Formylation of 4,7-Dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines Using Vilsmeier–Haack Conditions

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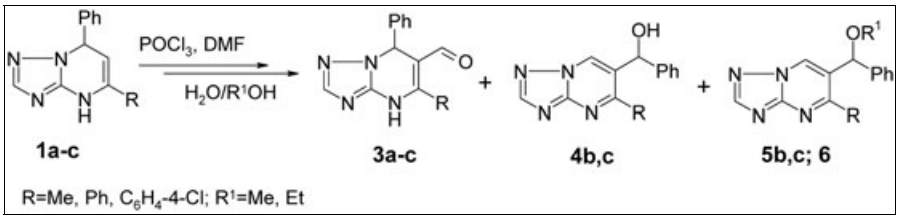

Formylation of 5-methyl-7-phenyl-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine **1a** using Vilsmeier–Haack conditions yields 5-methyl-7-phenyl-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidin-6-ylcarbaldehyde **3a**. 5,7-Diaryl-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines **1b**,**c** in this reaction apart from formylation undergo recyclization into 5-aryl-1,2,4-triazolo[1,5-*a*]pyrimidin-6-ylmethane derivatives **4b**,**c**, **5b**,**c**, and **6**. The structure of the synthesized compounds was determined on the basis of NMR, IR, and MS spectroscopic data and confirmed by the X-ray analysis of the 6-(ethoxy-phenyl-methyl)-5-phenyl-[1,2,4]triazolo[1,5-*a*]pyrimidine **6**, 5-phenyl-6-(1-phenyl-vinyl)-[1,2,4]triazolo[1,5-*a*]pyrimidine **11**, and 7-phenyl-6-(1-phenyl-vinyl)-[1,2,4]triazolo[4,3-*a*]pyrimidine **12**.

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INTRODUCTION

Dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines are of interest not only as drug-like molecules and objects for pharmacological trials, for example, as analogs of the well known inotropic and antiplatelet agent trapidil [1–4] or vasodilator bumepidil [1], but also as a convenient model structures for the research in the area of the synthetic chemistry of partially hydrogenated heterocycles. Investigations of their chemical properties, molecular structure, and imine–enamine tautomeric equilibrium have been reported in previous years [1,5–9].

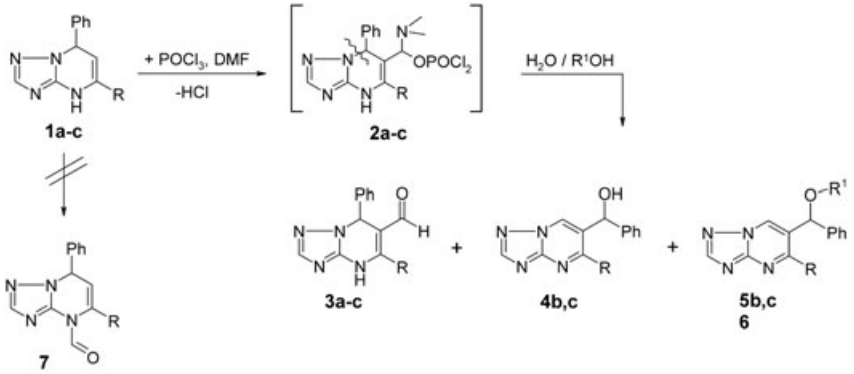
Aryl-substituted 4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines **1**, which contain an enamine substructure **—NH—C(R_1)=CH—**, represent ambident nucleophiles. The nitrogen atom N-4 is their hard, and the carbon atom C-6 is their soft center. In our previous investigation [5], we found that alkylation selectively took place at the N-4 atom but not at the C-6 atom, when soft electrophiles like CH_3I or hard electrophiles like Me_2SO_4 were used. The opposite results were obtained when the alkylation of compound **1a** or **1b** was performed using carbonyl 1,3-bielectrophilic agents such as 1,3-diarylpropen-1-ones or Mannich base hydrochlorides in the presence of sodium ethoxide [7, 8]. The carbon atom C-6 also became the place of electrophilic attack in the oxidation reaction by air oxygen in basic medium or under nitrosation by sodium nitrite in glacial acetic acid [5,6,9]. We used some of the obtained products as starting materials in the synthesis of novel heterocyclic systems [7–9]. Therefore, the functionalization of partially reduced pyrimidine ring opens wide opportunities for the synthesis of novel compounds on the basic of a dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine scaffold.

In this study, we aimed to examine the direction of the electrophilic attack in dihydropyrimidine ring of aryl-substituted 4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines **1a**–**c** in Vilsmeier–Haack reaction.

