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Diversity Oriented Synthesis of Polycyclic Heterocycles through the Condensation of 2-Amino[1,2,4]triazolo[1,5-*a*]pyrimidines with 1,3-Diketones

Dmitry A. Pyatakov,[†] Andrey N. Sokolov,[†] Alexander V. Astakhov,[†] Andrey Yu. Chernenko,[†] Artem N. Fakhrutdinov,[‡] Victor B. Rybakov,[§] Vladimir V. Chernyshev,[§,∥] and Victor M. Chernyshev*[,†]

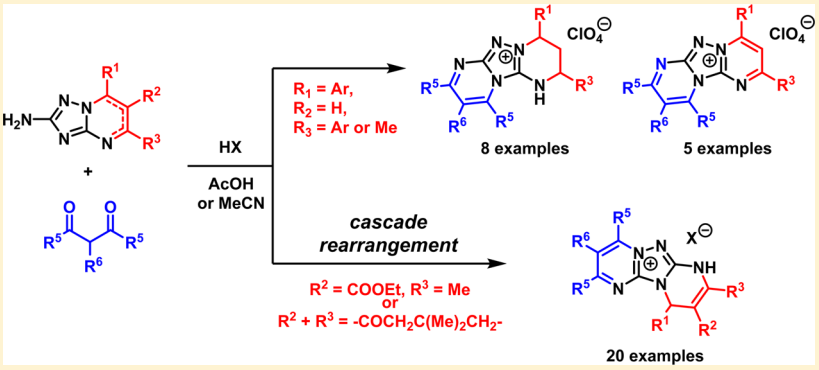
[†]Platov South-Russian State Polytechnic University (NPI), Prosveschenya 132, 346428 Novocherkassk, Russian Federation

[‡]Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky Prospect 47, Moscow 119991, Russian Federation

[§]M. V. Lomonosov Moscow State University, Leninskie Gory 1-3, Moscow, 119991, Russian Federation

[∥]A. N. Frumkin Institute of Physical Chemistry and Electrochemistry RAS, Leninsky prospect 31, Moscow 119071, Russian Federation

Supporting Information



ABSTRACT: The acid-catalyzed condensation between 2-aminosubstituted [1,2,4]triazolo[1,5-*a*]pyrimidines and their analogues with various saturation of the pyrimidine ring and 1,3-diketones or 1,1,3,3-tetramethoxypropane was evaluated as a new approach for the synthesis of diversely substituted polycyclic derivatives of triazolopyrimidine. The reaction of 4,5,6,7-tetrahydro- or aromatic aminotriazolopyrimidines results in selective formation of the corresponding [1,2,4]triazolo[1,5-*a*:4,3-*a*′]dipyrimidin-5-ium salts, and the condensation of substrates containing the 4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidine fragment is accompanied by a cascade rearrangement with unusual recyclization of the dihydropyrimidine ring to yield partially hydrogenated [1,2,4]triazolo[1,5-*a*:4,3-*a*′]dipyrimidin-5-ium or pyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-*b*]quinazolin-5-ium salts. The proposed methodology exhibits a wide scope, providing rapid access to polycondensed derivatives of the [1,2,4]triazolo[1,5-*a*]pyrimidine scaffold. DFT calculations of the Gibbs free energies of possible isomers were performed to rationalize the experimentally observed reactivity and selectivity.

INTRODUCTION

1,2,4-Triazolo[1,5-*a*]pyrimidines are purine analogues that are important in agricultural chemistry and medicine.[1,2] Triazolopyrimidine sulfonamide herbicides (e.g., Flumetsulam and Metosulam) have been employed in agriculture for approximately 20 years,[2a,b] and in the past decade, a new fungicide (Ametoctradin (Initium)[2c,d]) and herbicide (Pyroxsulam[2e]) have received approval for agricultural applications. Since the 1960s, Trapidil, which is a coronary vasodilator, has been used in medicine,[1a] and most recently, a new drug to treat hepatitis C (Filibuvir) passed stage II clinical trials.[1c] Compounds containing the [1,2,4]triazolo[1,5-*a*]pyrimidine core exhibit biological activity in a variety of therapeutic domains (i.e., anticancer,[3] antimalarial[4a] and anti-Leishmania,[4b,c] antibacterial,[5] antiviral,[6] including anti-HIV[6d,e] and anti-HCV,[1c,6f] anti-inflammatory,[7] hypoglycemic,[8] microtubule-stabilizing CNS,[9] hypnotic,[10] and other types of activities[11]).

Over the past years, in medicinal chemistry, polycyclic molecules containing the [1,2,4]triazolo[1,5-*a*]pyrimidine fragment annulated with different carbo- and heterocycles have become of interest because these compounds possess anticancer and anti-inflammatory activities.[3a,d,e,7,12] In most of these polycyclic molecules, the triazolopyrimidine fragment is annulated with other cycles at one of the edges of the pyrimidine hexagon. One of the most important approaches for the synthesis of these compounds is based on the reactions of partially hydrogenated triazolopyrimidines with electrophilic

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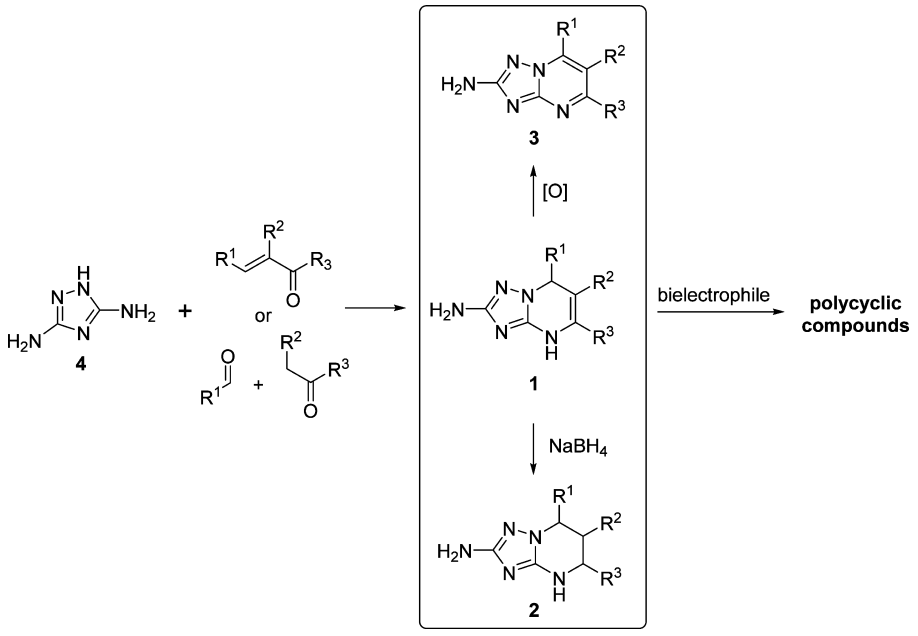
Scheme 1



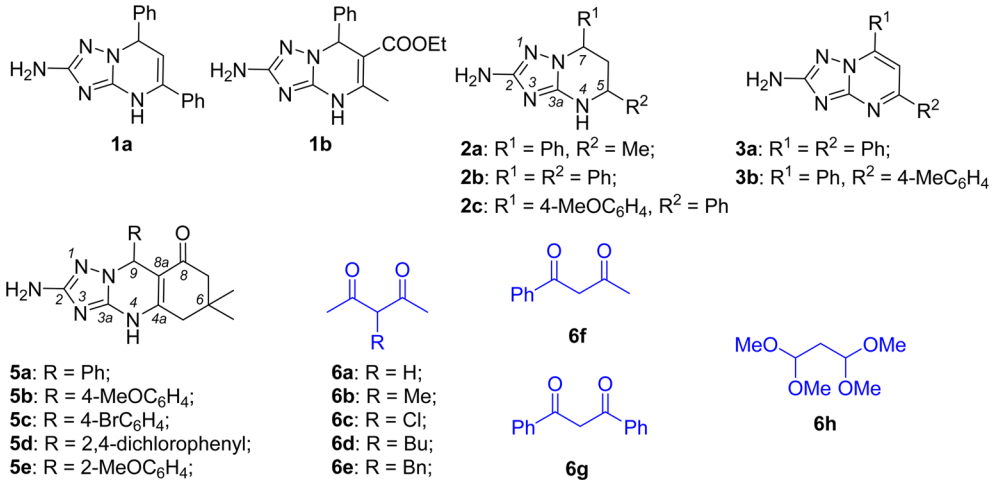


Figure 1. Structures of starting compounds **1**, **3**−**6**.

and bielectrophilic reagents.[10,12] However, the potential for annulation of new cycles from the side of the triazole fragment remains unexplored.

Recently, we have demonstrated the synthesis of polycyclic compounds by annulating new cycles to the triazole moiety of 2-amino-[1,2,4]triazolo[1,5-*a*]pyrimidines with various saturation of the pyrimidine ring by reactions with 3-chloropropanoyl chloride and *α*-bromoketones.[11] In these reactions, aminotriazolopyrimidines act as *N*,*N*′-binucleophilic synthons, resulting in the formation of a new ring through annulation reactions of the 2-NH_2 and N-3 atom. On the basis of these results, we hypothesized that cyclocondensation of 2-amino-[1,2,4]triazolo[1,5-*a*]pyrimidines and their analogues (**1**−**3**) with 1,3-dicarbonyl compounds may allow for the synthesis of various substituted polycondensed heterocycles. Compounds **1** can be obtained readily from the condensation of diaminotriazole **4** with *α*,ß-unsaturated carbonyls[13] or can be obtained from three-component reactions between triazole **4**, methylene-active carbonyl compounds, and aldehydes.[14] Compounds **1** are especially useful because the dihydropyrimidine motif is amenable to both aromatization by various oxidizing agents[13a,15] and reduction by sodium borohydride[16] to afford compounds **2** and **3** (Scheme 1).

In the current article, we describe the diversity oriented synthesis of multisubstituted polycondensed heterocycles by reactions of 2-amino-[1,2,4]triazolo[1,5-*a*]pyrimidines and analogues (**1**−**3**) with 1,3-diketones and 1,1,3,3-tetramethoxypropane. The proposed strategy allows for modulation of no less than five substituents in the resulting polycyclic systems with different annulation of the triazole and pyrimidine rings starting from readily available diaminotriazole **4** and carbonyl and dicarbonyl compounds.

RESULTS AND DISCUSSION

Partially hydrogenated 2-aminosubstituted triazolopyrimidines **1a**,[13] **1b**,[14c] **2a**−**c**,[16] triazoloquinazolines **5a**−**d**, and aromatic triazolopyrimidines **3a**,**b**[15] were used as substrates containing the 2-amino-[1,2,4]triazolo[1,5-*a*]pyrimidine fragment with various saturations of the pyrimidine ring (Figure 1). Previously undescribed aminotriazoloquinazolines **5c**,**e** were obtained by

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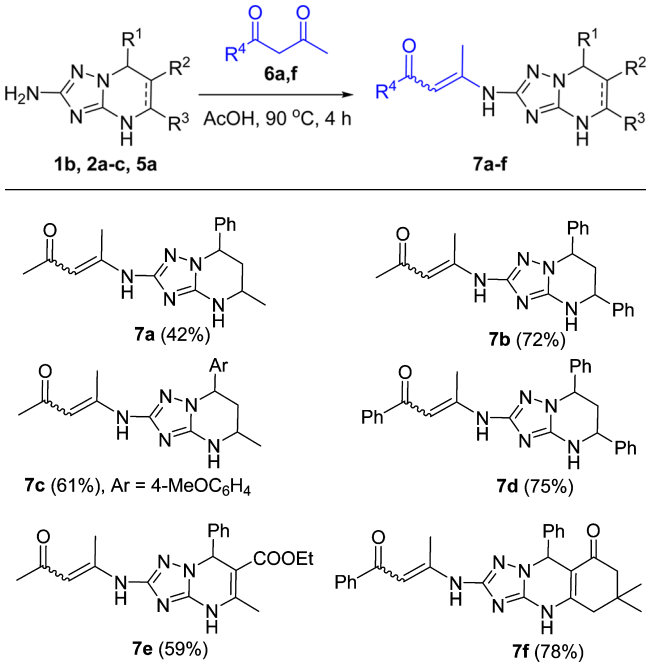
three-component condensation of diaminotriazole **4** with substituted benzaldehydes and 5,5-dimethylcyclohexane-1,3-dione similar to compounds **5a,b,d,f** (Scheme 1).[14a] 1,3-Diketones **6a−g** and 1,1,3,3-tetramethoxypropane **6h** (as equivalent of 1,3-dialdehyde) were applied as 1,3-dicarbonyls (Figure 1).

