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2-ACYLTHIOACETAMIDES IN THE BIGINELLI REACTION

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We have demonstrated for the first time a Biginelli reaction of 2-acylthioacetamides with aromatic aldehydes and ureas or thioureas, leading to N-Ar[1]-4-Ar[2]-6-R[1]-1-R[2]-2-oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carbothioamides. The regioselectivity of this process matched the concept of hard/soft Lewis acids and bases. It was established that nitrous acid or other oxidants converted the synthesized compounds into N-Ar[1]-4-Ar[2]-6-R[1]-1-R[2]-2-oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carboxamides, and not the expected 4-Ar[2]-6-R[1]-1-R[2]-5-(1,3-benzothiazol-2-yl)-1,2,3,4-tetrahydropyrimidin-2-ones(thiones).

Keywords: 2-acylthioacetamides, aromatic aldehydes, 2-oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carbothioamides, thioureas, ureas, three-component heterocyclization.

2-Acylthioacetamides are known as polyfunctional reagents useful as starting materials for the synthesis of various nitrogen- or sulfur-containing compounds [1]. Nevertheless, multicomponent reactions of 2-acylthioacetamides remain little known. Some examples are known of one-pot condensation between 2-acylthioacetamide and nitriles or aldehydes with activated methylene groups [2, 3], or with Meldrum's acid and aldehydes [4], leading to 1,4-dihydropyridines or 1,5-dihydro-4*H*-thiochromeno[2,3-*b*]pyridin-5-ones, respectively. However, the heterocyclization of 2-acylthioacetamides with aldehydes and ureas/thioureas (the Biginelli reaction) so far has not been investigated.

The Biginelli reaction is a general method for the synthesis of 3,4-dihydropyrimidin-2-ones with antiviral, antitumor, antihypertensive, antimalarial, and antituberculosis properties [5, 6]. This work is aimed at introducing 2-acylthioacetamides in the Biginelli reaction and investigating the regioselectivity in such reactions.

We established that the 2-acylthioacetamides **1a-d** reacted with the aldehydes **2a-f** and the ureas/thioureas **3a-c** in the presence of boric acid as a catalyst. The synthesis was performed in acetic acid at 100-110°C. The reaction did not proceed in the absence of boric acid. Using propionic acid instead of acetic acid and increasing the reaction mixture temperature to 130-135°C had essentially no impact on the product yield.

The reaction was selective and produced *N*-Ar[1]-4-Ar[2]-6-R[1]-1-R[2]-2-oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carbothioamides **4a-m** in 53-72% yields. The potential reaction products **5a-m** were not observed. Electron-donating substituents in the phenyl rings of the starting materials slightly improved the yields of the

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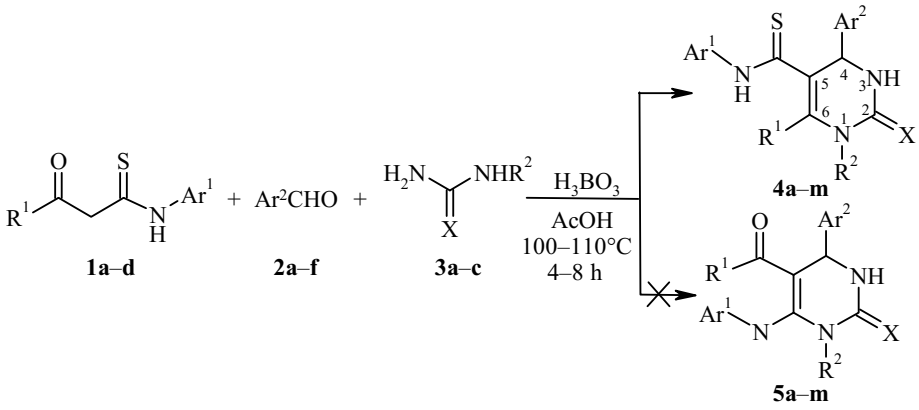
expected products (70-72%), compareed to electron-withdrawing substituents (51-58%). The reaction with unsymmetrical *N*-methylthiourea (**3c**) was selective and produced 1-methyl-1,2,3,4-tetrahydropyrimidine-2-thione **4k**.

2-Acylthioacetamides played the role of 1,2-reactive bifunctional reagents in this [2+1+3]-cyclocondensation reaction.

