ISSN 1070-4280, Russian Journal of Organic Chemistry, 2019, Vol. 55, No. 12, pp. 1896–1901. © Pleiades Publishing, Ltd., 2019.
Russian Text © The Author(s), 2019, published in Zhurnal Organicheskoi Khimii, 2019, Vol. 55, No. 12, pp. 1909–1915.

One-Pot Syntheses with 2-Substituted 6-Aminopyrimidin-4(3*H*)-ones: New 5-Aryl-5,8,9,10-tetrahydropyrimido[4,5-*b*]-quinoline-4,6(3*H*,7*H*)-diones and 5,5′-(Arylmethylene)-bis[6-amino-2-methylpyrimidin-4(3*H*)-ones]

A. A. Harutyunyan[a, b],* S. G. Israyelyan[b], H. A. Panosyan[b], M. R. Hakobyan[b], and T. R. Hovsepyan[b]**

[a] *Russian–Armenian (Slavic) University, Yerevan, 0051 Armenia*

[b] *Mnjoyan Institute of Fine Organic Chemistry, Scientific Technological Center of Organic and Pharmaceutical Chemistry, National Academy of Sciences of Armenia, Yerevan, 0014 Armenia*

*e-mail: *harutyunyan.arthur@yahoo.com; **tag.hovsepyan@mail.ru*

Received July 30, 2019; revised October 22, 2019; accepted October 24, 2019

Abstract—One-pot condensation of 2-substituted 6-aminopyrimidin-4(3*H*)-ones with aromatic aldehydes and 5,5-dimethylcyclohexane-1,3-dione (dimedone) in acetic acid without a catalyst afforded new substituted 5-aryl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-diones in good yields. The condensation of 2-methyl-6-aminopyrimidin-4(3*H*)-one with aromatic aldehydes at a molar ratio of 2:1 under similar conditions led to the exclusive formation of uncyclized 5,5′-(arylmethylene)bis[6-amino-2-methylpyrimidin-4(3*H*)-ones].

Keywords: 2-substituted 6-aminopyrimidin-4(3*H*)-ones, dimedone, aromatic aldehydes, one-pot condensations, pyrimido[4,5-*b*]quinolines.

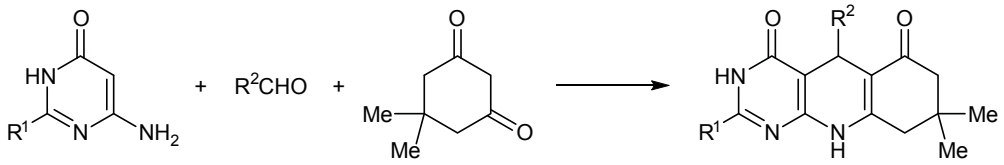
DOI: 10.1134/S1070428019120145

Interest in tri- and tetracyclic fused pyrimidines containing various pharmacologically important heterocyclic fragments is determined primarily by their diverse biological activity [1], such as antibacterial [2], antimalarial [3], antiviral [4], fungicidal [5], antitumor [6, 7], etc. We previously reported [8] the synthesis of pyrimido[4,5-*b*]quinoline derivatives by one-pot three-component cyclocondensation of 2-substituted 6-aminopyrimidin-4(3*H*)-ones **1** with aromatic or heterocyclic aldehydes **2** and 5,5-dimethylcyclohexane-1,3-dione (**3**, dimedone) in aqueous medium in the presence of benzyl(triethyl)ammonium chloride (BTEAC) as catalyst, as well as in the absence of a catalyst. The goal of the present work was to extend the scope of this reaction and obtain new tricyclic fused pyrimidines with account taken of the fact that its feasibility depends both on the presence of electron-donating substituents in the pyrimidine and on the reactivity of the aldehyde component.

In this study, the condensations were carried out in acetic acid which simultaneously served as solvent and catalyst, and the set of aldehydes used did not include those involved previously. The condensation of 2-substituted 6-aminopyrimidin-4(3*H*)-ones **1a**–**1c** with aromatic aldehydes **2a**–**2k** and dimedone (**3**) in boiling acetic acid occurred as a one-pot domino reaction and led to the formation of new 2-substituted 5-aryl-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-diones **4a**–**4l** in good yields (60–80%; Scheme 1). The product structure was confirmed by spectral data. The ^{1}H NMR spectra of **4a**–**4l** displayed a singlet at δ 4.66–5.10 ppm due to proton on C^5, as well as broadened singlets of the NH protons in the expected regions. The IR spectra of **4a**–**4l** characteristically showed absorption bands in the region 3670–3321 cm^{-1} due to N–H and O–H stretchings, as well as C=O stretching and N–H bending bands in the region 1729–1628 cm^{-1}.

