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SYNTHESIS OF 8-AMINO DERIVATIVES OF CONDENSED FURO[3,2-*d*]PYRIMIDINES

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A method for the synthesis of new 8-amine derivatives of pyrano[4",3":4',5']pyrido[3',2':4,5]furo-[3,2-d]pyrimidines based on 6-oxo derivatives of pyrano[3,4-c]pyridines has been developed.

Keywords: pyrano[3,4-*c*]pyridines, furo[2,3-*b*]pyridines, furo[3,2-*d*]pyrimidines, amination, condensation, synthesis, cyclization.

We have previously reported on the synthesis of condensed thieno[3,2-*d*]pyrimidines [1,2]. The present work is concerned with the extension of our studies in this field to the synthesis of condensed derivatives of furo[3,2-*d*]pyrimidines. As starting compounds we used 6-oxo derivatives of pyrano[3,4-*c*]pyridines **1** [3] which on interaction with ethyl chloroacetate were converted into the corresponding O-alkylated derivatives **2**. Cyclization of the latter into furo[2,3-*b*]pyridines **3** occurred only in absolute ethanol under the influence of sodium ethoxide. The presence in the furan ring of compound **3** of two similar functional groups permits cyclization by condensation of the latter with formamide. As a result we synthesized the condensed furo-[3,2-*d*]pyrimidones **4** which were converted into the corresponding chloro derivatives **5** under the influence of phosphorus oxychloride. Further reaction of the chloride with various amines led to the required 8-amino derivatives **6**.

EXPERIMENTAL

IR spectra of nujol mulls were recorded with a UR-20 spectrometer. ^{1}H NMR spectra of DMSO-d_6 solutions with TMS as internal standard were recorded on a Varian Mercury-300VX (300 MHz) instrument.

The course of reactions and the purity of the compounds synthesized were monitored by TLC on Silufol UV-254 plates.

Synthesis of Compounds 2a,b (General Method). Ethyl chloroacetate (13.48 g, 0.11 mol) was added dropwise with stirring to a suspension of pyrano[3,4-*c*]pyridine **1a,b** (0.1 mol) and potash (15 g, 0.11 mol) in dry DMF (150 ml). The temperature of the reaction mixture was maintained at 75-80°C for 2 h, then cooled to room temperature, and poured into cold water. The crystals of compound **2** formed were filtered off, washed with water, dried, and recrystallized from ethanol.

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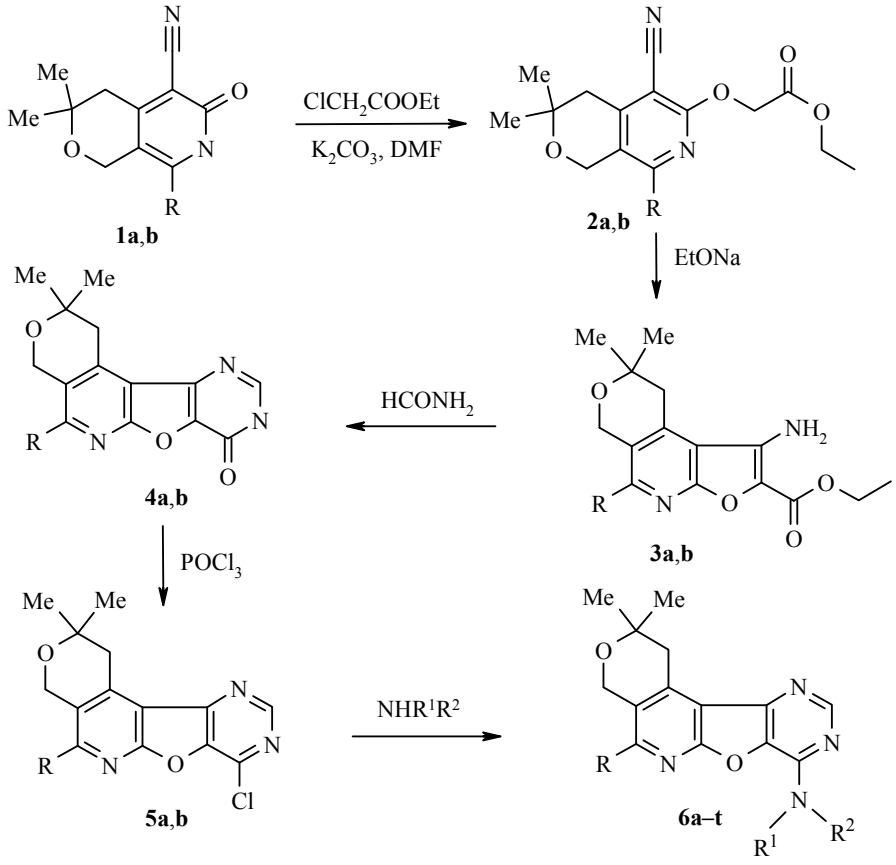

