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Synthesis and Properties of Derivatives of Pyrimidin-5-ylpropanoic Acids and 8-Aryl-4-methyl- and 4,6-Dimethyl-2-phenyl-5,6,7,8-tetrahydropyrido-[2,3-*d*]pyrimidin-7-ones

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Abstract—Proceeding from 3-(4-methyl-6-oxo-2-phenyl-1,6-dihydro-5-pyrimidinyl)propanoic and 2-methylpropanoic acids by successive reactions of chlorination, amination, and heterocyclization 4-amino-substituted pyrimidines were synthesized: 5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine derivatives and 4-methyl-2-phenyl-5,6-dihydrobenzo[4',5']imidazo[2',1':6,1]pyrido[2,3-*d*]pyrimidine which we had previously obtained by alternative method. Antibacterial properties of the synthesized compounds were studied.

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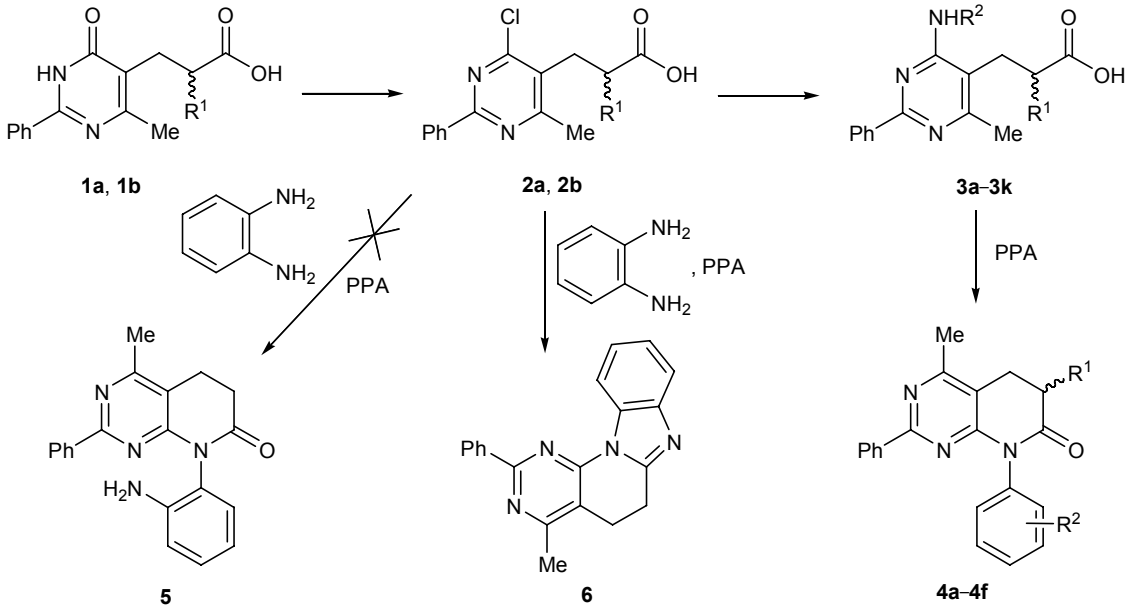
Heterocyclic compounds of the pyrido[2,3-*d*]pyrimidine series attract attention already for a long time as potential sources of new biologically active compounds of diverse effect [1, 2]. At the same time, 5,6,7,8-tetrahydro derivatives of this system are relatively few in number, and some of them show antienzymatic and antitumor activities [3, 4], therefore new compounds of this group may be of interest as pharmacologically active compounds.

In continuation of the studies on the synthesis and investigation of substituted pyrimidines and fused pyrimidines [5, 6], basing on the convenient initial compounds (pyrimidine-5-ylpropanoic acids **1a** and **1b** and their 4-chloroderivatives **2a** and **2b**) we carried out the synthesis of new 5,6,7,8-tetrahydropyrido[2,3-*d*]-pyrimidines and some derivatives of acid **1a** and studied their antibacterial properties.

The retrosynthetic analysis of the discussed heterocyclic system points to 4-amino-substituted pyrimidin-5-ylpropanoic acids **3a–3k** as key intermediate compounds, which convert into the target lactams **4a–4f** through the intermolecular nucleophilic cyclization.