In order to elucidate how particular structural fragments of **4a**–**4l** affect their biological activity, we made an attempt to synthesize according to a similar procedure 5-aryl-2,8-dimethyl-5,10-dihydropyrimi-

Scheme 1.



1a–1c **2a–2f** **3** **4a–4l**

1, R^1 = Me (**a**), NH_2 (**b**), OH (**c**); **2**, R^2 = 4-$O_2NC_6H_4$ (**a**), 4-FC_6H_4 (**b**), 4-$PhCH_2OC_6H_4$ (**c**), 2-HO-3-$MeOC_6H_3$ (**d**), 4-$Me_2NC_6H_4$ (**e**), 4-$Et_2NC_6H_4$ (**f**); **4**, R^1 = Me, R^2 = 2-HO-3-$MeOC_6H_3$ (**a**), 4-FC_6H_4 (**b**), 4-$Me_2NC_6H_4$ (**c**), 4-$Et_2NC_6H_4$ (**d**), 4-$O_2NC_6H_4$ (**e**), 4-$PhCH_2OC_6H_4$ (**f**); R^1 = NH_2, R^2 = 2-HO-3-$MeOC_6H_3$ (**g**), 4-$Me_2NC_6H_4$ (**h**), 4-$Et_2NC_6H_4$ (**i**), 4-$PhCH_2OC_6H_4$ (**j**); R^1 = OH, R^2 = 4-$Me_2NC_6H_4$ (**k**), 4-$E)_2NC_6H_4$ (**l**).

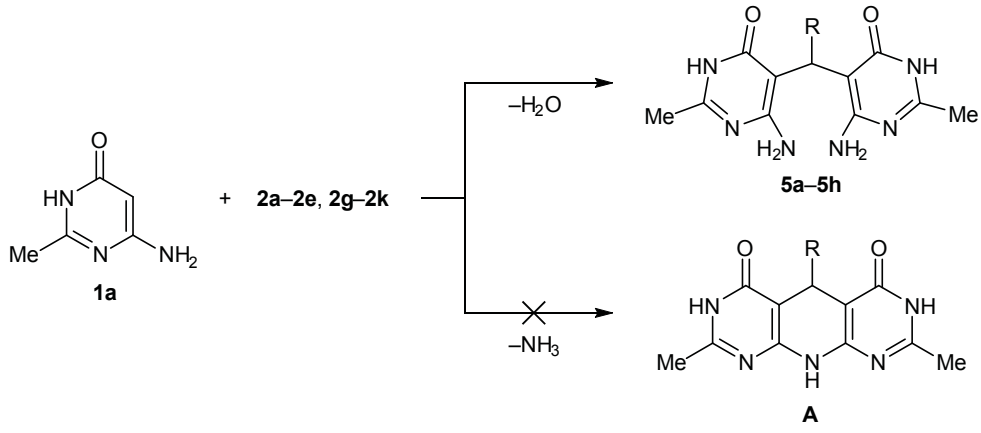
do[5′,4′:5,6]pyrido[2,3-*d*]pyrimidine-4,6(3*H*,7*H*)-diones **A**. For this purpose, we used 2 equiv of 2-methyl-6-aminopyrimidin-4(3*H*)-one (**1a**), 1 equiv of which was expected to replace the dimedone component. However, the reactions of **1a** with aromatic aldehydes **2a**–**2e**, **2i**, and **2k** at a molar ratio of 2:1 afforded only 5,5′-(arylmethylene)bis[6-amino-2-methylpyrimidin-4(3*H*)-ones] **5a**–**5h** which failed to undergo further cyclization to structure **A** (Scheme 2). Unlike bright yellow pyrimido[4,5-*b*]quinolines **4a**–**4l**, uncyclized products **5a**–**5h** were isolated as stable white crystalline solids. The IR spectra of **5a**–**5h** contained absorption bands due to N–H stretching vibrations at 3440, 3337, and 3180 cm^{-1}. The ^1H NMR spectra of **5a**–**5h** indicated that their molecules possess a symmetry plane passing through the ArCH moiety, so that the two 6-aminopyrimidin-4(3*H*)-one fragments become equivalent, and only one methyl and one NH signal were observed. However, protons of the NH_2 groups resonated as two broadened signals, presumably due to tautomeric processes in DMSO solution. The ^{13}C NMR spectrum of **5e** also confirmed symmetric structure of its molecule.