RESULTS AND DISCUSSION

It was found that 5-methyl-7-phenyl-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine **1a** undergoes reaction with small excess of $POCl_3$ in DMF for a 3 h period under condition of steam bath and afforded 6-carbaldehyde **3a** (Scheme 1) with high yield (see "Experimental" section). The reaction product was easily isolated from ice

Scheme 1. **1**–**5**: **a**, R=Me; **b**, R=Ph; **c**, R=C_6H_4-4Cl; **5**: R^1=Me; **6**: R=Ph, R^1=Et.



water and purified by crystallization from methanol. However, in the case of formylation 5,7-diaryl derivatives **1b**,**c** in the above-mentioned reaction conditions, we had obtained complicated mixture of products from which compounds **3b**,**c**, **4b**,**c**, and **5b**,**c** or **6** were crystallized. Yields of 6-carbaldehydes **3b**,**c** were low. In the reaction mixture, we also identified alcohols **4b**,**c** and alkoxy compounds **5b**,**c** or **6**. Compounds **5b**,**c** were formed in the case of decomposition of the reaction mixture by H_2O/MeOH and compound **6** obtained when H_2O/EtOH were used for this purpose. However, in H_2O/*i*-PrOH medium, formation of alkoxy derivatives was not observed. In these conditions, only 6-carbaldehydes **3b**,**c** and alcohols **4b**,**c** were detected. Products of the nitrogen atom N-4 formylation **7** have not been fixed in any case.

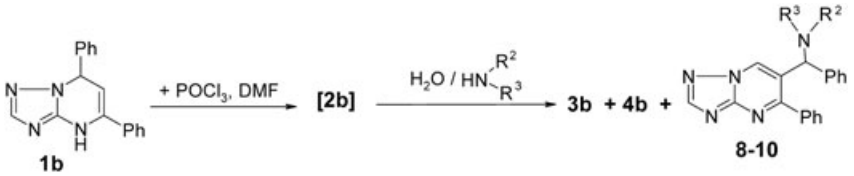
It should be noted that formation of **3b**, **4b**, and **8**–**10** compounds mixture also observed in the case utilization solutions of amines in 2-propanole for the decomposition of intermediate **2b** (Scheme 2). Piperidine, 4-methoxyphenylamine, and benzylamine were used as amine components in these reactions. The compounds **3b**, **4b**, and **8**–**10** were separated by crystallization from 2-propanole.

In our opinion, key role in the formation of alcohols **4b**,**c**, alkoxy **5b**,**c**, **6**, and amino-substituted derivatives **8**–**10** belongs to the intermediates **2**. We found that 6-carbaldehydes **3a**–**c** did not afford compounds **5** and **6** in acidic methanol or ethanol solution under long lasting refluxing. Hydroxy **4b**,**c**, alkoxy **5b**,**c**, **6**, and amino derivatives **8**–**10** probably formed in reaction mixture as a result of intramolecular rearrangement that accompanied decomposition of the intermediate products **2** under the action of H_2O and/or alcohol (amine). Under these conditions dihydropyrimidine ring opened and further cyclization took place with participation of the carbonyl electrophilic center and accompanied by heteroaromatization.

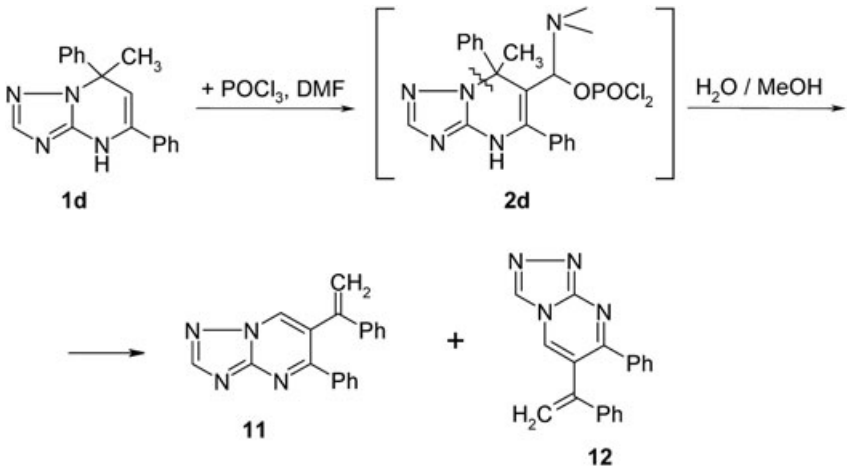
To prove this reaction mechanism, we have performed the formylation of 5,7-diphenyl-7-methyl-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine **1d** by $POCl_3$–DMF mixture. In this case, the CH_3 group played the role of the "marker." As a result (Scheme 3), we have obtained two isomers **11** and **12**. In this experiment, 6-carbaldehyde, alkoxy derivatives, or alcohols have not been obtained.

The structures of compounds **3a**–**c**, **4b**,**c**, **5b**,**c**, and **6** were confirmed by ^{1}H-, ^{13}C-NMR, IR, mass-spectroscopic data, and elemental analyses (see "Experimental" section). In mass spectra of the aldehydes **3a**–**c** obtained by EI method, peaks corresponding to the molecular ions are not the most intensive. At the first stage of fragmentation, these compounds lose CO. Intense peaks (100%) appear at *m*/*z* [M^+–C_6H_5] fragments. In the IR spectra of compounds **3a**–**c**, broad absorption band for associated imino group at 3416–2384 cm^{-1} and sharp absorption band for stretching vibration of carbonyl group at 1652–1632 cm^{-1}

Scheme 2. **8**: R^2+R^3=-C_5H_{10}; **9**: R^2=C_6H_4-4-OCH_3, R^3=H; **10**: R^2=CH_2-C_6H_5, R^3=H.



