# New tricyclic compounds with pyrimido[4,5-*d*]pyrimidine fragment, the 7,8-dihydro-1*H*-pyrimido[4,5,6-*de*]quinazoline derivatives*

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A reaction of 2-diaminomethylidenedimedone with aryl isocyanates leads to the formation of the corresponding ureas, which upon the action of sodium methoxide cyclize to 4-amino-7,8-dihydroquinazoline-2,5(1*H*,6*H*)-dione derivatives. The latter react with aryl isocyanates following the similar scheme to furnish 1,6-diaryl-8,8-dimethyl-7,8-dihydro-1*H*-pyrimido-[4,5,6-*de*]quinazoline-2,5(3*H*,6*H*)-diones, new tricyclic compounds containing pyrimido-pyrimidine fragment.

**Key words:** 2-diaminomethylidene-5,5-dimethylcyclohexane-1,3-dione, aryl isocyanates, 4-amino-7,8-dihydroquinazoline-2,5(1*H*,6*H*)-diones, cyclization, 7,8-dihydro-1*H*-pyrimido-[4,5,6-*de*]quinazoline-2,5(3*H*,6*H*)-dione derivatives, [1,5]-hydride shift.

Pyrimido[4,5-*d*]pyrimidines, close in the structure to pteridines and purines, are a biologically interesting system and exhibit various kinds of pharmacological activity: bronchodilatory,[1] antibacterial,[2,3] antiallergic,[4] antihypertensive,[5] as well as are inhibitors of phosphodiesterase[1] and dihydrofolatreductase.[6]

In continuation of our studies on the synthesis of pyrimido[4,5-*d*]pyrimidines,[7—12] in the present work we report on 7,8-dihydropyrimido[4,5,6-*de*]quinazoline-2,5-dione derivatives, tricyclic compounds containing a pyrimidopyrimidine fragment.

One of the simple and efficient ways for the construction of the pyrimido[4,5-*d*]pyrimidine system is based on the conversion of dioxoketene *N*,*N*-acetals with isocyanates.[8,11—13] Taking into account electronic and steric effects, it seems the most convenient to use ketene aminals unsubstituted at the nitrogen atoms, like, for example, in the scheme suggested by us for the synthesis of 3,6-diaryl-5-methylpyrimido[4,5-*d*]pyrimidine-2,4,7(1*H*,3*H*,6*H*)-triones.[12]

Recently, we have shown that ketene aminals of such a type can be obtained from 1,3-cyclohexanedione and dimedone.[14] In the present work, we consider heterocyclization involving 2-diaminomethylidene-5,5-dimethylcyclohexane-1,3-dione (**1**) and aryl isocyanates. It was found that ketene aminal **1** reacts with phenyl isocyanate **2a** and 4-chlorophenyl isocyanate **2b** in boiling toluene with the formation of ureas **3a**,**b**, which do not react with excess aryl isocyanate. Compounds **3a**,**b** upon the action of MeONa in MeOH were converted to the 4-amino-7,8-dihydroquinazoline-2,5(1*H*,6*H*)-dione derivatives **4a**,**b** (Scheme 1). Thus, the enamine fragment is involved into the heterocyclization, as in the case of the reaction of β-oxoester diaminomethylidene derivatives.[12]

Earlier, it has been reported on the synthesis of 2-ureidomethylidenecyclohexane-1,3-diones by a three-component reaction of 1,3-cyclohexanediones, triethyl orthoformate, and urea, however, these compounds were not used in further processes of heterocyclization.[15]

Bicyclic compounds **4a**,**b** are also able to react with aryl isocyanates in boiling toluene with the formation of ureas **5a**,**b** in 87—89% yields. Cyclization of the latter in the presence of MeONa in MeOH leads to 1,6-diaryl-8,8-dimethyl-7,8-dihydro-1*H*-pyrimido[4,5,6-*de*]quinazoline-2,5(3*H*,6*H*)-diones **6a**,**b**, whose yields were 80 and 65%, respectively.

The synthesized compounds **3**—**6** are well soluble in chloroform. Their structures were confirmed by the IR and $^1$H NMR spectroscopic data and mass spectrometric data, whereas heterocycles **4** and **6** were additionally characterized by the $^{13}$C NMR spectroscopic data and $^1$H/$^{13}$C HSQC and HMBC two-dimensional NMR spectra. Thus, the mass spectra (EI) of compounds **3**, **4**, and **6** exhibit peaks of molecular ions, whereas such peaks are absent in the spectra of ureas **5**, however, there are intensive peaks of the $[M - RNCO]^+$ and $[RNCO]^+$ ions. The IR spectra of compounds **3**—**6** are characterized by the presence of the absorption bands of the CO, NH, and (or) $NH_2$ group (see Experimental). In the $^1$H NMR spectra ($CDCl_3$) of ureas **3**, unlike in that of ketene aminal **1**, the two $CH_2$ groups have different chemical shifts (for example, for

