Benzannulation of 5-methyl-7-phenyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine with chalcones and their synthetic equivalents as a method for the synthesis of tetrazolo[5,1-*b*]quinazolines

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Derivatives of tetrahydrotetrazolo[5,1-*b*]quinazolines were synthesized by the reactions of 5-methyl-7-phenyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine with α,β-unsaturated carbonyl compounds and their synthetic equivalents in methanol in the presence of sodium methoxide. The spontaneous or specifically target oxidation of these derivatives gives rise to aromatic tetrazoloquinazolines. The reaction pathways and mechanisms were discussed. The structures of the resulting compounds were confirmed by IR and ^{1}H NMR spectroscopy, mass spectrometry, and elemental analysis.

Key words: partially hydrogenated tetrazolo[5,1-*b*]quinazolines, synthesis, cyclocondensation, heteroaromatization, chalcones.

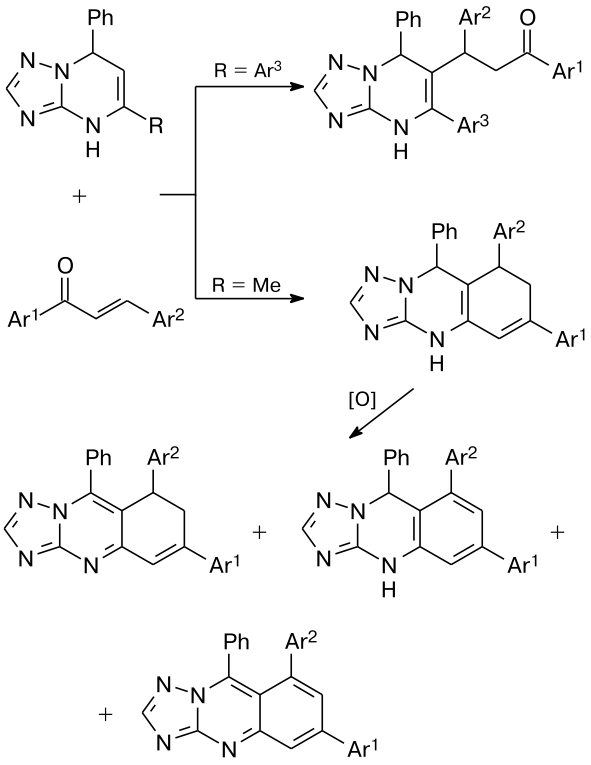
Fused azoloazine systems have attracted attention due primarily to the fact that they are widespread among natural biologically active compounds.[1] For the past several years, we have developed methods for the synthesis of these compounds and studied their chemical transformations, the emphasis being given to partially hydrogenated structures.[2—5]

Using aryl-substituted 4,7-dihydro-1,2,4-triazolo[1,5-*a*]-pyrimidines as examples, it was shown[3—5] that the reactions of this class of compounds with α,β-unsaturated carbonyl compounds and their synthetic equivalents afford Michael β-adducts at position 6 of the bicyclic moiety. The reaction with the use of 5-methyl-substituted triazolopyrimidine as the substrate is accompanied by the intramolecular cyclocondensation giving rise to tetrahydroazoloquinazoline systems.[3—5] The degree of hydrogenation can be varied using different oxidizing agents, thus preparing both dihydro derivatives and their aromatic products[5] (Scheme 1).

It is unusal that that the Me group at position 5 of the dihydropyrimidine ring is involved in the condensation step of this reaction. It should be noted that this fact remained unexplained.[3—5] Since data on the analogous reactions with other azoloazine systems are lacking in the literature, the aim of the present study was to examine whether this reaction can proceed with 5-methyl-7-phenyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine (**1**), whose synthesis has been described earlier.[6]

Initially, the reaction of compound **1** with chalcones **2a—g** was carried out under the conditions described earlier for triazolopyrimidine derivatives (by refluxing the components in MeOH in the presence of sodium methoxide).[4] In our case, this reaction afforded an unidentified mixture

Scheme 1



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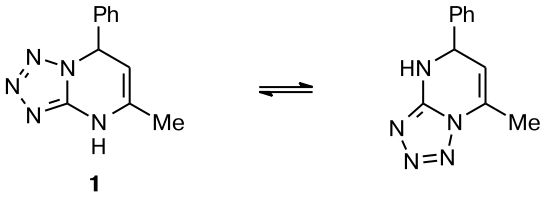
of products and was accompanied by partial resinification. Most likely, this is associated with the higher π-accepting ability of the tetrazole ring, which facilitates the side oxidation reactions. In addition, tetrazole derivatives can undergo the Dimroth rearrangement (Scheme 2) giving rise to isomeric compounds as impurities.[7,8]