Heating of compounds **1b**, **2a−c**, and **5a** with diketones **6a,f** in acetonitrile, ethanol, or acetic acid afforded the corresponding enaminoketones **7** (Table 1). The best yields of compounds

Table 1. Synthesis of Compounds 7a−f



7a−f were obtained when the reagents were heated in AcOH at 90 °C. At higher temperatures, sufficient tarring of the reaction mixtures was observed. However, at lower temperatures, the reaction time was too long. Notably, the reaction of amines **2b** and **5a** with unsymmetrical diketone **6f** progressed selectively at the acetyl group of **6f**, affording compounds **7d,f**. Dibenzoylmethane **6g** is unreactive under these conditions, which was most likely due to the low electrophilicity of the carbonyl groups conjugated with the benzene rings. In addition, under the studied conditions, we were unable to obtain enaminoketones from amine **1a** and aromatic amines **3a,b**. Intensive tarring and formation of a complex mixture of products occurred with amine **1a** due to instability of the dihydropyrimidine cycle. However, only starting compounds were isolated from the reaction mixtures after heating of amines **3a,b** with diketone **6a**, which is most likely due to the decreased nucleophilicity of the NH_2 group in compounds **3** resulting from the electron-withdrawing influence of the aromatic pyrimidine ring.

Compounds **7a−f** failed to cyclize under fusion or heating under reflux in acetic acid or DMF. Only gradual decomposition and sufficient tarring were observed under these conditions. Compounds **7a−f** underwent cyclization in the presence of strong mineral acids, which catalyze this reaction. However, the direction of the reaction depends on the saturation of the pyrimidine cycle in the starting compounds (**7**).

The derivatives of tetrahydrotriazolopyrimidine (compounds **7a−d**) with a short period of heating in acetonitrile or ethanol in the presence of a small excess of perchloric acid afforded tricyclic compounds **8a−c,h** (*Method A*, Table 2). In addition, compounds **8** and **9** are more effectively obtained by one-pot heating of amines **2a−c** and **3a,b** with diketones **6a−c,g** and $HClO_4$ in ethanol or acetic acid (*Methods B and C*, Table 2). Under these conditions, even poorly reactive dibenzoylmethane **6g** and low nucleophilic amines **3a,b** are involved in condensation. Presumably, enaminoketones **7** formed by the acid-catalyzed condensation of diketones at the NH_2 group are intermediates in the one-pot process.

The reaction of aminotriazolopyrimidine **1a** with diketone **6a** afforded a complex mixture of products from which only aromatic compound **9a** was isolated in 35% yield (Scheme 2). Apparently, compound **9a** results from the oxidative aromatization of intermediate **10**. However, an alternative route through an initial oxidative aromatization of compound **1a** to compound **3a** cannot be ruled out. The tendency to oxidative aromatization was also observed for the products of the reactions of compound **1a** with 3-chloropropanoyl chloride and α-bromoketones.[11] It is important to note that compounds **9a,b,e** have been previously described.[17] However, their structures were determined based on indirect data from ^{1}H NMR spectra.

The condensation of enaminoketones **7e,f**, in which the dihydropyrimidine fragment contains a carbonyl group in position 6 of the triazolopyrimidine core, proceeds in a different manner. These compounds in the presence of perchloric acid when heated under reflux in acetonitrile (compound **7e**) or acetic acid (compound **7f**) afford compounds **11a,b** (Scheme 3). The reaction includes recyclization of the dihydropyrimidine ring. Analogous products were obtained for one-pot heating of amines **1b** and **5a−e** with diketones **6a−g** and tetramethoxypropane **6h** in the presence of mineral acids (see below). Interestingly, according to the NMR spectra, a mixture of regioisomers, which presumably differ from each other by the positions of the methyl and phenyl groups on the aromatic pyrimidine ring, was formed during cyclization of compound **7f**. Compound **11b**, which apparently resulted from isomerization of starting enaminoketone **7f** through reversible hydrolysis and intermediate formation of diketone **6f** and amine **5a**, followed by acid-catalyzed condensation at the benzoyl group of the diketone (Scheme 3), was isolated as a major product from the mixture by crystallization.

The disclosed reaction between compounds **1b**, **5**, and **6** that resulted in the formation of compounds **11** may have a high preparative value for the synthesis of polycyclic compounds because the starting materials are readily available. Therefore, we optimized the preparative conditions using the reaction between compounds **5a** and **6a** as an example (Table 3).

First, we investigated the reaction in the presence of a 1 molar equiv of $HClO_4$ in various solvents heated under reflux with a 30% molar excess of diketone **6**. In ethanol, the reaction proceeds relatively slowly, resulting in a moderate yield of product **11c** (entry 1), which is contaminated by perchlorate from the starting aminoheterocycle based on the ^{1}H NMR spectra. In refluxing acetic acid, the reaction proceeds rapidly (entry 1). However, the resulting product contains unidentified impurities. Analogous impurities were detected in the product obtained from synthesis in neat 2,4-pentanedione (entry 3). Sufficient yields of the pure product (**11c**) were obtained in refluxing acetonitrile (entry 4) and especially in acetic acid at 90

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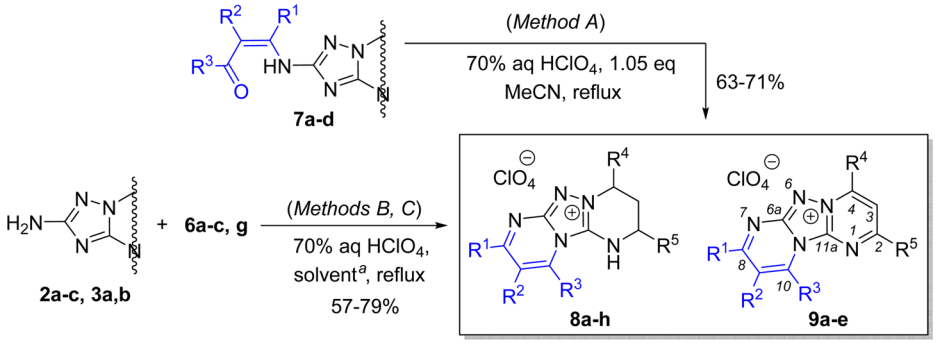
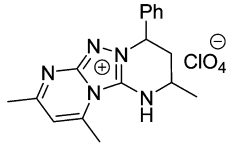
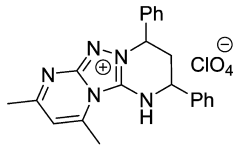
Table 2. Synthesis of Compounds 8a–h and 9a–e

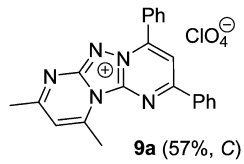




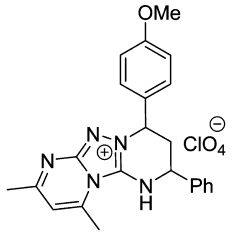
8a (65%, *A*; 58%, *B*)



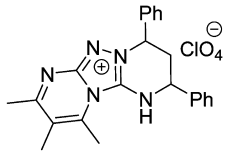
8b (71%, *A*; 61%, *B*)



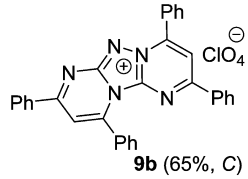
9a (57%, *C*)



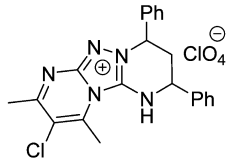
8c (69%, *A*; 59%, *B*)



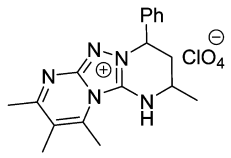
8d (65%, *B*)



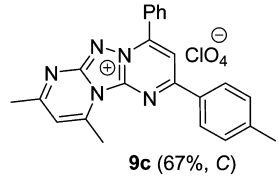
9b (65%, *C*)



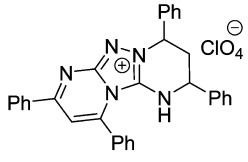
8e (61%, *B*)



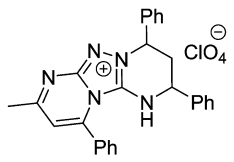
8f (72%, *B*)



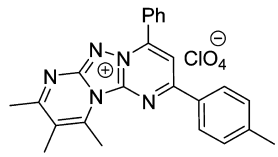
9c (67%, *C*)



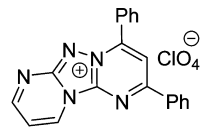
8g (72%, *C*)



8h (63%, *A*)



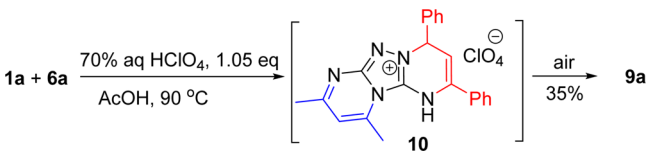
9d (70%, *C*)



9e (61%, *C*)

[a]See the Experimental Section for details.

Scheme 2



°C (entry 6). Therefore, we performed additional experiments in acetic acid at 90 °C with varied reaction times, reagent ratios, and strong acids as catalysts. Under the studied conditions, variations in the reaction time (entry 7) and the **5a**:**6a** molar ratio (entries 8, 9) did not increase the yield. In the presence of a 40% aqueous solution of HBr, only a trace yield of the desired product was detected by NMR in the resulting precipitate due to the low solubility of the hydrobromide of the starting aminoheterocycle in the reaction mixture (entry 10). For H_2SO_4, the yield of sulfate **11d** (entry 11) was slightly lower than that of perchlorate **1c** (entry 6). An increase in the amount of $HClO_4$ (entries 12, 13) did not increase the yield of **11c**. Therefore, the reaction conditions of entry 6 appeared to be the best for preparative one-pot synthesis.

With good reaction conditions in hand, the substrate scope of this reaction was investigated (Table 4).

It is important to note that our attempt to prepare polycyclic compounds **11** using a general approach similar to the synthesis of dihydroazolopyrimidines[18] based on a three-component condensation of aminoheterocycles with aldehydes and 1,3-dicarbonyl compounds was unsuccessful. The heating of aminotriazolopyrimidine **3c**, benzaldehyde, and 5,5-dimethyl-

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Scheme 3

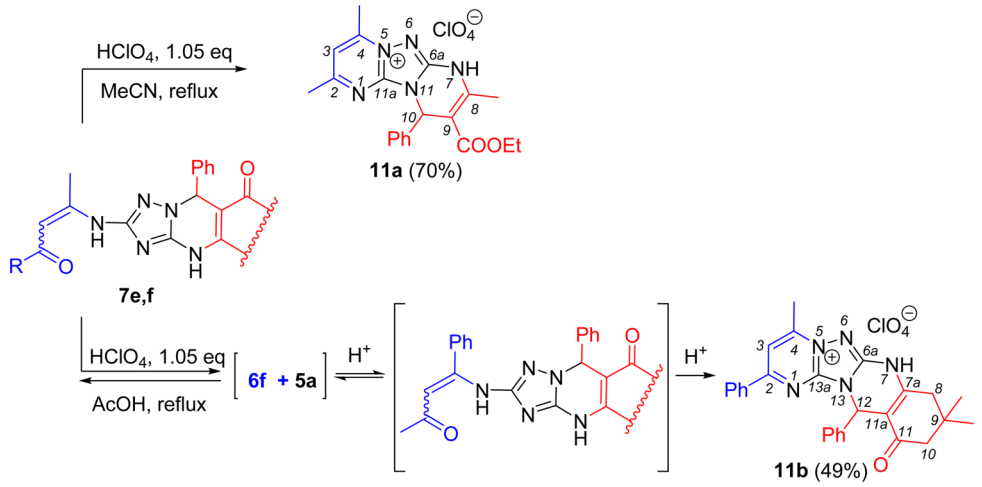
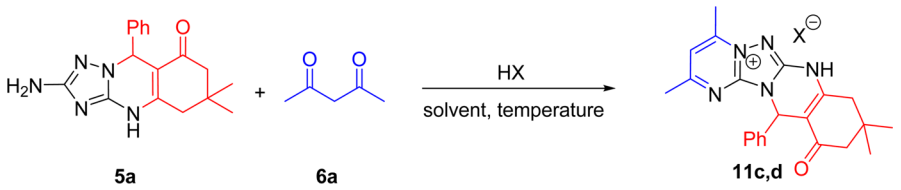


Table 3. Optimization of Reaction Conditions for the One-Pot Synthesis of Compounds 11



entry	solvent	temperature (°C)	time (h)	**6a** (equiv)	HX (equiv)	product	isolated yield (%)
1	EtOH	reflux	1	1.3	$HClO_4$ (1.05)	**11c**	57
2	AcOH	reflux	0.5	1.3	$HClO_4$ (1.05)	**11c**	71
3	neat	90	1	5	$HClO_4$ (1.05)	**11c**	67
4	MeCN	reflux	1	1.3	$HClO_4$ (1.05)	**11c**	63
5	AcOH	50	1	1.3	$HClO_4$ (1.05)	**11c**	59
6	**AcOH**	**90**	**1**	**1.3**	**$HClO_4$ (1.05)**	**11c**	**78**
7	AcOH	90	3	1.3	$HClO_4$ (1.05)	**11c**	75
8	AcOH	90	1	1.1	$HClO_4$ (1.05)	**11c**	72
9	AcOH	90	1	2	$HClO_4$ (1.05)	**11c**	63
10	AcOH	90	1	1.3	HBr (1.05)		trace
11	AcOH	90	1	1.3	H_2SO_4 (1.05)	**11d**	68
12	AcOH	90	1	1.3	$HClO_4$ (1.3)	**11c**	75
13	AcOH	90	1	1.3	$HClO_4$ (1.5)	**11c**	70

cyclohexane-1,3-dione **12** in acetic acid in the presence of $HClO_4$ afforded a mixture of the perchlorate of starting amine **13** and xanthenedione **14** (Scheme 4). Therefore, the acid-catalyzed condensation of compounds **1b** or **5** with 1,3-dicarbonyls is the only one-pot method available for the synthesis of polycyclic derivatives **11** containing both aromatic and dihydrogenated pyrimidine cycles annulated with a triazole ring in one molecule (Table 4).