Scheme 3



are most characteristic. The high resolution ^{1}H-NMR spectrum of the aldehyde **3a** shows signals suggesting the presence in their structure aryl ring and CH_3 group, the NH group (broad singlet at δ 11.18, which disappears after exchange for deuterium), the formyl proton (at δ 9.71) and two methine protons H-2 and H-7 (at δ 7.67 and δ 6.20 ppm), respectively. The spectra of the aldehydes **3b**,**c** differ from above-mentioned one only by the presence signals for two aryl rings and absence of CH_3 group signal. The presence in the formyl derivatives **3a**–**c** spectra singlets of the NH and H-7 protons confirms that the electrophilic substitution took place at C-6 reaction center and dihydro-system of the pyrimidine ring in aldehydes **5a**–**c** preserves.

The mass spectra of compounds **4b**,**c** contain low-intensity (10%) molecular ion peaks [M^+] with *m*/*z* 302 and 338/336, respectively. Intense peaks appear with *m*/*z* 272 (100) for compound **4b** and *m*/*z* 308/306 (32/100) for compound **4c**. These radical ions are generated by successive elimination of the CH_2O fragment from the starting molecules. In mass spectra of the alkoxy derivatives **5b**,**c**, **6** peaks corresponding to the molecular ions are also low intensive (13%). At the first stage of fragmentation these compounds lose alkyl group.

In the IR spectra of alcohols **4b**,**c** broad absorption of associated OH-group with maximum at 3192 and 3188 cm^{-1} correspondingly is noted. The IR spectra of alkoxy compounds **5b**,**c** and **6** unfortunately are low informative, they contain levy of the bands, which are peculiar to condensed heterocyclic systems with a few —C=N— bonds [10]. The ^{1}H-NMR spectra of alcohols **4b**,**c** exhibit multiplets of aromatic protons, singlets of H-2 and H-7 protons, and two doublets of the —CH—OH fragment in the downfield at δ 5.93 (CH) and δ 6.26 (OH) ppm with *J* 4.8–4.6 Hz. The signal from OH group was identified by deuterium exchange. The resonance of NH proton in these spectra and in the spectra of alkoxy derivatives **5b**, **c**, **6** was absented. Spectra of the compounds **5b**,**c** and **6** besides of multiplets of aromatic protons, singlets of H-2 and H-7 protons, contained signals of —CH—O-Alk fragment. The resonance of H-7 proton shifted downfield by 3 ppm compared with H-7 signals in the spectra of the aldehydes **3a**–**c**.

The structures of **8**–**10** also were proved by spectral methods. The mass spectrum of the piperidine derivative **8** contains molecular ion peak [M^+] with *m*/*z* 369 (11) and ion radical peaks 368 (44, M^+–H), 292 (43, M^+–C_6H_5), 285 (66, M^+–NC_5H_{10}), 207 (100, M^+–NC_5H_{10}–C_6H_5).

In the ^{1}H-NMR, spectrum of the compound **8** observed singlets of three methine protons and multiplets of phenyl and piperidyl fragments. The spectrum of amine derivative **9** was analogous to such of alcohols **4** and exhibited the resonance of NH and CH group as doublet correspondingly at δ 6.20 and δ 5.63 ppm with *J* 7.5 Hz. After exchange with deuterium doublet of the NH group disappeared and CH signal converted into singlet. In the spectrum of benzyl-substituted compound **10**, resonance of NH group was absented owing to proton exchange, but signal of the CH fragment connected with this imino group exhibited doublet at δ 4.97 ppm with *J* 3.8 Hz.

The products **11** and **12** have the same element content and molecular weight, but have different melting points and spectral IR, NMR characteristics. In mass spectra, both of the compounds **11** and **12** have low intensive molecular ions' peaks [M^+] with *m*/*z* 298. Intense peaks (100%) appear at *m*/*z* 221 [M^+–C_6H_5] fragments.

In IR spectra of **11** and **12**, absorption of carbonyl and associated imino groups were absented. Their ^{1}H-NMR spectra differed by the chemical shifts of the methine protons. Finally, the structures of compound **6** and isomeric triazolo[1,5-*a*]—**11** and—[3,4-*a*]pyrimidines **12** were established by an X-ray crystal structure analysis. Figures 1–3 show a perspective view of these molecules.