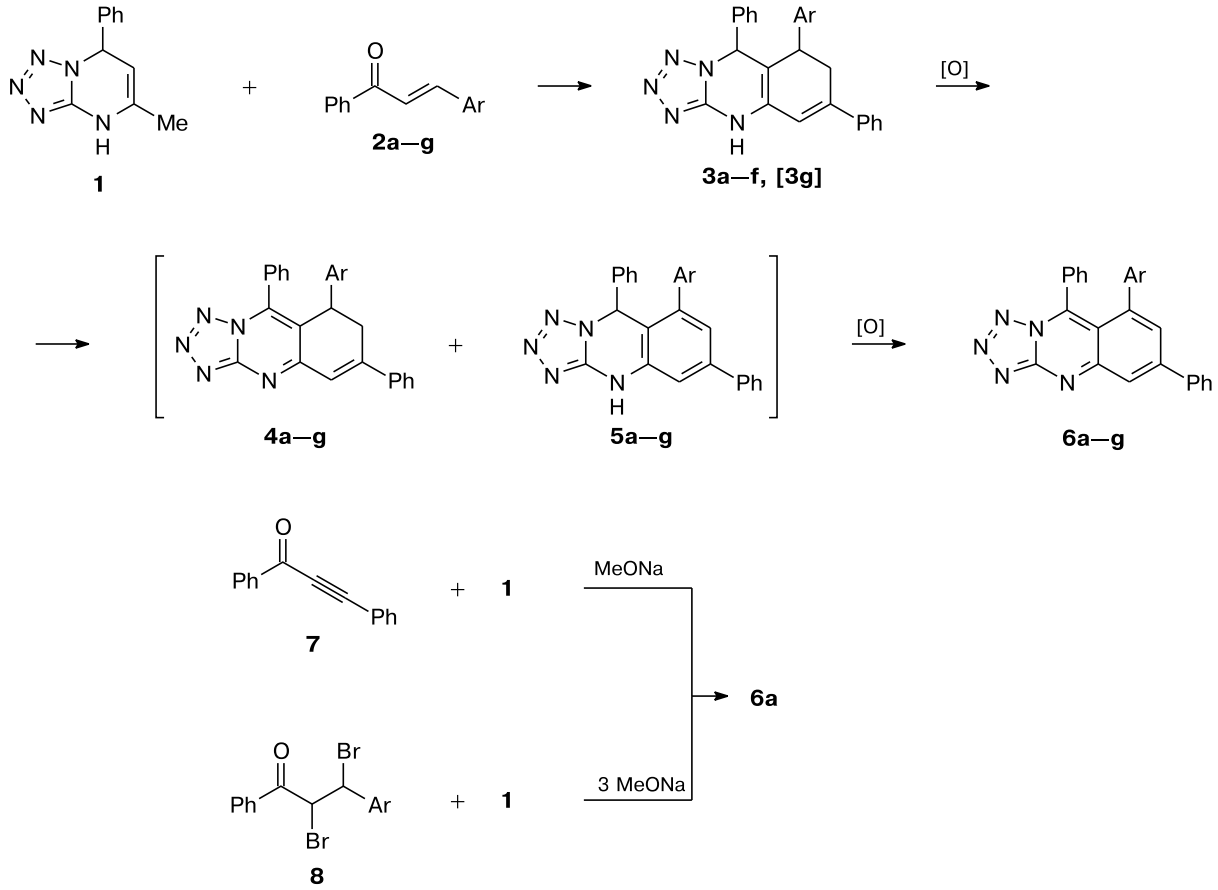
Scheme 2



Moderate heating (30—40 °C) of solutions of compounds **1** and **2a—e** in MeOH in the presence of sodium methoxide as the catalyst (Scheme 3) proved to be the method of choice for the synthesis of target compounds **3a—e** in moderate and good yields. However, under these conditions, substantial amounts of fully aromatic compounds **6a—f** were isolated as by-products as well. The synthesis under inert atmosphere (argon) in the oxygen-free solvent, which was preliminarily prepared by refluxing the solvent in an inert gas flow, produced tetrahydro compounds **3a—f** in substantially higher yield (compounds **3b—d** were obtained as virtually the only reaction products). To the contrary, compounds **6a—e** were prepared as the only products by refluxing the reaction mixtures in air over a long period of time.