Thus, we have synthesized new 2-substituted 5-aryl-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-diones and 5,5′-(arylmethylene)-bis[6-amino-2-methylpyrimidin-4(3*H*)-ones] by one-pot condensations of 2-substituted 6-aminopyrimidin-4(3*H*)-ones with aromatic aldehydes and dimedone in the absence of a catalyst. The proposed procedures ensure good yields and are environmentally benign, and the synthesized compounds are promising subjects for further applied studies.

EXPERIMENTAL

The solvents were distilled prior to use, and crystalline initial compounds were purified by recrystallization from appropriate solvents. The IR spectra were recorded in mineral oil on a Thermo Nicolet Avatar 330 spectrometer (USA). The ^1H and ^{13}C NMR spectra were measured on a Varian Mercury-300 VX spectrometer (USA) at 300.8 and 75.46 MHz, respectively, using DMSO-d_6–CCl_4 (1:3) as solvent and tetramethylsilane as internal standard. The elemental analyses were obtained with a Eurovector EA 3000 automated

Scheme 2.



1a **5a–5h** **A**

2, R = 4-ClC_6H_4 (**g**), 4-BrC_6H_4 (**h**), 4-$MeOC_6H_4$ (**i**), 2,3-$(MeO)_2C_6H_3$ (**j**), 1,3-benzodioxol-5-yl (**k**); **5**, R = 4-FC_6H_4 (**a**), 4-ClC_6H_4 (**b**), 4-BrC_6H_4 (**c**), 4-$O_2NC_6H_4$ (**d**), 4-$PhCH_2OC_6H_4$ (**e**), 4-$MeOC_6H_4$ (**f**), 2,3-$(MeO)_2C_6H_3$ (**g**), 1,3-benzodioxol-5-yl (**h**).

analyzer (Italy). Analytical TLC was performed on Silica gel 60 F_{254} plates using chloroform–ethanol (4:1) as eluent; spots were visualized under UV light.

General procedure for the synthesis of substituted pyrimido[4,5-*b*]quinolinediones 4a–4l. A mixture of 1 mmol of pyrimidine **1a**–**1c**, 1 mmol of aldehyde **2a**–**2f**, and 1 mmol of 5,5-dimethylcyclohexane-1,3-dione (**3**) in 10 mL of glacial acetic acid was refluxed for 8–10 h. The mixture was cooled to room temperature, and the precipitate was filtered off, washed with ethanol, and (if necessary) recrystallized from ethanol or DMF.

5-(2-Hydroxy-3-methoxyphenyl)-2,8,8-trimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4a). Yield 60%, mp 286–288°C, R_f 0.64. IR spectrum, ν, cm^{-1}: 3460, 3274, 3186 (NH, OH), 1634, 1583 (C=O, C=N, δNH). ^{1}H NMR spectrum, δ, ppm: 1.08 s (3H, CH_3), 1.11 s (3H, CH_3), 2.09 d (1H, CH_2, J = 16.1 Hz), 2.16 d (1H, CH_2, J = 16.1 Hz), 2.26 s (3H, 2-CH_3), 2.44 d (1H, CH_2, J = 17.2 Hz), 2.49 d (1H, CH_2, J = 17.2 Hz), 3.76 s (3H, OCH_3), 5.10 s (1H, CH), 6.43–6.49 m (1H) and 6.55–6.61 m (2H) (H_{arom}), 9.75 s (1H, OH), 9.79 br.s (1H, NH), 12.43 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 20.3 (2-CH_3), 27.1 (CH_3), 27.2 (CH), 28.8 (CH_3), 31.9 (C^8), 39.8 (CH_2), 50.0 (CH_2), 55.3 (OCH_3), 100.0, 109.1, 110.3 (CH), 119.0 (CH), 119.6 (CH), 134.7, 143.1, 149.2, 151.4, 153.1, 156.4, 163.3, 193.5. Found, %: C 66.29; H 6.28; N 11.33. $C_{21}H_{23}N_3O_4$. Calculated, %: C 66.12; H 6.07; N 11.01.

5-(4-Fluorophenyl)-2,8,8-trimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6-(3*H*,7*H*)-dione (4b). Yield 65%, mp >320°C, R_f 0.62. IR spectrum, ν, cm^{-1}: 3247, 3152, 3095 (NH), 1655, 1636, 1603 (δNH, C=N, C=O). ^{1}H NMR spectrum, δ, ppm: 0.90 s (3H, CH_3), 1.00 s (3H, CH_3), 2.01 d (1H, CH_2, J = 16.0 Hz), 2.17 d (1H, CH_2, J = 16.0 Hz), 2.20 s (3H, 2-CH_3), 2.39 d (1H, CH_2, J = 17.2 Hz), 2.45 d (1H, CH_2, J = 17.2 Hz), 4.91 s (1H, CH), 6.95–7.03 m (2H, H_{arom}), 7.15–7.22 m (2H, H_{arom}), 9.80 br.s (1H, NH), 12.00 br.s (1H, NH). Found, %: C 67.72; H 5.49; N 11.63. $C_{20}H_{20}FN_3O_2$. Calculated, %: C 67.97; H 5.70; N 11.89.