It should be pointed out that the heterocyclization reactions occurred at the carbonyl group, not the thiocarbonyl group of the starting 2-acylthioacetamides **1a-d**. Since the carbonyl group has a lower polarizability and smaller size than the thiocarbonyl group, and amino group is a hard nucleophile, the regioselectivity of this reaction was in agreement with the hard-soft acid-base theory.

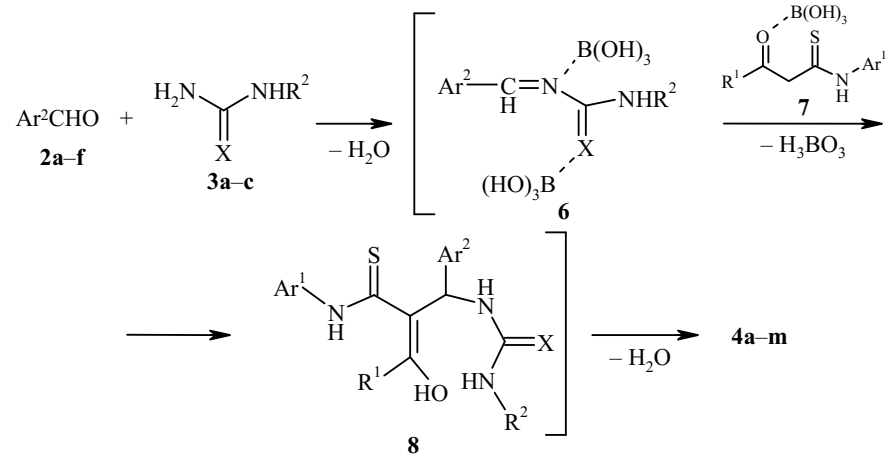


1a–d **2a–f** **3a–c** **4a–m** **5a–m**

1a,**d**, **4a**,**d**–**m**, **5a**,**d**–**m** Ar^1 = Ph; **1b**, **4b**, **5b** Ar^1 = 4-$MeOC_6H_4$; **1c**, **4c**, **5c** Ar^1 = 4-$O_2NC_6H_4$;
2a, **4a**–**c**,**h**,**i** , **5a**–**c**,**h**,**i** Ar^2 = Ph; **2b**, **4e**,**k**,**l**, **5e**,**k**,**l** Ar^2 = 4-$MeOC_6H_4$;
2c, **4f**,**m**, **5f**,**m** Ar^2 = 3-$O_2NC_6H_4$; **2d**, **4d**, **5d** Ar^2 = 4-FC_6H_4; **2e**, **4j**, **5j** Ar^2 = 2-thienyl;
2f, **4g**, **5g** Ar^2 = 2-furyl; **1a**–**c**, **4a**–**g**,**i**–**m**, **5a**–**g**,**i**–**m** R^1 = Me; **1d**, **4h**, **5h** R^1 = Ph;
3a,**b**, **4a**–**j**,**l**,**m**, **5a**–**j**,**l**,**m** R^2 = H; **3c**, **4k**, **5k** R^2 = Me
3a, **4**, **5 a**–**h** X = O; **3b**,**c**, **4**, **5 i**–**m** X = S

According to review articles [5, 6], a Biginelli reaction in acidic medium probably involves azomethine intermediates, formed from aldehyde and urea/thiourea. It has been proposed [7] that boric acid with azomethine and the 2-acylthioacetamide **1a-d** formed reactive adducts **6** and **7**, having highly electrophilic carbon atoms in the C=N and C=O groups, respectively.

The reaction of the adducts **6** and **7** apparently led to the intermediate **8**, which underwent intra-molecular cyclization accompanied by elimination of water and formation of the tetrahydropyrimidin-2-ones(thiones) **4a-m**.