The electronic character of the substituent in the chalcone component is of importance for the final composition of the reaction products. For example, the reaction of tetrazolopyrimidine **1** with chalcone **2a** performed under inert atmosphere for 30 min afforded a mixture of tetrahydrotetrazoloquinazoline **3a** and its aromatization product **6a** in a ratio of 60 : 40 (the reaction performed in air gave these compounds in a ratio of 30 : 70). Under analogous conditions, the reactions of chalcones containing electron-releasing substituents (dimethylamino (**2d**), methoxy

Scheme 3



Ar = 4-RC_6H_4, R = H (**a**), Me (**b**), OMe (**c**), NMe_2 (**d**), Cl (**e**), Br (**f**), NO_2 (**g**)

(**2c**), or methyl (**2b**) groups) gave rise to the products in the following ratios: **3d** : **6d** , = 95 : 5, **3c** : **6c** = 90 : 10, and **3b** : **6b** = 80 : 20 (in air, the ratios were 40 : 60, 35 : 65, and 50 : 50, respectively). The presence of the electron-withdrawing substituents Cl or Br (**2e** or **2f**, respectively) leads to an increase in the percentage of the fully aromatic products (25 : 75) (without inert atmosphere, the ratio was 10 : 90). In the case of chalcone **2g** containing the nitro group, only aromatized tetrazoloquinazoline **6g** was isolated (even under argon). In other words, the stronger the electron-withdrawing properties of the substituent R in the chalcone molecule, the higher the rate of dehydrogenation (oxidation), the higher the yield of aromatic compounds **6**, and the lower the yield of tetrahydrotetrazoloquinazolines **3**. The ratio of products **3** to **6** was estimated based on the ^{1}H NMR spectra (the presence of characteristic signals) and liquid chromatography data. Products **3** and **6** were separated by fractional crystallization from acetone, Pr^{i}OH, or their mixture (1 : 1) under inert atmosphere. In most cases, both groups of compounds (**3** and **6**) were isolated in the individual state. The presence of intermediate partially aromatic products **4** and **5** was confirmed by GLC-mass spectrometry of the substances precipitated from the reaction mixtures. However, attempts to isolate these intermediates in the pure form in amounts sufficient for further investigations failed. According to the GLC-mass spectrometric data (an acetonitrile—water mixture, gradient elution), heating of the reaction mixture containing tetrazolopyrimidine **1** and chalcone **2a** under argon for 20 min resulted in the formation of four products with molecular masses of 404 (59%), 402 (1%), 402 (2%), and 400 (38%). The starting compounds **1** and **2a** were not detected in this mixture.

Unlike the reaction of chalcone **2a**, the reactions of its acetylene analog **7** or 2,3-dibromo-1,3-diphenylpropan-1-one (**8**) with tetrazolopyrimidine **1** in methanol in the presence of MeONa (a threefold excess of sodium methoxide was used in the reaction with **8**) afforded exclusively aromatic product **6a** regardless of whether the reaction was performed under inert atmosphere or in air.

Apparently, the reaction of **1** with **7** proceeds by analogy with chalcone through the β-addition and cyclocondensation. As mentioned above, dihydro product **5a** is unstable and undergoes fast cyclization to give **6a**. The first step of the reaction of **1** with **8** would be expected to involve dehydrobromination.[9,10] The resulting β-bromochalcone (2-bromo-1,3-diphenylprop-1-en-3-one) behaves analogously to chalcones **2**. Thus, the reaction involves the β-addition and cyclocondensation followed by dehydrobromination and dehydrogenation. Moreover, the presence of the bromine atom leads to an increase in the electrophilicity of the β-C center of the chalcone molecule, *i.e.*, results in an increase in the reaction rate. In our opinion, the formation of intermediate propinone **7** under such mild conditions, which was hypothesized in the study,[5] is hardly probable.

We also performed the target aromatization of compounds **3a—f** under the conditions described in the study[5] (NBS in Pr^{i}OH, sodium nitrite and bromine in AcOH). As a result, we isolated the corresponding aromatic products **6a—f**.

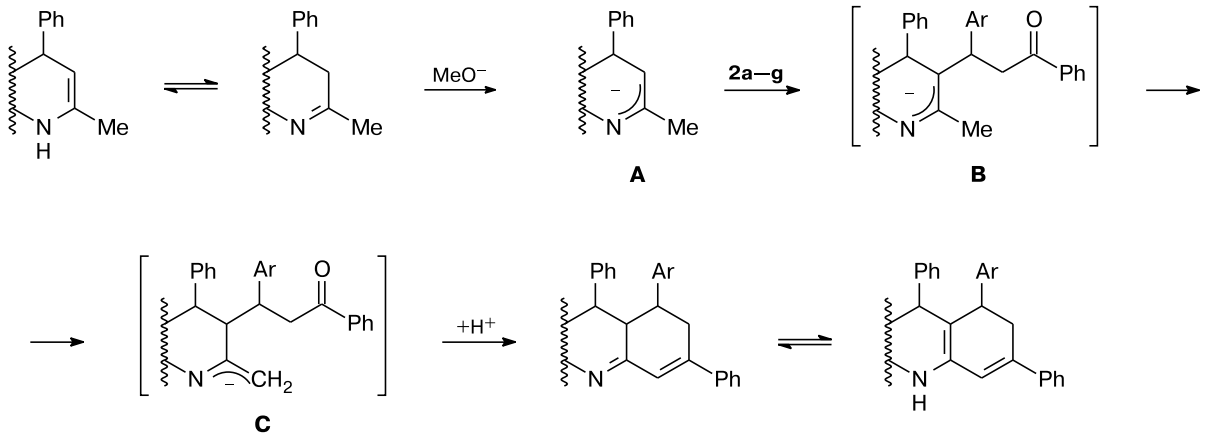
The structures of compounds **3a—f** and **6a—g** were determined by ^{1}H NMR and IR spectroscopy and mass spectrometry.