5-(4-Dimethylaminophenyl)-2,8,8-trimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4c). Yield 70%, mp 309–310°C, R_f 0.65. IR spectrum, ν, cm^{-1}: 3233, 3146 (NH), 1656, 1633, 1602 (δNH, C=N, C=O). ^{1}H NMR spectrum, δ, ppm: 1.00 s (3H, CH_3), 1.08 s (3H, CH_3), 2.02 d (1H, CH_2, J = 16.0 Hz), 2.10 d (1H, CH_2, J = 16.0 Hz), 2.21 s (3H, CH_3), 2.38 s (2H, CH_2), 2.85 s (6H, NMe_2), 4.81 s (1H, CH), 6.48–6.60 m (2H, H_{arom}), 7.01–7.09 m (2H, H_{arom}), 9.38 br.s (1H, NH), 11.89 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 20.3 (2-CH_3), 26.9 and 29.1 (8-CH_3), 31.8 (C^8), 32.1 (CH), 39.8 (NMe_2), 40.5 (CH_2), 50.3 (CH_2), 100.3, 109.9, 112.1 (2C, C_{arom}), 127.9 (2C, C_{arom}), 128.0, 132.9, 149.5, 152.0, 156.1, 161.2, 192.8. Found, %: C 69.57; H 6.71; N 14.53. $C_{22}H_{26}N_4O_2$. Calculated, %: C 69.81; H 6.92; N 14.80.

5-(4-Diethylaminophenyl)-2,8,8-trimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4d). Yield 75%, mp >320°C, R_f 0.62. IR spectrum, ν, cm^{-1}: 3231, 3149 (NH), 1653, 1633, 1594 (δNH, C=N, C=O). ^{1}H NMR spectrum, δ, ppm: 1.01 s (3H, CH_3), 1.08 s (3H, CH_3), 1.10 t (6H, $CH_2C\mathbf{H}_3$, J = 7.0 Hz), 2.03 d (1H, CH_2, J = 16.0 Hz), 2.10 d (1H, CH_2, J = 16.0 Hz), 2.21 s (3H, 2-CH_3), 2.38 s (2H, CH_2), 3.26 br.q (4H, NCH_2, J = 7.0 Hz), 4.78 s (1H, CH), 6.39–6.46 m (2H, H_{arom}), 6.96–7.03 m (2H, H_{arom}), 9.35 br.s (1H, NH), 11.88 br.s (1H, NH). Found, %: C 70.63; H 7.28; N 13.51. $C_{24}H_{30}N_4O_2$. Calculated, %: C 70.90; H 7.43; N 3.78.

2,8,8-Trimethyl-5-(4-nitrophenyl)-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4e). Yield 73%, mp >320°C, R_f 0.63. IR spectrum, ν, cm^{-1}: 3545, 3462, 3336 (NH), 1661, 1610, 1595 (δNH, C=O, C=N). ^{1}H NMR spectrum, δ, ppm: 0.98 s (3H, CH_3), 1.09 s (3H, CH_3), 2.01 d (1H, CH_2, J = 16.1 Hz), 2.13 d (1H, CH_2, J = 16.1 Hz), 2.22 s (3H, 2-CH_3), 2.41 s (2H, CH_2), 5.03 s (1H, CH), 7.45–7.49 m (2H, H_{arom}), 8.00–8.05 m (2H, H_{arom}), 9.66 br.s (1H, NH), 12.06 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 20.3 (CH_3), 26.8 (CH_3), 28.9 (CH_3), 31.8 (C^8), 34.4 (CH), 39.7 (CH_2), 50.0 (CH_2), 98.8, 108.4, 122.3 (2C), 128.5 (2C), 145.4, 150.7, 152.4, 153.6, 157.3, 161.0, 192.7. Found, %: C 63.57; H 5.67; N 14.41. $C_{20}H_{20}N_4O_4$. Calculated, %: C 63.31; H 5.31; N 14.76.