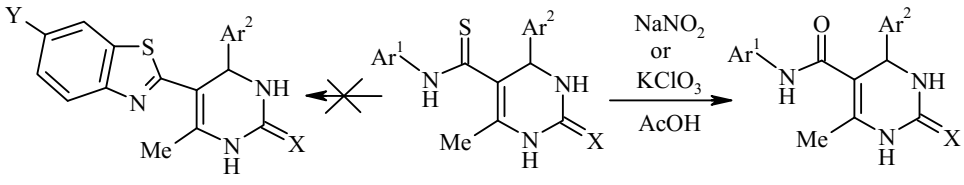
2a–f **3a–c** **6** **8** **4a–m**

We have previously demonstrated that interaction of 2-acylthioacetamides with nitrous acid induced a cyclization of the *N*-arylthioamide moiety to a benzothiazole [8]. A further research suggested that the 1,2,3,4-tetrahydropyrimidin-2-ones **4** could be oxidized to the 5-(benzothiazol-2-yl)-1,2,3,4-tetrahydropyrimidin-2-ones **9**.

However, data from the literature indicated that oxidation reactions of *N*-arylthioamides may proceed as heterocyclizations to 1,2,4-thiadiazoles [9] and benzothiazoles [10-12], and/or as desulfurization and conversion to amides [11-15]. The oxidants were nitrous acid [8, 9, 13], palladium chloride with atmospheric oxygen [10], phenyliodonium bis(trifluoroacetate) [11, 12], *N*-nitrosopiperidine and *N*-methyl-*N*-nitrosoaniline [14], ceric ammonium nitrate [12], and silver carbonate [15]. Other researchers have previously suggested that such reactions occur through a nitrosonium cation intermediate [13, 14], and by a radical cation mechanism [11, 12].

We should note that even with the same reagent (nitrous acid [8, 9, 13], phenyliodonium bis(trifluoroacetate) [11, 12]) the reactions can yield not only the heterocyclization products, but also products from the thioamide group oxidation to an amide group. The substrate structure is likely a major factor affecting these reactions.

We used the $NaNO_2$/AcOH and $KClO_3$/AcOH systems as oxidants. However, the attempt to convert the *N*-arylthioamide group of compounds **4a**,**b**,**d**,**e**,**i** into a benzothiazole system failed to close the ring and resulted in oxidation of the thioamide to an amide group. The reaction products in all cases were *N*-aryl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides **10a**-**e** in 40-48% yields.



9a–e **4a**,**b**,**d**,**e**,**i** **10a–e**

4a,**d**,**e**,**i**, **10a**,**b**,**d**,**e** Ar^1 = Ph; **4b**, **10c** Ar^1 = 4-$MeOC_6H_4$;
4a,**b**,**i**, **9a**,**c**,**e**, **10a**,**c**,**e** Ar^2 = Ph; **4**, **9d**, **10d** Ar^2 = 4-FC_6H_4; **4e**, **9b**, **10b** Ar^2 = 4-$MeOC_6H_4$;
4a,**b**,**d**,**e**, **9a**–**d**, **10a**–**d** X = O; **4i**, **9e**, **10e** X = S; **9a**,**b**,**d**,**e** Y = H; **9c** Y = MeO

The structures of the synthesized compounds were confirmed by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy, and the composition was determined by elemental analysis.

The ^{1}H NMR spectra of compounds **4a**-**m**, **10a**-**e** exhibited signals of all the structural fragments that contained protons. The characteristic signals were those of the 6-methyl group protons (1.89-2.10 ppm), 4-CH protons (5.35-6.00 ppm), 1-NH (8.58-8.82 ppm for the tetrahydropyrimidin-2-ones **4a**-**h**, **10a**-**d** and 9.88-10.14 ppm for the tetrahydropyrimidine-2-thiones **4i**-**m**, **10e**), 3-NH (7.48-9.46 ppm), NHCS (10.57-11.46 ppm), and NHCO (9.35-9.67 ppm). The vicinal 3-NH and 4-CH proton signals were typically present as broad singlets, probably due to the rapid deuterium exchange at the nitrogen atom. The most informative ^{13}C NMR signals of compounds **4a**,**d**,**e**,**i**,**h** and **10a**,**e** were those of the carbonyl groups (NHCONH (152.5-163.1 ppm), NHCO (164.9-165.2 ppm)) and the thiocarbonyl groups (NHCS (194.7-195.4 ppm), NHCSNH (173.4-174.0 ppm)).

The IR spectra of the compounds **4a**-**m**, **10a**-**e** contained absorption bands of NH groups (3350-3200 cm^{-1}), aromatic CH (3100-2950 cm^{-1}), and carbonyl groups (1660-1690 cm^{-1}).