It is reasonable to consider some key peculiarities of the synthesis of compounds **11**. In contrast to compound **1a** and other 4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidines unsubstituted in position 6 of the triazolopyrimidine core, compounds **1b** and **5** are resistant to oxidative aromatization in the reactions with dicarbonyls **6**. However, in these reactions, in contrast to reactions with other bielectrophiles,[11] the dihydrotriazolopyrimidine core undergoes a rearrangement that involves recyclization of the dihydropyrimidine ring (Scheme 5). It is also important to note that the formation of compounds **11**, most probably, involves two rearrangements that occur in a cascade fashion (Scheme 5). During the first stage of the reaction, compounds **1b** and **5** react with dicarbonyls **6** at the NH_2 and N-3 atom of the triazolopyrimidine core to form intermediates **15** as the kinetic products (Scheme 5) because all of the other studied substrates (**3**, **4**) react at the same nucleophilic centers. Although the direct formation of intermediates **16** cannot be excluded from consideration, it is important to note that compounds **1b** and **5** may react with other bielectrophiles only at N-3 and NH_2.[11] Intermediates **15** contain both the dihydro[1,2,4]triazolo[1,5-*a*]pyrimidine and aromatic [1,2,4]triazolo[4,3-*a*]pyrimidine fragments. [1,2,4]Triazolo[4,3-*a*]pyrimidines are prone to Dimroth rearrangement into [1,2,4]triazolo[1,5-*a*]pyrimidines, which are typically more thermodynamically stable.[1a,19] Apparently, intermediates **15** reversibly rearrange into intermediates **16**. We were able to isolate one of the intermediates (compound **16n**) in 52% yield by performing the reaction of compounds **5a** and **6h** at 20 °C for a short period of time (Scheme 6). Compound **16n** can be easily rearranged into compound **11n** by heating at 90 °C in an acetic acid solution (Scheme 6). Compounds **16** are thermodynamically unstable

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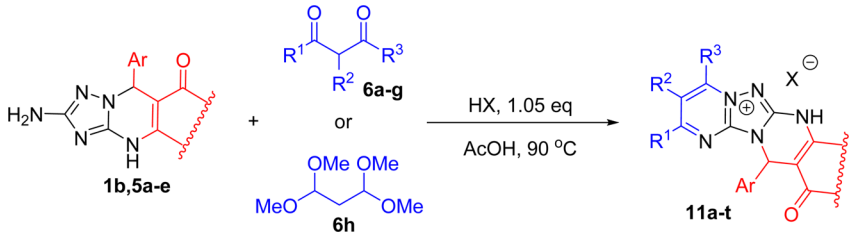
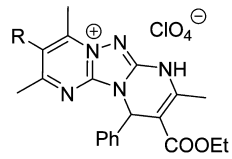
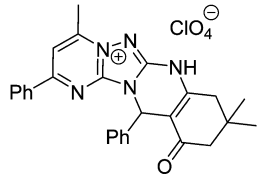
Table 4. Scope of the One-Pot Procedure for the Preparation of Polycyclic Compounds 11

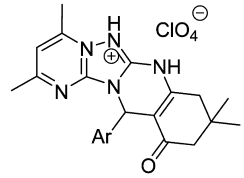




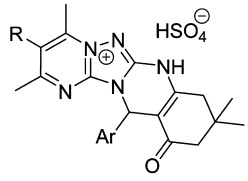
11a (67%) R = H
11p (90%) R = CH_3
11q (81%) R = Cl
11r (76%) R = Bn



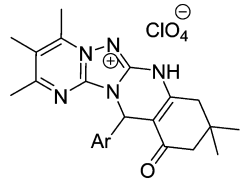
11b (45%)



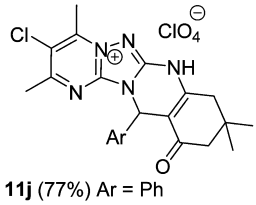
11c (78%) Ar = Ph
11e (67%) Ar = 4-$CH_3OC_6H_4$
11f (80%) Ar = 4-BrC_6H_4
11g (79%) Ar = 2,4-dichlorophenyl



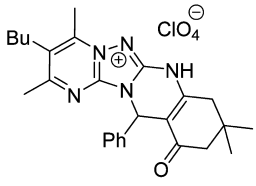
11d (68%) R = H; Ar = Ph
11t (57%) R = CH_3,
Ar = 4-BrC_6H_4



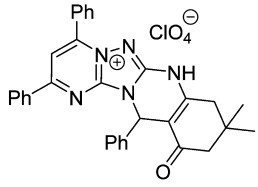
11h (82%) Ar = Ph
11i (85%) Ar = 2,4-dichlorophenyl



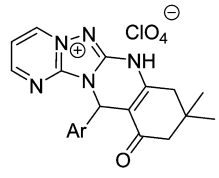
11j (77%) Ar = Ph
11k (70%) Ar = 2-$CH_3OC_6H_4$



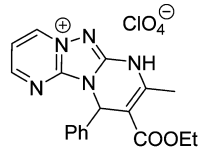
11l (54%)



11m (84%)

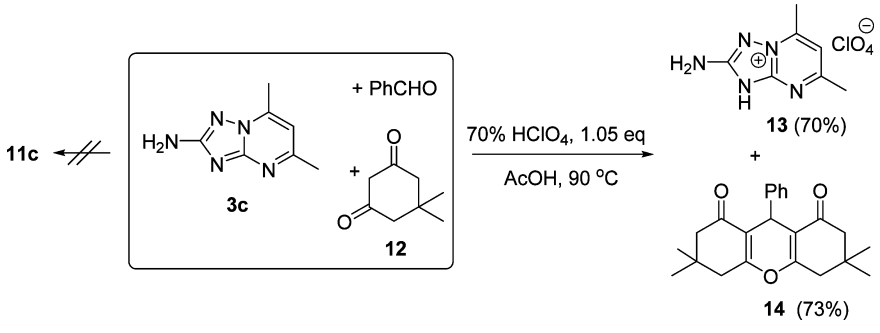


11n (74%) Ar = Ph
11o (69%) Ar = 4-$CH_3OC_6H_4$



11s (72%)

Scheme 4



due to electronic factors (two neighboring "pyrrole" nitrogen atoms)[11,20] and steric repulsions between R and Ar (Scheme 5). These factors promote Dimroth-type recyclization of the dihydropyrimidine ring. However, this rearrangement has an inverse direction for the majority of [1,2,4]triazolopyrimidines and can be characterized as a *retro*-Dimroth rearrangement.[19c]

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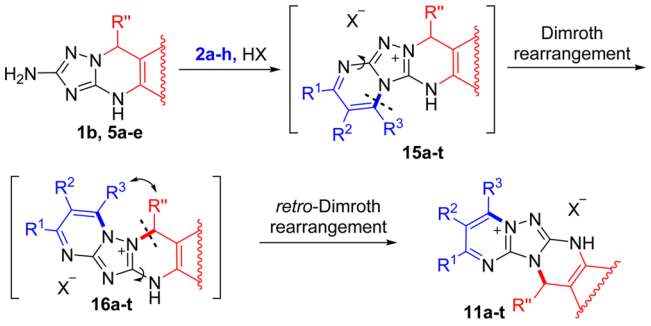
Scheme 5



The general direction of the cascade reaction is determined by the gain in energy from the formation of the more stable aromatic [1,2,4]triazolo[1,5-*a*]pyrimidine fragment in molecules **11**. It is important to note that this reaction is the first reported example of a Dimroth rearrangement of the dihydro[1,2,4]triazolo[1,5-*a*]pyrimidine fragment into a dihydro[1,2,4]triazolo[4,3-*a*]pyrimidine fragment. In addition, the rearrangement cascade shown in the Scheme 5 is quite unusual because it includes Dimroth rearrangements of both azine rings annulated with one azole cycle. All of the nitrogen atoms of the triazole ring participate in the translocations of the nitrogen atoms in the pyrimidine rings, and the triazole ring does not undergo recyclization. Detailed study of energy profiles for this cascade rearrangement, which may help to clarify the mechanism,[21] will be published elsewhere.

The following questions arise: What is the reason for these differences in the direction of the reactions for the formation of polycyclic compounds **8**, **9**, and **11** from the saturation of the pyrimidine ring in starting compounds **1**−**3** and **5**, and are similar rearrangements possible for compounds **8** and **9**?

To answer these questions, we performed computational analysis to determine the relative thermodynamic stability of various isomers of polycyclic compounds that could be theoretically expected as products of reactions between 2-amino[1,2,4]triazolo[1,5-*a*]pyrimidines **1**−**3**, **5**, and 1,3-dicarbonyls.

Quantum chemical calculations were performed using the Gaussian 09 suite of computational programs[22] at the DFT B3LYP/6-311++G(2d,2p) level.[23] The solvent effects were modeled by the integral equation formalism version of the polarizable continuum model (IEF-PCM) developed by Tomasi.[24] The character of the stationary points on the potential energy surface (local minimum) was confirmed by calculation of the Hessian matrix at the same level of theory within the harmonic approximation. All optimized geometries had only real frequencies. The computed energetic parameters and atomic coordinates of all of the species are provided in the Supporting Information.

We considered the thermodynamic stability of possible products of cyclocondensation on examples of model cations **8**, **9**, **11**, and **15**−**18** (see the Supporting Information). For the reactions of tetrahydrotriazolopyrimidines, only the equilibrium between possible isomeric products **8** and **17** was considered because recyclization of the tetrahydropyrimidine ring was not observed under the studied conditions. Analogously, only the equilibrium between isomers **9** and **18** was studied for the reactions of amines **3** because both pyrimidine cycles in products **9** are aromatic. Therefore, consideration of a rearrangement analogous to the rearrangement leading to **11** was pointless.

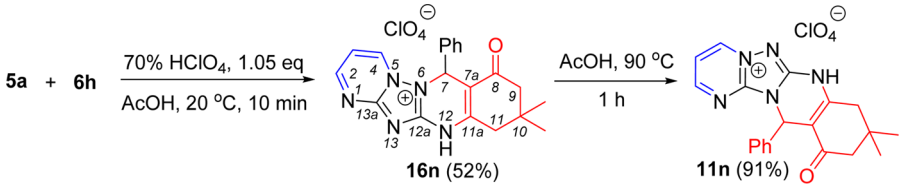
Several tautomers are possible for each isomer of compounds **8**, **11**, and **15**−**17** (see the Supporting Information). Therefore, the most stable tautomeric forms (**A**) shown in Scheme 7 were determined after geometry optimization and calculation of the Gibbs free energy (ΔG^{298}) for each tautomer (see the Supporting Information). The calculations of the relative Gibbs free energies (ΔG^{298}) of the isomers in the studied equilibriums (Scheme 7) were based on the assumption that only the most stable tautomers were present in the equilibrium mixtures. The equilibrium compositions of the mixtures of isomers were computed from standard Gibbs free energy functions through the following relationship: $\Delta G = -RT \ln K$, where ΔG is the difference between the Gibbs free energy for a given isomer and that calculated for the lowest energy and K is the equilibrium constant for these species.

The values of ΔG^{298} and the relative concentrations of the isomers in aqueous solutions are shown in the Scheme 7. In vacuum and DMSO solutions (see the Supporting Information), these parameters did not fundamentally change.