5-[4-(Benzyloxy)phenyl]-2,8,8-trimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4f). Yield 77%, mp 298–300°C, R_f 0.65. IR spectrum, ν, cm^{-1}: 3241, 3145, 3095 (NH), 1655, 1633, 1599 (δNH, C=N, C=O). ^{1}H NMR spectrum, δ, ppm: 0.99 s (3H, CH_3), 1.08 s (3H, CH_3), 2.02 d (1H, CH_2, J = 16.0 Hz), 2.10 d (1H, CH_2, J = 16.0 Hz), 2.22 s (3H, 2-CH_3), 2.38 s (2H, CH_2), 4.86 s (1H, CH), 4.97 s (2H, OCH_2), 6.70–6.76 m (2H, H_{arom}), 7.10–7.16 m (2H, H_{arom}), 7.22–7.40 m (5H, H_{arom}), 9.43 br.s

(1H, NH), 11.91 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 20.3 (CH_3), 26.9 (CH_3), 28.9 (CH_3), 31.8, 32.5, 50.3, 69.0, 100.1, 109.7, 113.4 (2C), 126.8 (2C), 127.0, 127.7 (2C), 128.3 (2C), 137.0, 139.0, 149.7, 152.1, 156.3, 156.4, 161.1, 192.7. Found, %: C 73.21; H 6.41; N 9.27. $C_{27}H_{27}N_3O_3$. Calculated, %: C 73.44; H 6.16; N 9.51.

2-Amino-5-(2-hydroxy-3-methoxyphenyl)-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4g). Yield 63%, mp >320°C, R_f 0.55. IR spectrum, ν, cm^{-1}: 3471, 3362, 3245, 3162 (NH, NH_2, OH), 1629, 1596 (δNH, C=O, C=C). ^{1}H NMR spectrum, δ, ppm: 1.09 s (3H, CH_3), 1.11 s (3H, CH_3), 2.06 d (1H, CH_2, J = 16.0 Hz), 2.15 d (1H, CH_2, J = 16.0 Hz), 2.43 d (1H, CH_2, J = 17.3 Hz), 2.48 d (1H, CH_2, J = 17.3 Hz), 3.76 s (3H, OCH_3), 5.00 s (1H, CH), 6.20 br.s (2H, NH_2), 6.45 m (1H) and 6.53–6.59 m (2H) (H_{arom}), 9.36 br.s (1H, NH), 10.03 br.s (1H, OH), 10.76 br.s (1H, NH). Found, %: C 62.57; H 5.38; N 14.36. $C_{20}H_{22}N_4O_4$. Calculated, %: C 62.81; H 5.79; N 14.65.

2-Amino-5-(4-dimethylaminophenyl)-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4h). Yield 71%, mp 319–320°C, R_f 0.62. IR spectrum, ν, cm^{-1}: 3419, 3246, 3189 (NH, NH_2), 1672, 1612, 1590 (δNH, C=N, C=O). ^{1}H NMR spectrum, δ, ppm: 0.99 s (3H, CH_3), 1.08 s (3H, CH_3), 1.99 d (1H, CH_2, J = 16.0 Hz), 2.09 d (1H, CH_2, J = 16.0 Hz), 2.36 s (2H, CH_2), 2.85 s (6H, NMe_2), 4.71 s (1H, CH), 5.96 s (2H, NH_2), 6.50–6.59 m (2H, H_{arom}), 7.02–7.07 m (2H, H_{arom}), 8.98 br.s (1H, NH), 10.24 br.s (1H, NH). Found, %: C 66.27; H 6.37; N 18.23. $C_{21}H_{25}N_5O_2$. Calculated, %: C 66.46; H 6.64; N 18.45.

2-Amino-5-(4-diethylaminophenyl)-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4i). Yield 76%, mp >320°C, R_f 0.59. IR spectrum, ν, cm^{-1}: 3438, 3264, 3195, 3110 (NH, NH_2), 1661, 1611 (δNH, C=O, C=N). ^{1}H NMR spectrum, δ, ppm: (3H, CH_3), 1.04 s (3H, CH_3), 1.06 t (6H, $CH_2C\mathbf{H}_3$, J = 6.9 Hz), 1.99 d (1H, CH_2, J = 16.0 Hz), 2.11 d (1H, CH_2, J = 16.0 Hz), 2.38 s (2H, CH_2), 3.21–3.30 br.q (4H, NCH_2, J = 6.9 Hz), 4.66 s (1H, CH), 6.11 br.s (2H, NH_2), 6.31–6.46 m (2H, H_{arom}), 6.91–7.00 m (2H, H_{arom}), 9.06 br.s (1H, NH), 10.20 br.s (1H, NH). Found, %: C 67.51; H 7.39; N 17.41. $C_{23}H_{29}N_5O_2$. Calculated, %: C 67.78; H 6.92; N 14.80.