The chlorination of initial acids **1a** [3] and **1b** [5] with $POCl_3$ with subsequent workup results in 4-chloro derivatives **2a** and **2b**. It is necessary to mention that unlike the quite stable substituted 4-chloropyrimidin-5-ylpropanoic acid **2a** the corresponding substituted 4-chloro-2-methylpropanoic acid **2b** at the attempt of purification is easily hydrolyzed into the initial 4-hydroxypyrimidine **1b**, therefore it should be brought into further reactions immediately after its preparation (see Experimental). By interaction of 4-chloroderivatives **2a** and **2b** with amines 4-aminopyrimidin-5-ylpropanoic acids **3a–3k** were synthesized, whose cyclodehydration in PPA afforded the corresponding 5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidines **4a–4f**. The attempt to synthesize 4-(2-aminoaniline) derivative of propanoic acid **1a** by the reaction of 4-chloropyrimidine **2a** with *o*-phenylenediamine in various solvents (ethanol, dioxane, butyl acetate, DMF) aiming at further cyclization into pyridopyrimidine **5**, unlike the similar synthesis with monoamines, was unsuccessful due to the formation of intractable mixture of compounds. At the same time boiling 4-chloropyrimidine **2a** and *o*-phenylenediamine in isobutyl alcohol followed by

Scheme 1.



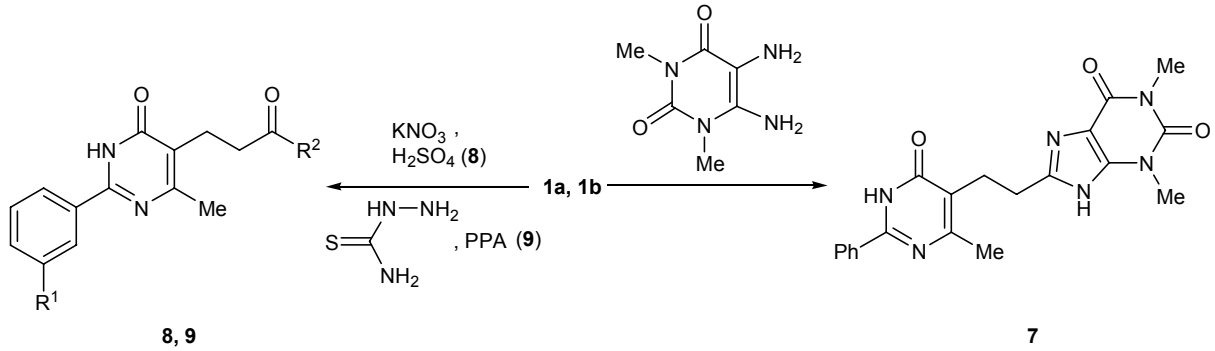
1, **2**, R^1 = H (**a**), Me (**b**); **3**, R^1 = H, R^2 = Ph (**a**), 2-MeC_6H_4 (**b**), 4-MeC_6H_4 (**c**), 4-$MeOC_6H_4$ (**d**), 4-$COOEtC_6H_4$ (**e**); R^1 = Me, R^2 = Ph (**f**), 2-MeC_6H_4 (**g**), 4-MeC_6H_4 (**h**), 2-$MeOC_6H_4$ (**i**), 4-$COOEtC_6H_4$ (**j**), H (**k**); **4**, R^1 = R^2 = H (**a**); R^1 = H, R^2 = 2-Me (**b**), 4-Me (**c**), 4-OMe (**d**); R^1 = Me, R^2 = H (**e**), 4-$COOC_2H_5$ (**f**).

heating the obtained adduct in PPA provided, instead of the expected substituted 5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidine **5**, 4-methyl-2-phenyl derivative of heterocyclic system 5,6-dihydrobenzo-[4',5']imidazo[2',1':6,1]pyrido[2,3-*d*]pyrimidine **6**, previously synthesized by a direct condensation of propanoic acid **1a** with *o*-phenylenediamine in PPA [5] (Scheme 1).

