalonamide **8c** and enamino diketone **1**, 2:1), 1.78 g (65% calculated from the thiomalonamide **8c**, from thiomalonamide **8c** and enamino diketone **2**, 1:1). Lemon-colored powder; mp >250°C (decomp., AcOH). IR spectrum, ν, cm^{-1}: 3285, 3180 (N–H), 1665, 1650 (C=O). ^{1}H NMR spectrum, δ, ppm : 4.00 (2H, s, C$\underline{H}_2$CONH); 6.95-7.13 (2H, m, H Ar); 7.24-7.37 (4H, m, H Ar); 7.57-7.70 (4H, m, H Ar); 8.83 (1H, s, H-4); 10.37 (1H, s, $CH_2CON\underline{H}$); 12.27 (1H, s, 5-$CON\underline{H}$); 14.37 (1H, br. s, NH). Found, %: C 62.89; H 4.57; N 15.32. $C_{19}H_{16}N_4O_2S$. Calculated, %: C 62.62; H 4.43; N 15.37.

***N*-(4-Methylphenyl)-2-{2-[(4-methylphenyl)amino]-2-oxoethyl}-6-thioxo-1,6-dihydropyrimidine-5-carboxamide (9d)**. Yield 1.59 g (54% calculated on thioamide **8d**, from the thioamide **8d** and enamino diketone **2**, 1:1), 3.53 g (60%, from thioamide **8d** and enamino diketone **2**, 2:1). Sandy-colored powder; mp > 250°C (decomp., AcOH). R_f 0.64. IR spectrum, ν, cm^{-1}: 3285, 3180 (N–H), 1672, 1650 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.29 (3H, s, CH_3); 2.32 (3H, s, CH_3); 3.96 (2H, s, C$\underline{H}_2$CONH); 7.04 (2H, d, ^3J = 8.2, H Ar); 7.09 (2H, d, ^3J = 8.4, H Ar); 7.44 (2H, d, ^3J = 8.4, H Ar); 7.56 (2H, d, ^3J = 8.2, H Ar); 8.93 (1H, s, H-4); 10.09 (1H, s, $CH_2CON\underline{H}$); 12.36 (1H, s, 5-CONH); 14.60 (1H, br. s, NH). Mass spectrum, *m*/*z*: 393.6 $[M+H]^+$, 786.0 $[2M+H]^+$. Found, %; C 64.57; H 5.29; N 14.25. $C_{21}H_{29}N_4O_2S$. Calculated, %: C 64.27; H 5.14; N 14.28.

***N*-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-6-thioxo-1,6-dihydropyrimidine-5-carboxamide (9e)**. Yield 2.51 g (64%, calculated on thiomalonamide **8e**, from the thiomalonamide **8e** and enamino diketone **2**, 1:1), Yellow powder; mp >250°C (decomp., DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz):

*Unresolved triplet

3.97 (2H, s, CH_2CONH); 7.37-7.43** (4H, m, H Ar); 7.55 (2H, d, ^3J = 8.7, H Ar); 7.64 (2H, d, ^3J = 8.8, H Ar); 8.92 (1H, s, H-4); 10.36 (1H, s, CH_2CONH); 12.53 (1H, s, 5-CONH). Found, %: C 44.01; H 2.79; N 10.63. $C_{19}H_{14}Br_2N_4O_2S$. Calculated, %: C 43.70; H 2.70; N 10.73.

4-(Alkylthio)-2-(2-amino-2-oxoethyl)pyrimidine-5-carboxamides 10a-v (General Method). Aqueous 10% KOH solution (2.1 ml, 4.1 mmol) was added to a suspension of thioxopyrimidine **9a-e** (4.0 mmol) in EtOH (20 ml), and the mixture was stirred until complete dissolution, with heating as necessary. A solution of alkylating agent (4.0 mmol of phenacyl bromide, chloroacetic ester, or chloroacetanilide derivative) in EtOH (6-7 ml) was added dropwise to the obtained solution. The reaction mixture was stirred for 3 h at 15-20°C, maintained for 72 h without stirring, then diluted with H_2O (10 ml), stirred for 5 h, and the solid was filtered off. The product was recrystallized as necessary from an appropriate solvent (in those cases the yields are indicated for the recrystallized product).

