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THREE-COMPONENT CONDENSATION OF 1,3-DIMETHYL-BARBITURIC ACID, ARYLGLYOXALS, AND SUBSTITUTED THIOUREAS

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4-Aryl-2-methylaminothiazoles and 5-aryl-2-mercapto-1-methylimidazoles, containing a fragment of 1,3-dimethylbarbituric acid, have been synthesized by the one-pot three-component condensation of 1,3-dimethylbarbituric acid, arylglyoxal hydrates, and N-methylthiourea. The analogous reaction involving N-arylthioureas proceeds regioselectively with the formation of 4-aryl-2-arylaminothiazoles. It was established that in the crystalline state 5-aryl-2-mercaptoimidazoles exist in the imidazoline-2-thione form.

Keywords: arylglyoxals, 5-(4-aryl-2-(methylamino)thiazol-5-yl)-6-hydroxy-1,3-dimethylpyrimidine-2,4-diones, 5-(5-aryl-1-methyl-2-thioxoimidazolidin-4-ylidene)-1,3-dimethylpyrimidine-2,4,6-triones, 1,3-dimethylbarbituric acid, *N*-methyl(aryl)thioureas, one-pot synthesis.

The thiazole ring is part of the composition of a series of biologically and pharmacologically important natural and synthetic products. Thus, the active chemical center of the coenzyme thiamine is the thiazolium fragment [1]. Derivatives of thiazole display antitumor activity [2], and are also used in medicine as antibiotics [3-5], anticonvulsants [6], preparations for treating ulcerous diseases [7, 8], and antimicrobial agents [9, 10]. This stimulates enhanced interest in the development of simple and convenient methods of synthesis and functionalization of the triazole nucleus.

We showed previously that a three-component one-pot condensation of 1,3-dimethylbarbituric acid (1,3-DMBA), arylglyoxals, and thiourea or *N*-arylthioureas led to a 2-aminothiazole derivatives [11]. With the aim of broadening the potential of this method for obtaining functionalized thiazoles, in the present work we have studied the three-component condensation of 1,3-DMBA **1** with arylglyoxal hydrates **2a-g** and *N*-methyl(aryl)thioureas **3a-d**. The reaction was carried out by refluxing the starting materials in ethanol. In the case of *N*-methylthiourea **3a**, high-melting products **4b-f** were isolated by filtration from the hot reaction mixture, and compounds **5a-f** from the cooled mother liquor, the melting points of which proved to be approximately 100°C lower, but the yields were somewhat higher than those of compounds **4b-f**. On using phenylglyoxal **2a** we successfully isolated only the low-melting compound **5a** from the reaction mixture.