In the course of the study some transformations of acid **1a** were also performed. For instance, as a result of its condensation with 5,6-diamino-1,3-dimethyl-1,2,3,4-tetrahydro-2,4-pyrimidinedione in conditions of synthesis of compound **6** from acid **1a** and *o*-phenylenediamine [5] we isolated a purine–pyrimidine conjugate **7**. Acid **1a** was transformed into *meta*-nitroderivative **8** under the action of equimolar amount of KNO_3 in H_2SO_4 and into amide **9** by melting with thiosemicarbadize in PPA. Compounds with asymmetrical carbon atom were obtained as racemic isomer mixtures (Scheme 2).

Investigation of bioactivity of compounds **2a**, **3a**–**3k**, **4a**–**4f**, **6** and **8** on strains of gram positive staphylococci (*St. aureus* 256, 1) and gram negative bacilli (*Sh. Flexneri* 6858, *E.coli* 0-55) showed that

Scheme 2.



8, R^1 = NO_2, R^2 = OH; **9**, R^1 = H, R^2 = NH_2.

the majority of the synthesized 4-substituted pyrimidines and the corresponding 5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidines lack antibacterial activity. Only several compounds, in particular, **3a**, **3b**, **3d**, **4a**, **4f** and **8**, exhibit weak activity, supressing the growth of gram positive and gram negative microbes. At the same time the mentioned compounds have significantly lower activity than furazolidone control.

EXPERIMENTAL

IR spectra were recorded on Nicolet Avatar 330 instrument from mulls in mineral oil, ^{1}H NMR spectra were registered on a spectrometer Varian Mercury-300 (300 MHz) in DMSO-d_6–CCl_4, 1 : 3, internal reference TMS. Melting points were determined on Boëtius micro-heating apparatus and were not corrected. TLC was carried out on Silufol UV-254 plates in a system ethanol–dichloroethane, 1 : 10 (compounds **2a**, **3a–3k**, **4a–4f**, **6**, **8** and **9**) and ethanol–dichloroethane, 1 : 4 (compound **7**), development in iodine vapor.

4-Chloropyrimidine-5-ylpropanoic acids 2a and 2b. A mixture of 0.01 mol of acid **1a** or **1b** in 20 mL $POCl_3$ was boiled at reflux for 4 h, the excess of $POCl_3$ was distilled off, the residue was poured on 100 g of ice and left in the cold for 4 h. Chloro derivative **2a** was filtered off and dried. Chloro derivative **2b** was extracted with dichloroethane (2 × 70 mL), the organic layer was washed with 50 mL of water, dried with Na_2SO_4 and on removing the solvent 2.4 g (83%) of oily chloroderivative **2b** was obtained and without further purification brought into reaction with amines.

3-(6-Methyl-2-phenyl-4-chloropyrimidin-5-yl)-propanoic acid (2a). Yield 73%, mp 168–169°C (ethanol), R_f 0.73. IR spectrum, ν, cm^{-1}: 1701 (CO), 1660 s (C=N). ^{1}H NMR spectrum, δ, ppm: 2.48–2.54 m, 3.01–3.07 m (2H each, CH_2CH_2), 7.41–7.46 m ($3H_{arom}$), 8.36–8.41 m ($2H_{arom}$), 11.99 b (1H, COOH). Found, %: N 9.86. $C_{14}H_{13}ClN_2O_2$. Calculated, %: N 10.12.

4-Aminoderivatives (3a–3j). A mixture of 0.01 mol of 4-chloropyrimidines **2a** and **2b** and 0.02 mol of the corresponding amine in 7 mL of dioxane was boiled at reflux during 7 h, left overnight, 20 mL of water was added, the precipitate was filtered off, dried, and recrystallized from DMF.

3-(4-Anilino-6-methyl-2-phenylpyrimidin-5-yl)-propanoic acid (3a). Yield 76%, mp 280–282°C, R_f 0.22. IR spectrum, ν, cm^{-1}: 3240 (NH), 1704 (CO), 1657 (C=N). ^{1}H NMR spectrum, δ, 2.35 s (3H, CH_3), 2.50–2.56 m (2H, CH_2CO), 2.74–2.82 m (2H, CH_2), 7.02 br.t ($1H_{arom}$, *J* 7.3 Hz), 7.25–7.31 m ($2H_{arom}$), 7.47–7.61 m ($5H_{arom}$), 8.05–8.11 m ($2H^o_{arom}$), 9.89 s (1H, NH), 12.60 br.s (1H, COOH). Found, %: N 12.45. $C_{20}H_{19}N_3O_2$. Calculated, %: N 12.60.