As shown in Scheme 7, molecules **11-A** and **9** are substantially more stable isomers in the corresponding equilibriums. Therefore, the so-called thermodynamic products were obtained in the reactions of compounds **1**, **3** with dicarbonyls **6**. The experimentally observed rearrangement of kinetic product **16n** into thermodynamic product **11n** is in good agreement with this conclusion.

Apparently, the formation of isomers **8-A** and **17-A** can be expected in cyclocondensations of compounds **2** with dicarbonyls **6**. Although the model cations **17-A** are slightly more stable than **8-A** in the case of R = H, the presence of bulky substituents in the real molecules shifts the equilibrium to the side of isomers **8-A**, as it is seen in the case of R = Ph (Scheme 7). It is important to note that we were unable to obtain isomers **17-A** or detect them in the uncrystallized products. Kinetic products **8** were formed under the studied reaction conditions. Our attempts to perform rearrangement of compounds **8** into **17** were futile. Only the starting compound was isolated from the reaction mixture after heating perchlorate **8b** in absolute refluxing ethanol or dry acetonitrile. Prolonged heating of **8b** in 95% ethanol or DMF was accompanied by solvolysis, affording perchlorate **19** (Scheme 8). Attempts to rearrange compounds **8** in alkaline medium were also unsuccessful. Compounds **8b,e,g** in an ethanol solution

Scheme 6



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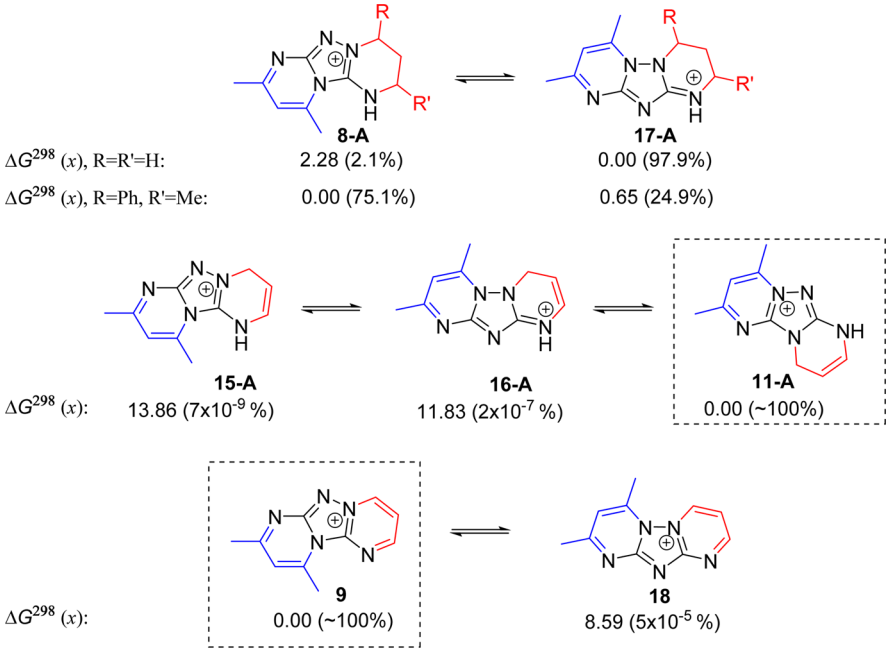
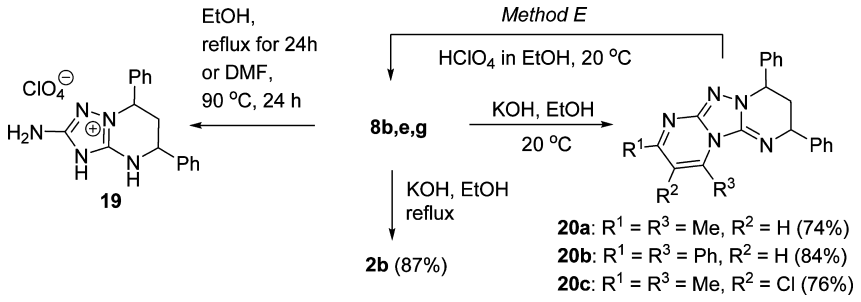
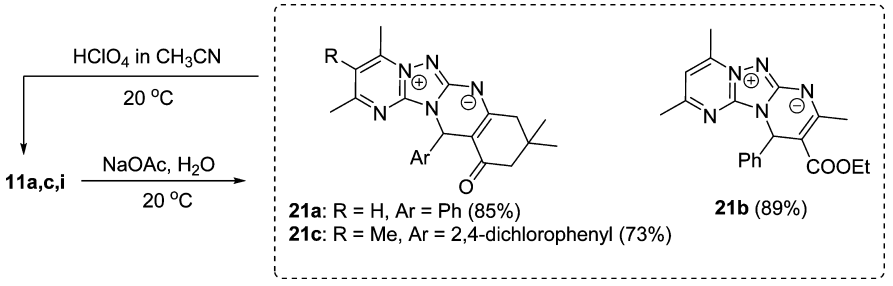
Scheme 7. Hypothetic Equilibriums, Calculated Relative Gibbs Free Energies (ΔG^{298}, kcal/mol), and Equilibrium Compositions (x, %) of Model Molecules of Isomeric Cations of Polycyclic Compounds in Aqueous Solution



Scheme 8



Scheme 9



containing KOH at room temperature yielded free bases **20a–c**, and only solvolysis product **2b** was isolated after heating under reflux (Scheme 8). Compounds **20a–c** formed initial perchlorates **8b,e,g** after treatment with perchloric acid in acetonitrile (Scheme 8).

Mesoionic free bases **21a–c** were also successfully prepared by treating perchlorates **11a,c,i** with an aqueous solution of sodium acetate (Scheme 9). The starting perchlorates can be readily obtained by the action of perchloric acid on bases **21** in acetonitrile (Scheme 9). Compounds **21** are stable in a crystalline state. However, in solution, these compounds decomposed within a few days to form complex mixtures of dark brown products.

Compounds **9** did not change when treated with aqueous solutions containing sodium acetate at room temperature. However, in ethanol solutions containing KOH, these compounds decomposed to yield complex mixtures of dark red products.

The structures of the synthesized compounds were established by HRMS and NMR spectroscopic data including $^{1}H-^{13}C$ heteronuclear correlation HSQC and HMBC spectra for the majority of compounds, NOESY spectrum for **8a**, and

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X-ray diffraction studies of **8h**, **11b**,**c**,**p**, **9a**, **16n**, and **20a** (for details, see the Supporting Information).

Some NMR spectral peculiarities and key correlation schemes in the HMBC and NOESY spectra used for the assignment of structures **8**, **9**, **11**, and **16n** are shown in Figure 2. In the ^{13}C NMR spectra of compounds **8**, the signals

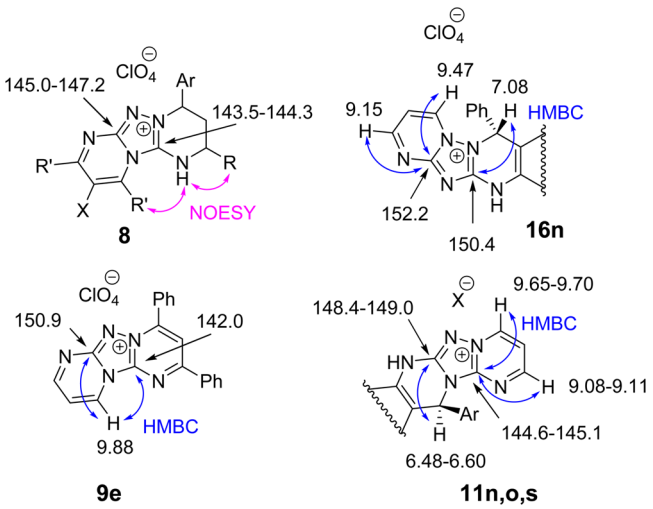

Figure 2. NMR spectral characteristics (chemical shifts, δ, ppm) of compounds **8**, **9e**, **11n,o,s**, and **16n** in DMSO-d_6 and key correlations in the NOESY and HMBC spectra.

corresponding to the carbon atoms of the triazole cycle were observed in the 143−147 ppm region, which is very close to the structurally analogous 3-amino-2-benzyl-[1,2,4]triazolo[4,3-*a*]-pyrimidin-2-ium salts.[25] The signals corresponding to the triazole carbons of compound **16n** are shifted downfield to 150−152 ppm, and in isomers **11**, these signals were observed in the 141−149 ppm region. It is important to note that the signal corresponding to H-7 (7.08 ppm) in the spectrum of compound **16n** is shifted downfield by ~0.5 ppm relative to the analogous signals of H-10 or H-12 (6.5−6.6 ppm) in isomers **11**.

CONCLUSION

In summary, we have developed a new methodology for the preparation of diversely substituted polycyclic derivatives of triazolopyrimidine based on acid-catalyzed cyclocondensation between 2-aminosubstituted [1,2,4]triazolo[1,5-*a*]pyrimidines with a pyrimidine ring with various saturation and 1,3-dicarbonyls. The orientation of the pyrimidine rings in the resulting polycondensed heterocycles depends on the saturation of the pyrimidine cycle in the starting aminotriazolopyrimidines. 4,5,6,7-Tetrahydro- and aromatic aminotriazolopyrimidines react with dicarbonyls at the 2-NH_2 and N-3 to selectively yield the corresponding [1,2,4]triazolo[1,5-*a*:4,3-*a*′]dipyrimidin-5-ium salts. 2-Aminosubstituted dihydrotriazolopyrimidine with no substituent in position 6 undergoes oxidative aromatization of the dihydropyrimidine ring. Cyclocondensation between stable-to-oxidation derivatives of 4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidines, which contain a carbonyl group as a substituent in position 6 of the triazolopyrimidine system, and 1,3-dicarbonyls is accompanied by a cascade rearrangement with unusual recyclization of the dihydropyrimidine ring to afford partially hydrogenated [1,2,4]triazolo[1,5-*a*:4,3-*a*′]dipyrimidin-5-ium and pyrimido-[1′,2′:1,5][1,2,4]triazolo[3,4-*b*]quinazolin-5-ium salts with reversed annulation of the aromatic and hydrogenated pyrimidine rings. The proposed methodology for the synthesis of polycyclic derivatives of triazolopyrimidine is based on the application of readily available starting compounds and demonstrates a broad substrate scope and high efficiency.

EXPERIMENTAL SECTION

General Information. Melting points were determined in open capillary tubes in a Thiele apparatus and are uncorrected. IR spectra were recorded using a single reflection diamond ATR system as a sampling accessory. ^1H NMR spectra were acquired at 500 MHz and ^{13}C {^1H} NMR spectra were acquired at 125 MHz in DMSO-d_6 using TMS as an internal standard. Mass spectra were recorded in the form of m/z (intensity relative to base 100) using electron impact ionization (70 eV). High-resolution mass spectra (HRMS) were obtained on a TOF MS instrument using electrospray ionization (ESI) in positive ion mode (interface capillary voltage − 4500 V).

Starting compounds **1a**,[13a] **1b**,[14b] **2a**−**c**,[16] **3a**,**b**,[15] **3c**,[26] and **5a**,**b**,**d**[14a] were prepared by known methods. All other chemicals are commercially available.

2-Amino-9-(4-bromophenyl)-6,6-dimethyl-5,6,7,9-tetrahydro[1,2,4]triazolo[5,1-*b*]quinazolin-8(4*H*)-one (5c). A magnetically stirred mixture of 3,5-diamino-1,2,4-triazole (1.0 g, 10.0 mmol), 4-bromobenzaldehyde (1.85 g, 10.0 mmol), 5,5-dimethylcyclohexane-1,3-dione (1.4 g, 10.0 mmol), and DMF (3 mL) was refluxed for 30 min, then diluted with ethanol (15 mL) and cooled to 20 °C. The precipitate formed was collected by filtration, recrystallized from DMF/EtOH (1:5), and dried at 120 °C to give **5c**. Yield 2.1 g (55%) of colorless crystals, mp > 300 °C. IR (cm^{-1}): 3461, 3302, 3181, 2955, 2818, 1661, 1645, 1598, 1570, 1515, 1459, 1411, 1365, 1336, 1253, 1012, 826, 751. ^1H NMR (500 MHz, DMSO-d_6): δ 0.95 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 2.05 (d, J = 16.2 Hz, 1H, 7-CH_2), 2.20 (d, J = 16.2 Hz, 1H, 7-CH_2), 2.45−2.54 (m, 2H, 5-CH_2), 5.20 (br s, 2H, NH_2), 5.90 (s, 1H, H-9), 7.11−7.12 (m, 2H, Ar), 7.46−7.47 (m, 2H, Ar), 10.79 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 26.9, 28.4, 32.1, 49.8, 56.6, 105.3, 120.5, 129.1, 131.0, 141.5, 145.6, 150.3, 162.1, 192.9 (signals of 3 carbons are overlapped). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{19}BrN_5O$ 388.0767; Found 388.0753.