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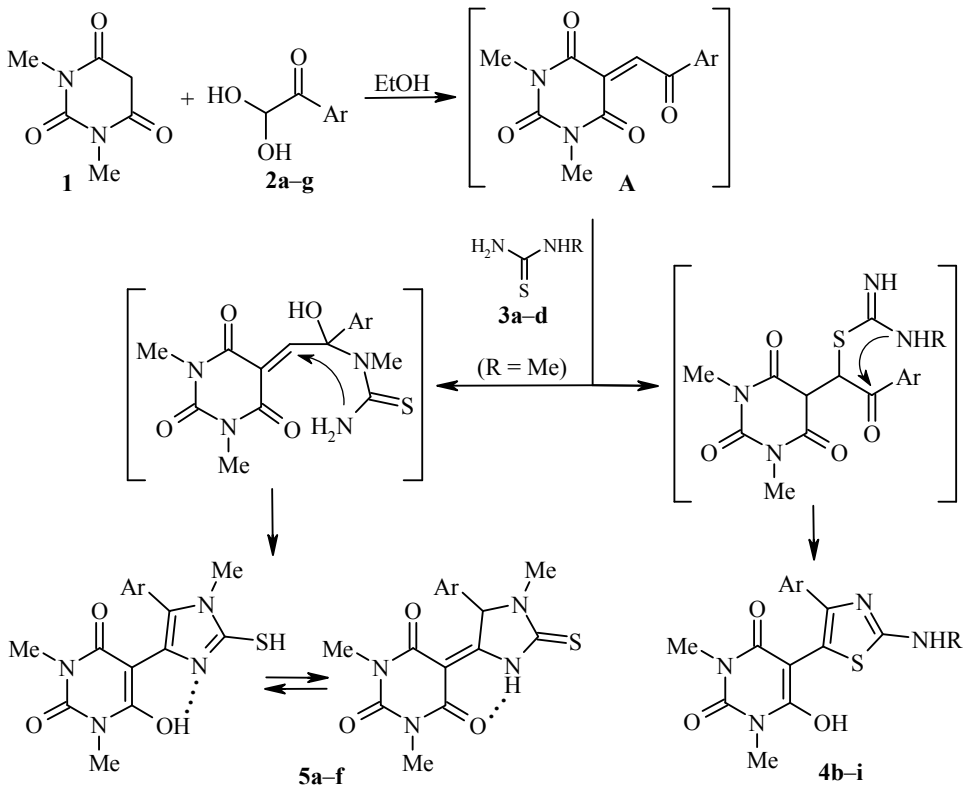
The formation of a thiazole ring in the reactions of arylglyoxals, 1,3-DMBA, and thiourea was considered previously and may occur through the formation of phenacylidene derivative **A** [12]. Nucleophilic addition of a mercapto group at the most electrophilic center of the exocyclic enone fragment, with subsequent cyclization, leads to thiazoles **4b-i**. The formation of imidazoles **5a-f** is probably linked to the competing 1,2-nucleophilic additions of the more basic center at the carbonyl group, and by the formation of a five-membered ring as a result of exotrigonal cyclization. The exclusive formation of thiazoles **4g-i** in the reactions of acid **1,** the corresponding arylglyoxal hydrates **2b**,**e**,**g**, and *N*-arylthioureas **3b-d** point in favor of such a hypothesis, which may be explained by the decrease of the nucleophilicity of the nitrogen atoms in *N*-arylthioureas [13], and as a result the lack of initial attack at the carbonyl group.



2a, **5a** Ar = Ph, **2b**, **4b**,**i**, **5b** Ar = 4-MeC_6H_4, **2c**, **4c**, **5c** Ar = 4-MeSC_6H_4, **2d**, **4d**, **5d** Ar = 4-ClC_6H_4, **2e**, **4e**,**h**, **5e** Ar = 4-BrC_6H_4, **2f**, **4f**, **5f** Ar = 4-O_2NC_6H_4, **2g**, **4g** Ar = 4-MeOC_6H_4, **3a**, **4b–f** R = Me, **3b**, **4g** R = Ph, **3c**, **4h** R = 2-MeC_6H_4, **3d**, **4i** R = 2-BrC_6H_4

The structures of the obtained compounds were established using physicochemical methods. The ^{1}H NMR spectra of compounds **4b-f** were similar to the spectra of previously described thiazoles [11]. They are characterized by multiplets for the aromatic protons, by the nine-proton singlet of the superimposed methyl groups of the thiourea fragment and the methyl groups of the dimethylbarbituric acid fragment, and also by the broadened singlets of the exchanged NH protons (9.0-9.2 ppm) and of the 6-OH protons of the pyrimidine ring (12.1-12.5 ppm). The special feature of the ^{1}H NMR spectra of thiazoles **4g-i** was absence of the 6-hydroxyl group signal as a result of the rapid exchange with water present in DMSO-d_6. An analogous picture was also observed for the previously described thiazoles containing a carbamoyl fragment at the ring position 2 [11].

In the ^{1}H NMR spectra of compounds **5a-f**, the *N*-methyl proton of the thiourea fragment was shifted towards lower field ($\delta \approx 3.4$ ppm), the six-proton singlet of the pyrimidine ring methyl groups was displayed at 3.1 ppm, and an exchanged broadened signal of the hydroxyl group proton was present at 12.0-12.2 ppm.