The EI mass spectra of tetrahydrotetrazoloquinazolines **3a—f** have the molecular ion peak $[M + 1]^+$ and the peak $[M - 27]^+$ (extrusion of a nitrogen molecule). The IR spectra of **3a—f** show characteristic stretching bands of the exocyclic C=C and C=N bonds, whereas the stretching bands of the C=O group are absent. It is difficult to separate the stretching bands of the N—H group because the latter group is associated and appears as a broadened band at 3680—3300 cm^{-1}. The ^{1}H NMR spectra are most characteristic for these compounds. These spectra show the proton signal of the NH group of the pyrimidine ring at δ 9.8—10.6, which appears as a broadened singlet, an AMX system of the protons at positions 7 and 8 of the cyclohexadiene fragment, as three doublets of doublets (sometimes partially degenerate) at δ 2.5—4.0, a singlet of the proton at position 9, a weakly split doublet of the proton at position 5 (allylic coupling with one of the protons of the AMX system), and a multiplet of aromatic protons. Since compounds **3a—f** contain two chiral centers, it could be expected that the reaction will afford a mixture of diastereomers. However, no doubling of the signals is observed in the ^{1}H NMR spectra of these compounds. Hence, it can be said with confidence that the reaction is diastereoselective.

The mass spectra of fully aromatic products **6a—g** have the molecular ion peak and the peak $[M - 28]^+$. In the ^{1}H NMR spectra, all signals are observed in the region of aromatic proton resonance, and it is difficult to separate the characteristic signals.

In our experiments, we varied the ratios of the reagents and the catalyst and performed the reactions under inert atmosphere and in air. As mentioned above, this was reflected in the ratio of aromatic to partially hydrogenated products. However, we failed to stop the reaction in the step giving rise to the β adduct. In all cases, the cyclocondensation proceeds at high rate. This is surprising taking into account that the carbonyl group of the dihydrochalcone fragment of the intermediate β adduct, in our opinion, should be characterized by moderate activity typical of aromatic ketones. At the same time, attempts to perform condensation of the methyl group in compound **1** with reactive carbonyl compounds, such as phenylglyoxal, 4-nitro- and 4-bromobenzaldehydes, and cinnamaldehyde, failed. Consequently, the cyclocondensation is determined primarily by the intramolecular factor, *e.g.*, the spatial proximity of the methyl and carbonyl groups in the β-adduct molecule.

Scheme 4



The activation of the methyl groups in azines is the classical situation. The reaction under study is unusual in that the methyl group of the partially hydrogenated pyrimidine system is involved in this reaction, the activation of this group being unexpected. In our opinion, this can be attributed to the fact that tetrazolopyrimidine **1** exists in solution as an equilibrium imine-enamine tautomeric mixture with the enamine tautomer predominating.[6] In alkaline media, these compounds undergo deprotonation and their reactions with chalcones afford exclusively the anionic forms **A**, **B**, and **C** in both steps (Scheme 4), which is also facilitated by the electron-withdrawing effect of the tetrazole ring. These forms are responsible for the lability of the hydrogen atoms involved in cyclocondensation and the fact that it is impossible to isolate the intermediate Michael adducts.

The formation of the ionic forms is additionally supported by the fact that the reaction mixtures turned bright yellow after the addition of sodium methoxide to a solution of the starting tetrazolopyrimidine **1** (before the addition of chalcones **2a—g**).

Experimental

The progress of the reactions was monitored and the purity of the reaction products was checked by TLC on Silufol UV-254 plates using 1 : 1 acetone—hexane or chloroform—hexane mixtures and pure chloroform as the eluents.

The ^{1}H NMR spectra were measured on Varian VX-200 Mercury and Bruker DRX-400 instruments operating at 200 and 400 MHz, respectively, with the use of DMSO-d_6 or a DMSO-d_6—CCl_4 mixture as the solvent and Me_4Si as the internal standard. The IR spectra were recorded on Specord M-82 and Specord IR-75 spectrophotometers in KBr pellets. The EI mass spectra were obtained on Hewlett—Packard LC/MSD 1100 and Finnigan MAT 4651P mass spectrometers at 70 eV.

The yields of the target compounds are given for the pure products (after separation).