3-[4-Methyl-6-(2-methylanilino)-2-phenylpyrimidin-5-yl]propanoic acid (3b). Yield 82%, mp 291–293°C, R_f 0.52. IR spectrum, ν, cm^{-1}: 3262 (NH), 1650 (CO), 1610 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.19 s (3H, CH_3), 2.38 s (3H, CH_3), 2.52–2.58 m (2H, CH_2), 2.77–2.84 m (2H, CH_2), 6.98–7.05 m ($1H_{arom}$), 7.07–7.16 m ($2H_{arom}$), 7.27–7.51 m ($4H_{arom}$), 8.10–8.16 m ($2H_{arom}$), 9.13 s (1H, NH), 12.51 br.s (1H, OH). Found, %: N 12.33. $C_{21}H_{21}N_3O_2$. Calculated, %: N 12.10.

3-[4-Methyl-6-(4-methylanilino)-2-phenylpyrimidin-5-yl]propanoic acid (3c). Yield 86%, mp 303–304°C, R_f 0.56. IR spectrum, ν, cm^{-1}: 3290 (NH), 1652 (CO), 1610 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3), 2.39 s (3H, CH_3), 2.47–2.53 m (2H, CH_2), 2.77–2.84 m (2H, CH_2), 6.97–7.03 m (2H, C_6H_4), 7.39–7.45 m (3H, Ph), 7.44–7.48 m (2H, C_6H_4), 8.13–8.18 m (2H, Ph), 9.56 s (1H, NH), 12.44 br.s (1H, OH). Found, %: N 12.42. $C_{21}H_{21}N_3O_2$. Calculated, %: N 2.10.

3-[4-Methyl-6-(4-methoxyanilino)-2-phenylpyrimidin-5-yl]propanoic acid (3d). Yield 84%, mp 301–302°C, R_f 0.39. IR spectrum, ν, cm^{-1}: 3294 (NH), 1648 (CO), 1610 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.39 s (3H, CH_3), 2.45–2.52 m (2H, CH_2), 2.77–2.84 m (2H, CH_2), 3.74 s (3H, OCH_3), 6.72–6.78 m (2H, C_6H_4), 7.40–7.52 m (3H, Ph), 7.46–7.51 m (2H, C_6H_4), 8.12–8.18 m (2H, Ph), 9.52 s (1H, NH), 12.41 br.s (1H, OH). Found, %: N 11.35. $C_{21}H_{21}N_3O_3$. Calculated, %: N 11.56.

3-[6-Methyl-2-phenyl-4-(4-ethoxycarbonylanilino)pyrimidine-5-yl]propanoic acid (3e). Yield 65%, mp 288–289°C, R_f 0.21. IR spectrum, ν, cm^{-1}: 3262 (NH), 1707 (CO), 1644 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 2.40 s (3H, CH_3), 2.55–2.60 m (2H, CH_2), 2.80–2.85 m (2H, CH_2), 4.29 q (2H, OCH_2, *J* 7.1 Hz), 7.39–7.49 m (3H, Ph), 7.68–7.73 m and 7.84–7.88 m (2H each, C_6H_4), 8.13–8.18 m (2H, Ph), 10.01 s (1H, NH), 12.44

br.s (1H, OH). Found, %: N 10.20. $C_{23}H_{23}N_3O_4$. Calculated, %: N 10.36.

(*RS*)-3-(4-Anilino-6-methyl-2-phenylpyrimidin-5-yl)-2-methylpropanoic acid (3f). Yield 75%, mp 289–290°C, R_f 0.62. IR spectrum, ν, cm^{-1}: 3281 (NH), 1644 (CO), 1600 (C=N). ^1H NMR spectrum, δ, ppm: 1.21 d (3H, C$\underline{H}_3$CH, ^3J 6.6 Hz), 2.36 s (3H, CH_3), 2.60 d.d (1H, $\underline{H}$CH-CH, ^2J 12.7, ^3J 5.7 Hz), 2.76–2.87 m (2H, HC$\underline{H}$-C$\underline{H}$), 6.93 m (1H), 7.18 m (2H) and 7.57 m (2H, NHPh), 7.39–7.49 m (3H) and 8.14 m (2H, Ph), 9.58 s (1H, NH), 12.42 b (1H, OH). Found, %: N 12.28. $C_{21}H_{21}N_3O_2$. Calculated, %: N 12.10.