Compounds **10** were also obtained in 27-82% yields by the condensation of acetoacetanilides with aldehydes and ureas [16]. We should note that this reaction required forcing conditions when no catalysts were used: a mixture of the starting materials was fused at the temperature range from 120°C to 150°C. Our reported method presents an alternative, which may be used depending on the availability of the starting acetoacetanilides and 2-acylthioacetamides.

Thus, we have demonstrated for the first time a Biginelli reaction with 2-acylthioacetamides. It was established that the reaction occurred between the hard reaction centers according to the hard-soft acid-base

theory. *N*-Ar[1]-4-Ar[2]-6-R[1]-1-R[2]-2-oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carbothioamides were synthesized and characterized, and the structure was confirmed by spectroscopy. The attempts at oxidation of these compounds with $NaNO_2$/AcOH or $KClO_3$/AcOH systems resulted in desulfurization and produced the respective carboxamides.

EXPERIMENTAL

IR spectra of compounds were acquired on a Vertex 70 spectrometer in KBr pellets. ^1H and ^{13}C NMR spectra were acquired on a Varian GEMINI 2000 instrument (400 and 100 MHz, respectively) in DMSO-d_6, with TMS as internal standard. Elemental analysis was performed on a Carlo Erba elemental analyzer. The melting points were determined with a PTP-1 apparatus. The 2-acylthioacetamides **1a-d** were synthesized by a literature method [17].

Preparation of *N*-Ar[1]-4-Ar[2]-6-R[1]-1-R[2]-2-Oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carbothioamides 4a-m (General Method). A solution of 2-thioacetamide **1a-d** (1.0 mmol), aldehyde **2a-f** (1.0 mmol), urea or thiourea **3a-c** (1.0 mmol), and boric acid (0.2 mmol) in acetic acid (2-3 ml) was heated for 4-8 h at 100-110°C. A crystalline precipitate of the tetrahydropyrimidine **4a-m** formed upon cooling. In cases when there was no precipitation, the reaction mixture was poured into aqueous NaCl solution. The precipitate was filtered off, dried, and purified by crystallization.

6-Methyl-2-oxo-*N*,4-diphenyl-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4a). Yield 65%; mp 235-237°C (PhCN). IR spectrum, ν, cm^{-1}: 3200-2950, 1675 (C=O), 1495, 1445, 1365, 1305. ^1H NMR spectrum, δ, ppm: 1.91 (3H, s, CH_3); 5.72 (1H, br. s, 4-CH); 7.17-7.58 (11H, m, H Ph, 3-NH); 8.62 (1H, s, 1-NH); 11.06 (1H, s, NHCS). ^{13}C NMR spectrum, δ, ppm: 16.9 (CH_3); 57.8 (C-4); 113.4, 123.6, 125.9, 126.2, 127.1, 128.2, 128.3, 131.7 (C Ph); 139.2 (C-5); 143.7 (C-6); 152.5 (C=O); 195.2 (C=S). Found, %: C 66.90; H 5.27; N 12.69; S 10.15. $C_{18}H_{17}N_3OS$. Calculated, %: C 66.85; H 5.30; N 12.99; S 9.91.

***N*-(4-Methoxyphenyl)-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4b)**. Yield 70%; mp 179-182°C ($MeNO_2$). IR spectrum, ν, cm^{-1}: 3200, 3100, 2950, 1680 (C=O), 1513, 1436, 1372, 1299. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.90 (3H, s, CH_3); 3.73 (3H, s, 4-CH_3O); 5.71 (1H, br. s, 4-CH); 6.85 (2H, d, *J* = 8.1, H Ar); 7.23-7.41 (7H, m, H Ph, 3-NH); 7.47 (2H, d, *J* = 8.1, H Ar); 8.58 (1H, s, 1-NH); 10.94 (1H, s, NHCS). Found, %: C 64.61; H 5.55; N 12.18; S 9.36. $C_{19}H_{19}N_3O_2S$. Calculated, %: C 64.57; H 5.42; N 11.89; S 9.07.