5-Methyl-7-phenyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine (1).[6] A mixture of 5-aminotetrazole (0.85 g, 0.01 mol) and benzylideneacetone (1.46 g, 0.01 mol) in amyl alcohol was refluxed under argon for 4 h. The solvent was concentrated *in vacuo*, the resinous precipitate was washed with Pr^iOH, and white crystals of product **1** were filtered off. The yield was 1.5 g (75%), m.p. 164—166 °C (*cf.* lit. data[6]: m.p. 164—166 °C).

6,8,9-Triphenyl-4,7,8,9-tetrahydrotetrazolo[5,1-*b*]quinazoline (3a) and its aromatization product (**6a**). *A*. A solution of benzylideneacetophenone (**2a**) (0.4 g, 0.002 mol) and 5-methyl-7-phenyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine (**1**) (0.4 g, 0.002 mol) in oxygen-free MeOH (10 mL), to which sodium (25 mg) was added in advance, was heated under argon to ~30—40 °C for 15 min. The precipitate that formed was filtered off and successively washed with MeOH and Me_2CO. The resulting mixture consisting of 6,8,9-triphenyltetrahydrotetrazolo[5,1-*b*]quinazoline (**3a**, 60%) and 6,8,9-triphenyl-4,7,8,9-tetrazolo[5,1-*b*]quinazoline (**6a**, 40%) was separated by crystallization from Pr^iOH. The yield of the crude product was 75%.

Compound 3a. The yield was 0.4 g (50%), a white crystalline compound, m.p. >300 °C. Found (%): C, 77.47; H, 5.19; N, 17.43. $C_{26}H_{21}N_5$. Calculated (%): C, 77.40; H, 5.25; N, 17.36. IR, ν/cm^{-1}: 1668 (C=C—NH), 1608 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6—CCl_4), δ: 2.65 dd, 1 H, $C\underline{H}_AH_M$, J = 16.0 Hz, J = 3.3 Hz); 3.30 dd, 1 H, $CH_A\underline{H}_M$, J = 5.0 Hz, J = 16.0 Hz); 3.71 dd, 1 H, CH_X, J = 3.3 Hz, J = 5.0 Hz); 6.50 (s, 1 H, CH); 6.62 (d, 1 H, CH, J = 2.5 Hz); 6.81—7.15 (m, 15 H, Ar—H); 10.62 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 404 $[M + H]^+$ (100), 402 $[M - H]^+$ (23), 376 $[(M - N_2) + H]^+$ (84).

Compound 6a. The yield was 0.17 g (21.5%), a yellow crystalline compound, m.p. 188—190 °C Found (%): C, 78.34; H, 4.26; N, 17.48. $C_{26}H_{17}N_5$. Calculated (%): C, 78.18; H, 4.29; N, 17.53. IR, ν/cm^{-1}: 1575 (C=N), 1594 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6—CCl_4), δ: 6.68—7.65 (m, 17 H, Ar—H). MS, m/z (I_{rel} (%)): 400 $[M]^+$ (100), 372 $[M - N_2]^+$ (98).

Compounds **3b—f** and **6b—g** were synthesized analogously.

8-(4-Methylphenyl)-6,9-diphenyl-4,7,8,9-tetrahydrotetrazolo[5,1-*b*]quinazoline (3b) and its aromatization product **6b**. The yield of the crude product (80 : 20) was 78%.

Compound 3b. The yield was 0.4 g (45%), a white crystalline compound, m.p. >300 °C. Found (%): C, 77.45; H, 5.64; N, 16.52. $C_{27}H_{23}N_5$. Calculated (%): C, 77.67; H, 5.55; N, 16.77.

IR, ν/cm^{-1}: 1669 (C=C—NH), 1608 (C=C). ^{1}H NMR (200 MHz, DMSO-d_6), δ: 2.24 (s, 3 H, Me); 2.61 dd, 1 H, C$\underline{H}_A$H$_M$, J = 15.7 Hz, J = 3.4 Hz); 3.23 dd, 1 H, CH$_A\underline{H}_M$, J = 5.1 Hz, J = 15.7 Hz); 3.62 dd, 1 H, CH$_X$, J = 3.4 Hz, J = 5.1 Hz); 6.46 (s, 1 H, CH); 6.63 (d, 1 H, CH, J = 1.7 Hz); 6.78—7.35 (m, 14 H, Ar—H); 10.10 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 418 [M + H]$^+$ (100), 416 [M – H]$^+$ (15), 391 [(M – N$_2$) + H]$^+$ (93).

Compound 6b. The yield was 0.1 g (12%), a yellow crystalline compound, m.p. 189—191 °C. Found (%): C, 78.49; H, 4.56; N, 16.88. $C_{27}H_{19}N_5$. Calculated (%): C, 78.43; H, 4.63; N, 16.94. IR, ν/cm^{-1}: 1578 (C=N), 1599 (C=C). ^{1}H NMR (200 MHz, DMSO-d_6), δ: 2.31 (s, 3 H, Me); 6.65—7.54 (m, 15 H, Ar—H); 6.69 (s, 1 H, 7-CH). MS, m/z (I_{rel} (%)): 413 [M]$^+$ (100), 385 [M – N$_2$]$^+$ (94).