We note that the ^{13}C NMR spectra of compounds **5** and the corresponding thiazoles **4** differed insignificantly. The carbon spectra of compounds **4b**,**c**,**e** were revised by a DEPT-135 experiment which

enabled the quaternary carbon atoms to be excluded from consideration and the correct assignment of the remaining signals to be carried out.

The mass spectra of compounds **4**, **5b**,**d** have the same values for the molecular ion peaks. A special feature of the fragmentation of compounds **5a-f** was the ejection of ionized methanimine molecule $[M\text{-}CH_2NH]^+$, the cleavage of an isothiocyanate radical $[M\text{-}CNS]^+$, and also the formation of a fragment ion $[M\text{-}C_2H_4N_2S]^+$. The main direction of fragmentation of thiazoles **4b**,**d** was the destruction of the thiazole ring with ejection of ionized *N*-methylcyanamide, molecule $[M\text{-}MeNHCN]^+$.

The obtained results enabled us to identify compounds **5a-f** as 5-aryl-2-mercapto-1-methylimidazoles containing a residue of 1,3-DMBA at the position 4. The presence of an aryl residue at position 5 of the ring was confirmed by NOE (Nuclear Overhauser Effect) experiment, carried out for the imidazole **5d**. Saturation of the *N*-methyl proton signal of the thiourea fragment led to a response from the *ortho* protons of the chlorophenyl radical, which indicated their spatial proximity.

Finally, the structures of compounds **5a-f** were confirmed by an X-ray structural investigation of one such representative **5c** (Fig. 1). In the crystalline phase, the compound assumed the thione form, stabilized by an intramolecular hydrogen bond N(3)–H(3N)···O(1) (H···O was 2.03 Å, N–H···O 124°). Bond C(3)–C(7) 1.385(3) Å was extended relative to the mean value of 1.340 Å [14]. Bonds C(7)–N(3) 1.340(3) Å and C(3)–C(4) 1.443(3) Å were shortened (mean values 1.355 and 1.509 Å, respectively) as a result of conjugation between the C(4)–O(1) carbonyl group and the thioamide group. The five-membered ring was in a "flattened envelope" conformation. The C(8) atom deviated from the plane of the remaining imidazole ring atoms by 0.14 Å.

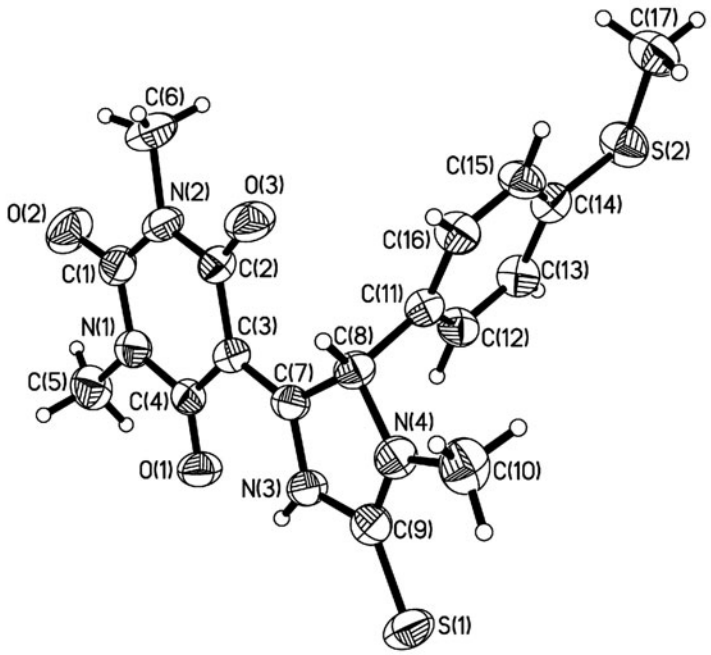


Fig. 1. Molecular structure of compound **5c** with atoms represented by thermal vibration ellipsoids of 50% probability.