1–5 a R = Me, **b** R = *i*-Pr; **6 a** R = Me, $R^1 + R^2 = –(CH_2)_4–$; **b** R = *i*-Pr, $R^1 + R^2 = –(CH_2)_4–$; **c** R = Me, $R^1 + R^2 = –(CH_2)_2O(CH_2)_2–$; **d** R = *i*-Pr, $R^1 + R^2 = –(CH_2)_2O(CH_2)_2–$; **e–j** R^1 = H, **e** R = Me, $R^2 = –CH_2CH_2OH$; **f** R = *i*-Pr, $R^2 = –CH_2CH_2OH$; **g** R = Me, R^2 = 2-methoxyethyl; **h** R = *i*-Pr, R^2 = 2- methoxyethyl; **i** R = Me, $R^2 = –CH_2CH_2NMe_2$; **j** R = *i*-Pr, $R^2 = –CH_2CH_2NMe_2$; **k** R = Me, $R^1 + R^2 = –(CH_2)_2NMe(CH_2)_2–$; **l** R = *i*-Pr, $R^1 + R^2 = –(CH_2)_2NMe(CH_2)_2–$; **m–t** R^1 = H, **m** R = Me, R^2 = 2-pyridylmethyl; **n** R = *i*-Pr, R^2 = 2-pyridylmethyl; **o** R = Me, R^2 = 3-pyridylmethyl; **p** R = *i*-Pr, R^2 = 3-pyridylmethyl; **q** R = Me, R^2 = 4-pyridylmethyl; **r** R = *i*-Pr, R^2 = 4-pyridylmethyl; **s** R = Me, R^2 = 2-morpholin-4-ylethyl; **t** R =*i*-Pr, R^2 = 2-morpholin-4-ylethyl

Ethyl 2-(5-Cyano-3,3,8-trimethyl-3,4-dihydro-1H-pyrano[3,4-*c*]pyridin-6-yloxy)acetate (2a). Yield 28.2 g (92.6%); mp 107-109°C (ethanol). IR spectrum, ν, cm^{-1}: 2220 (CN), 1680 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.26 (6H, s, $C(CH_3)_2$); 1.26 (3H, t, ^3J = 7.1, $CH_2C\underline{H}_3$); 2.32 (3H, s, CH_3); 2.78 (2H, s, CH_2); 4.19 (2H, q, ^3J = 7.1, $C\underline{H}_2CH_3$); 4.60 (2H, s, OCH_3); 4.93 (2H, s, CH_2CO). Found, %: C 63.11; H 6.54; N 9.15. $C_{16}H_{20}N_2O_4$. Calculated, %: C 63.14; H 6.62; N 9.20.

Ethyl 2-(5-Cyano-8-isopropyl-3,3-dimethyl-3,4-dihydro-1H-pyrano[3,4-*c*]pyridin-6-yloxy)acetate (2b). Yield 30.5 g (91.8%); mp 137-139°C (ethanol). IR spectrum, ν, cm^{-1}: 2220 (CN), 1690 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (6H, d, ^3J = 6.7, $CH(C\underline{H}_3)_2$); 1.27 (3H, t, ^3J = 7.1, $CH_2C\underline{H}_3$); 1.28 (6H, s, $C(CH_3)_2$); 2.79 (2H, s, CH_2); 2.89 (1H, sept, ^3J = 6.7, $C\underline{H}(CH_3)_2$); 4.17 (2H, q, ^3J = 7.1, $C\underline{H}_2CH_3$); 4.65 (2H, s, OCH_3); 4.89 (2H, s, $C\underline{H}_2CO$). Found, %: C 65.12; H 7.23; N 8.35. $C_{18}H_{24}N_2O_4$. Calculated, %: C 65.04; H 7.28; N 8.43.

Synthesis of Compounds 3a,b (General Method). Compound **2a,b** (0.1 mol) was added to a solution of sodium ethoxide, prepared from sodium (2.53 g, 0.11 mol) and absolute ethanol (300 ml). The mixture was boiled for 10-15 min, cooled, and added to ice. The crystal of furopyridines **3** were filtered off, washed with water, dried, and recrystallized from ethanol.