8-(4-Methoxyphenyl)-6,9-diphenyl-4,7,8,9-tetrahydrotetrazolo[5,1-*b*]quinazoline (3c) and its aromatization product **6c**. The yield of the crude product (90 : 10) was 68%.

Compound 3c. The yield was 0.5 g (50%), a white crystalline compound, m.p. >300 °C. Found (%): C, 74.45; H, 5.24; N, 16.27. $C_{27}H_{23}N_5O$. Calculated (%): C, 74.80; H, 5.35; N, 16.16. IR, ν/cm^{-1}: 1670 (C=C—NH), 1612 (C=C). ^{1}H NMR (200 MHz, DMSO-d_6), δ: 2.64 dd, 1 H, C$\underline{H}_A$H$_M$, J = 15.8 Hz, J = 3.4 Hz); 3.25 dd, 1 H, CH$_A\underline{H}_M$, J = 5.2 Hz, J = 15.8 Hz); 3.61 (s, 3 H, OMe); 3.75 dd, 1 H, CH$_X$, J = 3.4 Hz, J = 5.2 Hz); 6.52 (s, 1 H, CH); 6.58 (d, 1 H, CH, J = 2.4 Hz); 6.82—7.45 (m, 14 H, Ar—H); 10.21 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 434 [M + H]$^+$ (100), 432 [M – H]$^+$ (17), 406 [(M — N$_2$) + H]$^+$ (89).

Compound 6c. The yield was 0.07 g (5%), a yellow crystalline compound, m.p. 185—187 °C. Found (%): C, 75.54; H, 4.36; N, 16.38. $C_{27}H_{19}N_5O$. Calculated (%): C, 75.51; H, 4.46; N, 16.31. IR, ν/cm^{-1}: 1580 (C=N), 1601 (C=C). ^{1}H NMR (200 MHz, DMSO-d_6), δ: 3,58 (s, 3 H, OMe); 6.65—7.52 (m, 16 H, Ar—H). MS, m/z (I_{rel} (%)): 429 [M]$^+$ (100), 401 [M – N$_2$]$^+$ (87).

8-(4-Dimethylaminophenyl)-6,9-diphenyl-4,7,8,9-tetrahydrotetrazolo[5,1-*b*]quinazoline (3d) and its aromatization product **6d**. The yield of the crude product (95 : 5) was 70%.

Compound 3d. The yield was 0.7 g (75%), a yellow crystalline compound, m.p. >300 °C. Found (%): C, 75.38; H, 5.74; N, 18.52. $C_{28}H_{26}N_6$. Calculated (%): C, 75.31; H, 5.87; N, 18.82. IR, ν/cm^{-1}: 1667 (C=C—NH), 1610 (C=C). ^{1}H NMR (200 MHz, DMSO-d_6), δ: 2.62 (s, 6 H, NMe$_2$); 2.58 dd, 1 H, C$\underline{H}_A$H$_M$, J = 16.0 Hz, J = 3.6 Hz); 3.15 dd, 1 H, CH$_A\underline{H}_M$, J = 5.1 Hz, J = 16.0 Hz); 3.56 dd, 1 H, CH$_X$, J = 3.6 Hz, J = 5.1 Hz); 6.55 (s, 1 H, CH); 6.67 (d, 1 H, CH, J = 1.7 Hz); 6.82—7.40 (m, 14 H, Ar—H); 10.32 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 447.5 [M + H]$^+$ (100), 445 [M – H]$^+$ (12), 419.5 [(M – N$_2$) + H]$^+$ (98).

Compound 6d. The yield was 0.05 g (5%), a yellow crystalline compound, m.p. 185—186 °C. Found (%): C, 75.84; H, 5.09; N, 18.86. $C_{28}H_{22}N_6$. Calculated (%): C, 76.00; H, 5.01; N, 18.99. IR, ν/cm^{-1}: 1582 (C=N), 1598 (C=C). ^{1}H NMR (200 MHz, DMSO-d_6), δ: 2.65 (s, 6 H, NMe$_2$); 6.65—7.54 (m, 16 H, Ar—H). MS, m/z (I_{rel} (%)): 443 [M]$^+$ (100), 415 [M – N$_2$]$^+$ (74).

8-(4-Chlorophenyl)-6,9-diphenyl-4,7,8,9-tetrahydrotetrazolo[5,1-*b*]quinazoline (3e) and its aromatization product **6e**. The yield of the crude product (25 : 75) was 80%.