The molecular structures of the compound **6**, **11**, and **12** are very similar. The presence of two vicinal substituents in

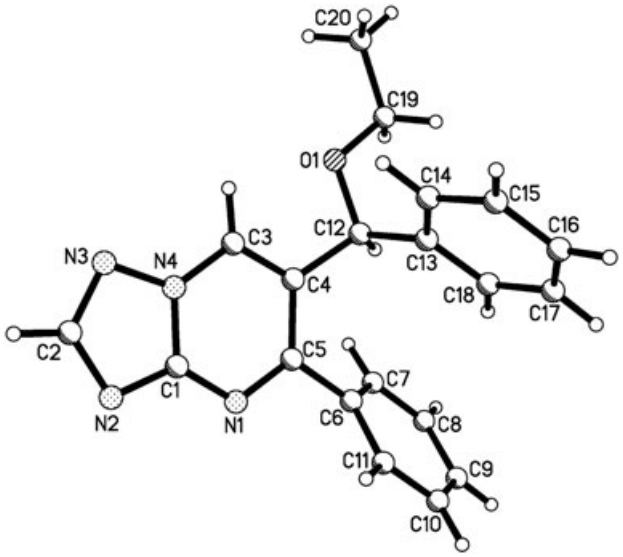


Figure 1. The molecular structure of the compound **6**.

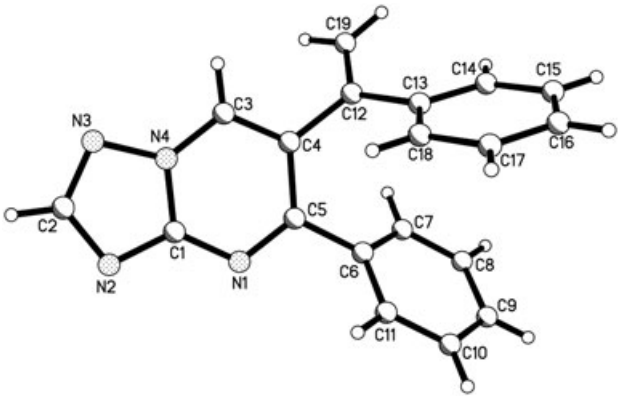


Figure 2. The molecular structure of the compound **11**.

pyrimidine ring leads to appearance of some steric strain. The repulsion between substituents is slightly weaker in the molecule **6**, where the C(12) atom is sp^3-hybridized as compared with molecules **11** and **12**, where the C(12) atom has sp^2-hybridization. Steric strain manifests itself in appearance of a number of shortened intramolecular contacts namely the H(7)…H(12) 2.25 Å (the van der Waals radii sum [11] is 2.34 Å), H(12)…C(7) 2.61 Å (2.87 Å), H(18)…C(7) 2.84 Å (2.87 Å), C(12)…C(7) 3.22 Å (3.42 Å), and C(18)…C(6) 3.37 Å (3.42 Å) for the molecule **6**, and the C(12)…C(7) 3.11 Å **11**, 3.10 Å **12**, C(13)…C(6) 3.19 Å **11**, 3.16 Å **12**, C(13)…C(7) 3.35 **11**, 3.21 Å **12**, C(18)…C(5) 3.33 Å **11**, 3.34 Å **12**, C(18)…C(6) 3.40 Å **11**, 3.32 Å **12** (the van der Waals radii is 3.42 Å), C(12)…H(7) 2.79 Å **11**, 2.77 Å **12**, H(18)…C(4) 2.65 Å **11**, 2.66 Å **12**, H(19a)…C(14) 2.71 Å **11**, 2.70 Å **12**, H (19b)…C(3) 2.78 Å **11**, 2.82 Å **12**, H(14)…C(19) 2.72 Å **11** and **12**, H(3)…C(19) 2.81 Å **11**, and **12** (the van der Waals radii is 2.87 Å), H(19a)…H(14) 2.30 Å **11**, 2.27 Å **12** for the molecules **11** and **12**. The repulsion between vicinal substituents leads also to the elongation of the C(4)—C (5) (1.436 (1) Å **6**, 1.446 (3) Å **11**, 1.433 (3) Å **12**) and C (4)—C(12) (1.520 (1) Å **6**, 1.493 (3) Å **11**, 1.492 (3) Å **12**) as compared with their mean values [12] 1.387 Å and 1.478 Å, respectively, and to the twisting of the C(4)—C (5) bond in the molecules **6** and **12** (the C(12)—C(4)—C (5)—C(6) torsion angle is –6.5 (1)° for **6** and –6.0 (4)° for **12**). The phenyl substituent at the C(5) atom is noncoplanar to the bicycle plane (the N(1)—C(5)—C(6)—C(11) torsion angle is –49.3 (1)° **6**, –46.9 (3)° **11**, –50.8 (4)° **12**).

The phenyl ring of the substituent at the C(4) atom in the molecule **6** is almost orthogonal to the pyrimidine ring, and it is turned relatively the C(4)—C(12) bond (the C(3)—C(4)—C(12)—C(13) and C(4)—C(12)—C(13)—C(14) torsion angles are 101.9 (1)° and 103.9 (1)°, respectively). The ethoxy group has almost *sp*-conformation with respect to the C(3)—C(4) bond (the C(3)—C(4)—C(12)—O(1) torsion angle is –19.5 (1)°) which is stabilized additionally by the H(3)…O(1) attractive interaction (2.28 Å) which cannot be considered as hydrogen bond because of too sharp C—H…O angle (99°). The ethyl group has *ap*-conformation relatively the C(4)—C(12) bond and the C(19)—C(20) bond is antiperiplanar to the C(12)—O(1) bond (the C(19)—O(1)—C(12)—C(4) and C(12)—O(1)—C(19)—C(20) torsion angles are –167.1 (1)° and –169.9 (1)°, respectively).