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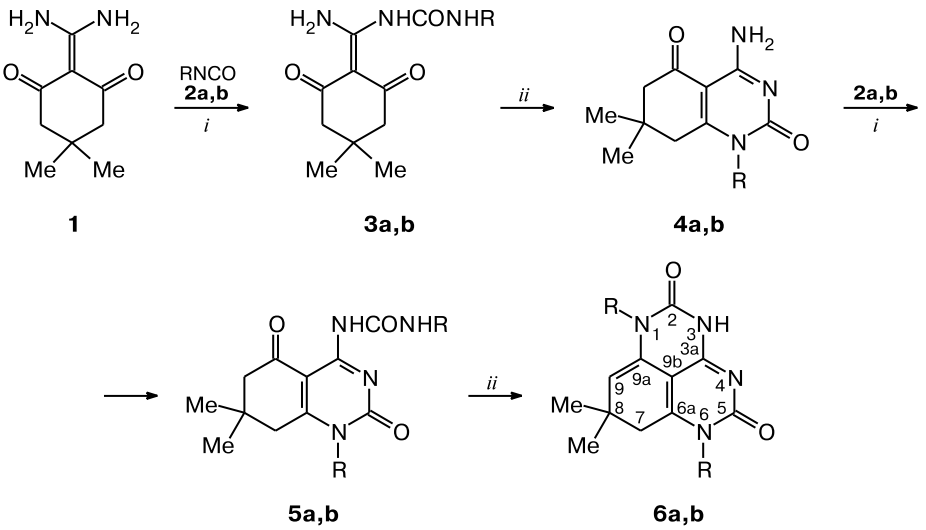
**Scheme 1**




R = Ph (**a**), 4-$ClC_6H_4$ (**b**)

**Reagents and conditions:** *i*. toluene, Δ; *ii*. MeONa, MeOH, Δ; AcOH, 20 °C.

compound **3a** they are at δ 2.30 and 2.37) and for dihydroquinazolines **4** and ureas **5**, the differences become more pronounced (for example, for compound **4a**: δ 2.28 and 2.40, for compound **5a**: δ 2.35 and 2.47). In addition, if ureas **3a**,**b** have four broad singlets from the NH and (or) $NH_2$ groups, each of the compounds **4a**,**b** and **5a**,**b** have only two broad singlets (nonequivalence of the protons of the $NH_2$ group in dihydroquinazolines **4a**,**b** indicates formation of a hydrogen bond between the $NH_2$ and CO groups). The $^1H$ NMR spectra ($CDCl_3$) of dihydropyrimidoquinazolines **6** exhibit singlets for the $CH_2$ group at δ ~2.2 and for the proton H(9) at δ ~4.0. If the $^{13}C$ NMR spectrum (DMSO-$d_6$) of dihydroquinazoline **4b** has a signal at δ 196.0 (C(5)), compounds **6** have the most low-field signal at δ 156.6. The $^1H/^{13}C$ HMBC two-dimensional NMR spectra of dihydropyrimidoquinazolines **6** exhibit the correlation peaks for the protons of the $CH_2$ group with the C(9b), C(9), C(8), C(6a) atoms and the methyl groups, whereas the protons H(9), with the C(9a), C(9b), C(8), C(7) atoms and the methyl groups. Attention should be paid to considerable differences in the chemical shifts for the C(9a) and C(6a) atoms in the $^{13}C$ NMR spectra (δ 130.7—130.9 and 154.8—155.0, respectively), which confirms that the structures of pyrimidine rings in compounds **6** significantly differ.