2-Amino-5-[4-(benzyloxy)phenyl]-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4j). Yield 75%, mp 308–310°C, R_f 0.64. IR spectrum, ν, cm^{-1}: 3448, 3248, 3194 (NH, NH_2), 1650, 1609 (δNH, C=N, C=C, C=O). ^{1}H NMR spectrum, δ, ppm: 0.90 s (3H, CH_3), 1.00 s (3H, CH_3), 1.98 d (1H, CH_2, J = 16.0 Hz), 2.14 d (1H, CH_2, J = 16.0 Hz), 2.38 d (1H, CH_2, J = 17.2 Hz), 2.42 d (1H, CH_2, J = 17.2 Hz), 4.75 s (1H, CH), 4.99 s (2H, OCH_2), 6.25 br.s (2H, NH_2), 6.76–6.81 m (2H, H_{arom}), 7.04–7.09 m (2H, H_{arom}), 7.27–7.42 m (5H, H_{arom}), 9.23 br.s (1H, NH), 10.30 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 26.8 (CH_3), 29.0 (CH_3), 32.0, 32.5, 50.2, 69.1, 92.3, 109.9, 113.7 (2C), 127.5 (2C), 127.6, 128.2 (2C), 128.3 (2C), 137.3, 140.2, 151.0, 153.8, 153.9, 156.2, 161.4, 193.7. Found, %: C 70.21; H 5.61; N 12.39. $C_{26}H_{26}N_4O_3$. Calculated, %: C 70.56; H 5.92; N 12.66.

5-(4-Dimethylaminophenyl)-2-hydroxy-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4k). Yield 63%, mp 300–302°C, R_f 0.61. IR spectrum, ν, cm^{-1}: 3482, 3320, 3172 (NH, OH), 1729, 1649, 1598 (δNH, C=N, C=O). ^{1}H NMR spectrum, δ, ppm: 0.98 s (3H, CH_3), 1.09 s (3H, CH_3), 2.04 d (1H, CH_2, J = 16.0 Hz), 2.14 d (1H, CH_2, J = 16.0 Hz), 2.38 s (2H, CH_2), 2.85 s (6H, NMe_2), 4.65 s (1H, CH), 6.50–6.58 m (2H, H_{arom}), 7.00–7.06 m (2H, H_{arom}); 8.25 br.s, 9.93 br.s, and 10.38 br.s (1H each, NH, OH). Found, %: C 67.11; H 6.42; N 14.52. $C_{22}H_{24}N_4O_3$. Calculated, %: C 67.32; H 6.16; N 14.27.

5-(4-Diethylaminophenyl)-2-hydroxy-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-4,6(3*H*,7*H*)-dione (4l). Yield 67%, mp 298–300°C, R_f 0.59. IR spectrum, ν, cm^{-1}: 3510, 3470, 3227, 3110 (NH, OH),1717, 1671, 1647, 1602, 1589 (δNH, C=N, C=C, C=O). ^{1}H NMR spectrum, δ, ppm: 0.98 s (3H, CH_3), 1.08 s (3H, CH_3), 1.10 t (6H, $CH_2C\mathbf{H}_3$, J = 7.0 Hz), 2.00 d (1H, CH_2, J = 16.0 Hz), 2.17 d (1H, CH_2, J = 16.0 Hz), 2.39 s (2H, CH_2), 3.28 br.q (4H, NCH_2, J = 7.0 Hz), 4.62 s (1H, CH), 6.39–6.48 m (2H, H_{arom}), 6.89–7.03 m (2H, H_{arom}); 8.32 br.s, 9.89 br.s, and 10.39 br.s (1H each, NH, OH). Found, %: C 67.34; H 6.67; N 13.48. $C_{23}H_{28}N_4O_3$. Calculated, %: C 67.62; H 6.90; N 13.71.

General procedure for the synthesis of 5,5′-(arylmethylene)bis[6-amino-2-methylpyrimidin-4(3*H*)-ones] 5a–5h. A mixture of 2 mmol of compound **1a** and 1 mmol of aldehyde **2a**–**2e** or **2g**–**2k** in 10 mL of glacial acetic acid was refluxed for 8–10 h. After

cooling, the precipitate was filtered off, washed with 1–2 mL of ethanol and recrystallized from acetic acid.