2-Amino-6,6-dimethyl-9-(2-methoxyphenyl)-5,6,7,9-tetrahydro[1,2,4]triazolo[5,1-*b*]quinazolin-8(4*H*)-one (5e). Compound **5e** was synthesized according to the procedure for preparation of compound **5c** using 2-methoxybenzaldehyde (1.36 g, 10.0 mmol). Yield 1.7 g (50%) of colorless crystals, mp 259−260 °C. IR (cm^{-1}): 3459, 3417, 3293, 3185, 3126, 2951, 2881, 2830, 1659, 1640, 1596, 1569, 1513, 1466, 1366, 1245, 1116, 1035, 861, 742. ^1H NMR (500 MHz, DMSO-d_6): δ 0.91 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.95 (d, J = 16.2 Hz, 1H, 7-CH_2), 2.17 (d, J = 16.2 Hz, 1H, 7-CH_2), 2.38 (d, J = 16.8 Hz, 1H, 5-CH_2), 2.49−2.53 (m, 1H, 5-CH_2), 3.66 (s, 3H, CH_3O), 5.07 (br s, 2H, NH_2), 6.10 (s, 1H, H-9), 6.81−6.89 (m, 2H, Ar), 7.14−7.17 (m, 2H, Ar), 10.63 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 26.2, 28.8, 32.0, 39.6, 49.9, 53.8, 55.5, 105.1, 111.3, 119.8, 128.7, 129.5, 129.6, 146.0, 150.4, 157.2, 161.6, 192.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{18}H_{22}N_5O_2$ 340.1768; Found 340.1764.

General Procedure for the Synthesis of Compounds 7a−d. A magnetically stirred mixture of the appropriate amine **1b**, **2a**−**c** (2 mmol), diketone **6a**,**f** (4 mmol), and AcOH (1 mL) was heated at 90 °C for 4 h, then cooled to room temperature and diluted with ethanol (5 mL). The solid precipitate was collected by filtration and recrystallized from an appropriate solvent.

*4-[(5-Methyl-7-phenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]-pyrimidin-2-yl)amino]pent-3-en-2-one (**7a**).* Yield 0.261 g (42%) of colorless crystals, mp 188−189 °C (from DMF/EtOH 1:3). IR (cm^{-1}): 3232, 2967, 2927, 2927, 1620, 1601, 1579, 1544, 1457, 1381, 1362, 1424, 1288 1031, 992, 759. ^1H NMR (500 MHz, DMSO-d_6): δ 1.14 (d, J = 4.6 Hz, 3H, 5-CH_3), 1.67−1.73 (m, 1H, 6-CH_2), 1.95 (s, 3H, CH_3CO), 2.13 (s, 3H, CH_3), 2.27−2.29 (m, 1H, 6-CH_2), 3.59 (m,

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1H, H-5), 5.15 (s, 1H, H-7), 5.17 (s, 1H, H-3 of pent-3-en-2-one), 7.15−7.33 (m, 6H, Ph + NH), 12.39 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 20.5 (5-CH_3), 20.7 (CH_3), 29.1 ($\underline{C}H_3CO$), 40.9 (C-6), 45.3 (C-5), 58.2 (C-7), 98.6 (C-3 of pent-3-en-2-one), 126.8 (2C), 127.5, 128.3 (2C), 140.3 (carbons of Ph), 154.46 (C-3a), 154.54 (C-2), 157.6 (C-4 of pent-3-en-2-one), 195.8 (CO). MS (EI, 70 eV), *m*/*z* (%): 311 (38) $[M]^+$, 268 (39), 192 (78), 164 (89), 150 (24), 131 (28), 125 (15), 115 (12), 104 (16), 91 (28), 77 (19), 69 (27), 43 (100). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{17}H_{22}N_5O$ 312.1819; Found 312.1819.

4-[(5,7-Diphenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]-pyrimidin-2-yl)amino]pent-3-en-2-one (**7b**). Yield 0.537 g (72%) of colorless crystals, mp 161−162 °C (from acetonitrile). IR (cm^{-1}): 3251, 3031, 1620 (shoulder), 1603, 1579, 1550, 1514, 1496, 1427, 1355, 1284, 1199, 1028, 920, 837, 751. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.97 (s, 3H, CH_3CO), 2.03−2.10 (m, 1H, 6-CH_2), 2.16 (s, 3H, CH_3), 2.41−2.43 (m, 1H, 6-CH_2), 4.69−4.71 (m, 1H, H-5), 5.20 (s, 1H, H-3 of pent-3-en-2-one), 5.34−5.35 (m, 1H, H-7), 7.23−7.44 (m, 10H, 2Ph), 7.57 (br s, 1H, NH), 12.44 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 20.7, 29.0, 42.0, 53.5, 58.3, 98.6, 118.4, 126.4 (2C), 126.9 (2C), 127.5, 128.2 (2C), 128.3 (2C), 139.8, 141.3 (carbons of 2Ph), 154.6, 154.8, 157.5, 195.9. MS (EI, 70 eV), *m*/*z* (%): 373 (22) $[M]^+$, 330 (26), 254 (50), 226 (74), 212 (13), 193 (14), 115 (46), 104 (42), 91 (29), 77 (35), 43 (100). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{22}H_{24}N_5O$ 374.1975; Found 374.1970.

4-{[7-(4-Methoxyphenyl)-5-phenyl-4,5,6,7-tetrahydro[1,2,4]-triazolo[1,5-a]pyrimidin-2-yl]amino}pent-3-en-2-one (**7c**). Yield 0.492 g (61%) of colorless crystals, mp 166−167 °C (from acetonitrile). IR (cm^{-1}): 3239, 2951, 2835, 1605, 1579, 1551, 1512, 1430, 1351, 1280, 1247, 1202, 1173, 1030, 826, 772. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.96 (s, 3H, CH_3CO), 2.03−2.09 (m, 1H, 6-CH_2), 2.16 (s, 3H, CH_3), 2.35−2.37 (m, 1H, 6-CH_2), 3.72 (s, 3H, CH_3O), 4.67−4.69 (m, 1H, H-5), 5.19 (s, 1H, H-3 of pent-3-en-2-one), 5.26−5.27 (m, 1H, H-7), 6.86−6.87 (m, 2H, Ar), 7.16−7.43 (m, 7H, Ar), 7.52 (br s, 1H, NH), 12.43 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 20.7 (CH_3), 29.1 ($\underline{C}H_3CO$), 42.1 (C-6), 53.7 (C-5), 55.0 (CH_3O), 58.0 (C-7), 98.6 (C-3 of pent-3-en-2-one), 113.6, 126.5, 127.5, 128.2, 128.3, 131.6, 141.5 (carbons of aromatic), 154.5 (C-3a), 154.7 (C-2), 157.6 (C-4 of pent-3-en-2-one), 158.7 ($CH_3O\underline{C}_{Ar}$), 195.8 (C═O). MS (EI, 70 eV), *m*/*z* (%): 403 (19) $[M]^+$, 360 (11), 254 (58), 252 (23), 226 (95), 223 (33), 145 (10), 134 (30), 131 (19), 121 (15), 115 (29), 106 (20), 104 (21), 91 (32), 77 (28), 43 (100). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{23}H_{26}N_5O_2$ 404.2081; Found 404.2078.

3-[(5,7-Diphenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]-pyrimidin-2-yl)amino]-1-phenylbut-2-en-1-one (**7d**). Yield 0.652 g (75%) of yellowish crystals, mp 185−186 °C (from acetonitrile). IR (cm^{-1}): 3214, 3062, 3033, 2973, 2914, 1591, 1582, 1536, 1469, 1418, 1313, 1289, 1275, 1222, 1027, 747. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.07−2.14 (m, 1H, 6-CH_2), 2.35 (s, 3H, CH_3), 2.43−2.46 (m, 1H, 6-CH_2), 4.73−4.75 (m, 1H, H-5), 5.36−5.39 (m, 1H, H-7), 6.06 (s, 1H, H-2 of 1-phenylbut-2-en-1-one), 7.26−7.53 (m, 13H, Ar), 7.65 (br s, 1H, NH), 7.90−7.92 (m, 2H, Ar), 13.15 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 21.1 (CH_3), 41.9 (C-6), 53.4 (C-5), 58.3 (C-7), 94.7 (C-2 of 1-phenylbut-2-en-1-one), 126.3, 126.8, 127.4, 128.1, 128.2, 131.2, 138.7, 139.6, 141.2 (carbons of 3Ph, signals are partially overlapped), 154.3 (C-3a), 154.8 (C-2), 160.1 (C-3 of 1-phenylbut-2-en-1-one), 187.5 (CO). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{27}H_{26}N_5O$ 436.2132; Found 436.2122.

Ethyl 5-Methyl-2-{[4-oxopent-2-en-2-yl]amino}-7-phenyl-4,7-dihydro[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylate (**7e**). Yield 0.225 g (59%) of colorless crystals, mp 232−233 °C (from DMF/EtOH 1:3). IR (cm^{-1}): 3231, 3106, 3061, 2974, 2887, 1697, 1617, 1552, 1531, 1453, 1379, 1288, 1252, 1169, 1077, 838, 774. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.03 (t, *J* = 7.1 Hz, 3H, $OCH_2\underline{C}H_3$), 1.98 (s, 3H, CH_3CO), 2.19 (s, 3H, 5-CH_3), 2.39 (s, 3H, CH_3), 3.93−3.96 (m, 2H, $OC\underline{H}_2CH_3$), 5.26 (s, 1H, H-3 of 4-oxopent-2-ene group), 6.14 (s, 1H, H-7), 7.21−7.33 (m, 5H, Ph), 10.80 (s, 1H, NH), 12.51 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.7, 18.2, 20.7, 29.1, 59.0, 59.3, 97.7, 99.4, 126.8, 127.8, 128.3, 141.6 (carbons of Ph), 146.1, 146.2, 155.9, 156.9, 164.9, 196.5. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{20}H_{23}N_5O_3Na$ 404.1693; Found 404.1687.

6,6-Dimethyl-2-{[4-oxo-4-phenylbut-2-en-2-yl]amino}-9-phenyl-5,6,7,9-tetrahydro[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-one (**7f**). Yield 0.707 g (78%) of colorless crystals, mp 232−233 °C (from DMF/EtOH 1:3). IR (cm^{-1}): 3028, 2955, 2865, 2792, 2732, 2682, 1620 (shoulder), 1582, 1546, 1515, 1445, 1315, 1282, 1149, 1059, 836, 752. ^{1}H NMR (500 MHz, DMSO-d_6): δ 0.97 (s, 3H, 6-CH_3), 1.04 s, 3H, 6-CH_3), 2.10 (d, *J* = 16.7 Hz, 1H, H-7), 2.22 (d, *J* = 16.7 Hz, 1H, H-7), 2.53−2.54 (m, 2H, H-5), 6.10 (s, 1H, CH), 6.12 (s, 1H, H-9), 7.21−7.52 (m, 8H, Ph), 7.89−7.90 (m, 2H, Ph), 11.14 (s, 1H, NH), 13.18 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 21.9, 27.5, 29.0, 32.8, 40.8, 50.5, 58.3, 96.3, 106.6, 127.5, 127.7, 128.4, 128.9, 129.0, 132.2, 139.4, 141.8 (carbons of 2Ph), 147.0, 150.6, 156.4, 160.4, 188.9, 193.6. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{27}H_{27}N_5O_2Na$ 476.2057; Found 476.2052.

General Procedure for the Synthesis of Compounds 8a−f, 9a−e. *Method A.* A magnetically stirred mixture of the appropriate enamine **7a−d** (1 mmol), a 70% aqueous solution of $HClO_4$ (0.152 g, 1.05 mmol), and acetonitrile (4 mL) was refluxed for 1 h. The precipitate formed after cooling to 20 °C was collected by filtration and recrystallized from acetonitrile/EtOH (1:3).

Method B. A magnetically stirred mixture of the appropriate compound **2a−c** (1 mmol), diketone **6a−c,g** (1.3 mmol), a 70% aqueous solution of $HClO_4$ (0.152 g, 1.05 mmol), and ethanol (4 mL) was refluxed for 2 h. The precipitate formed after cooling to 20 °C was collected by filtration and recrystallized from acetonitrile/EtOH (1:3).

Method C. A magnetically stirred mixture of the appropriate compound **2b**, **3a**,**b** (1 mmol), diketone **6a**,**b**,**g** or 1,1,3,3-tetramethoxypropane **6h** (1.3 mmol), a 70% aqueous solution of $HClO_4$ (0.152 g, 1.05 mmol), and AcOH (0.5 mL for the synthesis of **9a−e**, 1.0 mL for the preparation of **8g**) was refluxed for 2 h (or 5 min for compound **9e**) and then diluted with ethanol (3 mL). The precipitate formed after cooling to room temperature was collected by filtration and recrystallized from acetonitrile (compounds **9a−e**) or DMF/EtOH 1:3 (compounds **8g**).