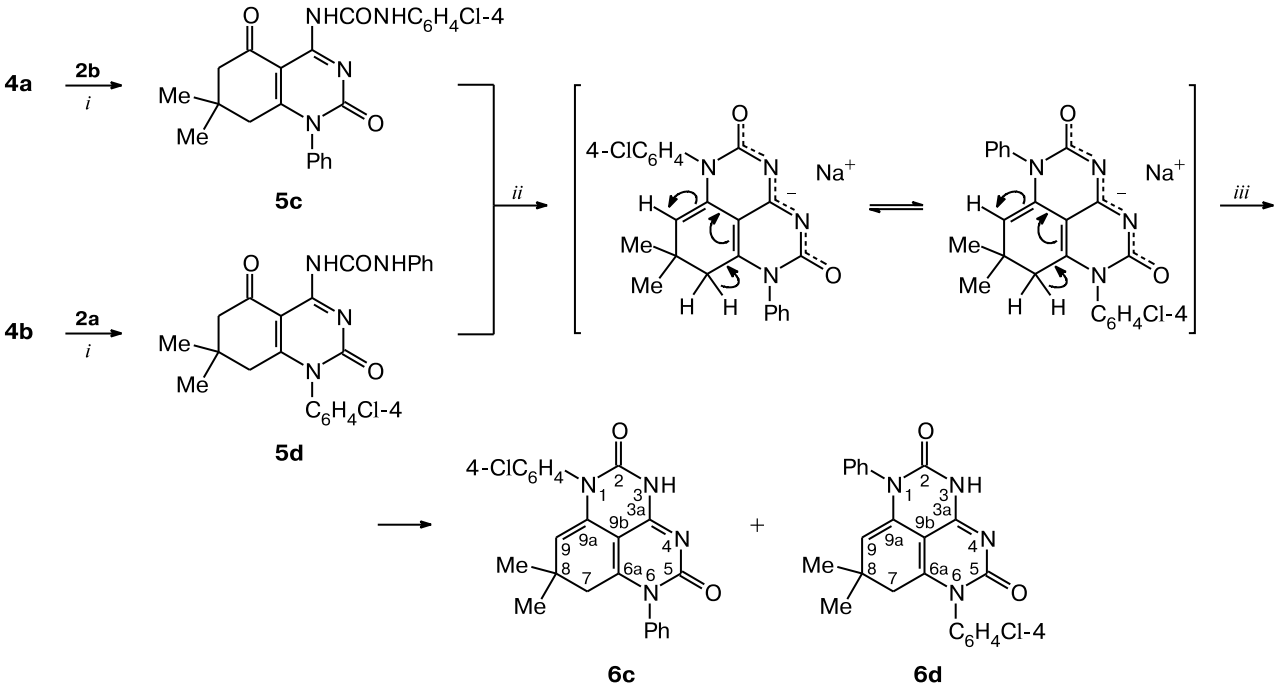
Varying isocyanates in the steps of preparation of bicyclic and tricyclic systems, one can obtain dihydropyrimidoquinazolinediones with different substituents at positions N(1) and N(6) (Scheme 2). By analogy with compounds **5a**,**b**, ureas **5c**,**d** were synthesized for this purpose (the yields were 86—98%), whose intramolecular cyclization upon the action of MeONa in MeOH led to the formation of isomeric compounds with the suggested structures **6c**,**d** (the yields were 67 and 80%, respectively).

The IR and mass spectral data, as well as $^1H$ NMR spectra (300 MHz) obtained for dihydropyrimidoquinazolinediones resemble the spectral data for similar heterocycles **6a**,**b** with the same substituents at the N(1) and N(6) atoms. However, their $^{13}C$ NMR spectra, as well as $^1H$ NMR spectra (600 MHz) in both $CDCl_3$ and DMSO-$d_6$ exhibit a double set of closely placed signals (the $^1H$ NMR spectra in DMSO-$d_6$ have two signals not only for the aromatic protons and H(9) protons, but also for the protons of the $CH_2$ group). Recording the $^1H$ NMR spectra in DMSO-$d_6$ at 60 °C, as well as in the presence of trifluoroacetic acid, produced no changes. These data indicate that the cyclization of both the urea **5c** and the urea **5d** leads to isomeric compounds **6c** and **6d** in virtually equal ratio. Recording the $^1H/^1H$ COSY, $^1H/^{13}C$ HSQC and HMBC and $^1H/^{15}N$ HMBC two-dimensional NMR spectra allowed us to assign almost all the signals for compounds **6c** and **6d** in the $^1H$ and $^{13}C$ NMR spectra (see Experimental). Heterocycles **6c** and **6d** do not differ in their chromatographic lability.

It can be suggested that an equilibrium between the corresponding salts is reached upon the action of a base due to the proton transfer over the cyclohexane ring, which disappears after acidification with acetic acid. Apparently, this process can be interpreted as a [1,5]-hydride shift (see review 16).

In conclusion, when pyrimidine ring is built as a part of the bi- and tricyclic systems, 2-diaminomethylidene-

**Scheme 2**




**Reagents and conditions:** *i.* toluene, Δ; *ii.* MeONa, MeOH, Δ; *iii.* AcOH, 20 °C.

cyclohexane-1,3-diones can be used not only as *N*,*N*-binucleophiles (like amidines),[14] but also as functionalized enaminones.

## Experimental

$^1$H NMR spectra were recorded on a Bruker AM-300 spectrometer (300 MHz), $^1$H NMR spectra of tricyclic compounds **6**, $^{13}$C NMR spectra, and $^1$H/$^1$H COSY, $^1$H/$^{13}$C HSQC and HMBC, $^1$H/$^{15}$N HMBC two-dimensional NMR spectra were recorded on a Bruker Avance 600 spectrometer (600, 150, and 60.8 MHz for $^1$H, $^{13}$C, and $^{15}$N, respectively). Signals for the residual protons of the deuterated solvents were used as a reference in $^1$H NMR spectra (7.27 for $CDCl_3$ and 2.50 for DMSO-$d_6$) and multiplet signals of the deuterated solvents, in the $^{13}$C NMR spectra (39.50 for DMSO-$d_6$ and 77.00 for $CDCl_3$). Chemical shifts of $^{15}$N were measured relatively to the external standard $MeNO_2$ (the high-field chemical shifts are given with the negative sign). IR spectra were recorded on a Specord-M82 spectrometer, and mass spectra, on a Kratos MS-30 instrument (EI, 70 eV, temperature of the ionization chamber was 250 °C, a direct injection of compounds). We used in the syntheses aryl isocyanates purchased from Lancaster, anhydrous toluene was obtained by distillation over sodium, methanol was purified by fractional distillation. 2-Diaminomethylidene-5,5-dimethylcyclohexane-1,3-dione **1** was synthesized according to the described by us procedure.[14] Column chromatography was performed on Merck silica gel 60 (0.063—0.200 mm).