(*RS*)-3-[4-Methyl-6-(2-methylanilino)-2-phenylpyrimidin-5-yl]-2-methylpropanoic acid (3g). Yield 58%, mp 296–298°C, R_f 0.46. IR spectrum, ν, cm^{-1}: 3269 (NH), 1652 (CO), 1610 (C=N). ^1H NMR spectrum, δ, ppm: 1.21 d (3H, CHC$\underline{H}_3$, J 6.8 Hz), 2.10 s (3H, CH_3), 2.35 s (3H, CH_3), 2.60 d.d (1H, $\underline{H}$CH-CH, ^2J 13.0, ^3J 6.3 Hz), 2.78 d.d (1H, HC$\underline{H}$-CH, ^2J 13.0, ^3J 7.7 Hz), 2.88–3.00 m (1H, C$\underline{H}$CH$_3$), 6.97–7.03 m (1H), 7.05–7.12 m ($2H_{arom}$), 7.30–7.35 m ($1H_{arom}$), 7.42–7.53 m ($3H_{arom}$), 8.11–8.15 m ($2H_{arom}$), 9.03 br.s (1H, NH), 12.50 b (1H, OH). Found, %: N 11.44. $C_{22}H_{23}N_3O_2$. Calculated, %: N 11.63.

(*RS*)-3-[4-Methyl-6-(4-methylanilino)-2-phenylpyrimidin-5-yl]-2-methylpropanoic acid (3h). Yield 79%, mp 286–288°C, R_f 0.47. IR spectrum, ν, cm^{-1}: 3257 (NH), 1647 (CO), 1600 (C=N). ^1H NMR spectrum, δ, ppm: 1.19 d (3H, CH$\underline{CH}_3$, ^3J 6.7 Hz), 2.27 s (3H, CH_3), 2.34 m (3H, CH_3), 2.60 d.d (1H, $\underline{H}$CH-CH, ^2J 12.2, ^3J 5.2 Hz), 2.75–2.88 m (2H, HC$\underline{H}$-C$\underline{H}$), 6.98 m (2H), 7.43 m (2H, C_6H_4), 7.39–7.47 m (3H), 8.14 m (2H, Ph), 9.47 s (1H, NH), 12.42 br.s (1H, OH). Found, %: N 11.56. $C_{22}H_{23}N_3O_2$. Calculated, %: N 11.63.

(*RS*)-3-[4-Methyl-6-(2-methoxyanilino)-2-phenylpyrimidin-5-yl]-2-methylpropanoic acid (3i). Yield 65%, mp 242–243°C, R_f 0.57. IR spectrum, ν, cm^{-1}: 3323 (NH), 1650 (CO), 1600 (C=N). ^1H NMR spectrum, δ, ppm: 1.22 d (3H, CHC$\underline{H}_3$, ^3J 6.8 Hz), 2.32 s (3H, CH_3), 2.61 d.d (1H, $\underline{H}$CH-CH, ^2J 13.1, ^3J 6.5 Hz), 2.79 d.d (1H, HC$\underline{H}$-CH, ^2J 13.1, ^3J 7.4 Hz), 2.93 m (1H, C$\underline{H}$CH$_3$), 3.76 s (3H, OCH_3), 6.85 m (2H), 6.94 m (1H) and 8.10 m (1H, C_6H_4), 7.40–7.49 m (3H) and 8.16 m (2H, Ph), 8.30 s (1H, NH), 12.48 b (1H, OH). Found, %: N 11.72. $C_{22}H_{23}N_3O_3$. Calculated, %: N 11.13.