5,5′-[(4-Fluorophenyl)methylene]bis[6-amino-2-methylpyrimidin-4(3*H*)-one] (5a). Yield 76%, mp >320°C, R_f 0.63. IR spectrum, ν, cm^{-1}: 3465, 3323, 3171 (NH, NH_2), 1623, 1558 (C=O, C=N). ^{1}H NMR spectrum, δ, ppm: 2.18 s (6H, CH_3), 5.54 s (1H, CH), 6.01 br.s (2H, NH_2), 6.82–6.90 m (2H, H_{arom}), 7.03–7.11 m (2H, H_{arom}), 7.41 br.s (2H, NH_2), 11.60 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 20.2 (CH_3), 32.6 (CH), 95.3, 113.2, 113.5, 127.9, 128.1, 134.7, 155.5. Found, %: C 57.12; H 4.67; N 23.69. $C_{17}H_{17}FN_6O_2$. Calculated, %: C 57.30; H 4.81; N 23.58.

5,5′-[(4-Chlorophenyl)methylene]bis[6-amino-2-methylpyrimidin-4(3*H*)-one] (5b). Yield 61%, mp >320°C, R_f 0.61. IR spectrum, ν, cm^{-1}: 3452, 3319, 3152 (NH, NH_2), 1649, (C=O, C=N, δNH). ^{1}H NMR spectrum, δ, ppm: 2.19 s (6H, CH_3), 5.54 s (1H, CH), 5.97 br.s (2H, NH_2), 7.04–7.09 m (2H, H_{arom}), 7.10–7.15 m (2H, H_{arom}), 7.45 br.s (2H, NH_2), 11.62 br.s (2H, NH). Found, %: C 54.61; H 4.43; N 22.37. $C_{17}H_{17}ClN_6O_2$. Calculated, %: C 54.77; H 4.60; N 22.54.

5,5′-[(4-Bromophenyl)methylene]bis[6-amino-2-methylpyrimidin-4(3*H*)-one] (5c). Yield 52%, mp >320°C, R_f 0.60. IR spectrum, ν, cm^{-1}: 3451, 3315, 3120 (NH, NH_2), 1616 (C=O, C=N). ^{1}H NMR spectrum, δ, ppm: 2.19 s (6H, CH_3), 5.52 s (1H, CH), 5.97 br.s (2H, NH_2), 6.99–7.04 m (2H, H_{arom}), 7.23–7.28 m (2H, H_{arom}), 7.35 br.s (2H, NH_2), 11.58 br.s (2H, NH). Found, %: C 48.71; H 4.41; N 20.37. $C_{17}H_{17}BrN_6O_2$. Calculated, %: C 48.93; H 4.11; N 20.11.

5,5′-[(4-Nitrophenyl)methylene]bis[6-amino-2-methylpyrimidin-4(3*H*)-one] (5d). Yield 62%, mp >320°C, R_f 0.62. IR spectrum, ν, cm^{-1}: 3425 s, 3337 s, 3194 s (NH, NH_2), 1714 s, 1621 s, 1519 s (C=O, δNH, C=N). ^{1}H NMR spectrum, δ, ppm: 2.18 s (6H, CH_3), 5.59 s (1H, CH), 6.81 br.s (2H, NH_2), 7.10 br.s (2H, NH_2), 7.22–7.27 m (2H, H_{arom}), 8.06–8.11 m (2H, H_{arom}), 11.68 br.s (2H, NH). Found, %: C 53.22; H 4.17; N 25.38. $C_{17}H_{17}N_7O_4$. Calculated, %: C 53.26; H 4.47; N 25.58.

5,5′-{[4-(Benzyloxy)phenyl]methylene}bis-[6-amino-2-methylpyrimidin-4(3*H*)-one] (5e). Yield 62%, mp >320°C, R_f 0.64. IR spectrum, ν, cm^{-1}: 3435, 3331, 3169 (NH, NH_2), 1619, (C=O, δNH, C=N). ^{1}H NMR spectrum, δ, ppm: 2.18 s (6H, CH_3), 5.02 s (2H, OCH_2), 5.51 s (1H, CH), 5.93 br.s (2H, NH_2), 6.73–6.78 m (2H, H_{arom}), 6.95–7.00 m (2H, H_{arom}), 7.23–7.28 m (1H, H_{arom}), 7.30–7.36 m (2H, H_{arom}), 7.38–7.43 m (2H, H_{arom}), 7.30 br.s (2H, NH_2), 11.55 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 20.2 (CH_3), 32.5 (CH), 69.0 (OCH_2), 113.3 (2C), 126.9 (2C), 127.0 (2C), 127.5 (CH), 127.7 (2C), 131.1, 137.2, 155.4, 155.7. Found, %: C 64.72; H 5.31; N 18.75. $C_{24}H_{24}N_6O_3$. Calculated, %: C 64.84; H 5.44; N 18.91.