**2-[Amino(*N*´-phenylureido)methylidene]-5,5-dimethylcyclohexane-1,3-dione (3a).** Phenyl isocyanate (0.18 mL, 1.6 mmol) was added to ketene aminal **1** (0.2 g, 1.1 mmol) in anhydrous toluene (3 mL), and the mixture was refluxed for 8 h, cooled to 20 °C, a precipitate that formed was filtered off, washed with toluene and light petroleum, and recrystallized from MeOH to obtain urea **3a** (0.23 g, 71%), m.p. 219—220 °C. Found (%): C, 63.43; H, 6.10; N, 13.81. $C_{16}H_{19}N_3O_3$. Calculated (%): C, 63.77; H, 6.36; N, 13.94. MS, *m*/*z* ($I_{rel}$ (%)): 301 $[M]^+$ (6), 209 $[M - PhNH]^+$ (24), 182 $[M - PhNCO]^+$ (49), 119 $[PhNCO]^+$ (70), 93 $[PhNH_2]^+$ (100). IR ($CHCl_3$), ν/cm$^{-1}$: 3336 (NH), 3030—2950 (NH, CH), 1708 (CO), 1644, 1532. $^1$H NMR ($CDCl_3$), δ: 0.99 (s, 6 H, 2 Me); 2.30 (s, 2 H, $CH_2$); 2.37 (s, 2 H, $CH_2$); 7.16 (t, 1 H, *p*-$H_{Ph}$, *J* = 7.5 Hz); 7.35 (t, 2 H, *m*-$H_{Ph}$, *J* = 7.5 Hz); 7.41 (d, 2 H, *o*-$H_{Ph}$, *J* = 7.5 Hz); 8.32 (br.s, 1 H, NHPh); 9.67 (br.s, 1 H, $NH_2$); 11.43 (br.s, 1 H, $NH_2$); 13.89 (br.s, 1 H, NH).

**2-[Amino(*N*´-4-chlorophenylureido)methylidene]-5,5-dimethylcyclohexane-1,3-dione (3b)** was synthesized similarly to urea **3a** from ketene aminal **1** and 4-chlorophenyl isocyanate, the yield was 77%, m.p. 239—240 °C (from methanol). Found (%): C, 57.49; H, 5.02; Cl, 10.70; N, 12.48. $C_{16}H_{18}ClN_3O_3$. Calculated (%): C, 57.23; H, 5.40; Cl, 10.56; N, 12.51. MS, *m*/*z* ($I_{rel}$ (%)): 335 $[M]^+$ (3), 209 $[M - ClC_6H_4NH]^+$ (100), 166 $[M - ClC_6H_4NCO - Me - H]^+$ (28), 153 $[ClC_6H_4NCO]^+$ (27), 127 $[ClC_6H_4NH_2]^+$ (55). IR (KBr), ν/cm$^{-1}$: 3296 (NH), 3210—2950 (NH, CH), 1700 (CO), 1636, 1528. $^1$H NMR ($CDCl_3$), δ: 1.01 (s, 6 H, 2 Me); 2.31 (s, 2 H, $CH_2$); 2.38 (s, 2 H, $CH_2$); 7.31 (d, 2 H, $C_6H_4$, *J* = 7.5 Hz); 7.40 (d, 2 H, $C_6H_4$, *J* = 7.5 Hz); 8.33 (br.s, 1 H, N*H*$C_6H_4$); 9.61 (br.s, 1 H, $NH_2$); 11.47 (br.s, 1 H, $NH_2$); 13.97 (br.s, 1 H, NH).

**4-Amino-7,7-dimethyl-1-phenyl-7,8-dihydroquinazoline-2,5-(1*H*,6*H*)-dione (4a).** A solution of MeONa in MeOH (0.5 mL,

0.53 mmol) was added to urea **3a** (0.16 g, 0.53 mmol) in MeOH (5 mL), and the mixture was refluxed for 1 h, cooled to 20 °C, acidified with AcOH, the solvent was evaporated *in vacuo* to dryness. The residue was diluted with water, a precipitate was filtered off, washed with diethyl ether to obtain dihydroquinazoline **4a** (0.12 g, 80%), m.p. 286—287 °C. Found (%): C, 67.95; H, 5.67; N, 14.47. $C_{16}H_{17}N_3O_2$. Calculated (%): C, 67.83; H, 6.05; N, 14.83. MS, *m/z* ($I_{rel}$ (%)): 283 $[M]^+$ (100), 268 $[M - Me]^+$ (44), 241 $[M - H_2NCN]^+$ (23), 226 $[M - Me - H_2NCN]^+$ (24), 147 $[M - Me - PhNCO - 2H]^+$ (42), 117 $[PhNCO - 2H]^+$ (33). IR ($CHCl_3$), ν/cm$^{-1}$: 3480, 3320 (NH), 3010—2960 (NH, CH), 1688 (CO), 1648, 1608, 1512. $^1$H NMR ($CDCl_3$), δ: 1.02 (s, 6 H, 2 Me); 2.28 (s, 2 H, $CH_2$); 2.40 (s, 2 H, $CH_2$); 6.45 (br.s, 1 H, $NH_2$); 7.18 (d, 2 H, Ph, *J* = 7.5 Hz); 7.52 (m, 3 H, Ph); 9.00 (br.s, 1 H, $NH_2$).