Method D. A magnetically stirred mixture of compound **1a** (1 mmol), diketone **6a** (1.3 mmol), a 70% aqueous solution of $HClO_4$ (0.152 g, 1.05 mmol), and AcOH (1.0 mL) was heated at 90 °C for 2 h and then diluted with ethanol (3 mL). The precipitate of compound **9a** formed after cooling to room temperature was collected by filtration and recrystallized from DMF/EtOH (1:3).

Method E. A mixture of compound **20a−c** (1 mmol), a 70% aqueous solution of $HClO_4$ (0.152 g, 1.05 mmol), and EtOH (5 mL) was stirred at 20 °C for 20 min. The precipitated perchlorate **8b**,**e**,**g** was collected by filtration, washed with EtOH, and dried at 80 °C to give.

2,8,10-Trimethyl-4-phenyl-1,2,3,4-tetrahydro[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**8a**). Yield 0.768 g (65%, *Method A*), 0.685 g (58%, *Method B*) of colorless crystals, mp 194−195 °C. IR (cm^{-1}): 3369, 3081, 1647, 1582, 1549, 1496, 1457, 1376, 1338, 1228, 1079, 1033, 730. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.37 (d, 3H, *J* = 6.2 Hz, 2-CH_3), 2.04−2.08 (m, 1H, H-3), 2.43 (s, 3H, 8-CH_3), 2.54−2.56 (m, 1H, H-3), 2.84 (s, 3H, 10-CH_3), 3.91−3.95 (m, 1H, H-2), 5.56−5.59 (m, 1H, H-4), 6.83 (s, 1H, H-9), 7.35−7.43 (m, 5H, Ph), 8.33 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 17.7 (10-CH_3), 19.9 (2-CH_3), 24.9 (8-CH_3), 37.6 (C-3), 47.2 (C-2), 60.3 (C-4), 111.5 (C-9), 127.7, 128.43, 128.47, 137.5 (carbons of Ph), 143.8 (C-11a), 145.4 (C-10), 147.2 (C-6a), 169.8 (C-8). MS (EI, 70 eV), *m*/*z* (%): 294 (7) $[M - ClO_4]^+$, 293 (30) $[M - HClO_4]^+$, 278 (43), 189 (20), 174 (59), 148 (34), 107 (40), 104 (34), 91 (27), 77 (34), 67 (100), 51 (33), 44 (49). HRMS (ESI-TOF) *m*/*z*: $[M - ClO_4]^+$ Calcd for $C_{17}H_{20}N_5$ 294.1713; Found 294.1713.

8,10-Dimethyl-2,4-diphenyl-1,2,3,4-tetrahydro[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**8b**). Yield 0.971 g (71%, *Method A*), 0.834 g (61%, *Method B*), 1.272 g (93%, *Method E*) of colorless crystals, mp 221−222 °C. IR (cm^{-1}): 3307, 3079, 3041, 2952, 1643, 1582, 1547, 1455, 1323, 1224, 1203, 1079, 1021, 764, 723. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.33−2.39 (m, 1H, H-3), 2.47 (s,

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3H, CH_3), 2.67−2.69 (m, 1H, H-3), 2.87 (s, 3H, CH_3), 5.03−5.05 (m, 1H, H-2), 5.72−5.74 (m, 1H, H-4), 6.88 (s, 1H, H-9), 7.35−7.43 (m, 8H, Ar), 7.54−7.55 (m, 2H, Ar), 9.10 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 17.7 (10-CH_3), 25.0 (8-CH_3), 39.2 (C-3), 54.6 (C-2), 60.3 (C-4), 111.6 (C-9), 126.5, 127.9, 128.0, 128.4, 128.5, 128.6, 136.7, 139.9 (carbons of 2Ph), 144.2 (C-11a), 145.4 (C-10), 147.2 (C-6a), 169.9 (C-8). MS (EI, 70 eV), *m*/*z* (%): 356 (5) [M − ClO_4]$^+$, 355 (21) [M − $HClO_4$]$^+$, 250 (100), 107 (12), 104 (19), 77 (12), 67 (28), 44 (55). HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{22}H_{22}N_5$ 356.1870; Found 356.1873.

*4-(4-Methoxyphenyl)-8,10-dimethyl-2-phenyl-1,2,3,4-tetrahydro-[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**8c**).* Yield 1.005 g (69%, *Method A*), 0.860 g (59%, *Method B*) of colorless crystals, mp 173−174 °C. IR (cm^{-1}): 3607, 3529, 3253, 3000, 1646, 1578, 1514, 1457, 1321, 1246, 1176, 1081, 1019, 837, 770. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.33−2.39 (m, 1H, H-3), 2.46 (s, 3H, CH_3), 2.61−2.64 (m, 1H, H-3), 2.87 (s, 3H, CH_3), 3.75 (s, 3H, CH_3O), 5.02−5.03 (m, 1H, H-2), 5.67−5.68 (m, 1H, H-4), 6.87 (s, 1H, H-9), 6.93−6.94 (m, 2H, Ar), 7.32−7.56 (m, 7H, Ar), 9.06 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 17.7 (10-CH_3), 25.0 (8-CH_3), 39.2 (C-3), 54.7 (C-2), 55.2 (CH_3O), 60.0 (C-4), 111.6 (C-9), 113.8, 126.5, 128.1, 128.5, 128.6, 129.4, 140.0 (carbons of aromatic), 144.0 (C-11a), 145.3 (C-10), 147.1 (C-6a), 159.4 ($CH_3O\underline{C}_{Ar}$), 169.8 (C-8). MS (EI, 70 eV), *m*/*z* (%): 385 (1) [M − $HClO_4$]$^+$, 250 (100), 134 (94), 119 (43), 107 (27), 103 (10), 91 (65), 89 (19), 77 (26), 67 (66), 65 (40), 51 (26), 44 (66). HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{23}H_{24}N_5O$ 386.1975; Found 386.1974.

*8,9,10-Trimethyl-2,4-diphenyl-1,2,3,4-tetrahydro[1,2,4]triazolo-[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**8d**).* Yield 0.305 g (65%, *Method B*) of colorless crystals, mp 203−204 °C. IR (cm^{-1}): 3629, 3536, 3297, 1638, 1577, 1540, 1459, 1323, 1200, 1088, 1020, 755. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.22 (s, 3H, 9-CH_3), 2.35−2.37 (m, 1H, H-3), 2.51 (s, 3H, 8-CH_3), 2.65−2.67 (m, 1H, H-3), 2.86 (s, 3H, 10-CH_3), 5.01−5.02 (m, 1H, H-2), 5.71−5.72 (m, 1H, H-4), 7.37−7.54 (m, 10H, Ar), 9.07 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.1 (9-CH_3), 14.8 (10-CH_3), 24.9 (8-CH_3), 39.2 (C-3), 54.6 (C-2), 60.4 (C-4), 117.7 (C-9), 126.5, 127.9, 128.0, 128.4, 128.5, 128.6, 136.9, 140.0 (carbons of 2Ph), 140.8 (C-10), 144.1 (C-11a), 146.0 (C-6a), 170.7 (C-8). HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{23}H_{24}N_5$ 370.2026; Found 370.2019.

*9-Chloro-8,10-dimethyl-2,4-diphenyl-1,2,3,4-tetrahydro[1,2,4]-triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**8e**).* Yield 0.299 g (61%, *Method B*), 0.441 g (90%, *Method E*) of yellowish crystals, mp 201−202 °C. IR (cm^{-1}): 3299, 2939, 1642, 1632, 1570, 1539, 1460, 1326, 1280, 1084, 1056, 1033, 763, 737. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.33−2.40 (m, 1H, H-3), 2.61 (s, 3H, 8-CH_3), 2.69−2.72 (m, 1H, H-3), 3.00 (s, 3H, 10-CH_3), 5.04−5.06 (m, 1H, H-2), 5.76−5.79 (m, 1H, H-4), 7.36−7.45 (m, 8H, Ar), 7.53−7.55 (m, 2H, Ar), 9.36 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 15.7 (10-CH_3), 24.8 (8-CH_3), 38.9 (C-3), 54.6 (C-2), 60.6 (C-4), 118.3 (C-9), 126.5, 127.8, 128.1, 128.4, 128.59, 128.63, 136.5, 139.6 (carbons of 2Ph), 142.4 (C-10), 144.3 (C-11a), 145.0 (C-6a), 167.2 (C-8). HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{22}H_{21}ClN_5$ 390.1480; Found 390.1470.

*2,8,9,10-Tetramethyl-4-phenyl-1,2,3,4-tetrahydro[1,2,4]triazolo-[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**8f**).* Yield 0.293 g (72%, *Method B*) of colorless crystals, mp 233−234 °C. IR (cm^{-1}): 3297, 2990, 2941, 1633, 1576, 1537, 1486, 1400, 1331, 1302, 1240, 1081, 756, 714. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.32 (d, *J* = 6.2 Hz, 3H, 2-CH_3), 1.94−2.02 (m, 1H, H-3), 2.16 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 2.48−2.51 (m, 1H, H-3), 2.77 (s, 3H, CH_3), 3.82−3.88 (m, 1H, H-2), 5.51−5.54 (m, 1H, H-4), 7.32−7.34 (m, 5H, Ph), 8.26 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.7, 15.3, 20.5, 25.4, 38.2, 47.7, 60.9, 118.1, 128.2, 128.9, 129.0, 138.2 (carbons of Ph), 141.3, 144.3, 146.7, 171.2. HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{18}H_{22}N_5$ 308.1870; Found 308.1876.

*2,4,8,10-Tetraphenyl-1,2,3,4-tetrahydro[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**8g**).* Yield 0.457 g (79%, *Method C*), 0.550 g (95%, *Method E*) of yellow crystals, mp 273−274 °C. IR (cm^{-1}): 3408, 3067, 3030, 2897, 1653, 1631, 1576, 1526, 1478, 1398, 1244, 1093, 1081, 752. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.34−2.42 (m, 1H, H-3), 2.65−2.68 (m, 1H, H-3), 4.82−4.85 (m, 1H, H-2), 5.71−5.74 (m, 1H, H-4), 7.27−7.65 (m, 16H, Ar), 7.80 (s, 1H, H-9), 7.92 (br s, 1H, NH), 7.97−8.05 (m, 2H, Ar), 8.31−8.32 (m, 2H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6): δ 40.2, 55.6, 61.2, 110.6, 126.8, 128.5, 128.6, 128.7, 128.8, 129.05, 129.08, 129.3, 129.7, 130.7, 132.5, 133.4, 135.2, 137.4, 140.5 (carbons of 4Ph, signals of two carbon atoms of benzene rings are overlapped), 144.3, 147.0, 148.0, 163.9. HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{32}H_{26}N_5$ 480.2183; Found 480.2177.

*8-Methyl-2,4,10-triphenyl-1,2,3,4-tetrahydro[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**8h**).* Yield 0.326 g (63%, *Method A*) of yellow crystals, mp 245−246 °C. IR (cm^{-1}): 3224, 3068, 1643, 1629, 1580, 1536, 1475, 1458, 1331, 1072, 1018, 1001, 761, 749, 720. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.37−2.44 (m, 1H, H-3), 2.61 (s, 3H, CH_3), 2.68−2.71 (m, 1H, H-3), 4.86−4.88 (m, 1H, H-2), 5.74−5.75 (m, 1H, H-4), 7.19 (s, 1H, H-9), 7.32−7.53 (m, 10H, Ar), 7.65−7.70 (m, 3H, Ar), 7.86 (br s, 1H, NH),7.90−8.02 (m, 2H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6): δ 25.0 (CH_3), 39.5 (C-3), 54.7 (C-2), 60.4 (C-4), 113.8 (C-9), 126.1, 127.8, 128.27, 128.31, 128.4, 129.6, 131.7, 136.7, 139.7(carbons of 3Ph, signals of three carbon atoms of benzene rings are overlapped), 143.5 (C-11a), 144.5 (C-10), 146.9 (C-6a), 169.2 (C-8). HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{27}H_{24}N_5$ 418.2026; Found 418.2019.