Ethyl 1-amino-5,8,8-trimethyl-8,9-dihydro-6H-pyrano[4,3-*d*]furo[2,3-*b*]pyridine-2-carboxylate (3a). Yield 25.5 g (83.8%); mp 255-256°(ethanol). IR spectrum, ν, cm^{-1}: 3340 (NH_2), 1660 (CO). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.30 (6H, s, $C(CH_3)_2$); 1.40 (3H, ^3J = 7.1, $CH_2C\underline{H}_3$); 2.39 (3H, s, CH_3); 3.10 (2H, s, CH_2); 4.33 (2H, q, ^3J = 7.1, $C\underline{H}_2CH_3$); 4.67 (2H, s, OCH_3); 5.75 (2H, br. s, NH_2). Found, %: C 63.16; H 6.59; N 9.21. $C_{16}H_{20}N_2O_4$. Calculated, %: C 63.14; H 6.62; N 9.20.

Ethyl 1-Amino-5-isopropyl-8,8-dimethyl-8,9-dihydro-6H-pyrano[4,3-*d*]furo[2,3-*b*]pyridine-2-carboxylate (3b). Yield 28 g (84.2%); mp 261-263°C (ethanol). IR spectrum, ν, cm^{-1}: 3360 (NH_2), 1670 (CO). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.24 (6H, d, ^3J = 6.7, $CH(C\underline{H}_3)_2$); 1.30 (6H, s, $C(CH_3)_2$); 1.40 (3H, t, ^3J = 7.1, $CH_2C\underline{H}_3$); 2.96 (1H, sept, ^3J = 6.7, $C\underline{H}(CH_3)_2$); 3.13 (2H, s, CH_2); 4.33 (2H, q, ^3J = 7.1, $C\underline{H}_2CH_3$); 4.79 (2H, s, OCH_2); 5.74 (2H, br. s, NH_2). Found, %: C 65.15; H 7.21; N 8.45. $C_{18}H_{24}N_2O_4$. Calculated, %: C 65.04; H 7.28; N 8.43.

Synthesis of Compounds 4a,b (General Method). A mixture of compound **3a,b** (0.1 mol) and formamide (200 ml) was boiled for 4 h. After cooling, the separated crystals were filtered off, washed with water, dried, and recrystallized from DMSO.

2,2,5-Trimethyl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo[3,2-*d*]pyrimidin-8-one (4a). Yield 24 g (84%); mp > 360°C. IR spectrum, ν, cm^{-1}: 3180 (NH), 1650 (CO). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.33 (6H, s, $C(CH_3)_2$); 2.48 (3H, s, CH_3); 3.22 (2H, s, CH_2); 4.71 (2H, s, OCH_2); 7.97 (1H, s, N=CH); 12.86 (1H, br. s, NH). Found, %: C 63.05; H 5.12; N 14.65. $C_{15}H_{15}N_3O_3$. Calculated, %: C 63.15; H 5.30; N 14.73.

5-Isopropyl-2,2-dimethyl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo[3,2-*d*]pyrimidin-8-one (4b). Yield 25.5 g (81.4%); mp >360°C. IR spectrum, ν, cm^{-1}: 3180 (NH), 1650 (CO). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.30 (6H, d, ^3J = 6.7, $CH(C\underline{H}_3)_2$); 1.33 (6H, s, $C(CH_3)_2$); 3.03 (1H, sept, ^3J = 6.7, $C\underline{H}(CH_3)_2$); 3.26 (2H, s, CH_2); 4.87 (2H, s, OCH_2); 7.97 (1H, s, N=CH); 12.86 (1H, br. s, NH). Found, %: C 65.22; H 6.05; N 13.37. $C_{17}H_{19}N_3O_3$. Calculated, %: C 65.16; H 6.11; N 13.41.

Synthesis of Compounds 5a,b (General Method). A mixture of compound **4a,b** (0.1 mol) and phosphorus oxychloride (250 ml) was boiled for 4h. The remaining phosphorus oxychloride was evaporated off to dryness, ice water was added, the crystals of compound **5** were filtered off, washed with water, dried and recrystallized from ethanol.

8-Chloro-2,2,5-trimethyl-1,4-dihydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo[3,2-*d*]pyrimidine (5a). Yield 27.3 g (89.9%); mp 198-199°C (ethanol). IR spectrum, ν, cm^{-1}: 1600 (C=C Ar). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.35 (6H, s, $C(CH_3)_2$); 2.58 (3H, s, CH_3); 3.31 (2H, s, CH_2); 4.84 (2H, s, OCH_2); 8.89 (1H, s, N=CH). Found, %: C 59.24; H 4.54; N 13.75. $C_{15}H_{14}ClN_3O_2$. Calculated, %: C 59.31; H 4.65; N 13.83.