2-(2-Amino-2-oxoethyl)-4-[(2-amino-2-oxoethyl)thio]pyrimidine-5-carboxamide (10a). Yield 0.69 g (33%). White powder; mp >250°C (DMF). ^{13}C APT NMR spectrum, δ, ppm: 33.7 (CH_2); 46.7 (SCH_2); 123.5 (C-5); 154.9* (C-6); 165.8 (C-2); 166.4 (5-$CONH_2$); 169.2 (C-4); 170.3 (SCH_2CONH_2); 170.4 (2-CH_2CONH_2). Mass spectrum, *m*/*z*: 270.6 $[M+H]^+$, 539.8 $[2M+H]^+$. Found, %: C 40.27; H 4.25; N 25.95. $C_9H_{11}N_5O_3S$. Calculated, %: C 40.14; H 4.12; N 26.01.

2-(2-Amino-2-oxoethyl)-4-[(2-oxo-2-phenylethyl)thio]pyrimidine-5-carboxamide (10b). Yield 0.48 g (36%). White powder; mp >200°C (acetone–MeOH, 1:2). ^{13}C APT NMR spectrum, δ, ppm; 36.6 (CH_2); 45.6 (SCH_2); 122.6 (C-5); 128.1* (CH Ar); 128.6* (CH Ar); 133.1* (CH Ar); 136.5 (C-1 Ar); 154.4* (C-6); 165.1 (C-2); 165.8 (5-$CONH_2$); 168.3 (C-4); 169.3 (2-CH_2CONH_2); 194.5 (PhCO). Found, %: C 54.44; H 4.30; N 17.05. $C_{15}H_{14}N_4O_3S$. Calculated, %: C 54.53; H 4.27; N 16.96.

2-(2-Amino-2-oxoethyl)-4-({2-[(4-chlorophenyl)amino]-2-oxoethyl}thio)pyrimidine-5-carboxamide (10c). Yield 0.70 g (46%). White powder; mp 226-228°C (decomp., AcOH). ^{13}C NMR spectrum, δ, ppm: 34.7 (CH_2); 46.0 (SCH_2); 120.8 (C Ar); 122.6 (C-5); 126.8 (C Ar); 128.5 (C Ar); 137.9 (C Ar); 154.5 (C-6); 165.2 (C-2); 165.8 (5-$CONH_2$); 166.9 (C-4); 168.7 (2-CH_2CONH_2); 169.7 (CONHAr). Mass spectrum, *m*/*z*: 380.8 $[M+H]^+$, 759.8 $[2M+H]^+$. Found, %: C 47.35; H 3.79; N 18.35. $C_{15}H_{14}ClN_5O_3S$. Calculated, %: C 47.43; H 3.72; N 18.44.

Propyl {[2-(2-Anilino-2-oxyethyl)-5-(*N*-phenylcarbamoyl)pyrimidin-4-yl]thio}acetate (10d). Yield 0.59 g (32%). White powder, mp 210-212°C (EtOH–acetone, 1:1). Mass spectrum, *m*/*z*: 465.0 $[M+H]^+$, 463.0 $[M-H]^-$. Found, %: C 61.92; H 5.36; N 12.00. $C_{24}H_{24}N_4O_4S$. Calculated, %: C 62.05; H 5.21; N 12.06.

4-({2-[(4-Bromophenyl)amino]-2-oxoethyl}thio)-*N*-(4-methylphenyl)-2-{2-[(4-methylphenyl)amino]-2-oxoethyl}pyrimidine-5-carboxamide (10e). Yield 0.87 g (36%). White powder; mp >250°C (DMF). Found, %: C 57.85; H 4.46; N 11.49. $C_{29}H_{26}BrN_5O_3S$. Calculated, %: C 57.62; H 4.34; N 11.59.

Ethyl [(2-{2-[(4-Methylphenyl)amino]-2-oxoethyl}-5-[*N*-(4-methylphenyl)carbamoyl]pyrimidin-4-yl)thio]acetate (10f). Yield 0.52 g (27%). Colorless crystals; mp 218-220°C (AcOH). Found, %: C 62.65; H 5.46; N 11.89. $C_{25}H_{26}N_4O_4S$. Calculated, %: C 62.74; H 5.48; N 11.71.

Ethyl 2-({[(5-{[(4-Methylphenyl)amino]carbonyl}-2-{2-[(4-methylphenyl)amino]-2-oxoethyl}pyrimidin-4-yl)thio]acetyl}amino)-4,5,6,7-tetrahydro-1-benzo[*b*]thiophene-3-carboxylate (10g). Yield 1.05 g (40%). Beige powder; mp >250°C (AcOH). Found, %: C 61.94; H 5.49; N 10.79. $C_{34}H_{35}N_5O_5S_2$. Calculated, %: C 62.08; H 5.36; N 10.65.