Imidazoles **5a-f** in DMSO-d_6 solution existed predominantly in the thiol form. The fraction of the thione form of compounds **5a-e** did not exceed 25%, as indicated by the integral intensity of the imidazole ring H-5 proton signal at 5.04-5.08 ppm (data not given in Experimental), and also by the absence of thioamide group signal at the 170-180 ppm region of the ^{13}C NMR spectra. The thione form was not detected in the ^{1}H NMR spectra of compound **5f**. It should be emphasized that both tautomeric forms of compound **5** were additionally stabilized by intramolecular hydrogen bonds.

We note that the synthesized imidazolones **5a-f** contain a structural fragment of the medication timazol (1-methylimidazoline-2-thione), which is a synthetic antithyroid (thyreostatic) agent and is used in medicinal practice for a specific treatment of thyroid gland hyperactivity [15]. Consequently, a further investigation of the pharmacological activity of the obtained imidazoles is justified.

In the investigation of three-component condensation, a competition has been discovered between the different nucleophilic centers of *N*-methylthiourea. This led to the formation of both thiazole and imidazole rings. In the case of *N*-arylthioureas the interaction proceeded regioselectively with the formation of 2-aminofunctionalized thiazoles.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Varian VX-200 Mercury instrument (200 MHz), and the ^{13}C NMR spectra on a Bruker AM-400 spectrometer (100 MHz) in DMSO-d_6, internal standard was TMS. The mass spectra were recorded on a Hewlett-Packard LC/MSD 1100 instrument, ionization method EI (70 eV). Elemental analysis was carried out on a LECO CHNS-900 instrument. Melting points were determined on a Kofler hot stage apparatus. A check on the reaction progress and purity of the obtained compounds was effected by TLC on Silufol UV-254 plates in the systems: PhMe–EtOAc, 1:1, CH_2Cl_2–2-PrOH, 10:1, visualization with iodine vapor.

5-(4-Aryl-2-methylaminothiazol-5-yl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-diones 4b-f and 5-(5-Aryl-1-methyl-2-sulfanyl-1*H*-imidazol-4-yl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-diones 5a-f (General Method). A mixture of equimolar quantities (about 1.0 mmol) of 1,3-DMBA **1**, arylglyoxal hydrates **2a-f**, and thiourea **3a** in EtOH (10 ml) was refluxed for 5-30 min until the start of precipitation of solid compounds **4b-f** (when using arylglyoxal hydrate **2a**, compound **4a** was not formed). After rapid cooling to room temperature, compounds **4b-f** were filtered off and washed on the filter with EtOH. Compounds **5a-f** precipitated as solids from the filtrate after 1-3 h at room temperature and were purified by recrystallization from EtOH.

5-(4-Aryl-2-arylaminothiazol-5-yl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-diones 4g-i were synthesized analogously to compounds **4b-f** from 1,3-DMBA **1**, arylglyoxal hydrates **2b**,**e**,**g** and thioureas **3b-d**. Since compounds **5** were not formed in this case, the reaction mixture was maintained at room temperature for 1 day, and products **4g-i** were filtered off.