8-Chloro-5-isopropyl-2,2-dimethyl-1,4-dihydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo[3,2-*d*]pyri-midine (5b). Yield 29 g (87.4%); mp 192-194°C (ethanol). IR spectrum, ν, cm^{-1}: 1600 (C=C Ar). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.33 (6H, d, ^3J = 6.7, $CH(C\underline{H}_3)_2$); 1.38 (6H, s, $C(CH_3)_2$); 3.11 (1H, sept, ^3J = 6.7, $C\underline{H}(CH_3)_2$); 3.36 (2H, s, CH_2); 4.95 (2H, s, OCH_2); 8.90 (1H, s, N=CH). Found, %: C 62.48; H 5.42; N 12.60. $C_{17}H_{18}ClN_3O_3$. Calculated, %: C 61.54; H 5.47; N 12.66.

Synthesis of Compounds 6a-t (General Method). A mixture of chloride **5a,b** (0.01 mol) and the corresponding amine (0.022 mol) in absolute ethanol (50 ml) was boiled for 10 h. The reaction mixture was cooled, water added (100 ml), the crystals formed were filtered off, washed with water, dried, and recrystallized from ethanol.

2,2,5-Trimethyl-8-pyrrolidin-1-yl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo-[3,2-*d*]pyrimidine (6a). Yield 2.94 g (86.9%); mp 195-197°C (ethanol). IR spectrum, ν, cm^{-1}: 1610 (C=C Ar). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $C(CH_3)_2$); 2.09 (4H, m, $2CH_2$); 2.47 (3H, s, CH_3); 3.30 (2H, s, CH_2); 3.92 (4H, m, $N(CH_2)_2$); 4.75 (2H, s, OCH_2). 8.33 (1H, s, N=CH). Found, %: C 67.41; H 6.45; N 16.49. $C_{19}H_{22}N_4O_2$. Calculated, %: C 67.44; H 6.55; N 16.56.

5-Isopropyl-2,2-dimethyl-8-pyrrolidin-1-yl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidine (6b). Yield 3.4g (92.8%); mp 186-187°C (ethanol). IR spectrum, ν, cm^{-1}: 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.30 (6H, d, ^3J = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.35 (6H, s, C(CH$_3$)$_2$); 2.09 (4H, m, 2CH$_2$); 3.05 (1H, sept, ^3J = 6.7, C<u>H</u>(CH$_3$)$_2$); 3.33 (2H, s, CH$_2$); 3.94 (4H, m, N(CH$_2$)$_2$); 4.86 (2H, s, OCH$_2$); 8.32 (1H, s, N=CH). Found, %: C 68.75; H 7.08; N 15.11. $C_{21}H_{26}N_4O_2$. Calculated, %: C 68.83; H 7.15; N 15.29.

2,2,5-Trimethyl-8-(morpholin-4-yl)-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo-[3,2-*d*]pyrimidine (6c). Yield 3.2 g (90.3%); mp 213-214°C (ethanol). IR spectrum, ν, cm^{-1}: 1590 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, C(CH$_3$)$_2$); 2.47 (3H, s, CH$_3$); 3.29 (2H, s, CH$_2$); 3.82 (4H, m, N(CH$_2$)$_2$); 4.06 (4H, m, O(CH$_2$)$_2$); 4.75 (2H, s, OCH$_2$); 8.39 (1H, s, N=CH). Found, %: C 64.29; H 6.18; N 15.74. $C_{19}H_{22}N_4O_3$. Calculated, %: C 64.39; H 6.26; N 15.81.

5-Isopropyl-2,2-dimethyl-8-(morpholin-4-yl)-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidine (6d). Yield 3.6 g (94.1%); mp 179-180°C (ethanol). IR spectrum, ν, cm^{-1}: 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.29 (6H, d, ^3J = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.35 (6H, s, C(C<u>H</u>$_3$)$_2$); 3.05 (1H, sept, ^3J = 6.7, C<u>H</u>(CH$_3$)$_2$); 3.34 (2H, s, CH$_2$); 3.81 (4H, m, N(CH$_2$)$_2$); 4.08 (4H, m, O(CH$_2$)$_2$); 4.86 (2H, s, OCH$_2$); 8.40 (1H, s, N=CH). Found, %: C 65.86; H 6.78; N 14.51. $C_{21}H_{26}N_4O_3$. Calculated, %: C 65.95; H 6.85; N 14.65.