***N*-(4-Methylphenyl)-4-({2-[(4-ethylphenyl)amino]-2-oxo-ethyl}thio)2-{2-[(4-methylphenyl)amino]-2-oxoethyl}pyrimidine-5-carboxamide (10h)**. Yield 0.82 g (37%). Beige, finely crystalline powder; mp >250°C (AcOH). Found, %: C 67.19; H 5.73; N 12.73. $C_{31}H_{31}N_5O_3S$. Calculated, %: C 67.25; H 5.64; N 12.65.

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*Overlap of two doublets. Signal of endocyclic NH proton is not displayed, evidently due to deuterium exchange.

**Signal in antiphase.

4-({2-[(2-Chlorophenyl)amino]-2-oxoethyl}thio)-*N*-(4-methylphenyl)-2-{2-[(4-methylphenyl)amino]-2-oxoethyl}pyrimidine-5-carboxamide (10i). Yield 0.43 g (19%). White powder; mp >250°C (AcOH). Found, %: C 62.05; H 4.80; N 12.71. $C_{29}H_{26}ClN_5O_3S$. Calculated, %: C 62.19; H 4.68; N 12.50.

4-({2-[(3-Methoxyphenyl)amino]-2-oxoethyl}thio)-*N*-(4-methylphenyl)-2-{2-[(4-methylphenyl)amino]-2-oxoethyl}pyrimidine-5-carboxamide (10j). Yield 0.38 g (17%). White powder, mp >250°C (AcOH). Found, %: C 64.77; H 5.40; N 12.57. $C_{30}H_{29}N_5O_4S$. Calculated, %: C 64.85; H 5.26; N 12.60.

4-({2-[(2-Methoxyphenyl)amino]-2-oxoethyl}thio)-*N*-(4-methylphenyl)-2-{2-[(4-methylphenyl)-amino]-2-oxoethyl}pyrimidine-5-carboxamide (10k). Yield 0.42 g (19%). White powder; mp 187-189°C (AcOH). Mass spectrum, *m*/*z*: 556.0 $[M+H]^+$, 554.1 $[M-H]^-$. Found, %: C 64.72; H 5.34; N 12.69. $C_{30}H_{29}N_5O_4S$. Calculated, %: C 64.85; H 5.26; N 12.60.

4-[(2-Anilino-2-oxoethyl)thio]-*N*-(4-bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}pyrimidine-5-carboxamide (10l). Yield 0.84 g (32%). White powder; mp >250°C. Found, %: C 49.70; H 3.30; N 10.57. $C_{27}H_{21}Br_2N_5O_3S$. Calculated, %: C 49.48; H 3.23; N 10.69.

4-{[2-(Benzylamino)-2-oxoethyl]thio}-*N*-(4-bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-pyrimidine-5-carboxamide (10m). Yield 1.04 g (39%). Beige powder; mp 233-235°C. Found, %: C 50.07; H 3.54; N 10.39. $C_{28}H_{23}Br_2N_5O_3S$. Calculated, %: C 50.24; H 3.46; N 10.46.

***N*-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-4-({2-[(2-methylphenyl)amino]-2-oxoethyl}thio)pyrimidine-5-carboxamide (10n)**. Yield 0.83 g (31%). Beige powder; mp >240°C (decomp.). Found, %: C 50.10; H 3.50; N 10.49. $C_{28}H_{23}Br_2N_5O_3S$. Calculated, %: C 50.24; H 3.46; N 10.46.

***N*-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-4-({2-[(4-methylphenyl)amino]-2-oxoethyl}thio)pyrimidine-5-carboxamide (10o)**. Yield 1.10 g (41%). White powder; mp >300°C (acetone–DMF, 4:1). Found, %: C 50.15; H 3.59; N 10.59. $C_{28}H_{23}Br_2N_5O_3S$. Calculated, %: C 50.24; H 3.46; N 10.46.

***N*-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-4-({2-[(2-ethylphenyl)amino]-2-oxoethyl}thio)pyrimidine-5-carboxamide (10p)**. Yield 0.71 g (26%). White powder; mp >250°C. Found, %: C 50.85; H 3.73; N 10.14. $C_{29}H_{25}Br_2N_5O_3S$. Calculated, %: C 50.97; H 3.69; N 10.25.