**4-Amino-1-(4-chlorophenyl)-7,7-dimethyl-7,8-dihydroquinazoline-2,5(1*H*,6*H*)-dione (4b)** was synthesized similarly to dihydroquinazoline **4a** from urea **3b**, the yield was 62%, m.p. 290—291 °C. Found (%): C, 60.17; H, 4.65; Cl, 11.19; N, 13.17. $C_{16}H_{16}ClN_3O_2$. Calculated (%): C, 60.48; H, 5.08; Cl, 11.16; N, 13.22. MS, *m/z* ($I_{rel}$ (%)): 317 $[M]^+$ (55), 316 $[M - H]^+$ (100), 302 $[M - Me]^+$ (14), 127 $[ClC_6H_4NH_2]^+$ (17), 101 (62). IR ($CHCl_3$), ν/cm$^{-1}$: 3480, 3320 (NH), 3030—2960 (NH, CH), 1680 (CO), 1648, 1608, 1512. $^1$H NMR ($CDCl_3$), δ: 1.05 (s, 6 H, 2 Me); 2.29 (s, 2 H, $CH_2$); 2.42 (s, 2 H, $CH_2$); 6.35 (br.s, 1 H, $NH_2$); 7.15 (d, 2 H, $C_6H_4$, *J* = 8.0 Hz); 7.52 (d, 2 H, $C_6H_4$, *J* = 8.0 Hz); 9.03 (br.s, 1 H, $NH_2$). $^1$H NMR (DMSO-$d_6$), δ: 0.93 (s, 6 H, 2 Me); 2.29 (s, 2 H, $CH_2$); 2.36 (s, 2 H, $CH_2$); 7.35 (d, 2 H, *o*-$H_{C_6H_4}$, *J* = 7.8 Hz); 7.59 (d, 2 H, *m*-$H_{C_6H_4}$, *J* = 7.8 Hz); 8.01 (br.s, 1 H, $NH_2$); 8.69 (br.s, 1 H, $NH_2$). $^{13}$C NMR (DMSO-$d_6$), δ: 27.39 (2 Me); 31.46 (C(7)); 41.71 (C(8)); 50.19 (C(6)); 99.62 (C(4a)); 129.48 (*o*-$C_{C_6H_4}$); 130.22 (*m*-$C_{C_6H_4}$); 133.25 (*p*-$C_{C_6H_4}$); 136.76 (*ipso*-$C_{C_6H_4}$); 153.44 (C(4)); 163.17 (C(2)); 166.05 (C(8a)); 196.04 (C(5)). Assignment of the signals performed was based on the $^1$H/$^{13}$C HMBC two-dimensional NMR.

**7,7-Dimethyl-1-phenyl-4-(*N*´-phenylureido)-7,8-dihydroquinazoline-2,5(1*H*,6*H*)-dione (5a).** Phenyl isocyanate (0.03 mL, 0.3 mmol) was added to dihydroquinazoline **4a** (0.06 g, 0.2 mmol) in anhydrous toluene (3 mL), and the mixture was refluxed for 6 h, cooled to 20 °C. A precipitate that formed was filtered off, washed with toluene, dried *in vacuo*, and recrystallized from MeOH to obtain urea **5a** (0.07 g, 87%), m.p. > 300 °C. Found (%): C, 68.78; H, 5.47; N, 13.77. $C_{23}H_{22}N_4O_3$. Calculated (%): C, 68.64; H, 5.51; N, 13.92. MS, *m/z* ($I_{rel}$ (%)): 283 $[M - PhNCO]^+$ (67), 282 $[M - PhNCO - H]^+$ (100), 268 $[M - PhNCO - Me]^+$ (12), 119 $[PhNCO]^+$ (80), 93 $[PhNH_2]^+$ (81). IR ($CHCl_3$), ν/cm$^{-1}$: 3184 (NH), 3030—2960 (NH, CH), 1696 (CO), 1648, 1596, 1528. $^1$H NMR ($CDCl_3$), δ: 1.04 (s, 6 H, 2 Me); 2.35 (s, 2 H, $CH_2$); 2.47 (s, 2 H, $CH_2$); 7.09 (t, 1 H, *p*-$H_{Ph}$, *J* = 7.5 Hz); 7.21 (d, 2 H, *o*-$H_{Ph}$, *J* = 7.5 Hz); 7.32 (m, 3 H, *m*-$H_{Ph}$, *p*-$H_{Ph}$); 7.59 (m, 4 H, *o*-$H_{Ph}$, *m*-$H_{Ph}$); 11.45 (br.s, 1 H, NH); 11.85 (br.s, 1 H, NH).