*8,10-Dimethyl-2,4-diphenyl[1,2,4]triazolo[1,5-a:4,3-a′]-dipyrimidin-5-ium Perchlorate (**9a**).* Yield 0.257 g (57%, *Method C*), 0.068 g (35%, *Method D*) of yellowish crystals, mp 285−286 °C. IR (cm^{-1}): 3075, 3005, 1636, 1597, 1561, 1500, 1445, 1382, 1244, 1091, 1078, 769, 725. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.77 (s, 3H, CH_3), 3.31 (s, 3H, CH_3), 7.54 (s, 1H, H-9), 7.71−7.84 (m, 6H, Ar), 8.36−8.37 (m, 2H, Ar), 8.61−8.62 (m, 2H, Ar), 9.01 (s, 1H, H-3). ^{13}C NMR (125 MHz, DMSO-d_6): δ 18.6 (CH_3), 25.8 (CH_3), 113.6 (C-3), 114.0 (C-9), 127.7, 128.8, 129.0, 129.6, 130.4, 133.1, 133.5, 133.8 (carbons of 2Ph), 143.3 (C-11a), 148.2 (C-8 or C-10), 149.3 (C-2 or C-4), 151.8 (C-6a), 162.1 (C-2 or C-4), 175.3 (C-8 or C-10). HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{22}H_{18}N_5$ 352.1557; Found 352.1553.

*2,4,8,10-Tetraphenyl[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**9b**).* Yield 0.374 g (65%, *Method C*) of yellow crystals, mp > 300 °C. IR (cm^{-1}): 3065, 1627, 1596, 1562, 1504, 1492, 1367, 1356, 1309, 1238, 1086, 762. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.59−7.61 (m, 2H, Ar), 7.70−7.75 (m, 3H, Ar), 7.80−7.95 (m, 7H, Ar), 8.07−8.08 (m, 2H, Ar), 8.11−8.13 (m, 2H, Ar), 8.43−8.44 (m, 3H, Ar + H-9), 8.63−8.64 (m, 2H, Ar), 9.01 (s, 1H, H-3). ^{13}C NMR (125 MHz, DMSO-d_6): δ 111.9 (C-9), 114.2 (C-3), 128.3, 129.0, 129.2, 129.58, 129.63, 129.7, 129.8, 130.0, 130.3, 131.0, 132.2, 133.7, 134.08, 134.12, 134.6, 134.8 (carbons of benzene rings), 143.1 (C-11a), 149.6 (C-8 or C-10), 149.9 (C-2 or C-4), 153.1 (C-6a), 161.9 (C-2 or C-4), 168.8(C-8 or C-10). HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{32}H_{22}N_5$ 476.1870; Found 476.1861.

*8,10-Dimethyl-2-(4-methylphenyl)-4-phenyl[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**9c**).* Yield 0.302 g (67%, *Method C*) of cream-colored crystals, mp > 300 °C. IR (cm^{-1}): 3082, 1637, 1603, 1570, 1488, 1447, 1382, 1349, 1255, 1075, 829, 771, 723. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.50 (s, 3H, CH_3), 2.80 (s, 3H, CH_3), 3.33 (s, 3H, CH_3), 7.55−7.56 (m, 3H, Ar + H-9), 7.82−7.86 (m, 3H, Ar), 8.38−8.39 (m, 2H, Ar), 8.54−8.55 (m, 2H, Ar), 8.99 (s, 1H, H-3). ^{13}C NMR (125 MHz, DMSO-d_6): δ 19.2, 21.7, 26.4, 113.7, 114.5, 128.3, 129.3, 129.5, 130.8, 131.0, 131.7, 133.6, 143.8, 144.9, 148.7, 149.7, 152.3, 162.7, 175.7. HRMS (ESI-TOF) *m*/*z*: [M − ClO_4]$^+$ Calcd for $C_{23}H_{20}N_5$ 366.1713; Found 366.1712.

*8,9,10-Trimethyl-2-(4-methylphenyl)-4-phenyl[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**9d**).* Yield 0.336 g (70%, *Method C*) of yellow crystals, mp 281−282 °C. IR (cm^{-1}): 3067, 1638, 1603, 1568, 1519, 1487, 1368, 1381, 1213, 1079, 1014, 829, 767, 748. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.50 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 2.84 (s, 3H, CH_3), 3.39 (s, 3H, CH_3), 7.55−7.56 (m, 2H, Ar), 7.82−7.85 (m, 3H, Ar), 8.37−8.38 (m, 2H, Ar), 8.51−8.53 (m, 2H, Ar), 8.96 (s 1H, H-3). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.9, 16.0, 21.7, 26.1, 113.5, 121.4, 128.4, 129.2, 129.5, 130.8, 130.9, 131.8, 133.5,

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143.7, 144.65, 144.70, 149.5, 151.0, 162.1, 176.2. HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{24}H_{22}N_5$ 380.1870; Found 380.1869.

*2,4-Diphenyl[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**9e**).* Yield 0.258 g (61%, *Method C*) of cream-colored crystals, mp 268−269 °C. IR (cm^{-1}): 3098, 3075, 1635, 1600, 1558, 1527, 1369, 1250, 1079, 926, 768. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.76−7.84 (m, 7H, Ar + H-9), 8.40−8.42 (m, 2H, Ar), 8.72−8.74 (m, 2H, Ar), 9.08 (s, 1H, H-3), 9.43 (br s, 1H, H-8), 9.88−9.89 (m, 1H, H-10). ^{13}C NMR (125 MHz, DMSO-d_6): δ 113.0 (C-9), 114.0 (C-3), 127.3, 128.8, 128.9, 129.4, 130.3, 133.1, 133.4, 133.6 (carbons of 2Ph), 134.0 (C-10), 142.0 (C-11a), 149.5 (C-2 or C-4), 150.9 (C-6a), 162.9 (C-2 or C-4), 165.7 (C-8). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{20}H_{14}N_5$ 324.1244; Found 324.1245.

General Procedure for the Synthesis of Compounds 11a−t. *Method A.* A magnetically stirred mixture of the appropriate enaminoketone **7e,f** (1 mmol), a 70% aqueous solution of $HClO_4$ (0.152 g, 1.05 mmol), and acetonitrile (4 mL, for the preparation of **11a**) or AcOH (1 mL for the preparation of **11b**) was refluxed for 1 h. The precipitate formed after cooling to 20 °C was collected by filtration and recrystallized from acetonitrile/EtOH (1:3).

Method B. A magnetically stirred mixture of the appropriate amine **1b**, **5a−e** (1 mmol), diketone **6a−g** or tetramethoxypropane **6h** (1.3 mmol), a 70% aqueous solution of $HClO_4$ (0.152 g, 1.05 mmol, for the preparation of compounds **11a−c,e−s**) or concentrated H_2SO_4 (0.11 g, 1.05 mmol, for the preparation of **11d,t**), and AcOH (0.5 mL) was heated at 90 °C for 1 h and then diluted with ethanol (2 mL). The precipitate formed after cooling to room temperature was collected by filtration and recrystallized.

Method C. A mixture of compound **21a−c** (1 mmol), a 70% aqueous solution of $HClO_4$ (0.152 g, 1.05 mmol), and EtOH (5 mL) was stirred at 20 °C for 20 min. The precipitate formed was collected by filtration, washed with EtOH, and dried at 80 °C.

*9-(Ethoxycarbonyl)-2,4,8-trimethyl-10-phenyl-7,10-dihydro-[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**11a**).* Yield 0.276 g (70%, *Method A*), 0.264 g (67%, *Method B*), 0.362 g (92%, *Method C*) of colorless crystals, mp 226−227 °C (from EtOH). IR (cm^{-1}): 3234, 3173, 3082, 2980, 1707, 1666, 1640, 1599, 1531, 1441, 1378, 1270, 1249, 1073, 762. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.08 (t, 3H, $CH_2C\underline{H}_3$), 2.53 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 2.72 (s, 3H, CH_3), 3.99−4.05 (m, 2H, $C\underline{H}_2CH_3$), 6.52 (s, 1H, H-10), 7.30−7.38 (m, 3H, Ar), 7.47−7.49 (m, 2H, Ar), 7.67 (s, 1H, H-3), 11.97 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.7 ($CH_2\underline{C}H_3$), 16.1 (CH_3), 18.1 (CH_3), 24.4 (8-CH_3), 56.0 (C-10), 60.1 ($\underline{C}H_2CH_3$), 99.9 (C-9), 116.0 (C-3), 127.9, 128.5, 128.9, 138.2 (carbons of Ph), 143.5 (C-6a or C-13a), 144.9 (C-8), 147.5 (C-6a or C-13a), 150.3 (C-4), 163.8 (CO), 168.4 (C-2). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{20}H_{22}N_5O_2$ 364.1768; Found 364.1769.

*4,9,9-Trimethyl-11-oxo-2,12-diphenyl-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11b**).* Yield 0.466 g (49%, *Method A*), 0.441 g (45%, *Method B*) of colorless crystals, mp > 300 °C (from acetonitrile). IR (cm^{-1}): 3275, 3202, 3143, 3089, 3011, 2967, 2934, 2875, 1671, 1639, 1604, 1375, 1330, 1254, 1109, 1038, 928, 756. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.06 (s, 3H, 9-CH_3), 1.12 (s, 3H, 9-CH_3), 2.21 (d, J = 16.4 Hz, 1H, 10-CH_2), 2.32 (d, J = 16.4 Hz, 1H, 10-CH_2), 2.69−2.77 (m, 2H, 8-CH_2), 2.84 (s, 3H, 4-CH_3), 6.60 (s, 1H, H-12), 7.28−7.31 (m, 1H, Ar), 7.38−7.41 (m, 2H, Ar), 7.61−7.69 (m, 5H, Ar), 8.31−8.32 (m, 2H, Ar), 8.45 (s, 1H, H-3), 12.42 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 17.1 (4-CH_3), 27.5 (9-CH_3), 28.6 (9-CH_3), 32.9 (C-9), 40.2 (C-8), 50.2 (C-10), 55.6 (C-12), 107.6 (C-11a), 112.4 (C-3), 128.6, 128.8, 129.0, 129.3, 130.1, 133.7, 134.3, 138.6 (carbons of 2Ph), 145.0 (C-6a or C-13a), 148.4 (C-6a or C-13a), 149.6 (C-7a), 152.1 (C-4), 162.6 (C-2), 193.5 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{27}H_{26}N_5O$ 436.2132; Found 436.2130.

*2,4,9,9-Tetramethyl-11-oxo-12-phenyl-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11c**).* Yield 0.303 g (78%, *Method B*), 0.389 g (95%, *Method C*) of colorless crystals, mp 268−269 °C (from EtOH). IR (cm^{-1}): 3143, 3084, 3025, 2963, 1670, 1658, 1607, 1437, 1380, 1335, 1247, 1116, 1077, 1050, 1026, 929. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.01 (s, 3H, 9-CH_3), 1.09 (s, 3H, 9-CH_3), 2.19 (d, J = 16.3 Hz, 1H, 10-CH_2), 2.30 (d, J = 16.3 Hz, 1H, 10-CH_2), 2.64−2.70 (m, 2H, 8-CH_2), 2.66 (s, 3H, CH_3), 2.75 (s, 3H, CH_3), 6.47 (s, 1H, H-12), 7.28−7.37 (m, 3H, Ar), 7.46−7.48 (m, 2H Ar), 7.70 (s, 1H, H-3), 12.32 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.1 (CH_3), 24.5 (CH_3), 26.9 (9-CH_3), 28.0 (9-CH_3), 32.4 (C-9), 39.7 (C-8), 49.6 (C-10), 54.7 (C-12), 107.1 (C-11a), 116.1 (C-3), 127.8, 128.4, 128.7, 137.9 (carbons of Ph), 144.0 (C-6a or C-13a), 147.6 (C-6a or C-13a), 149.0 (C-7a), 150.4 (C-4), 168.7 (C-2), 192.8 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{22}H_{24}N_5O$ 374.1975; Found 374.1975.

*2,4,9,9-Tetramethyl-11-oxo-12-phenyl-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Hydrogen Sulfate (**11d**).* Yield 0.273 g (68%, *Method B*) of colorless crystals, mp 275−276 °C (from *i*-PrOH). IR (cm^{-1}): 3055, 2935, 2739, 1666, 1648, 1594, 1445, 1382, 1341, 1224, 1156, 1041, 881, 739. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.01 (s, 3H, 9-CH_3), 1.09 (s, 3H, 9-CH_3), 2.16−2.32 (m, 2H, 10-CH_2), 2.65 (s, 3H, CH_3), 2.70−2.72 (m, 2H, 8-CH_2), 2.75(s, 3H, CH_3), 6.47 (s, 1H, H-12), 7.27−7.37 (m, 3H, Ar), 7.46−7.47 (m, 2H, Ar), 7.73 (s, 1H), 12.34 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.2, 24.5, 26.9, 28.1, 32.4, 42.2, 49.6, 54.7, 107.1, 116.2, 127.8, 128.5, 128.7, 138.1, 144.0, 147.6, 149.2, 150.4, 168.7, 192.9. HRMS (ESI-TOF) m/z: $[M - HSO_4]^+$ Calcd for $C_{22}H_{24}N_5O$ 374.1975; Found 374.1970.