6-Methyl-*N*-(4-nitrophenyl)-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4c). Yield 55%; mp 238-240°C (PhCN). IR spectrum, ν, cm^{-1}: 3345, 3230, 3090, 2930, 1690 (C=O), 1615, 1600, 1525, 1500, 1462, 1431. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.97 (3H, s, CH_3); 5.71 (1H, br. s, 4-CH); 7.25-7.35 (5H, m, H Ph); 7.56 (1H, s, 3-NH); 7.80 (2H, d, *J* = 8.4, H Ar); 8.20 (2H, d, *J* = 8.4, H Ar); 8.81 (1H, s, 1-NH); 11.40 (1H, s, NHCS). Found, %: C 58.74; H 4.27; N 14.97; 8.48. $C_{18}H_{16}N_4O_3S$. Calculated, %: C 58.68; H 4.38; N 15.21; S 8.70.

4-(4-Fluorophenyl)-6-methyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4d). Yield 64%; mp 162-165°C (EtOH). IR spectrum, ν, cm^{-1}: 3200, 3100, 2950, 1660 (C=O), 1510, 1446, 1365, 1307. ^1H NMR spectrum, δ, ppm: 1.93 (3H, s, CH_3); 5.70 (1H, br. s, 4-CH); 7.11-7.43 (8H, m, H Ar, 3-NH); 7.54-7.62 (2H, m, H Ar); 8.64 (1H, s, 1-NH); 11.06 (1H, s, NHCS). ^{13}C NMR spectrum, δ, ppm: 16.6 (CH_3); 57.2 (C-4); 113.3, 115.0, 115.3, 123.6, 126.0, 128.3, 128.5, 132.0 (C Ar); 139.6 (C-5); 152.4 (C-6); 162.4 (C=O); 195.2 (C=S). Found, %: C 63.44; H 4.87; N 12.04; S 9.25. $C_{18}H_{16}FN_3OS$. Calculated, %: C 63.32; H 4.72; N 12.31; S 9.39.

4-(4-Methoxyphenyl)-6-methyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4e). Yield 72%; mp 184-185°C ($MeNO_2$). IR spectrum, ν, cm^{-1}: 3200, 3100, 2950, 1660 (C=O), 1610, 1555, 1510, 1445. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.91 (3H, s, CH_3); 5.66 (1H, br. s, 4-CH); 6.88 (2H, d, *J* = 8.2, H Ar); 7.23–7.40 (6H, m, H Ph, 3-NH); 7.59 (2H, d, *J* = 8.2, H Ar); 8.60 (1H, s, 1-NH); 11.06 (1H, s, NHCS).

^{13}C NMR spectrum, δ, ppm: 16.7 (CH_3); 54.9 (OCH_3); 57.3 (C-4); 113.3, 123.5, 123.7, 125.7, 127.5, 128.4, 131.6, 135.8 (C Ar); 139.2 (C-5); 152.4 (C-6); 158.0 (C=O); 195.4 (C=S). Found, %: C 64.63; H 5.58; N 12.13; S 8.80. $C_{19}H_{19}N_3O_2S$. Calculated, %: C 64.57; H 5.42; N 11.89; S 9.07.

6-Methyl-4-(3-nitrophenyl)-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4f). Yield 51%; mp 170-172°C (EtOH). IR spectrum, ν, cm^{-1}: 3350, 3200, 3100, 2950, 1670 (C=O), 1600, 1525, 1495, 1465. ^{1}H NMR spectrum, δ, ppm: 1.97 (3H, s, CH_3); 5.77 (1H, br. s, 4-CH); 7.17-7.22 (1H, m, H Ar); 7.31-7.36 (2H, m, H Ar); 7.51-7.83 (5H, m, H Ar, 3-NH); 8.12-8.17 (2H, m, H Ph); 8.82 (1H, s, 1-NH); 11.17 (1H, s, NHCS). Found, %: C 58.79; H 4.10; N 14.95; S 8.98. $C_{18}H_{16}N_4O_3S$. Calculated, %: C 58.68; H 4.38; N 15.21; S 8.70.