**1-(4-Chlorophenyl)-4-(*N*´-4-chlorophenylureido)-7,7-dimethyl-7,8-dihydroquinazoline-2,5(1*H*,6*H*)-dione (5b)** was synthesized similarly to urea **5a** from dihydroquinazoline **4b** and 4-chlorophenyl isocyanate, the yield was 89%, m.p. 290—291 °C (sublimes). Found (%): C, 58.26; H, 4.14; Cl, 15.09; N, 11.72. $C_{23}H_{20}Cl_2N_4O_3$. Calculated (%): C, 58.61; H, 4.28; Cl, 15.04; N, 11.89. MS, *m/z* ($I_{rel}$ (%)): 318 $[M - ClC_6H_4NCO]^+$ (42), 317 $[M - ClC_6H_4NCO - H]^+$ (57), 316 $[M - ClC_6H_4NCO - 2H]^+$ (100), 153 $[ClC_6H_4NCO]^+$ (58). IR (KBr), ν/cm$^{-1}$: 3150—2950 (NH, CH), 1700 (CO), 1652, 1600, 1528. $^1$H NMR ($CDCl_3$), δ: 1.06 (s, 6 H, 2 Me); 2.36 (s, 2 H, $CH_2$); 2.48 (s, 2 H, $CH_2$); 7.14 (d, 2 H, $C_6H_4$, *J* = 7.5 Hz); 7.28 (d, 2 H, $C_6H_4$, *J* = 7.5 Hz); 7.53 (d, 2 H, $C_6H_4$, *J* = 7.5 Hz); 7.58 (d, 2 H, $C_6H_4$, *J* = 7.5 Hz); 11.45 (br.s, 1 H, NH); 11.86 (br.s, 1 H, NH).

**4-(*N*´-4-Chlorophenylureido)-7,7-dimethyl-1-phenyl-7,8-dihydroquinazoline-2,5(1*H*,6*H*)-dione (5c)** was synthesized similarly to urea **5a** from dihydroquinazoline **4a** and 4-chlorophenyl isocyanate, the yield was 98%, m.p. 255—256 °C (sublimes). Found (%): C, 62.88; H, 4.75; Cl, 8.06; N, 12.69. $C_{23}H_{21}ClN_4O_3$. Calculated (%): C, 63.23; H, 4.84; Cl, 8.11; N, 12.82. MS, *m/z* ($I_{rel}$ (%)): 283 $[M - ClC_6H_4NCO]^+$ (85), 282 $[M - ClC_6H_4NCO - H]^+$ (97), 268 $[M - ClC_6H_4NCO - Me]^+$ (69), 153 $[ClC_6H_4NCO]^+$ (100), 127 $[ClC_6H_4NH_2]^+$ (34). IR ($CHCl_3$), ν/cm$^{-1}$: 3175 (NH), 3020—2960 (NH, CH), 1700 (CO), 1652, 1604, 1528. $^1$H NMR ($CDCl_3$), δ: 1.04 (s, 6 H, 2 Me); 2.36 (s, 2 H, $CH_2$); 2.47 (s, 2 H, $CH_2$); 7.21 (m, 2 H, Ph); 7.29 (m, 2 H, $C_6H_4$); 7.58 (m, 5 H, $C_6H_4$, Ph); 11.46 (br.s, 1 H, NH); 11.94 (br.s, 1 H, NH).

**1-(4-Chlorophenyl)-7,7-dimethyl-4-(*N*´-phenylureido)-7,8-dihydroquinazoline-2,5(1*H*,6*H*)-dione (5d)** was synthesized similarly to urea **5a** from dihydroquinazoline **4b** and phenyl isocyanate, the yield was 86%, m.p. 270—271 °C (sublimes). Found (%): C, 63.07; H, 4.53; Cl, 8.16; N, 12.68. $C_{23}H_{21}ClN_4O_3$. Calculated (%): C, 63.23; H, 4.84; Cl, 8.11; N, 12.82. MS, *m/z* ($I_{rel}$ (%)): 317 $[M - PhNCO]^+$ (73), 316 $[M - PhNCO - H]^+$ (100), 302 $[M - PhNCO - Me]^+$ (15), 127 $[ClC_6H_4NH_2]^+$ (22); 119 $[PhNCO]^+$ (46). IR ($CHCl_3$), ν/cm$^{-1}$: 3190 (NH), 3020—2960 (NH, CH), 1696 (CO), 1652, 1604, 1528. $^1$H NMR ($CDCl_3$), δ: 1.04 (s, 6 H, 2 Me); 2.34 (s, 2 H, $CH_2$); 2.46 (s, 2 H, $CH_2$); 7.16 (m, 3 H, *o*-$H_{C_6H_4}$, *p*-$H_{Ph}$); 7.33 (m, 2 H, *m*-$H_{Ph}$); 7.57 (m, 4 H, *m*-$H_{C_6H_4}$, *o*-$H_{Ph}$); 11.42 (br.s, 1 H, NH); 11.80 (br.s, 1 H, NH).