2-(2,2,5-Trimethyl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo[3,2-*d*]pyrimi-din-8-ylamino)-1-ethanol (6e). Yield 3.0 g (91.4%); mp 244-246°C (ethanol). IR spectrum, ν, cm^{-1}: 3330 (NH), 1610 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, C(CH$_3$)$_2$); 2.48 (3H, s, CH$_3$); 3.30 (2H, s, CH$_2$); 3.64 (4H, m, NHC<u>H</u>$_2$C<u>H</u>$_2$); 4.35 (1H, br. s, OH); 4.76 (2H, s, OCH$_2$); 7.58 (1H, br. s, NH); 8.34 (1H, s, N=CH). Found, %: C 62.07; H 6.04; N 17.14. $C_{17}H_{20}N_4O_3$. Calculated, %: C 62.18; H 6.14; N 17.06.

2-(5-Isopropyl-2,2-dimethyl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo[3,2-*d*]-pyrimidin-8-ylamino)-1-ethanol (6f). Yield 3.1 g (87%); mp 225-227°C (ethanol). IR spectrum, ν, cm^{-1}: 3350 (NH), 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.29 (6H, d, ^3J = 6.7, CH(C<u>H</u>$_3$)$_2$), 1.35 (6H, s, C(CH$_3$)$_2$); 3.05 (1H, sept, C<u>H</u>(CH$_3$)$_2$); 3.32 (2H, s, CH$_2$); 3.65 (4H, m, NHCH$_2$CH$_2$); 4.43 (1H, br. s, OH); 4.86 (2H, s, OCH$_2$); 7.55 (1H, br. s, NH); 8.34 (1H, s, N=CH). Found, %: 64.11; H 6.72; N 15.69. $C_{19}H_{24}N_4O_3$. Calculated, %: C 64.03; H 6.79; N 15.72.

N-(2-Methoxyethyl)-2,2,5-trimethyl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo-[3,2-*d*]pyrimidine-8-amine (6g). Yield 3.1 g (90.5%); mp 168-170°C (ethanol). IR spectrum: ν, cm^{-1}: 3310 (NH), 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, C(CH$_3$)$_2$); 2.48 (3H, s, CH$_3$); 3.30 (2H, s, CH$_2$); 3.36 (3H, s, OCH$_3$); 3.58 (2H, t, ^3J = 5.8, C<u>H</u>$_2$OCH$_3$); 3.71 (2H, q, ^3J = 5.8, NHC<u>H</u>$_2$); 4.76 (2H, s, OCH$_2$); 7.71 (1H, t, ^3J = 5.9, NH); 8.35 (1H, s, N=CH). Found, %: C 63.03; H 6.42; N 16.31. $C_{18}H_{22}N_4O_3$. Calculated, %: C 63.14; H 6.48; N 16.36.

N-(2-Methoxyethyl)-5-isopropyl-2,2-dimethyl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidine-8-amine (6h). Yield 3.4 g (91.8%); mp 170-172°C (ethanol). IR spectrum, ν, cm^{-1}: 3290 (NH), 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.29 (6H, d, ^3J = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.35 (6H, s, C(CH$_3$)$_2$); 3.06 (1H, sept, ^3J = 6.7, C<u>H</u>(CH$_3$)$_2$); 3.32 (2H, s, CH$_2$); 3.34 (3H, s, OCH$_3$); 3.58 (2H, t, ^3J = 5.9, C<u>H</u>$_2$OCH$_3$); 3.73 (2H, q, ^3J = 5.9, NHC<u>H</u>$_2$); 4.86 (2H, s, OCH$_2$); 7.67 (1H, t, ^3J = 5.9, NH); 8,35 (1H, s, N=CH). Found, %: C 64.72; H 6.95; N 15.02. $C_{20}H_{26}N_4O_3$. Calculated, %: C 64.85; H 7.07; N 15.12.