Significant disturbance of the conjugation between triazolopyrimidine fragment and π-systems of the substituents is observed in the molecules **11** and **12** (the C(3)—C(4)—C(12)—C(19) and C(4)—C(12)—C(13)—C(18) torsion angles are –54.0 (4)° **11** 50.8 (4)° **12** and –27.6 (4)° **11** –26.8 (4)° **12**, respectively).

CONCLUSION

Thus, 4,7-dihydro-5,7-diphenyl-1,2,4-triazolo[1,5-*a*]pyrimidines using Vilsmeier–Haack conditions not only formed

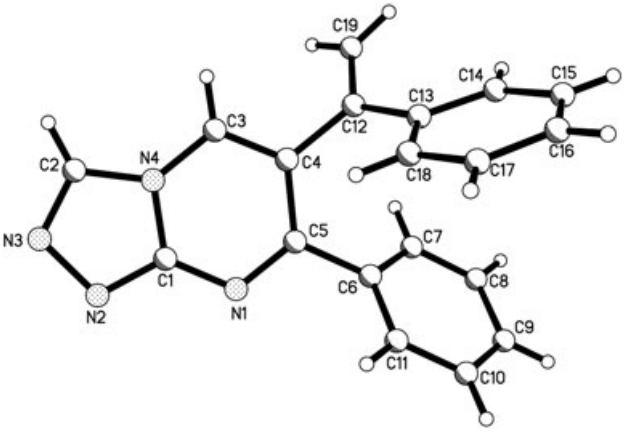


Figure 3. The molecular structure of the compound **12**.

6-carbaldehydes, but rearranged to alkoxy, hydroxyl derivatives and/or vinyl-[1,2,4]triazolo[1,5-*a*]- or -[4,3-*a*] pyrimidines.

EXPERIMENTAL

All melting points were measured using Koeffler melting point apparatus and are uncorrected. IR spectra were taken on a Specord M-82 spectrometer in KBr pellet. ^{1}H-, ^{13}C-NMR spectra were recorded at Varian Mercury VX200 at 200 MHz (50 MHz for ^{13}C) and Bruker AM300 spectrometer at 300 MHz in DMSO-d_6, using TMS as an internal standard (chemical shifts in parts per million). Mass spectra were taken on a Varian 1200L DIP; ionization mode: EI; electron energy 70 eV. Elemental analyses were determined using a Perkin-Elmer 2400 instrument.

Starting dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines **1a–d** were obtained by known methods [5,13]. All other chemicals are commercially available.

General procedure for the formylation of the 4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines (3a–d). For the preparation of the compound **3a**, a mixture of dihydrotriazolo[1,5-*a*]pyrimidine **1a** (0.86 g, 3 mmol), $POCl_3$ (0.32 mL, 3.5 mmol), and 3 mL DMF was heated at the steam bath for 3 h. Then, reaction mixture was stirred in ice water, neutralized by solution of the NaOH to pH 6 and amorphous precipitate of the carbaldehyde **3a** removed by filtration, purified by recrystallization from a MeOH. In the case of formylation compounds **3b**,**c** at the analogous conditions obtained amorphous precipitate refluxed in MeOH (10 mL) for 5 min and filtered insoluble compounds **3b**,**c**. Then after cooling of solution, crystals of the compounds **4b**,**c** and **5b**,**c** were formed and separated consequently. Ethoxy derivative **6** was obtained from EtOH. Compounds **11** and **12** were synthesized from dihydrotriazolo[1,5-*a*]pyrimidine **3d** by the same procedure and were crystallized from 2-propanol.

General procedure for the preparation amino derivatives (8–10). For the preparation of the compounds **8–10** the dihydrotriazolo[1,5-*a*]pyrimidine **1b** was formylated by above-mentioned method and obtained amorphous precipitate refluxed in 2-propanol (7 mL) with 3 mmol of the appropriate amine for 5 min and filtered insoluble compound **3b**. Then, after cooling of solution, crystals of the compounds **4b** and **8** (or **9**, **10**) were formed and separated consequently.