N-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-4-({2-[(4-ethylphenyl)amino]-2-oxoethyl}thio)pyrimidine-5-carboxamide (10q). Yield 0.63 g (23%). Beige powder; mp >250°C. Found, %: C 50.89; H 3.78; N 10.28. $C_{29}H_{25}Br_2N_5O_3S$. Calculated, %: C 50.97; H 3.69; N 10.25.

***N*-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-4-({2-[(2,6-dimethylphenyl)amino]-2-oxoethyl}thio)pyrimidine-5-carboxamide (10r)**. Yield 0.41 g (15%). White powder; mp 252-254°C (AcOH). Found, %: C 51.11; H 3.78; N 10.11. $C_{29}H_{25}Br_2N_5O_3S$. Calculated, %: C 50.97; H 3.69; N 10.25.

N-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-4-({2-[(2,4-dimethylphenyl)amino]-2-oxoethyl}thio)pyrimidine-5-carboxamide (10s). Yield 0.93 g (34%). Sandy-colored powder; mp >235°C (decomp., DMF). Found, %: C 50.91; H 3.73; N 10.18. $C_{29}H_{25}Br_2N_5O_3S$. Calculated, %: C 50.97; H 3.69; N 10.25.

***N*-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-4-({2-[(3-chloro-2-methylphenyl)-amino]-2-oxoethyl}thio)pyrimidine-5-carboxamide (10t)**. Yield 0.99 g (35%). White powder; mp >250°C (DMF). Found, %: C 47.61; H 3.23; N 10.02. $C_{28}H_{22}Br_2ClN_5O_3S$. Calculated, %: C 47.78; H 3.15; N 9.95.

N-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-4-{[2-(4-methylphenyl)-2-oxoethyl]-thio}pyrimidine-5-carboxamide (10u). Yield 0.58 g (22%). Sandy-colored powder; mp 240-242°C (decomp., AcOH–DMF, 2:1). Found, %: C 51.27; H 3.37; N 8.70. $C_{28}H_{22}Br_2N_4O_3S$. Calculated, %: C 51.39; H 3.39; N 8.56.

***N*-(4-Bromophenyl)-2-{2-[(4-bromophenyl)amino]-2-oxoethyl}-4-{[2-(4-chlorophenyl)-2-oxo-ethyl]-thio}pyrimidine-5-carboxamide (10v)**. Yield 1.11 g (41%). Beige powder; mp 239-240°C (decomp., AcOH–DMF, 2:1). Found, %: C 47.97; H 3.02; N 8.37. $C_{27}H_{19}Br_2ClN_4O_3S$. Calculated, %: C 48.06; H 2.84; N 8.30.