5,5′-[(4-Methoxyphenyl)methylene]bis[6-amino-2-methylpyrimidin-4(3*H*)-one] (5f). Yield 65%, mp >320°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3455, 3322, 3165 (NH, NH_2), 1613 (C=O, C=N, δNH). ^{1}H NMR spectrum, δ, ppm: 2.18 s (6H, CH_3), 3.73 s (3H, OCH_3), 5.52 s (1H, CH), 5.99 br.s (2H, NH_2), 6.65–6.70 m (2H, H_{arom}), 6.95–7.00 m (2H, H_{arom}), 7.37 br.s (2H, NH_2), 11.59 br.s (2H, NH). Found, %: C 58.37; H 5.28; N 22.63. $C_{18}H_{20}N_6O_3$. Calculated, %: C 58.69; H 5.47; N 22.81.

5,5′-[(2,3-Dimethoxyphenyl)methylene]bis-[6-amino-2-methylpyrimidin-4(3*H*)-one (5g). Yield 72%, mp >320°C, R_f 0.68. IR spectrum, ν, cm^{-1}: 3331, 3173 (NH, NH_2), 1622 (C=O, C=N, δNH). ^{1}H NMR spectrum, δ, ppm: 2.16 s (6H, CH_3), 3.52 s (3H, OCH_3), 3.78 s (3H, OCH_3), 5.60 s (1H, CH), 6.40 br.s (4H, NH_2), 6.70–6.85 m (3H, H_{arom}), 11.50 br.s (2H, NH). Found, %: C 57.11; H 5.31; N 20.87. $C_{19}H_{22}N_6O_4$. Calculated, %: C 57.28; H 5.57; N 21.10.

5,5′-[(1,3-Benzodioxol-5-yl)methylene]bis-[6-amino-2-methylpyrimidin-4(3*H*)-one (5h). Yield 70%, mp >320°C, R_f 0.66. IR spectrum, ν, cm^{-1}: 3452, 3321, 3166 (NH, NH_2), 1612, (C=O, C=N, δNH). ^{1}H NMR spectrum, δ, ppm: 2.18 s (6H, CH_3), 5.46 s (1H, CH), 5.89 s (2H, OCH_2O), 6.34 br.s (2H, NH_2), 6.49–6.55 m (2H, H_{arom}), 6.63 d (1H, H_{arom}, J = 7.9 Hz), 7.25 br.s (2H, NH_2), 11.53 br.s (2H, NH). Found, %: C 56.32; H 4.51; N 22.39. $C_{18}H_{18}N_6O_4$. Calculated, %: C 56.54; H 4.74; N 22.08.

CONFLICT OF INTERESTS

The authors declare the absence of conflict of interests.

REFERENCES

1. Bharate, J.B., Vishwakarma, R.A., and Bharate, S.B., *RSC Adv.*, 2015, vol. 5, p. 42020. https://doi.org/10.1039/C5RA07798B
2. Bhaskar, G., Arun, Y., Balachandran, C., Saikumar, C., and Perumol, P., *Eur. J. Med. Chem.*, 2012, vol. 51, p. 79. https://doi.org/10.1016/j.ejmech.2012.02.024

3. Joshi, A.A. and Visvanathan, C.L., *Bioorg. Med. Chem. Lett*., 2006, vol. 16, p. 2613. https://doi.org/10.1016/j.bmcl.2006.02.038
4. Hiramoto, K., Nasuhara, A., Michiloshi, K., Kato, T., and Kikugawa, K., *Mutat. Res., Genet. Toxicol. Environ. Mutagen*., 1997, vol. 47, p. 395. https://doi.org/10.1016/s1383-5718(97)00141-1
5. El-Gazzar, A.B.A., Wl-Enany, M.M., and Mahmoud, M.N., *Bioorg. Med. Chem*., 2008, vol. 16, p. 3261. https://doi.org/10.1016/j.bmc.2007.12.012
6. Jnsuasty, B., Beccera, D., Quiroga, J., Abonia, R., Noguaras, M., and Cobo, J., *J. Heterocycl. Chem*., 2013, vol. 50, p. 506. https://doi.org/10.1002/jhet.1510
7. Melik-Ogandzhanyan, R.G., Ovsepyan, T.R., Karakhanyan, G.S., Israelyan, S.G., Arsenyan, F.G., Nersesyan, L.E., and Agaronyan, A.S., *Mezhdunar. Zh. Prikl. Fundam. Issled*., 2016, vol. 6, p. 455.
8. Hovsepyan, T.R., Karakhanyan, G.S., Israelyan, S.G., and Panosyan, G.A., *Russ. J. Gen. Chem*., 2018, vol. 88, p. 1114. https://doi.org/10.1134/S1070363218060117