5-Methyl-7-phenyl-4,7-dihydro[1,2,4]triazolo[1,5-a]pyrimidin-6-carbaldehyde (3a). This compound was obtained in yield 83% as white needles (methanol), mp 292–295°C; IR (KBr): 3316–2660 (NH, H-bond), 1648 (CO) cm^{-1}; ^{1}H-NMR: (300 MHz, DMSO-d_6): δ 11.2 (br s, 1H, NH), 9.71 (s, 1H, CH), 7.67 (s, 1H, CH), 6.20 (s, 1H, CH), 7.2–7.3 (m, 5H, phenyl), 2.45 (s, 3H, Me); ^{13}C-NMR (50 MHz, DMSO-d_6): δ 56.12, 79.01, 127.00, 126.48 (C-6), 127.48, 127.67, 127.79, 127.89, 128.79 (*p*-C-Ar), 134.66 (C-7), 137.33, 142.21, 153.32 (C-3a), 156.15 (C-2), 163.84 (C-5); MS: *m*/*z* (relative intensity, %): 240 (88), 223 (14), 211 (33), 195 (25), 184 (18), 170 (26), 163 (100), 134 (14), 77 (25); Anal. Calcd. for $C_{13}H_{12}N_4O$: C, 64.99; H, 5.03; N 23.32; Found: C, 65.01; H, 5.06; N 23.34.

4,7-Dihydro-5,7-diphenyl-1,2,4-triazolo[1,5-a]pyrimidin-6-carbaldehyde (3b). This compound was obtained in yield 30% as white crystals (methanol), mp >300°C; IR (KBr): 3416–2736 (NH, H-bond), 1646 (CO) cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 11.5 (br s, 1H, NH), 9.06 (s, 1H, CH), 7.75 (s, 1H, CH), 6.35 (s, 1H, CH), 7.3–7.6 (m, 10H, phenyl); MS: *m*/*z* (relative intensity, %): 302 (62), 274 (26), 247 (24), 232 (34), 225 (100), 207 (34), 189 (17), 129 (13), 77 (32); Anal. Calcd. for $C_{18}H_{14}N_4O$: C, 71.51; H, 4.67; N 18.53; Found: C, 71.54; H, 4.70; N 18.55.

5-(4-Chlorophenyl)-7-phenyl-4,7-dihydro[1,2,4]triazolo[1,5-a]pyrimidin-6-carbaldehyde (3c). This compound was obtained in yield 31% as white crystals (methanol), mp 275–278°C; IR (KBr): 3404–2500 (NH, H-bond), 1652 (CO) cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 11.5 (br s, 1H, NH), 9.06 (s, 1H, CH), 7.74 (s, 1H, CH), 6.35 (s, 1H, CH), 7.7–7.6 (d.d, 4H, *J* 8.2 Hz, Ar-H), 7.3 (m, 5H, phenyl); MS: *m*/*z* (relative intensity, %): 338/336 (9/27), 310/308 (7/20), 282/280 (8/24), 268/266 (9/27), 261/259 (32/100), 243/241 (10/33), 233/231 (14/45), 189 (16); Anal. Calcd. for $C_{18}H_{13}ClN_4O$: C, 64.20; H, 3.89; N 16.64; Found: C, 64.22; H, 3.93; N 16.67.

Phenyl(5-phenyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)methanol (4b). This compound was obtained in yield 21% as white crystals (methanol), mp 211–213°C; IR (KBr): 3192, 1624, 1504, 1492 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.23 (s, 1H, CH), 8.67 (s, 1H, CH), 7.0–7.4 (m, 10H, phenyl), 6.27 (d, 1H, *J* 4.6 Hz, OH), 5.93 (d, 1H, *J* 4.6 Hz, CH); ^{13}C-NMR (50 MHz, DMSO-d_6): δ 69.43, 126.57, 126.93 (C-6), 127.03 (*p*-C-Ar), 127.68, 127.76, 128.14, 128.90 (*p*-C-Ar), 134.96 (C-7), 137.43, 142.29, 153.31 (C-3a), 156.19 (C-2), 163.52 (C-5); MS: *m*/*z* (relative intensity, %): 302 (54), 274 (11), 225 (11), 171 (12), 128 (10), 105 (30), 77 (100); Anal. Calcd. for $C_{18}H_{14}N_4O$: C, 71.51; H, 4.67; N 18.53; Found: C, 71.54; H, 4.68; N 18.55.

[5-(4-Chlorophenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl]-phenyl-methanol (4c). This compound was obtained in yield 19% as white crystals (methanol), mp 212–215°C; IR (KBr): 3188, 1624, 1520, 1492 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.22 (s, 1H, CH), 8.68 (s, 1H, CH), 7.0–7.5 (m, 9H, Ar-H), 6.26 (d, 1H, *J* 4.8 Hz, OH), 5.93 (d, 1H, *J* 4.8 Hz, CH); MS: *m*/*z* (relative intensity, %): 338/336 (6/18), 308/306 (32/100), 281/279 (29/89), 243/241 (8/24), 231/229 (10/30), 225/223 (11/32), 216/214 (12/36), 189 (13); Anal. Calcd. for $C_{18}H_{13}ClN_4O$: C, 64.20; H, 3.89; N 16.64; Found: C, 64.21; H, 3.88; N 16.65.