Compound 3e. The yield was 0.14 g (16%), a white crystalline compound, m.p. >300 °C. Found (%): C, 71.38; H, 4.74; Cl, 8.23; N, 15.82. $C_{26}H_{20}ClN_5$. Calculated (%): C, 71.31; H, 4.60; Cl, 8.10; N, 15.99. IR, ν/cm^{-1}: 1668 (C=C—NH), 1607 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6—CCl_4), δ: 2.68 dd, 1 H, C$\underline{H}_A$H$_M$, J = 15.8 Hz, J = 3.5 Hz); 3.22 dd, 1 H, CH$_A\underline{H}_M$, J = 5.2 Hz, J = 15.8 Hz); 3.61 dd, 1 H, CH$_X$, J = 3.5 Hz, J = 5.5 Hz); 6.62 (s, 1 H, CH); 6.74 (d, 1 H, CH, J = 1.6 Hz); 6.88—7.50 (m, 14 H, Ar—H); 9.94 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 439 [M + H]$^+$ (98), 436 [M – H]$^+$ (19), 411 [(M – N$_2$) + H]$^+$ (82).

Compound 6e. The yield was 0.35 g (40%), a yellow crystalline compound, m.p. 188—190 °C. Found (%): C, 72.06; H, 3.68; Cl, 8.13; N, 16.11. $C_{26}H_{16}ClN_5$. Calculated (%): C, 71.97; H, 3.72; Cl, 8.17; N, 16.14. IR, ν/cm^{-1}: 1580 (C=N), 1598 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6—CCl_4), δ: 6.78 (s, 1 H, 7-CH); 6.80—7.45 (m, 15 H, Ar—H). MS, m/z (I_{rel} (%)): 434 [M]$^+$ (92), 408 [M – N$_2$]$^+$ (100).

8-(4-Bromophenyl)-6,9-diphenyl-4,7,8,9-tetrahydrotetrazolo[5,1-*b*]quinazoline (3f) and its aromatization product **6f**. The yield of the crude product (25 : 75) was 74%.

Compound 3f. The yield was 0.15 g (15.5%), a white crystalline compound, m.p. >300 °C. Found (%): C, 64.68; H, 4.24; Br, 16.53; N, 14.51. $C_{26}H_{20}BrN_5$. Calculated (%): C, 64.74; H, 4.18; Br, 16.56; N, 14.52. IR, ν/cm^{-1}: 1670 (C=C—NH), 1610 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6—CCl_4), δ: 2.70 dd, 1 H, C$\underline{H}_A$H$_M$, J = 15.4 Hz, J = 3.7 Hz); 3.30 dd, 1 H, CH$_A\underline{H}_M$, J = 5.2 Hz, J = 15.4 Hz); 3.81 dd, 1 H, CH$_X$, J = 3.7 Hz, J = 5.2 Hz); 6.40 (s, 1 H, CH); 6.62 (d, 1 H, CH, J = 1.9 Hz); 6.90—7.50 (m, 14 H, Ar—H); 10.50 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 483 [M + H]$^+$ (50), 481 [M + H]$^+$ (52), 479 [M – H]$^+$ (35), 453 [(M – N$_2$) + H]$^+$ (48), 455 [(M – N$_2$) + H]$^+$ (47).

Compound 6f. The yield was 0.36 g (37.6%), a yellow crystalline compound, m.p. 188—190 °C. Found (%): C, 65.24; H, 3.41; Br, 16.53; N, 14.61. $C_{26}H_{16}BrN_5$. Calculated (%): C, 65.28; H, 3.37; Br, 16.70; N, 14.64. IR, ν/cm^{-1}: 1574 (C=N), 1596 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6—CCl_4), δ: 6.65—7.50 (m, 16 H, Ar—H). MS, m/z (I_{rel} (%)): 477 [M]$^+$ (50), 479 [M]$^+$ (50), 449 [M – N$_2$]$^+$ (47), 451 [M – N$_2$]$^+$ (45).

8-(4-Nitrophenyl)-6,9-diphenyltetrazolo[5,1-*b*]quinazoline (6g). The yield was 0.45 g (50%), a yellow crystalline compound, m.p. 195—197 °C. Found (%): C, 70.24; H, 3.61; N, 18.68. $C_{26}H_{16}N_6O_2$. Calculated (%): C, 70.26; H, 3.63; N, 18.91. IR, ν/cm^{-1}: 1576 (C=N), 1596 (C=C). ^{1}H NMR (200 MHz, DMSO-d_6), δ: 6.65—7.52 (m, 16 H, Ar—H). MS, m/z (I_{rel} (%)): 445 [M]$^+$ (100), 417 [M – N$_2$]$^+$ (96).

Compound 6a. *B*. A solution of dibromobenzylideneacetophenone (0.6 g, 0.002 mol) and 5-methyl-7-phenyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine (0.4 g, 0.002 mol) in oxygen-free MeOH (10 mL), to which sodium (50 mg) was added in advance, was heated to ~30—40 °C using a reflux condenser under argon for 15 min. The precipitate that formed was filtered off, successively washed with MeOH and Me_2CO, and crystallized from Pr^{i}OH. The yield was 68%, a yellow crystalline compound, m.p. 186—190 °C. The spectroscopic data are identical to those described above (method *A*).