(*RS*)-3-[4-Methyl-2-phenyl-6-(4-ethoxycarbonylanilino)pyrimidin-5-yl]-2-methylpropanoic acid (3j). Yield 69%, mp 256–258°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3262 (NH), 1707 (CO), 1648 (C=N). ^1H NMR spectrum, δ, ppm: 1.22 d (3H, CHC$\underline{H}_3$, J 6.8 Hz), 1.37 t (3H, $CH_2C\underline{H}_3$, J 7.1 Hz), 2.35 s (3H, 6-CH_3), 2.62 d.d (1H, $\underline{H}$CH-CH, ^2J 13.0, ^3J 6.1 Hz), 2.82 d.d (1H, HC$\underline{H}$-CH, ^2J 13.0, ^3J 7.6 Hz), 2.85–2.96 m (1H, C$\underline{H}$CH$_3$), 4.28 q (2H, $OC\underline{H}_2CH_3$, J 7.1 Hz), 7.38–7.48 m (2H, Ph), 7.67–7.72 m and 7.81–7.87 m (2H each, C_6H_4), 8.12–8.17 m (2H, Ph), 9.93 br.s (1H, NH), 12.44 b (1H, OH). Found, %: N 9.76. $C_{24}H_{25}N_3O_4$. Calculated, %: N 10.02.

(*RS*)-3-(4-Amino-6-methyl-2-phenylpyrimidin-5-yl)-2-methylpropanoic acid (3k). A solution of 2.90 g (0.01 mol) of 4-chloropyrimidine **2b** in 30 mL of saturated alcohol solution of ammonia was stirred for 4 h at 100°C, distilled till dryness, the residue was treated with water, filtered off, dried, and recrystallized from DMF. Yield 70%, mp 273–274°C, R_f 0.54. IR spectrum, ν, cm^{-1}: 3378, 3178 (NH_2), 1646 (CO), 1607 (C=N). ^1H NMR spectrum, δ, ppm: 1.09 d (3H, C$\underline{H}_3$CH, ^3J 6.7 Hz), 2.35 s (3H, CH_3), 2.45–2.73 m (3H, $CHCH_2$), 6.30 b (1H). 6.93 b (1H, NH_2), 7.40–7.47 m ($3H_{arom}$), 8.15 m ($2H_{arom}$), 12.40 b (1H, OH).

Pyrido[2,3-*d*]pyrimidines (4a–4f). A mixture of 0.01 mol of 4-amino derivatives **3** and 5 g of PPA was heated for 3 h on Wood's metal bath at 170–180°C, cooled to room temperature, and neutralized with aqueous ammonia. After 3 h of standing in the cold the precipitate was filtered off and recrystallized from alcohol.

4-Methyl-2,8-diphenyl-5,6,7,8-tetrahydropyrido-[2,3-*d*]pyrimidin-7(8*H*)-one (4a). Yield 67%, mp 252–254°C, R_f 0.45. IR spectrum, ν, cm^{-1}: 1703 (CO), 1657 (C=N). ^1H NMR spectrum, δ, ppm: 2.57 s (3H, CH_3), 2.85–2.90 m (2H, CH_2), 3.07–3.13 m (2H, CH_2), 7.18–7.34 m (5H), 7.40–7.53 m ($3H_{arom}$), 7.97–8.02 m ($2H_{arom}$). Found, %: N 13.17. $C_{20}H_{17}N_3O$. Calculated, %: N 13.32.

4-Methyl-8-(2-methylphenyl)-2-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-7(8*H*)-one (4b). Yield 71%, mp 248–250°C, R_f 0.63. IR spectrum, ν, cm^{-1}: 1695 (CO), 1650 (C=N). ^1H NMR spectrum, δ, ppm: 2.07 s (3H, $CH_3C_6H_4$), 2.57 s (3H, CH_3), 2.85–2.90 m (2H, CH_2), 3.08–3.14 m (2H, CH_2), 7.07–7.11 m (1H), 7.23–7.37 m (6H), 7.94–7.98 m ($2H_{arom}$).

Found, %: N 12.48. $C_{21}H_{19}N_3O$. Calculated, %: N 12.76.

4-Methyl-8-(4-methylphenyl)-2-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-7(8*H*)-one (4c). Yield 70%, mp 216–218°C, R_f 0.83. IR spectrum, ν, cm^{-1}: 1691 (CO), 1650 (C=N). ^1H NMR spectrum, δ, ppm: 2.49 s (3H, $CH_3C_6H_4$), 2.56 s (3H, CH_3), 2.82–2.88 m (2H, CH_2), 3.05–3.10 m (2H, CH_2), 7.05–7.09 m (2H), 7.25–7.35 m (5H), 7.99–8.04 m ($2H_{arom}$). Found, %: N 12.48. $C_{21}H_{19}N_3O$. Calculated, %: N 12.76.