**8,8-Dimethyl-1,6-diphenyl-7,8-dihydro-1*H*-pyrimido[4,5,6-*de*]quinazoline-2,5(3*H*,6*H*)-dione (6a).** A solution of MeONa in MeOH (0.2 mL, 0.2 mmol) was added to urea **5a** (0.08 g, 0.2 mmol) in MeOH (5 mL), and the mixture was refluxed for 10 min, cooled to 20 °C, acidified with AcOH, the solvent was evaporated *in vacuo* to dryness. The residue was diluted with water, a precipitate was filtered off and recrystallized from the benzene—methanol mixture to obtain compound **6a** (0.06 g, 80%), m.p. 308—309 °C. Found (%): C, 71.50; H, 5.19; N, 14.30. $C_{23}H_{20}N_4O_2$. Calculated (%): C, 71.86; H, 5.24; N, 14.57. MS, *m/z* ($I_{rel}$ (%)): 384 $[M]^+$ (7), 369 $[M - Me]^+$ (100), 326 $[M - 2 Me - CO]^+$ (13), 250 $[M - Me - PhNCO]^+$ (4), 119 $[PhNCO]^+$ (17), 93 $[PhNH_2]^+$ (73). IR ($CHCl_3$), ν/cm$^{-1}$: 3392 (NH), 3024, 1712 (CO), 1652, 1632, 1560. $^1$H NMR ($CDCl_3$), δ: 0.93 (s, 6 H, 2 Me); 2.22 (s, 2 H, $CH_2$); 3.99 (s, 1 H, H(9)); 7.22 (d, 2 H, *o*-$H_{Ph}$, *J* = 8.0 Hz); 7.28 (d, 2 H, *o*-$H_{Ph}$, *J* = 8.0 Hz); 7.53 (m, 6 H, *m*-H, 2 Ph; *p*-H, 2 Ph); 7.97 (br.s, 1 H, NH). $^{13}$C NMR ($CDCl_3$), δ: 28.62 (2 Me); 32.31 (C(8)); 40.16 (C(7)); 95.12 (C(9b)); 106.95 (C(9)); 127.75 (*o*-$C_{Ph}$); 128.88 (*o*-$C_{Ph}$); 128.92 (*p*-$C_{Ph}$); 129.50 (*p*-$C_{Ph}$); 129.98 (*m*-$C_{Ph}$); 130.06 (*m*-$C_{Ph}$); 130.88 (C(9a)); 136.16 (*ipso*-$C_{Ph}$); 136.68 (*ipso*-$C_{Ph}$); 155.02 (C(6a)); 148.93, 156.02, 156.56 (C(2), C(3a), C(5)). Assignment of the signals performed was based on the $^1$H/$^{13}$C HMBC two-dimensional NMR.

**1,6-Di(4-chlorophenyl)-8,8-dimethyl-7,8-dihydro-1*H*-pyrimido[4,5,6-*de*]quinazoline-2,5(3*H*,6*H*)-dione (6b)** was synthesized similarly to compound **6a** from urea **5b**, the yield was 65%, m.p. 295—296 °C (from the benzene—methanol mixture). Found (%):

C, 60.92; H, 4.27; Cl, 15.62; N, 12.15. $C_{23}H_{18}Cl_2N_4O_2$. Calculated (%): C, 60.94; H, 4.00; Cl, 15.64; N, 12.36. MS, *m/z* ($I_{rel}$ (%)): 453 $[M]^+$ (1), 439 (72), 437 $[M - Me - H]^+$ (100). IR ($CHCl_3$), ν/cm$^{-1}$: 3400 (NH), 3020, 1712 (CO), 1652, 1628, 1560. $^1$H NMR ($CDCl_3$), δ: 0.94 (s, 6 H, 2 Me); 2.21 (s, 2 H, $CH_2$); 4.00 (s, 1 H, H(9)); 7.17 (d, 2 H, *o*-$H_{C_6H_4}$, *J* = 8.0 Hz); 7.22 (d, 2 H, *o*-$H_{C_6H_4}$, *J* = 8.0 Hz); 7.50 (m, 4 H, *m*-H, 2 $C_6H_4$). $^{13}$C NMR ($CDCl_3$), δ: 28.60 (2 Me); 32.33 (C(8)); 40.11 (C(7)); 95.03 (C(9b)); 106.91 (C(9)); 129.26 (*o*-$C_{C6H4}$); 130.28 (*m*-C, 2 $C_6H_4$); 130.37 (*o*-$C_{C_6H_4}$); 130.72 (C(9a)); 134.56 (*ipso*-$C_{C_6H_4}$); 134.86 (*p*-$C_{C_6H_4}$); 135.02 (*ipso*-$C_{C_6H_4}$); 135.58 (*p*-$C_{C_6H_4}$); 154.81 (C(6a)); 148.80, 155.53, 156.59 (C(2), C(3a), C(5)). Assignment of the signals performed was based on the $^1$H/$^{13}$C HMBC two-dimensional NMR.