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REFERENCES

1. L. A. Rodinovskaya, V. K. Promonenkov, Yu. A. Sharanin, V. P. Litvinov, and A. M. Shestopalov, in: M. I. Kabachnik (editor), *Results of Science and Technology. Organic Chemistr*y [in Russian], Vol. 17, VINITI, Moscow (1989), p. 3.
2. B. Stanovnik and J. Svete, *Chem. Rev.*, **104**, 2433 (2004).
3. J. V. Greenhill, *Chem. Soc. Rev.*, **6**, 277 (1977).
4. A.-Z. A. Elassar and A. A. El-Khair, *Tetrahedron*, **59**, 8463 (2003).
5. G. Negri, C. Kascheres, and A. J. Kascheres, *J. Heterocycl. Chem*., **41**, 461 (2004).
6. S. M. Riyadh, I. A. Abdelhamid, H. M. Al-Matar, N. M. Hilmy, and M. H. Elnagdi, *Heterocycles*, **75**, 1849 (2008).
7. P. Lue and J. V. Greenhill, *Adv. Heterocycl. Chem.*, **67**, 207 (1996).
8. C. Camoutsis and G. Pairas, *Trends Heterocycl. Chem*., **9**, 237 (2003).
9. F. A. L'Eplattenier, L. Vuitel, H. Junek, and O. S. Volfbeis, *Synthesis*, 543 (1976).
10. G. Bouillon and K. Schank, *Chem. Ber.*, **113**, 2630 (1980).
11. O. S. Wolfbeis, *Chem. Ber.*, **114**, 3471 (1981).
12. O. S. Wolfbeis, E. Ziegler, A. Knierzinger, H. Wipfler, and I. Trummer, *Monatsh. Chem.*, **111**, 93 (1980).
13. V. V. Dotsenko, S. G. Krivokolysko, A, N. Chernega, and V. P. Litvinov, *Izv. Akad. Nauk*, *Ser. Khim.*, 1432 (2002). [*Russ. Chem. Bull*., *Int. Ed.*, **51**, 1556 (2002).]
14. A. Knierzinger and O. S. Wolfbeis, *J. Heterocycl. Chem.*, **17**, 225 (1980).
15. V. K. Ahluwalia, M. K. Sharma, and R. Sharma, *Indian J. Chem*., *Sect. B: Org. Chem. Incl. Med. Chem.*, **32B**, 1272 (1993).
16. I. Trummer, E. Ziegler, and O. S. Wolfbeis, *Synthesis*, 225 (1981).
17. G. Zacharias, O. S. Wolfbeis, and H. Junek, *Monatsh. Chem.*, **105**, 1283 (1974).
18. H. Junek, O. S. Wolfbeis, H. Sprintschnik, and H. Wolny, *Monatsh. Chem.*, **108**, 689 (1977).
19. O. S. Wolfbeis and E. Ziegler, *Z. Naturforsch.*, **31B**, 1519 (1976).
20. A. D. Yukhnevich and E. Yu. Gudriniece, *Izv. Akad. Nauk LatvSSR*, *Ser. Khim.*, 694 (1973).
21. M. Vanejevs, C. Jatzke, S. Renner, S. Müller, M. Hechenberger, T. Bauer, A. Klochkova, I. Pyatkin, D. Kazyulkin, E. Aksenova, S. Shulepin, O. Timonina, A. Haasis, A. Gutcaits, C. G. Parsons, V. Kauss, and T. Weil, *J. Med. Chem.*, **51**, 634 (2008).
22. S. Nagarajan, M. R. Doddareddy, H. Choo, Y. S. Cho, K.-S. Oh, B. H. Lee, and A. N. Pae, *Bioorg. Med. Chem.*, **17**, 2759 (2009).
23. A. H. Mermerian, A. Case, R. L. Stein, and G. D. Cuny, *Bioorg. Med. Chem. Lett.*, **17**, 3729 (2007).
24. R. Dayam, L. Q. Al-Mawsawi, Z. Zawahir, M. Witvrouw, Z. Debyser, and N. Neamati, *J. Med. Chem.*, **51**, 1136 (2008).
25. P. N. Ibrahim, H. Cho, B. England, S. Gilette, D. R. Artis, R. Zuckerman, and C. Zhang, US Pat. Appl. 2006041006.
26. V. V. Dotsenko, S. G. Krivokolysko, *Khim. Geterotsikl. Soedin.*, 1680 (2012). [*Chem. Heterocycl. Compd.*, **48**, 1568 (2012)].
27. A. M. El-Sayed and O. A. A. Allah, *Phosphorus, Sulfur Silicon Relat. Elem.*, **170**, 75 (2001).
28. A. Lorente, J. L. Balcázar, and F. Florencio, *J. Chem. Soc*., *Perkin Trans. 1*, 3377 (1992).
29. R. P. Tkachev, O. S. Bityukova, V. D. Dyachenko, V. P. Tkacheva, and A. D. Dyachenko, *Zh. Obshch. Khim.*, **77**, 125 (2007). [*Russ. J. Gen. Chem.*, **77**, 116 (2007)].
30. V. A. Pechenyuk, P. V. Kuznetsov, and L. B. Dashkevich, *Zh. Org. Khim.*, **11**, 1345 (1975).
31. V. N. Britsyun, V. A. Doroshchuk, N. V. Bogdan, V. N. Zaitsev, and M. O. Lozinskii, *Ukr. Khim. Zh.*, **73** (5), 40 (2007).
32. W. Walter and R. F. Becker, *Justus Liebigs Ann. Chem.*, **727**, 71 (1969).

33. G. G. Danagulyan, *Khim. Geterotsikl. Soedin.*, 1445 (2005). [*Chem. Heterocycl. Compd.*, **41**, 1205 (2005)].
34. K. Sasse, *Justus Liebigs Ann. Chem.,* **1976**, 768 (1976).
35. W. Schaper, *Synthesis*, 861 (1985).
36. M. Ohto and Y. Kato, *Yakugaku Zasshi,* **67**, 136 (1947).