4-Methyl-8-(4-methoxyphenyl)-2-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-7(8*H*)-one (4d). Yield 80%, mp 170–172°C, R_f 0.80. IR spectrum, ν, cm^{-1}: 1691 (CO), 1652 (C=N). ^1H NMR spectrum, δ, ppm: 2.56 s (3H, CH_3), 2.82–2.87 m (2H, CH_2), 3.04–3.10 m (2H, CH_2), 3.89 s (3H, OCH_3), 6.97–7.02 m and 7.08–7.13 m (2H each, C_6H_4), 7.26–7.36 m (3H) and 8.01–8.06 m (2H, Ph). Found, %: N 12.41. $C_{21}H_{19}N_3O_2$. Calculated, %: N 12.17.

(*RS*)-4,6-Dimethyl-2,8-diphenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-7-one (4e). Yield 65%, mp 214–215°C, R_f 0.65. IR spectrum, ν, cm^{-1}: 1704 (CO) 1650 (C=N). ^1H NMR spectrum, δ, ppm: 1.36 d (3H, CHC<u>H</u>$_3$, ^3J 6.6 Hz), 2.56 s (3H, CH_3), 2.79 d.d (1H, <u>H</u>CH-CH, ^2J 15.2, ^3J 11.8 Hz), 2.91 m (1H, C<u>H</u>CH$_3$), 3.19 d.d (1H, HCH-CH, ^2J 15.2, ^3J 5.6 Hz), 7.19 m (2H), 7.24–7.32 m (3H), 7.40–7.53 m (3H) and 7.99 m (2H, $2C_6H_5$). Found, %: N 12.58. $C_{21}H_{19}N_3O$. Calculated, %: N 12.76.

Ethyl (*RS*)-4-(4,6-dimethyl-7-oxo-2-phenyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-8-yl) benzoate (4f). Yield 69%, mp 210–211°C, R_f 0.60. IR spectrum, ν, cm^{-1}: 1715 (CO), 1692 (C=N). ^1H NMR spectrum, δ, ppm: 1.29 d (3H, CHC<u>H</u>$_3$, *J* 6.7 Hz), 1.37 t (3H, C<u>H</u>$_3$CH$_2$O, *J* 7.1 Hz), 2.55 s (3H, 4-CH_3), 2.82 d.d (1H, <u>H</u>CH-CH, *J* 15.5, 12.3 Hz), 3.01 m (1H, C<u>H</u>CH$_3$), 3.21 d.d (1H, HC<u>H</u>-CH, *J* 15.5, 6.0 Hz), 4.37 q (2H, OCH_2, *J* 7.1 Hz), 7.33–7.40 m (3H, $H^{3,3',4'}$, Ph), 7.44 m (2H, $H^{3',5'}$, C_6H_4), 7.95 m (2H, $H^{2',6'}$, Ph), 8.10 m (2H, $H^{2',6'}$, C_6H_4). Found, %: N 10.60. $C_{24}H_{23}N_3O_3$. Calculated, %: N 10.47.

4-Methyl-2-phenyl-5,6-dihydrobenzo[4',5']-imidazo[2',1':6,1]pyrido[2,3-*d*]pyrimidine (6). A solution of 2.76 g (0.01 mol) of chloropyrimidine **2a** and 1.08 g (0.01 mol) of *o*-phenylenediamine in 20 mL of anhydrous isobutyl alcohol was boiled at reflux for 3 h, light-yellow precipitate started to appear already after 40 min. The reaction mixture was left overnight, a solution of 0.8 g (0.01 mol) of $NaHCO_3$ in 20 mL of water was added, stirred for 15 min, distilled till dryness, the residue was washed with water, filtered off, dried, and heated on Wood's metal bath with 5 g of PPA for 2 h at 210–220°C. The cooled melt was neutralized with solution of NH_4OH, the reaction product was filtered off and recrystallized from alcohol. Yield 55%, mp 176–178°C, no melting point depression was observed with the sample of compound obtained by the method [5], R_f 0.60. IR spectrum, ν, cm^{-1}: 1644 (C=N). ^1H NMR spectrum, δ, ppm: 2.64 s (3H, CH_3), 3.16 m (2H), 3.32 m (2H, CH_2CH_2), 7.29 m (1H), 7.37 m (1H), 7.63 m (1H) and 8.61 m (1H, C_6H_4), 7.46–7.55 m (3H) and 8.49 m (2H, Ph). Found, %: N 17.80. $C_{20}H_{16}N_4$. Calculated, %: N 17.94.