N-(2-Dimethylaminoethyl)-2,2,5-trimethyl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidine-8-amine (6i). Yield 3.4 g (87.2%); mp 167-168°C (ethanol). IR spectrum, ν, cm^{-1}: 3350 (NH), 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, C(CH$_3$)$_2$); 2.27 (6H, s, N(CH$_3$)$_2$); 2.48 (3H, s, CH$_3$); 2.56 (2H, t, ^3J = 6.6, C<u>H</u>$_2$C(CH$_3$)$_2$); 3.30 (2H, s, CH$_2$); 3.65 (2H, td, ^3J = 6.6, ^3J = 5.6, NHC<u>H</u>$_2$); 4.76 (2H, s, OCH$_2$); 7.44 (1H, t, ^3J = 5.6, NH); 8.34 (1H, s, N=CH). Found, %: C 64.15; H 6.98; N 19.59. $C_{19}H_{25}N_5O_2$. Calculated, %: C 64.21; H 7.09; N 19.70.

N-(2-Dimethylaminoethyl)-5-isopropyl-2,2-dimethyl-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidine-8-amine (6j). Yield 3.5 g (91.3%); mp 146-148°C (ethanol). IR spectra, ν, cm^{-1}: 3320 (NH), 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J* , Hz): 1.28 (6H, d, ^3J = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.36 (6H, s, C(CH$_3$)$_2$); 2.26 (6H, s, N(CH$_3$)$_2$); 2.56 (2H, t, ^3J = 6.5, C<u>H</u>$_2$N(CH$_3$)$_2$); 3.04 (1H, sept, ^3J = 6.7, C<u>H</u>(CH$_3$)$_2$); 3.32 (2H, s, CH$_2$); 3.64 (2H, td, ^3J = 6.5, ^3J = 5.8, NHC<u>H</u>$_2$); 4.86 (2H, s, OCH$_2$); 7.40 (1H, t, ^3J = 5.8, NH); 8.35 (1H, s, N=CH). Found, %: C 65.61; H 7.52; N 18.15. $C_{21}H_{29}N_5O_2$. Calculated, %: C 65.77; H 7.62; N 18.26.

2,2,5-Trimethyl-8-(4-methylpiperazin-1-yl)-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidine (6k). Yield 3.3 g (89.8%); mp 215-217°C (ethanol). IR spectrum, ν, cm^{-1}: 1610 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.37 (6H, s, C(CH$_3$)$_2$); 2.28 (3H, s, NCH$_3$); 2.48 (3H, s, CH$_3$); 2.51 (4H, m, CH$_3$N(C<u>H</u>$_2$)$_2$); 3.30 (2H, s, CH$_2$); 4.08 (4H, m, N(C<u>H</u>$_2$)$_2$); 4.76 (2H, s, OCH$_2$); 8.37 (1H, s, N=CH). Found, %: C 65.22; H 6.79; N 19.14. $C_{20}H_{25}N_5O_2$. Calculated, %: C 65.38; H 6.86; N 19.06.

5-Isopropyl-2,2-dimethyl-8-(4-methylpiperazin-1-yl)-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']-pyrido[3',2':4,5]furo[3,2-*d*]pyrimidine (6l). Yield 3.5 g (88.5%); mp 200-202°C (ethanol). IR spectrum, ν, cm^{-1}: 1590 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.31 (6H, d, ^3J = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.35 (6H, s, C(CH$_3$)$_2$); 2.30 (3H, s, NCH$_3$); 2.54 (4H, m, CH$_3$N(C<u>H</u>$_2$)$_2$); 3.04 (1H, sept, ^3J = 6.7, C<u>H</u>(CH$_3$)$_2$); 3.34 (2H, s, CH$_2$); 4.09 (4H, m, N(C<u>H</u>$_2$)$_2$); 4.86 (2H, s, OCH$_2$); 8.37 (1H, s, N=CH). Found, %: C 66.77; H 7.28; N 17.65. $C_{22}H_{29}N_5O_2$. Calculated, %: C 66.81; H 7.39; N 17.71.

2,2,5-Trimethyl-N-(2-pyridylmethyl)-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo-[3,2-*d*]pyrimidine-8-amine (6m). Yield 3.2 g (85.2%); mp 162-164°C (ethanol). IR spectrum ν, cm^{-1}: 3330 (NH), 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 (6H, s, C(CH$_3$)$_2$); 2.51 (3H, s, CH$_3$); 3.31 (2H, s, CH$_2$); 4.78 (2H, s, OCH$_2$); 4.86 (2H, d, ^3J = 5.9, NHC<u>H</u>$_2$); 7.18 (1H, ddd, ^3J = 7.5, ^3J = 4.9, ^4J = 1.0, H-5'); 7.35 (1H, dt, ^3J = 7.9, ^4J = 1.0, H-3'); 7.64 (1H, ddd, ^3J = 7.9, ^3J = 7.5, ^4J = 1.8, H-4'); 8.30 (1H, t, ^3J = 5.9, NH); 8.35 (1H, s, N=CH); 8.50 (1H, ddd, ^3J = 4.9, ^4J = 1.8, ^4J = 1.0, H-6'). Found, %: C 67.09; H 5.60; N 18.59. $C_{21}H_{21}N_5O_2$. Calculated, %: C 67.18; H 5.64; N 18.65.