6-Hydroxy-1,3-dimethyl-5-[2-methylamino-4-(4-methylphenyl)thiazol-5-yl]pyrimidine-2,4(1*H*,3*H*)-dione (4b). Yield 0.11 g (30%). Cream-colored powder. Mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.27 (3H, s, ArC<u>H</u>$_3$); 3.01 (9H, s, 3NC<u></u>H$_3$); 7.14 (2H, d, *J* = 8.1, H-3,5 Ar); 7.31 (2H, d, *J* = 8.1, H-2,6 Ar); 9.02 (1H, s, NH); 12.40 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 20.8 (Ar<u>C</u>H$_3$); 28.4 (2NCH$_3$); 32.1 (NHCH$_3$); 79.9 (C-5'); 120.4 (C-5); 128.0, 129.5, 130.8, 131.5 (C Ar); 137.7 (C-4); 150.0 (C-2); 161.8 (2C=O); 168.2 (COH). Mass spectrum, *m/z* (I_{rel}, %): 358 $[M]^+$ (100), 332 (5), 302 $[M\text{-}MeNHCN]^+$ (9), 270 (7), 265 (15), 115 (8), 114 (5), 91 (10), 56 (10). Found, %: C 56.88; H 5.12; N 15.52. $C_{17}H_{18}N_4O_3S$. Calculated, %: C 56.97; H 5.06; N 15.63.

6-Hydroxy-1,3-dimethyl-5-[2-methylamino-4-(4-methylsulfanylphenyl)thiazol-5-yl]pyrimidine-2,4(1*H*,3*H*)-dione (4c). Yield 0.12 g (30%). Cream-colored powder. Mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.53 (3H, s, SCH$_3$); 3.00 (9H, s, 3NCH$_3$); 7.21 (2H, d, *J* = 8.0, H-3,5 Ar); 7.39 (2H, d, *J* = 8.0, H-2,6 Ar); 9.10 (1H, s, NH); 12.48 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 14.1 (SCH$_3$); 27.9 (2NCH$_3$); 32.4 (NHCH$_3$); 80.0 (C-5'); 122.0 (C-5); 128.9, 125.2, 129.8, 136.3 (C Ar); 138.7 (C-4); 151.1 (C-2); 160.9 (2C=O); 167.8 (COH). Found, %: C 52.35; H 4.59; N 14.42; S 16.56. $C_{17}H_{18}N_4O_3S_2$. Calculated, %: C 52.29; H 4.65; N 14.35; S 16.42.

5-[4-(4-Chlorophenyl)-2-methylaminothiazol-5-yl]-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (4d). Yield 0.13 g (35%). Cream-colored powder. Mp 290-292°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.07 (9H, s, 3NCH$_3$); 7.39 (2H, d, *J* = 8.8, H-3,5 Ar); 7.45 (2H, d, *J* = 8.8, H-2,6 Ar); 9.12 (1H, s, NH); 12.11 (1H, s, OH).

^{13}C NMR spectrum, δ, ppm: 27.8 ($2NCH_3$); 32.1 ($NHCH_3$); 78.2 (C-5'); 120.4 (C-5); 129.2, 130.1, 130.8, 131.1 (C Ar); 135.5 (C-4); 153.0 (C-2); 161.8 (2C=O); 168.2 (COH). Mass spectrum (for ^{35}Cl isotope), *m/z* (I_{rel}, %): 378 $[M]^+$ (100), 322 $[M\text{-}MeNHCN]^+$ (7), 264 (25), 229 (30), 201 (15), 180 (10), 137 (12), 100 (100), 76 (11). Found, %: C 50.80; H 4.04; N 14.71. $C_{16}H_{15}ClN_4O_3S$. Calculated, %: C 50.73; H 3.99; N 14.79.

5-[4-(4-Bromophenyl)-2-methylaminothiazol-5-yl]-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (4e). Yield 0.12 g (29%). Finely crystalline cream-colored powder. Mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.02 (9H, s, $3NCH_3$); 7.41 (2H, d, *J* = 8.6, H-3,5 Ar); 7.51 (2H, d, *J* = 8.6, H-2,6 Ar); 9.07 (1H, s, NH); 12.15 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 27.9 ($2NCH_3$); 32.5 ($NHCH_3$); 78.8 (C-5'); 121.8 (C-5); 127.9, 131.0, 131.6, 132.2 (C Ar); 136.7 (C-4); 151.1 (C-2); 160.9 (2C=O); 168.8 (COH). Found, %: C 45.31; H 3.64; N 13.33. $C_{16}H_{15}BrN_4O_3S$. Calculated, %: C 45.40; H 3.57; N 13.24.