C. A solution of 1,3-diphenylpropynone (0.4 g, 0.002 mol) and 5-methyl-7-phenyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine (0.4 g, 0.002 mol) in oxygen-free MeOH (10 mL), to which sodium (25 mg) was added in advance, was heated to ~30—40 °C using a reflux condenser under argon for 15 min. The precipitate that formed was filtered off, successively washed with MeOH and Me_2CO, and crystallized from Pr^{i}OH. The yield was 55%, a yellow crystalline compound, m.p. 187—189 °C. The spectroscopic data are identical to those described above (method *A*).

Fully aromatic tetrazolo[5,1-*b*]quinazolines **6a—f** (general procedures).

1. A mixture of 8-aryl-6,9-diphenyl-4,7,8,9-tetrahydrotetrazolo[5,1-*b*]quinazoline **3a—f** (0.5 mmol) and NBS (0.15 g, 1 mmol) was dissolved in Pr^iOH (10 mL) and refluxed for 30 min. The crystals of **6a—f** that formed were filtered off and recrystallized from Pr^iOH. The yields were 75—85%.

2. A mixture of 8-aryl-6,9-diphenyl-4,7,8,9-tetrahydrotetrazolo[5,1-*b*]quinazoline **3a—f** (0.6 mmol) and sodium nitrite (0.06 g, 0.7 mmol) was dissolved in AcOH (5 mL) and refluxed for 1 h. Products **6a—f** were precipitated with water and recrystallized from Pr^iOH. The yields were 60—76%.

3. A mixture of 8-aryl-6,9-diphenyl-4,7,8,9-tetrahydrotetrazolo[5,1-*b*]quinazoline **3a—f** (0.5 mmol) and bromine (0.06 mL, 1 mmol) was dissolved in AcOH (5 mL). The reaction mixture was refluxed for 1 h and treated with an excess of a concentrated aqueous sodium hydroxide solution. Products **6a—f** that precipitated were filtered off and recrystallized from Pr^iOH. The yields were 75—85%.

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References

1. Kh. M. Shakhidoyatov, in *Azotistye geterotsikly i alkaloidy* [*Nitrogen Heterocycles and Alkaloids*], Eds V. G. Kartsev, G. A. Tolstikov, Iridium-Press, Moscow, 2001, 186 (in Russian).
2. V. D. Orlov, S. M. Desenko, *Azageterotsikly na osnove aromaticheskikh nepredel´nykh ketonov* [*Azaheterocycles Based on Aromatic Unsaturated Ketones*], Folio, Kharkov, 1998, 148 pp. (in Russian).
3. V. Lipson, S. Desenko, O. Zhikol, A. Kaganovsky, I. Ignatenko, N. Vorobyova, D. Sidorenko, *Int. Conf. "Chemistry of Nitrogen-Containing Heterocycles" (CNCH-2003)*, Kharkov, 2003, p. 20.
4. V. V. Lipson, I. V. Ignatenko, S. M. Desenko, S. V. Shishkina, O. V. Shishkin, S. A. Komykhov, N. V. Logvinenko, V. D. Orlov, H. Meier, *J. Heterocycl. Chem.*, 2003, **40**, 1081.
5. V. V. Lipson, S. M. Desenko, I. V. Ignatenko, O. V. Shishkin, S. V. Shishkina, *Izv. Akad. Nauk, Ser. Khim.*, 2006, 335 [*Russ. Chem. Bull., Int. Ed.*, 2006, **55**, 345].
6. S. M. Desenko, E. S. Gladkov, S. A. Komykhov, O. V. Shishkin, V. D. Orlov, *Khim. Geterotsikl. Soedin.*, 2001, 811 [*Chem. Heterocycl. Compd.*, 2001, **37**, 811 (Engl. Transl.)].
7. N. N. Kolos, B. V. Paponov, V. D. Orlov, *Khim. Geterotsikl. Soedin.*, 2003, 310 [*Chem. Heterocycl. Compd.*, 2003, **39**, 310 (Engl. Transl.)].
8. N. N. Kolos, B. V. Paponov, V. D. Orlov, M. I. Lvovskaja, A. O. Doroshenko, O. V. Shishkin, *J. Mol. Struct.*, 2006, 114.
9. *Organic Syntheses*, Ed. H. Gilman, 2nd ed., John Wiley and Sons, New York—London, 1944, Coll. Vol. **1**.
10. N. N. Kolos, V. D. Orlov, E. Yu. Yur´eva, E. V. Zhidkova, *Khim. Geterotsikl. Soedin.*, 1993, 1409 [*Chem. Heterocycl. Compd.*, 1993, **29**, 1210 (Engl. Transl.)].

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