6-(Methoxy(phenyl)methyl)-5-phenyl-[1,2,4]triazolo[1,5-a]pyrimidine (5b). This compound was obtained in yield 35% as white crystals (methanol), mp 144–146°C; IR (KBr): 3092, 2940, 2828, 1624, 1520, 1492, 1296 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.20 (s, 1H, CH), 8.68 (s, 1H, CH), 6.9–7.5 (m, 10H, phenyl), 5.53 (s, 1H, CH), 3.27 (s, 3H, OMe); MS: *m*/*z* (relative intensity, %): 316 (28), 301 (10), 284 (34), 207 (10), 180 (12), 130 (15), 121 (37), 115 (19), 105 (27), 77 (100); Anal. Calcd. for $C_{19}H_{16}N_4O$: C, 72.14; H, 5.10; N 17.71; Found: C, 72.12; H, 5.12; N 17.73.

5-(4-Chlorophenyl)-6-(methoxy-phenyl-methyl)-[1,2,4]triazolo [1,5-a]pyrimidine (5c). This compound was obtained in yield 42% as white crystals (methanol), mp 179–182°C; (KBr): 3088, 2940, 2832, 1624, 1596, 1520, 1488, 1308 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.21 (s, 1H, CH), 8.69 (s, 1H, CH), 7.1–7.5 (m, 9H, Ar-H), 5.53 (s, 1H, CH), 3.36 (s, 3H, OMe); MS: *m*/*z* (relative intensity, %): 352/350 (8/25), 337/335 (12/36), 243/241 (31/100), 230/228 (12/34), 216/214 (11/33), 205 (14); Anal. Calcd. for $C_{19}H_{15}ClN_4O$: C, 65.05; H, 4.31; N 15.97; Found: C, 65.07; H, 4.34; N 16.01.

6-(Ethoxy-phenyl-methyl)-5-phenyl-[1,2,4]triazolo[1,5-a] pyrimidine (6). This compound was obtained in yield 38% as white crystals (ethanol), mp 125–127°C. IR (KBr): 2972, 2924, 1620, 1520, 1492, 1300 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.12 (s, 1H, CH), 8.67 (s, 1H, CH), 7.1–7.5 (m, 10H, phenyl), 5.65 (s, 1H, CH), 3.40 (q, 2H, CH_2), 1.09 (t, 3H, Me); MS: *m/z* (relative intensity, %): 330 (13), 301 (100), 284 (10), 257 (12), 223 (30), 207 (73), 181 (12), 171 (11); Anal. Calcd. for $C_{20}H_{18}N_4O$: C, 72.71; H, 5.49; N 16.96; Found: C, 72.74; H, 5.52; N 17.71.

5-Phenyl-6-(phenyl-piperidin-1-yl-methyl)-[1,2,4]triazolo [1,5-a]pyrimidine (8). This compound was obtained in yield 64% as yellow crystals (2-propanol), mp 183–186°C; IR (KBr): 2964, 2936, 2860, 2804, 1616, 1516, 1492 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.50 (s, 1H, CH), 8.75 (s, 1H, CH), 7.0–7.6 (m, 10H, phenyl), 4.72 (s, 1H, CH), 2.43–1.55 (m, 10H, $(CH_2)_5$); MS: *m/z* (relative intensity, %): 369 (11), 368 (44), 292 (43), 285 (66), 207 (100), 180 (29), 174 (53), 153 (13), 140 (24), 115 (14), 91 (12), 77 (45); Anal. Calcd. for $C_{23}H_{23}N_5$: C, 74.77; H, 6.27; N 18.95; Found: C, 74.79; H, 6.30; N 18.98.

(4-Methoxy-phenyl)-[phenyl-(5-phenyl-[1,2,4]triazolo[1,5-a] pyrimidin-6-yl)-methyl]-amine (9). This compound was obtained in yield 60% as yellow crystals (2-propanol), mp 95–97°C; IR (KBr): 3252, 3060, 3048, 2972, 1624, 1508 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.02 (s, 1H, CH), 8.70 (s, 1H, CH), 7.2–7.3 (m, 5H, phenyl), 7.5–7.5 (m, 5H, phenyl), 6.5–6.7 (dd, 4H, *J* 7.8 Hz, Ar-H), 6.20 (d, 1H, *J* 7.5 Hz, NH), 5.63 (d, 1H, 7.5 Hz, CH), 3.6 (s, 3H, OMe); ^{13}C-NMR (50 MHz, DMSO-d_6): δ 56.79, 55.09, 114.11, 114.52, 125.00 (C-6), 127.08 (p-C-Ar), 127.37, 127.83, 127.86, 128.09, 129.00 (p-C-Ar), 135.48 (C-7), 137.20, 140.48, 140.52, 153.29 (C-3a), 156.17 (C-2), 164.47 (C-5); MS: *m/z* (relative intensity, %): 407 (40), 285 (27), 256 (15), 216 (15), 207 (100), 122 (26); Anal. Calcd. for $C_{25}H_{21}N_5O$: C, 73.69; H, 5.19; N 17.19; Found: C, 73.72; H, 5.21; N 17.22.