8-Isopropyl-2,2-dimethyl-N-(2-pyridylmethyl)-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidine-8-amine (6n). Yield 3.4 g (84.3%); mp 209-210°C (ethanol). IR spectrum, ν, cm^{-1}: 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.30 (6H, d, ^3J = 6.7, CH(C<u>H</u>$_3$)$_2$); 1.35 (6H, s, C(CH$_3$)$_2$); 3.06 (1H, sept, ^3J = 6.7, C<u>H</u>(CH$_3$)$_2$); 3.33 (2H, s, CH$_2$); 4.86 (2H, s, OCH$_2$); 4.87 (2H, d, ^3J = 5.9, NHC<u>H</u>$_2$); 7.18, 1H, dd, ^3J = 7.6, ^3J = 4.6, H-5'); 7.34 (1H, d, ^3J = 7.9, H-3'); 7.64 (1H, ddd, ^3J = 7.9, ^3J = 7.6, ^4J = 1.8, H-4'); 8.26 (1H, t, ^3J = 5.9, NH); 8.35 (1H, s, N=CH); 8.50 (1H, dd, ^3J = 4.6, ^4J = 1.8, H-6'). Found, %: C 68.39; H 6.18; N 17.29. $C_{23}H_{25}N_5O_2$. Calculated, %: C 68.47; H 6.25; N 17.36.

2,2,5-Trimethyl-N-(3-pyridylmethyl)-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo-[3,2-*d*]pyrimidine-8-amine (6o). Yield 3.5 g (93.2%); mp 180-182°C (ethanol). IR spectrum, ν, cm^{-1}: 3370 (NH), 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, C(CH$_3$)$_2$); 2.48 (3H, s, CH$_3$); 3.30 (2H, s, CH$_2$); 4.76 (2H, s, OCH$_2$); 4.77 (2H, d, ^3J =6.0, NHC<u>H</u>$_2$); 7.22 (1H, ddd, ^3J = 7.8, ^3J = 4.8, ^4J = 0.8, H-5'); 7.77 (1H, ddd, ^3J = 7.8, ^4J = 2.1, ^4J =1.7, H-6'); 8.37 (1H, s, N=CH); 8.39 (1H, dd, ^3J = 4.8, ^4J = 1.7, H-4'); 8.52 (1H, t, ^3J = 6.0, NH); 8.60 (1H, d, ^4J = 2.1, H-2'). Found, %: C 67.11; H 5.69; N 18.52. $C_{21}H_{21}N_5O_2$. Calculated, %: C 67.18; H 5.64; N 18.65.

5-Isopropyl-2,2-dimethyl-N-(3-pyridylmethyl)-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidin-8-amine (6p). Yield 3.5 g (86.7%); mp 223-224°C (ethanol). IR spectrum, ν, cm^{-1}: 3350 (NH), 1610 (C=C Ar). ^{1}H NMR spectrum, δ , ppm (*J*, Hz): 1.29 (6H, d, ^3J = 6.6, CH(C<u>H</u>$_3$)$_2$); 1.34 (6H, s, C(CH$_3$)$_2$); 3.04 (1H, sept, ^3J = 6.6, C<u>H</u>(CH$_3$)$_2$, 3.22 (2H, s, CH$_2$); 4.77 (2H, d, ^3J = 6.1, NHC<u>H</u>$_2$); 4.86 (2H, s, OCH$_2$); 7.22 (1H, ddd, ^3J = 7.8, ^3J = 4.8, ^4J = 0.8, H-5'); 7.75 (1H, ddd, ^3J = 7.8, ^4J = 2.1, ^4J = 1.6, H-6'); 8.37 (1H, s, N=CH); 8.39 (1H, dd, ^3J = 4.8, ^4J = 1.6, H-4'); 8.52 (1H, t, ^3J = 6.1, NH); 8.59 (1H, d, ^4J =2.1, H-2'). Found, %: C 68.49; H 6.28; N 17.26. $C_{23}H_{25}N_5O_2$. Calculated, %: C 68.47; H 6.25; N 17.36.