6-Hydroxy-1,3-dimethyl-5-[2-methylamino-4-(4-nitrophenyl)thiazol-5-yl]pyrimidine-2,4(1H,3*H*)-dione (4f). Yield 0.12 g (31%). Pale-yellow crystals. Mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.01 (9H, s, $3NCH_3$); 7.62 (2H, d, *J* = 8.6, H-2,6 Ar); 8.17 (2H, d, *J* = 8.6, H-3,5 Ar); 9.20 (1H, s, NH); 12.15 (1H, s, OH). Found, %: C 49.40; H 3.94; N 18.04. $C_{16}H_{15}N_5O_5S$. Calculated, %: C 49.35; H 3.88; N 17.99.

6-Hydroxy-1,3-dimethyl-5-[4-(4-methoxyphenyl)-2-phenylaminothiazol-5-yl]pyrimidine-2,4(1*H*,3*H*)-dione (4g). Yield 0.36 g (82%). White powder. Mp 281-282°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.13 (6H, s, $2NCH_3$); 3.61 (3H, s, OCH_3); 6.88 (2H, d, *J* = 8.0, H-3,5 Ar); 6.98 (1H, t, *J* = 7.2, H-4 Ph); 7.30-7.37 (2H, m, H-3,5 Ph); 7.53-7.63 (4H, m, H-2,6 Ph, H-2,6 Ar); 10.29 (1H, s, NH). Mass spectrum, *m/z* (I_{rel}, %): 436 $[M]^+$ (100), 323 (10), 322 (30), 279 (5), 202 (10), 176 (12), 194 (10), 135 (12), 77 (70), 76 (13). Found, %: C 60.38; H 4.69; N 12.77. $C_{22}H_{20}N_4O_4S$. Calculated, %: C 60.54; H 4.62; N 12.84.

5-[4-(4-Bromophenyl)-2-(2-methylphenyl)aminothiazol-5-yl]-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (4h). Yield 0.31 g (62%). White powder. Mp 263-264°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.28 (3H, s, $ArC\underline{H}_3$); 3.09 (6H, s, $2NCH_3$); 7.22-7.30 (3H, m, H Ar); 7.45-7.65 (5H, m, H Ar); 9.92 (1H, s, NH). Mass spectrum (for ^{79}Br isotope), *m/z* (I_{rel}, %): 498 $[M]^+$ (100), 350 (50), 311 (10), 227 (20), 160 (25), 133 (80), 132 (50), 131 (30), 104 (18), 76 (5). Found, %: C 52.72; H 3.70; N 11.10. $C_{22}H_{19}BrN_4O_3S$. Calculated, %: C 52.91; H 3.83; N 11.22.

5-[2-(2-Bromophenyl)amino-4-(4-methylphenyl)thiazol-5-yl]-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (4i). Yield 0.34 g (68%). White powder. Mp 260-262°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.26 (3H, s, $ArC\underline{H}_3$); 3.09 (6H, s, $2NCH_3$); 7.08-7.12 (3H, m, H Ar); 7.34-7.44 (3H, m, H Ar); 7.70 (1H, d, *J* = 7.6, H Ar); 7.90 (1H, d, *J* = 7.6, H Ar); 9.95 (1H, s, NH). Mass spectrum (for ^{79}Br isotope), *m/z* (I_{rel} %): 498 $[M]^+$ (35), 420 (25), 419 (100), 305 (35), 270 (5), 153 (12), 115 (15), 91 (12). Found, %: C 52.80; H 3.69; N 11.27. $C_{22}H_{19}BrN_4O_3S$. Calculated, %: C 52.91; H 3.83; N 11.22.