4-(2-Furyl)-6-methyl-2-oxo-*N*-phenylthiocarbamoyl-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4g). Yield 53%; mp 145-147°C (EtOH). IR spectrum, ν, cm^{-1}: 3200, 3100, 2955, 1670 (C=O), 1600, 1510, 1445, 1365. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.89 (3H, s, CH_3); 5.76 (1H, br. s, 4-CH); 6.25-6.29 (1H, m, H Ar); 6.37 (1H, d, *J* = 4.0, H Ar); 7.17-7.23 (1H, m, H Ph); 7.32-7.38 (2H, m, H Ar); 7.55-7.63 (4H, m, H Ar, 3-NH); 8.73 (1H, s, 1-NH); 11.20 (1H, s, NHCS). Found, %: C 61.57; H 5.09; N 13.22; S 10.46. $C_{16}H_{15}N_3O_2S$. Calculated, %: C 61.32; H 4.82; N 13.41; S 10.23.

2-Oxo-*N*,4,6-triphenyl-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4h). Yield 60%; mp 232-234°C (EtOH). IR spectrum, ν, cm^{-1}: 3350, 3300, 3100, 3000, 1680 (C=O), 1595, 1530, 1490, 1460, 1430. ^{1}H NMR spectrum, δ, ppm: 5.68 (1H, br. s, 4-CH); 7.05-7.63 (16H, m, H Ph, 3-NH); 8.78 (1H, s, 1-NH); 10.57 (1H, s, NHCS). ^{13}C NMR spectrum, δ, ppm: 58.2 (C-4); 123.4, 124.2, 125.6, 126.2, 126.5, 127.1, 127.5, 128.1, 128.6, 129.3, 130.0, 133.9 (C Ph); 143.1 (C-5); 152.8 (C-6); 163.1 (C=O); 195.0 (C=S). Found, %: C 71.73; H 5.23; N 11.04; S 8.12. $C_{23}H_{19}N_3OS$. Calculated, %: C 71.66; H 4.97; N 10.90; S 8.32.

6-Methyl-*N*,4-diphenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4i). Yield 70%; mp 251-253°C (PhCN). IR spectrum, ν, cm^{-1}: 3350, 3200–3000, 2950, 1560, 1490, 1440, 1345. ^{1}H NMR spectrum, δ, ppm: 1.97 (3H, s, CH_3); 5.71 (1H, br. s, 4-CH); 7.25-7.55 (8H, m, H Ph); 7.57-7.63 (2H, m, H Ph); 9.26 (1H, s, 3-NH); 9.91 (1H, s, 1-NH); 11.21 (1H, s, NHCS). ^{13}C NMR spectrum, δ, ppm: 16.3 (CH_3); 58.1 (C-4); 114.8, 123.4, 124.2, 125.9, 126.4, 126.9, 127.5, 128.9 (C Ph); 138.6 (C-5); 142.4 (C-6); 173.4 (C=S); 194.7 (C=S). Found, %: C 63.89; H 4.88; N 12.25; S 19.17. $C_{18}H_{17}N_3S_2$. Calculated, %: C 63.68; H 5.05; N 12.38; S 18.89.

6-Methyl-*N*-phenyl-4-(2-thienyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4j). Yield 68%; mp 220-222°C ($MeNO_2$). IR spectrum, ν, cm^{-1}: 3350, 3150, 2955, 1580, 1554, 1480, 1440. ^{1}H NMR spectrum, δ, ppm: 1.99 (3H, s, CH_3); 6.00 (1H, br. s, 4-CH); 6.95-6.99 (2H, m, H Ar); 7.18-7.23 (1H, m, H Ar); 7.35-7.45 (3H, m, H Ar); 7.60-7.64 (2H, m, H Ph); 9.46 (1H, s, 3-NH); 10.05 (1H, s, 1-NH); 11.32 (1H, s, NHCS). Found, %: C 55.38; H 4.55; N 12.26; S 28.12. $C_{16}H_{15}N_3S_3$. Calculated, %: C 55.62; H 4.38; N 12.16; S 27.84.

4-(4-Methoxyphenyl)-1,6-dimethyl-*N*-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4k). Yield 60%; mp 225-227°C ($MeNO_2$). IR spectrum. ν, cm^{-1}: 3180, 3030, 2900, 1605, 1535, 1509, 1450, 1370. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.10 (3H, s, CH_3); 3.47 (3H, s, NCH_3); 3.73 (3H, s, CH_3O); 5.56 (1H, d, *J* = 3.0, 4-CH); 6.88 (2H, d, *J* = 8.1, H Ar); 7.18-7.22 (3H, m, H Ph); 7.34-7.40 (2H, m, H Ph); 7.69 (2H, d, *J* = 8.1, H Ar); 9.37 (1H, d, *J* = 3.0, 3-NH); 11.46 (1H, s, NHCS). Found, %: C 62.90; H 5.34; N 11.23; S 16.49. $C_{20}H_{21}N_3OS_2$. Calculated, %: C 62.63; H 5.52; N 10.96; S 16.72.