2,2,5-Trimethyl-N-(4-pyridylmethyl)-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]furo-[3,2-*d*]pyrimidine-8-amine (6q). Yield 3.6 g (95.9%); mp 219-220°C (ethanol). IR spectrum, ν, cm^{-1}: 3360 (NH), 1610 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $CCH_3)_2$); 2.49 (3H, s, CH_3); 3.30 (2H, s, CH_2); 4.76 (2H, d, ^3J = 6.1, NHC$\underline{H}_2$); 4.77 (2H, s, OCH_2); 7.32 (2H, m, H-3',5'); 8.33 (1H, s, N=CH); 8.42 (2H, m, H-2',6'); 8.55 (1H, t, ^3J =6.1, NH). Found, %: C 67.15; H 5.60; N 18.59. $C_{21}H_{21}N_5O_2$. Calculated, %: C 67.18; H 5.64; N 18.65.

5-Isopropyl-2,2-dimethyl-N-(4-pyridylmethyl)-1,4-dihydro-2H-pyrano[4",3":4',5']pyrido[3',2':4,5]-furo[3,2-*d*]pyrimidine-8-amine (6r). Yield 3.7 g (91.7%); mp 260-262°C (ethanol). IR spectrum, ν, cm^{-1}: 3360 (NH), 1590 (C=C, Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.30 (6H, d, ^3J = 6.6, CH(C$\underline{H}_3)_2$); 1.35 (6H, s, $C(CH_3)_2$); 3.07 (1H, sept, ^3J = 6.6, C$\underline{H}(CH_3)_2$); 3.33 (2H, s, CH_2); 4.77 (2H, d, ^3J = 6.1, NHC$\underline{H}_2$); 4.87 (2H, s , OCH_2); 7.31 (2H, m, H-3',5'); 8.34 (1H, s, N=CH); 8.42 (2H, m, H-2',6'); 8.56 (1H, t, ^3J = 6.1, NH). Found, %: C 68.36; H 6.17; N 17.13. $C_{23}H_{25}N_5O_2$. Calculated, %: C 68.47; H 6.25; N 17.36.

2,2,5-Trimethyl-N-[2-morpholin-4-yl)ethyl]-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidine-8-amine (6s). Yield 3.4 g (85.5%); mp 188-189°C (ethanol). IR spectrum, ν, cm^{-1}: 3340 (NH), 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, $C(CH_3)_2$); 2.48 (3H, s, CH_3); 2.52 (4H, m, $N(CH_2)_2$); 2.62 (2H, t, ^3J = 6.6, C$\underline{H}_2$N$(CH_2)_2$); 3.30 (2H, s, CH_2); 3.60 (4H, m, $O(CH_2)_2$); 3.67 (2H, td, ^3J = 6.6, ^3J = 5.7, NHC$\underline{H}_2$); 4.76 (2H, s, OCH_2); 7.60 (1H, t, ^3J = 5.7, NH); 8.33 (1H, s, N=CH). Found, %: C 63.35; H 6.79; N 17.54. $C_{21}H_{27}N_5O_3$. Calculated, %: C 63.46; H 6.85; N 17.62.

5-Isopropyl-2,2-dimethyl-N-[2-(morpholin-4-yl)ethyl]-1,4,8,9-tetrahydro-2H-pyrano[4",3":4',5']pyrido-[3',2':4,5]furo[3,2-*d*]pyrimidine-8-amine (6t). Yield 3.6 (84.6%); mp 228-230°C (ethanol). IR spectrum, ν, cm^{-1}: 3350 (NH), 1600 (C=C Ar). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.29 (6H, d, ^3J = 6.7, CH(C$\underline{H}_3)_2$), 1.35 (6H, s, $C(CH_3)_2$); 2.50 (4H, m, $N(CH_2)_2$); 2.61 (2H, t, ^3J =6.7, C$\underline{H}_2$N$(CH_2)_2$); 3.05 (1H, sept, ^3J = 6.7, C$\underline{H}(CH_3)_2$); 3.32 (2H, s, CH_2); 3.60 (4H, m, $O(CH_2)_2$); 3.68 (2H, td, ^3J = 6.6, ^3J = 5.5, NHC$\underline{H}_2$); 4.87 (2H, s, OCH_2); 7.58 (1H, t, ^3J = 5.5, NH); 8.33 (1H, s, N=CH). Found, %: C 64.86; H 7.27; N 16.41. $C_{23}H_{31}N_5O_3$. Calculated, %: C 64.92; H 7.34; N 16.46.

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