Benzyl-[phenyl-(5-phenyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl-) methyl]-amine (10). This compound was obtained in yield 24% as yellow crystals, mp 98°C; IR (KBr): 3268, 3060, 1620, 1516, 1488 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.48 (s, 1H, CH), 8.68 (s, 1H, CH), 7.0–7.5 (m, 15H, phenyl), 4.97 (d, 1H, *J* 3.6 Hz, CH), 3.62 (d, 2H, *J* 4.0 Hz, CH_2); MS: *m/z* (relative intensity, %): 391 (14), 390 (12), 314 (44), 312 (26), 300 (100), 285 (56), 207 (97), 202 (16), 196 (51), 189 (13), 180 (30), 153 (11), 104 (11), 91 (46); Anal. Calcd. for $C_{25}H_{21}N_5$: C, 76.70; H, 5.41; N 17.89; Found: C, 76.73; H, 5.43; N 17.91.

5-Phenyl-6-(1-phenyl-vinyl)-[1,2,4]triazolo[1,5-a]pyrimidine (11). This compound was obtained in yield 42% as light yellow crystals (2-propanol), mp 160–162°C; IR (KBr): 3048, 1620, 1516, 1488 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.46 (s, 1H, CH), 8.76 (s, 1H, CH), 7.13–7.62 (m, 10H, phenyl), 5.95 (s, 1H, CH), 5.71 (s, 1H, CH); ^{13}C-NMR (50 MHz, DMSO-d_6): δ 118.87, 126.21, 123.80 (C-6), 127.41 (*p*-C-Ar), 127.30, 127.64, 128.29, 128.94 (*p*-C-Ar), 136.48 (C-7), 137.50, 138.43, 143.01, 153.89 (C-3a), 156.12 (C-2), 162.41 (C-5); MS: *m/z* (relative intensity, %): 298 (17), 297 (26), 271 (10), 270 (14), 227 (14), 221 (100), 215 (19), 202 (17), 189 (14), 179 (28), 152 (14); Anal. Calcd. for $C_{19}H_{14}N_4$: C, 76.49; H, 4.73; N 18.78; Found: C, 76.52; H, 4.74; N 18.80.

7-Phenyl-6-(1-phenyl-vinyl)-[1,2,4]triazolo[4,3-a]pyrimidine (12). This compound was obtained in yield 37% as light yellow crystals (2-propanol), mp 220–221°C; IR (KBr): 3116, 3052, 1624, 1516, 1492 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 9.28 (s, 1H, CH), 9.04 (s, 1H, CH), 7.15–7.60 (m, 10H, phenyl), 5.65 (s, 1H, CH), 5.90 (s, 1H, CH); MS: *m/z* (relative intensity, %): 298 (21), 297 (29), 271 (12), 270 (17), 227 (18), 221 (100), 215 (24), 202 (15), 189 (12), 179 (31), 152 (16); Anal. Calcd. for $C_{19}H_{14}N_4$: C, 76.49; H, 4.73; N 18.78; Found: C, 76.53; H, 4.76; N 18.82.

Table 1

The crystallographic data and experimental parameters for compounds **6**, **11**, and **12**.

Parameter	**6**	**11**	**12**
Formula	$C_{20}H_{18}N_4O$	$C_{19}H_{14}N_4$	$C_{19}H_{14}N_4$
Unit cell dimensions			
A (Å)	9.0403 (5)	9.823 (2)	6.994 (2)
b (Å)	9.9674 (7)	19.861 (5)	28.25 (1)
C (Å)	11.1218 (8)	8.274 (2)	8.283 (2)
α (°)	107.936 (6)	90	90
β (°)	107.401 (6)	106.61 (2)	112.04 (2)
γ (°)	104.184 (6)	90	90
V (Å^3)	844.7 (1)	1546.8 (6)	1516.6 (8)
T (K)	293	193	193
F(0 0 0)	348	624	624
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	*P*1	$P2_1/c$	$P2_1/c$
Z	2	4	4
μ (mm^{-1})	0.083	0.079	0.081
D_{calc} (g cm^{-3})	1.299	1.281	1.307
$2\Theta_{max}$ (grad)	60	50	50
Measured reflections	9904	2896	3121
Independent reflections	4902	2695	2674
R_{int}	0.014	0.039	0.040
Reflections with $F > 4\sigma(F)$	2820	1320	1291
R_1	0.036	0.049	0.055
wR_2	0.085	0.123	0.103
S	0.833	0.911	0.979
CCDC	779,096	779,097	779,098

The X-ray diffraction study. X-ray diffraction studies were performed using an automatic "Xcalibur 3" diffractometer (CCD detector, ω-scans) for the compound **6** and on the "Siemens P3/PC" diffractometer (point detector, Θ/2Θ-scan) for **11** and **12** with graphite monochromated MoK_α radiation. The structures were solved by direct method using SHELXTL package [14]. Crystallographic data and parameters of experiments are listed in Table 1.

The positions of the hydrogen atoms were located from electron density difference maps and refined by "riding" model with $U_{iso} = nU_{eq}$ of the carrier atom (n = 1.5 for methyl groups and n = 1.2 for other hydrogen atoms) for structures **11** and **12**. Hydrogen atoms in the structure **6** were refined in isotropic approximation. All nonhydrogen atoms were refined using anisotropic approximation. The final atomic coordinates and crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

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