4-(4-Methoxyphenyl)-6-methyl-N-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4l). Yield 73%; mp 170-172°C ($MeNO_2$). IR spectrum, ν, cm^{-1}: 3300, 3170, 2970, 1595, 1565, 1522, 1472, 1440. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.97 (3H, s, CH_3); 3.73 (3H, s, CH_3O); 5.64 (1H, br. s, 4-CH); 6.90 (2H, d, *J* = 8.3, H Ar); 7.18-7.25 (3H, m, H Ph); 7.30-7.37 (2H, m, H Ph); 7.60 (2H, d, *J* = 8.3, H Ar); 9.21 (1H, s, 3-NH); 9.88 (1H, s, 1-NH); 11.21 (1H, s, NHCS). Found, %: C 62.02; H 5.35; N 11.55; S 17.08. $C_{19}H_{19}N_3OS_2$. Calculated, %: C 61.76; H 5.18; N 11.37; S 17.36.

6-Methyl-4-(3-nitrophenyl)-*N*-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbothioamide (4m). Yield 58%; mp 185-188°C ($MeNO_2$). IR spectrum, ν, cm^{-1}: 3300, 3170, 2975, 1563, 1525, 1475, 1440, 1350. ^1H NMR spectrum, δ, ppm: 2.02 (3H, s, CH_3); 5.77 (1H, br. s, 4-CH); 7.18-7.22 (1H, m, H Ar); 7.32-7.37 (2H, m, H Ar); 7.57-7.72 (4H, m, H Ar); 8.10-8.17 (2H, m, H Ph); 9.44 (1H, s, 3-NH); 10.14 (1H, s, 1-NH); 11.33 (1H, s, NHCS). Found, %: C 56.50; H 4.38; N 14.73; S 16.94. $C_{18}H_{16}N_4O_2S_2$. Calculated, %: C 56.23; H 4.19; N 14.57; S 16.68.

Preparation of *N*-Ar^1-4-Ar^2-6-R^1-1-R^2-2-Oxo(thioxo)-1,2,3,4-tetrahydropyrimidine-5-carboxamides 10a-e (the method by nitrous acid oxidation). A suspension of tetrahydropyrimidine **4a**,**b**,**e**,**d**,**i** (1.0 mmol) and $NaNO_2$ (172.5 mg, 2.5 mmol) in acetic acid (3 ml) was stirred for 8 h at 5°C and poured into 50 ml of cold water. The precipitate of tetrahydropyrimidine **10a-e** was filtered off, dried, and purified by crystallization.

Preparation of *N*-Ar^1-4-Ar^2-6-R^1-1-R^2-2-Oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides 10a,c (the method by potassium chlorate oxidation). A solution of tetrahydropyrimidine **4a**,**b** (3 mmol) and $KClO_3$ (122.5 mg, 1.0 mmol) in acetic acid (5 ml) was stirred for 2 h at 30-40°C, cooled, and poured into 50 ml of cold water. The precipitate of tetrahydropyrimidine **10a**,**c** was filtered off, dried, and purified by crystallization.

6-Methyl-2-oxo-*N*,4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide (10a). Yield 48%; mp 240-243°C (PhCN) (246-248°C (EtOH) [16]). IR spectrum, ν, cm^{-1}: 3230, 3100, 2980, 1675 (C=O), 1620, 1595, 1520, 1440. ^1H NMR spectrum, δ, ppm: 2.04 (3H, s, CH_3); 5.40 (1H, br. s, 4-CH); 6.95-7.02 (1H, m, H Ph); 7.18-7.29 (7H, m, H Ph, 3-NH); 7.50 (3H, m, H Ph); 8.63 (1H, s, 1-NH); 9.47 (1H, s, NHCO). ^{13}C NMR spectrum, δ, ppm: 17.1 (Me); 55.0 (C-4); 105.4, 119.5, 123.0, 126.1, 127.2, 128.4, 128.6, 138.4 (C Ph); 139.1 (C-5); 144.2 (C-6); 152.6 (C-2); 165.2 (NHCO). Found, %: C 70.37; H 5.29; N 13.90. $C_{18}H_{17}N_3O_2$. Calculated, %: C 70.34; H 5.58; N 13.67.