**1-(4-Chlorophenyl)-8,8-dimethyl-6-phenyl-7,8-dihydro-1*H*-pyrimido[4,5,6-*de*]quinazoline-2,5(3*H*,6*H*)-dione (6c) and 6-(4-chlorophenyl)-8,8-dimethyl-1-phenyl-7,8-dihydro-1*H*-pyrimido-[4,5,6-*de*]quinazoline-2,5(3*H*,6*H*)-dione (6d)** were synthesized similarly to compound **6a** from urea **5c** and **5d**. After concentration, the residue was purified by column chromatography on $SiO_2$ (chloroform) to obtain a mixture of unseparable isomers **6c** and **6d** (the ratio 1 : 1 according to the $^1$H NMR spectral data), the yields were 67 and 80% from **5c** and **5d**, respectively, m.p. 284—285 °C. Found (%): C, 66.17; H, 4.62; Cl, 8.45; N, 13.00. $C_{23}H_{19}ClN_4O_2$. Calculated (%): C, 65.95; H, 4.57; Cl, 8.46; N, 13.38. MS, *m/z* ($I_{rel}$ (%)): 418 $[M]^+$ (29), 403 $[M - Me]^+$ (100), 148 (24). IR ($CHCl_3$), ν/cm$^{-1}$: 3400 (NH), 3020—2920 (NH, CH), 1712 (CO), 1668, 1652, 1628, 1560. $^1$H NMR (600 MHz, $CDCl_3$), δ, isomer **6c**/isomer **6d**: 0.94/0.94 (s, 6 H, 2 Me); 2.22/2.22 (s, 2 H, $CH_2$); 3.99/4.00 (s, 1 H, H(9)); 7.16—7.25/7.16—7.25 (m, 4 H, *o*-$H_{C_6H_4}$, *o*-$H_{Ph}$); 7.47—7.52/7.47—7.52 (m, 5 H, *m*-$H_{C_6H_4}$, *m*-$H_{Ph}$, *p*-$H_{Ph}$); a signal for the proton from NH is very broad and resonates in the region ~8.70 $^1$H NMR (600 MHz, DMSO-$d_6$), δ, isomer **6c**/isomer **6d**: 0.87/0.87 (s, 6 H, 2 Me); 2.20/2.22 (s, 2 H, $CH_2$); 3.81/3.79 (s, 1 H, H(9)); 7.32/7.27 (d, 2 H, *o*-$H_{Ph}$, *J* = 7.8 Hz); 7.32/7.39 (d, 2 H, *o*-$H_{C_6H_4}$, *J* = 7.8 Hz); 7.49/7.44 (t, 1 H, *p*-$H_{Ph}$, *J* = 7.8 Hz); 7.55/7.53 (t, 2 H, *m*-$H_{Ph}$, *J* = 7.8 Hz); 7.57/7.59 (d, 2 H, *m*-$H_{C_6H_4}$, *J* = 7.8 Hz). $^{13}$C NMR (DMSO-$d_6$), δ, isomer **6c**/isomer **6d**: 28.23/28.23 (2 Me); 31.40/31.40 (C(8)); 39.41/39.30 (C(7)); 93.77/93.98 (C(9b)); 104.50/104.63 (C(9)); 127.88/128.84 (*o*-$C_{Ph}$); 128.54/128.02 (*p*-$C_{Ph}$); 129.16/129.21 (*m*-$C_{Ph}$); 129.43/129.31 (*m*-$C_{C_6H_4}$); 130.87/129.93 (*o*-$C_{C_6H_4}$); 130.87/130.87 (C(9a)); 132.66/133.26 (*p*-$C_{C_6H_4}$); 135.53/135.87 (*ipso*-$C_{C_6H_4}$), 136.96/136.61 (*ipso*-$C_{Ph}$); 154.34/154.19 (C(6a)); 148.96, 154.62, 154.70, 156.74, 156.91 (C(2), C(3a), C(5) from two isomers. $^{15}$N NMR based on the $^1$H/$^{15}$N HMBC two-dimensional NMR spectrum (correlation on the *ortho*-protons of the aryl groups, the $CH_2$ or CH protons, DMSO-$d_6$), δ, isomer **6c**/isomer **6d**: −250/−248 (N(1)); −205/−207 (N(6)). The $^1$H/$^1$H COSY, $^1$H/$^{13}$C HMBC and HSQC, and $^1$H/$^{15}$N HMBC two-dimensional NMR spectra were used to assign signals in the $^1$H and $^{13}$C NMR spectra and to determine whether they belong to compound **6c** or **6d**.

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