1,3-Dimethyl-8-[2-(4-methyl-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-yl)ethyl]-1*H*-purine-2,6-(3*H*,9*H*)-dione (7). A mixture of 2.58 g (0.01 mol) of acid **1a** and 1.70 g (0.01 mol) of 5,6-diamino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione in 15 g of PPA was heated for 3 h on Wood's metal bath at 210–220°C, cooled to room temperature, the melt was neutralized with aqueous ammonia, the precipitate was filtered off, washed with water, dried, and recrystallized from DMF. Yield 60%, mp >300°C, R_f 0.61. IR spectrum, ν, cm^{-1}: 3150 (NH), 1704, 1700 (CO), 1648 (C=N). ^1H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3), 2.91 br.s (4H, CH_2CH_2), 3.28 s (3H, NCH_3), 3.50 s (3H, NCH_3), 7.39–7.50 m (3H, Ph), 8.12–8.20 m (2H, Ph), 12.50 b (1H, NH), 13.07 br.s (1N, NH). Found, %: N 21.15. $C_{20}H_{20}N_6O_3$. Calculated, %: N 21.42.

3-[4-Methyl-2-(3-nitrophenyl)-6-oxo-1,6-dihydro-pyrimidin-5-yl]propanoic acid (8). To a mixture of 2.58 g (0.01 mol) of acid **1a** in 10 g of conc. H_2SO_4 cooled with flowing water was added in small portions 1.11 g (0.011 mol) of KNO_3, the reaction mixture was heated for 1 h at 130–135°C and poured on 100 g of ice. The precipitated product was filtered off, dried, and recrystallized from ethanol. Yield 76%, mp 268–270°C, R_f 0.49. IR spectrum, ν, cm^{-1}: 1700 (CO), 1652 (C=N). ^1H NMR spectrum, δ, ppm: 2.43 s (3H, CH_3), 2.41–2.46 m (2H, CH_2), 2.72–2.79 m (2H, CH_2), 7.70 d.d (1H, H^5, Ar, ^1J 8.1, ^2J 7.9 Hz), 8.31 d.d.d (1H, H^6, Ar, ^1J 8.1, ^2J 2.0, ^3J 0.9 Hz), 8.59 d.d.d (1H, H^4, Ar, ^1J 7.9, ^2J 2.0, ^3J 0.9 Hz), 9.06 t (1H, H^2, Ar, *J* 2.0 Hz), 12.24 b (2H, NH, COOH). Found, %: N 13.69. $C_{14}H_{13}N_3O_5$. Calculated, %: N 13.86.

3-(4-Methyl-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-yl)propanamide (9). A mixture of 2.58 g (0.01 mol) of acid **1a** and 1.37 g (0.015 mol) of thiosemicarbazide in 5 g of PPA was heated for 1 h on Wood's metal bath at 165°C, cooled, neutralized with aqueous ammonia, the precipitate was filtered off, dried, and recrystallized from ethanol. Yield 73%, mp 263–264°C, R_f 0.63. IR spectrum, ν, cm^{-1}: 3269, 3070 (NH_2), 1640 (CO), 1610 (C=N). ^1H NMR spectrum, δ, ppm: 2.24 s (3H, CH_3), 2.80 br.t (2H, CH_2, *J* 7.4 Hz), 3.00 br.t (2H, CH_2, *J* 7.4 Hz), 6.97 b (1H) and 6.97 br.s (1H, NH_2), 7.47–7.59 m (3H) and 8.07–8.12 m (2H, Ph), 12.62 b (1H, NH). Found, %: N16.17. $C_{14}H_{15}N_3O_2$. Calculated, %: N 16.33.

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