6-Hydroxy-5-(1-methyl-5-phenyl-2-sulfanyl-1*H*-imidazol-4-yl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (5a). Yield 0.20 g (58%). Pale-sandy crystals. Mp 228-229°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.07 (6H, s, $2NCH_3$); 3.41 (3H, s, 1'-CH_3); 7.27-7.33 (5H, m, H Ph); 12.32 (1H, s, OH). Mass spectrum, *m/z* (I_{rel}, %): 344 $[M]^+$ (100), 315 $[M\text{-}CH_2NH]^+$ (5), 286 $[M\text{-}CNS]^+$ (7), 256 $[M\text{-}C_2H_4N_2S]^+$ (8), 215 (5), 118 (5), 91 (6), 58 (5). Found, %: C 55.60; H 4.59; N 16.37. $C_{16}H_{16}N_4O_3S$. Calculated, %: C 55.80; H 4.68; N 16.27.

6-Hydroxy-5-[2-mercapto-1-methyl-5-(4-methylphenyl)-2-sulfanyl-1*H*-imidazol-4-yl]-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (5b). Yield 0.19 g (53%). Pale-yellow crystals. Mp 208-210°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.28 (3H, s, $ArC\underline{H}_3$); 3.11 (6H, s, $2NCH_3$); 3.35 (3H, s, 1'-CH_3); 7.20-7.32 (4H, m, H Ar); 12.05 (1H, s, OH). Mass spectrum, *m/*z (I_{rel}, %): 358 $[M]^+$ (100), 329 $[M\text{-}CH_2NH]^+$ (3), 300 $[M\text{-}CNS]^+$ (10), 270 $[M\text{-}C_2H_4N_2S]^+$ (10), 156 (8), 116 (15), 91 (20), 88 (3), 58 (18). Found, %: C 56.85; H 5.12; N 15.70. $C_{17}H_{18}N_4O_3S$. Calculated, %: C 56.97; H 5.06; N 15.63.

6-Hydroxy-5-[2-mercapto-1-methyl-5-(4-methylsulfanylphenyl)-2-sulfanyl-1*H*-imidazol-4-yl]-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (5c). Yield 0.16 g (40%). Pale-yellow crystals. Mp 196-198°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.47 (3H, s, SCH_3); 3.12 (6H, s, $2NCH_3$); 3.37 (3H, s, 1'-CH_3); 7.22-7.37 (4H, m, H Ar); 12.04 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 14.8 (SCH_3); 28.8 ($2NCH_3$); 33.9 (1'-CH_3); 80.5 (C-5'); 116.7 (C-5); 126.2, 126.6, 130.1, 139.3 (C Ar); 130.8 (C-4); 151.6 (C-2); 161.6 (2C=O); 168.7 (COH).

Mass spectrum, *m/z* (I_{rel}, %): 390 $[M]^+$ (100), 361 $[M-CH_2NH]^+$ (5), 332 $[M-CNS]^+$ (10), 302 $[M-C_2H_4N_2S]^+$ (15), 149 (20), 110 (5), 88 (5), 58 (20). Found, %: C 52.20; 4.69; N 14.27. $C_{17}H_{18}N_4O_3S_2$. Calculated, %: C 52.29; 4.65; N 14.35.

5-[5-(4-Chlorophenyl)-1-methyl-2-sulfanyl-1*H*-imidazol-4-yl]-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (5d). Yield 0.16 g (42%). Pale-yellow crystals. Mp 200-201°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.11 (6H, s, $2NCH_3$); 3.43 (3H, s, 1'-CH_3); 7.32 (2H, d, *J* = 7.8, H-3,5 Ar); 7.43 (2H, d, *J* = 7.8, H-2,6 Ar); 12.05 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 28.8 ($2NCH_3$); 33.4 (1'-CH_3); 79.0 (C-5'); 116.0 (C-5); 129.0, 130.9, 131.1, 131.5, 132.5 (C-4, C Ar); 151.0 (C-2); 161.8 (2C=O); 169.0 (COH). Mass spectrum (for ^{35}Cl isotope), *m/z* (I_{rel}, %): 378 $[M]^+$ (100), 349 $[M-CH_2NH]^+$ (5), 320 $[M-CNS]^+$ (10), 290 $[M-C_2H_4N_2S]^+$ (10), 156 (8), 111 (15), 88 (4), 58 (12). Found, %: C 50.65; H 4.07; N 14.72. $C_{16}H_{15}ClN_4O_3S$. Calculated, %: C 50.73; H 3.99; N 14.79.