4-(4-Methoxyphenyl)-6-methyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide (10b). Yield 45%; mp 222-223°C (PhCN). IR spectrum, ν, cm^{-1}: 3240, 3100, 2950, 1675 (C=O), 1625, 1600, 1510, 1450. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.04 (3H, s, CH_3); 3.71 (3H, s, CH_3O); 5.35 (1H, br. s, 4-CH); 6.86 (2H, d, *J* = 8.4, H Ar); 6.94-7.00 (2H, m, H Ph); 7.18-7.24 (3H, m, H Ph); 7.40 (1H, s, 3-NH); 7.53 (2H, d, *J* = 8.4, H Ar); 8.62 (1H, s, 1-NH); 9.45 (1H, s, NHCO). Found, %: C 67.40; H 5.39; N 12.72. $C_{19}H_{19}N_3O_3$. Calculated, %: C 67.64; H 5.68; N 12.46.

***N*-(4-Methoxyphenyl)-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide (10c)**. Yield 42%; mp 229-230°C (PhCN). IR spectrum, ν, cm^{-1}: 3250, 3100, 2950, 1680 (C=O), 1670 (C=O), 1620, 1515, 1465, 1410. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.03 (3H, s, CH_3); 3.69 (3H, s, CH_3O); 5.37 (1H, br. s, 4-CH); 6.78 (2H, d, *J* = 9.0, H Ar); 7.27-7.33 (5H, m, H Ph); 7.42 (2H, d, *J* = 9.0, H Ar); 7.48 (1H, s, 3-NH); 8.59 (1H, s, 1-NH); 9.35 (1H, s, NHCO). Found, %: C 67.90; H 5.95; N 12.45. $C_{19}H_{19}N_3O_3$. Calculated, %: C 67.64; H 5.68; N 12.46.

4-(4-Fluorophenyl)-6-methyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide (10d). Yield 41%; mp 190-193°C ($MeNO_2$). IR spectrum, ν, cm^{-1}: 3280, 3100, 2950, 1670 (C=O), 1630, 1600, 1505, 1440. ^1H NMR spectrum, δ, ppm: 2.05 (3H, s, CH_3); 5.39 (1H, br. s, 4-CH); 6.96-7.02 (1H, m, H Ph); 7.08-7.12 (2H, m, H Ar); 7.20-7.24 (2H, m, H Ar); 7.30-7.35 (2H, m, H Ar); 7.49-7.56 (3H, m, H Ar, 3-NH); 8.68 (1H, s, 1-NH); 9.49 (1H, s, NHCO). Found, %: C 66.47; H 5.24; N 13.05. $C_{18}H_{16}FN_3O_2$. Calculated, %: C 66.45; H 4.96; N 12.92.

6-Methyl-*N*,4-diphenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (10e). Yield 40%; mp 160-162°C ($MeNO_2$). IR spectrum, ν, cm^{-1}: 3270, 3100, 3000, 1675 (C=O), 1630, 1595, 1525, 1490, 1440. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.07 (3H, s, CH_3); 5.40 (1H, br. s, 4-CH); 6.93-7.03 (1H, m, H Ph); 7.25-7.35 (6H, m, H Ph); 7.50-7.54 (3H, m, H Ph); 9.35 (1H, s, 3-NH); 9.67 (1H, s, NHCO); 9.91 (1H, s, 1-NH). ^{13}C NMR spectrum, δ, ppm: 16.3 (CH_3); 55.2 (C-4); 120.2, 123.2, 124.0, 125.5, 126.6, 127.3, 129.0, 134.7 (C Ph); 139.3 (C-5); 142.9 (C-6); 164.9 (C=O); 174.0 (C=S). Found, %: C 66.93; H 5.40; N 13.90; S 10.07. $C_{18}H_{17}N_3OS$. Calculated, %: C 66.85; H 5.30; N 12.99; S 9.91.

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