5-[5-(4-Bromophenyl)-1-methyl-2-sulfanyl-1*H*-imidazol-4-yl]-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (5e). Yield 0.17 g (40%). Pale-yellow crystals. Mp 192-193°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.10 (6H, s, $2NCH_3$); 3.38 (3H, s, 1'-CH_3); 7.29 (2H, d, *J* = 8.2, H-3,5 Ar); 7.58 (2H, d, *J* = 8.2, H-2,6 Ar); 12.05 (1H, s, OH). Mass spectrum (for ^{79}Br isotope), *m/z* (I_{rel}, %): 422 $[M]^+$ (100), 393 $[M-CH_2NH]^+$ (6), 364 $[M-CNS]^+$ (11), 334 $[M-C_2H_4N_2S]^+$ (9), 156 (8), 155 (13), 88 (4), 58 (12). Found, %: C 45.30; H 3.45; N 13.16. $C_{16}H_{15}BrN_4O_3S$. Calculated, %: C 45.40; H 3.57; N 13.24.

6-Hydroxy-1,3-dimethyl-5-[1-methyl-5-(4-nitrophenyl)-2-sulfanyl-1*H*-imidazol-5-yl]pyrimidine-2,4(1*H*,3*H*)-dione (5f). Yield 0.14 g (37%). Yellow crystals. Mp 200-202°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.01 (6H, s, $2NCH_3$); 3.43 (3H, s, 1'-CH_3); 7.58 (2H, d, *J* = 8.6, H-2,6 Ar); 8.17 (2H, d, *J* = 8.6, H-3,5 Ar); 12.20 (1H, s, OH). Mass spectrum, *m/z* (I_{rel}, %): 389 $[M]^+$ (100), 360 $[M-CH_2NH]^+$ (8), 331 $[M-CNS]^+$ (10), 301 $[M-C_2H_4N_2S]^+$ (14), 122 (20), 110 (10), 88 (8), 58 (20). Found, %: C 49.20; H 3.84; N 17.84. $C_{16}H_{15}N_5O_5S$. Calculated, %: C 49.35; H 3.88; N 17.99.

X-Ray Structural Investigation of Compound 5c. Crystals of compound **5c** were monoclinic, $C_{17}H_{18}N_4O_3S_2$, at 20°C: *a* 5.9678(5), *b* 15.4918(11), *c* 19.5066(14) Å; β 97.080(7)°; *V* 1789.7(2) Å^3; *M* 390.47; *Z* 4; space group $P2_1/c$, d_{calc} 1.449 g/cm^3, μ(MoKα) 0.323 mm^{-1}, *F*(000) 816. The parameters of the unit cell and the intensities of 10916 reflections (5208 independent, R_{int} 0.049) were measured on an Xcalibur-3 diffractometer (MoKα radiation, CCD detector, graphite monochromator, ω-scanning, $2\theta_{max}$ 60°). The structure was solved by the direct method with the SHELXTL software package [16]. The positions of hydrogen atoms were determined by an electron density difference synthesis and were refined isotropically, with the exception of the methyl group hydrogen atoms which were refined with a "rider" model with U_{iso} = 1.5 U_{eq}. The structure was refined on F^2 with a full-matrix least-squares method in an anisotropic approximation for the non-hydrogen atoms to wR_2 0.105 for 5208 reflections (R_1 0.056 on 2556 reflections with $F>4\sigma(F)$, *S* 0.89). All the crystallographic data have been deposited at the Cambridge Crystallographic Data Center (deposit CCDC 874086).

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