*12-(4-Methoxyphenyl)-2,4,9,9-tetramethyl-11-oxo-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]-quinazolin-5-ium Perchlorate (**11e**).* Yield 0.287 g (67%, *Method B*) of yellowish crystals, mp 246−247 °C (from *i*-PrOH). IR (cm^{-1}): 3207, 2960, 2872, 1665, 1591, 1513, 1440, 1380, 1243, 1092, 1048, 1022, 849, 762. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.03 (s, 3H, 9-CH_3), 1.09 (s, 3H, 9-CH_3), 2.19 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.30 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.67 (s, 3H, CH_3), 2.68−2.70 (m, 2H, 8-CH_2), 2.74 (s, 3H, CH_3), 3.71 (s, 3H, CH_3O), 6.43 (s, 1H, H-12), 6.88−6.90 (m, 2H, Ar), 7.38−7.40 (m, 2H, Ar), 7.69 (s, 1H, H-3), 12.29 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.1 (CH_3), 24.5 (CH_3), 26.9 (CH_3), 28.1 (CH_3), 32.4 (C-9), 39.7 (C-8), 49.7 (C-10), 54.2 (C-12), 55.1 (CH_3O), 107.2 (C-11a), 113.8 (carbon of benzene ring), 116.0 (C-3), 129.2, 130.2 (carbons of benzene ring), 144.0 (C-6a or C-13a), 147.6 (C-6a or C-13a), 148.8 (C-7a), 150.3 (C-4), 159.4 (CH_3O-$\underline{C}_{Ar}$), 168.6 (C-2), 192.9 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{23}H_{26}N_5O_2$ 404.2081; Found 404.2076.

*2-(4-Bromophenyl)-2,4,9,9-tetramethyl-11-oxo-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11f**).* Yield 0.386 g (80%, *Method B*) of yellowish crystals, mp 202−203 °C (from EtOH). IR (cm^{-1}): 3209, 3146, 3085, 2962, 2877, 1666, 1597, 1441, 1382, 1273, 1246, 1089, 1010, 841, 764. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.02 (s, 3H, 9-CH_3), 1.09 (s, 3H, 9-CH_3), 2.19 (d, J = 16.1 Hz, 1H, 10-CH_2), 2.29 (d, J = 16.1 Hz, 1H, 10-CH_2), 2.65−2.69 (m, 5H, 8-CH_2 + CH_3), 2.75 (s, 3H, CH_3), 6.45 (s, 1H, H-12), 7.43−7.45 (m, 2H, Ar), 7.54−7.56 (m, 2H, Ar), 7.70 (s, 1H, H-3), 12.38 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.1 (CH_3), 24.5 (CH_3), 27.0 (CH_3), 28.0 (CH_3), 32.4 (C-9), 39.5 (C-8), 49.6 (C-10), 54.3 (C-12), 106.6 (C-11a), 116.1 (C-3), 122.0, 130.3, 131.3, 137.2 (carbons of benzene ring), 144.0 (C-6a or C-13a), 147.5 (C-6a or C-13a), 149.4 (C-7a), 150.3 (C-4), 168.7 (C-2), 192.9 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{22}H_{23}BrN_5O$ 452.1080; Found 452.1057.

*12-(2,4-Dichlorophenyl)-2,4,9,9-tetramethyl-11-oxo-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]-quinazolin-5-ium Perchlorate (**11g**).* Yield 0.374 g (79%, *Method B*) of yellowish crystals, mp 279−280 °C (from AcOH/benzene 1:4). IR (cm^{-1}): 3140, 3091, 2959, 1658, 1641, 1592, 1526, 1443, 1377, 1343, 1274, 1116, 1076, 866, 767. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.01 (s, 3H, 9-CH_3), 1.07 (s, 3H, 9-CH_3), 2.13 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.27 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.58 (s, 3H, CH_3), 2.61−2.68 (m, 2H, 8-CH_2), 2.74 (s, 3H, CH_3), 6.73 (s, 1H, H-12), 7.40−7.42 (m, 1H, Ar), 7.51−7.64 (m, 2H, Ar), 7.69 (s, 1H, H-3), 12.44 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.7 (CH_3), 25.2 (CH_3), 27.5 (CH_3), 28.7 (CH_3), 32.9 (C-9), 40.3 (C-8), 50.3 (C-10), 53.5 (C-12), 106.4 (C-11a), 116.9 (C-3), 128.1, 129.5, 134.6, 134.74,

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134.78 (carbons of benzene ring, signals are partially overlapped), 144.7 (C-6a or C-13a), 148.1 (C-6a or C-13a), 150.2 (C-7a), 150.9 (C-4), 169.4 (C-2), 193.6 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{22}H_{22}Cl_2N_5O$ 442.1196; Found 442.1180.

*2,3,4,9,9-Pentamethyl-11-oxo-12-phenyl-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11h**).* Yield 0.351 g (82%, *Method B*) of colorless crystals, mp 269−270 °C (from EtOH). IR (cm^{-1}): 3204, 3149, 3089, 3028, 2962, 2873, 1669, 1632, 1598, 1447, 1373, 1335, 1245, 1116, 1050, 1037, 1003, 931, 740. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.02 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.20 (d, J = 16.4 Hz, 1H, 10-CH_2), 2.31 (d, J = 16.4 Hz, 1H, 10-CH_2), 2.37 (s, 3H, CH_3), 2.65−2.70 (m, 5H, 8-CH_2 + CH_3), 2.78 (s, 3H, CH_3), 6.48 (s, 3H, H-12), 7.28−7.37 (m, 3H, Ar), 7.48 (d, J = 7.4 Hz, 2H, Ar), 12.30 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.5 (CH_3), 13.7 (CH_3), 24.0 (CH_3), 26.7 (CH_3), 27.9 (CH_3), 32.2 (C-9), 39.7 (C-8), 49.5 (C-10), 54.4 (C-12), 106.8 (C-11a), 123.5 (C-3), 127.6, 128.3, 128.5, 137.9 (carbons of Ph), 141.7 (C-6a or C-13a), 147.1 (C-6a or C-13a), 147.7 (C-4), 148.9 (C-7a), 167.7 (C-2), 192.7 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{23}H_{26}N_5O$ 388.2132; Found 388.2128.

*12-(2,4-Dichlorophenyl)-2,3,4,9,9-pentamethyl-11-oxo-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11i**).* Yield 0.417 g (85%, *Method B*), 0.442 g (90%, *Method C*) of yellowish crystals, mp 208−209 °C (from EtOH). IR (cm^{-1}): 2956, 2869, 1666, 1589, 1452, 1379, 1340, 1274, 1100, 1051, 857, 757. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.01 (s, 3H, 9-CH_3), 1.08 (s, 3H, 9-CH_3), 2.13 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.27 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.33 (s, 3H, CH_3), 2.58 (s, 3H, CH_3), 2.61−2.68 (m, 2H, 8-CH_2), 2.76 (s, 3H, CH_3), 6.73 (s, 1H, H-12), 7.40 (d, J = 7.2 Hz, 1H, Ar), 7.48−7.64 (m, 2H, Ar), 12.39 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 14.3 (CH_3), 14.5 (CH_3), 24.8 (CH_3), 27.5 (9-CH_3), 28.7 (9-CH_3), 32.9 (C-9), 40.2 (C-8), 50.3 (C-10), 53.2 (C-12), 106.4 (C-11a), 124.5 (C-3), 128.1, 129.5, 134.6, 134.8, 134.9 (carbons of benzene ring, signals are partially overlapped), 142.6 (C-6a or C-13a), 147.8 (C-6a or C-13a), 148.5 (C-4), 150.3 (C-7a), 168.6 (C-2), 193.6 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{23}H_{24}Cl_2N_5O$ 456.1352; Found 456.1329.

*3-Chloro-2,4,9,9-tetramethyl-11-oxo-12-phenyl-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11j**).* Yield 0.340 g (77%, *Method B*) of colorless crystals, mp 213-214 °C (from *i*-PrOH). IR (cm^{-1}): 3214, 3150, 3082, 2961, 2878, 1662, 1590, 1452, 1379, 1246, 1104, 1059, 1018, 805, 760, 720. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.03 (s, 3H, 9-CH_3), 1.10 (s, 3H, 9-CH_3), 2.20 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.31 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.67−2.76 (m, 5H, CH_3 + 8-CH_2), 2.87 (s, 3H, 4-CH_3), 6.51 (s, 1H, H-12), 7.29−7.38 (m, 3H, Ph), 7.48−7.50 (m, 2H, Ph), 12.48 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 15.0 (CH_3), 24.2 (CH_3), 26.9 (9-CH_3), 28.1 (9-CH_3), 32.4 (C-9), 39.5 (C-8), 49.6 (C-10), 55.0 (C-12), 107.1 (C-11a), 123.3 (C-3), 127.9, 128.5, 128.8, 137.7 (carbons of benzene ring), 142.0 (C-6a or C-13a), 148.1 (C-6a or C-13a), 148.8 (C-7a), 148.9 (C-4), 165.7 (C-2), 192.9 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{22}H_{23}ClN_5O$ 408.1586; Found 408.1579.

*3-Chloro-12-(2-methoxyphenyl)-2,4,9,9-tetramethyl-11-oxo-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11k**).* Yield 0.315 g (69%, *Method B*) of colorless crystals, mp 269−270 °C (from DMF/EtOH 1:3). IR (cm^{-1}): 3233, 2956, 2842, 1671, 1637, 1592, 1496, 1453, 1378, 1336, 1268, 1110, 1060, 1026, 755. ^{1}H NMR (500 MHz, DMSO-d_6): δ 0.92 (s, 3H, 9-CH_3), 1.07 (s, 3H, 9-CH_3), 2.09 (d, J = 16.4 Hz, 1H, 10-CH_2), 2.29 (d, J = 16.4 Hz, 1H, 10-CH_2), 2.51−2.54 (m, 1H, 8-CH_2), 2.67 (s, 3H, CH_3), 2.69−2.72 (m, 1H, 8-CH_2), 2.85 (s, 3H, CH_3), 3.67 (s, 3H, CH_3O), 6.52 (s, 1H, H-12), 6.95−6.96 (m, 2H, Ar), 7.25−7.28 (m, 1H, Ar), 7.54−7.56 (m, 1H, Ar), 12.37 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 15.1, 24.2, 25.9, 28.5, 32.2, (signal of C-8 is overlapped by DMSO signal), 49.1, 53.6, 55.4, 105.5, 111.6, 119.8, 123.2, 124.4, 130.4, 131.6, 142.0, 148.6, 148.9, 149.0, 157.4, 165.5, 192.8. HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{23}H_{25}ClN_5O_2$ 438.1691; Found 438.1685.

*3-Butyl-2,4,9,9-tetramethyl-11-oxo-12-phenyl-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11l**).* Yield 0.233 g (54%, *Method B*) of colorless crystals, mp 186−187 °C (from EtOH). IR (cm^{-1}): 3199, 3142, 3080, 3030, 2958, 2872, 1663, 1636, 1593, 1450, 1378, 1337, 1255, 1095, 1052, 928, 840. ^{1}H NMR (500 MHz, DMSO-d_6): δ 0.94 (t, J = 6.9 Hz, 3H, $(CH_2)_3C\underline{H}_3$), 1.03 (s, 3H, 9-CH_3), 1.10 (s, 3H, 9-CH_3), 1.40−1.51 (m, 4H, $CH_2(C\underline{H}_2)_2CH_3$), 2.19 (d, J = 16.3 Hz, 1H, 10-CH_2), 2.31 (d, J = 16.3 Hz, 1H, 10-CH_2), 2.66−2.74 (m, 5H, CH_3 + 8-CH_2), 2.77−2.81 (m, 5H, CH_3 + $C\underline{H}_2(CH_2)_2CH_3$), 6.47 (s, 1H, H-12), 7.28−7.38 (m, 3H, Ar), 7.48−7.50 (m, 2H, Ar), 12.31 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.3 ($(CH_2)_3\underline{C}H_3$), 13.5 (CH_3), 21.8 (CH_2), 23.3 (CH_3), 26.7 (9-CH_3), 26.8 (CH_2), 27.9 (9-CH_3), 30.0 (CH_2), 32.2 (C-9), 39.5 (C-8, overlapped by DMSO signal), 49.5 (C-10), 54.4 (C-12), 106.9 (C-11a), 127.3 (C-3), 127.7, 128.3, 128.5, 137.9 (carbons of benzene ring), 141.8(C-6a or C-13a), 147.2(C-6a or C-13a), 148.1 (C-7a), 148.9(C-4), 167.3 (C-2), 192.7 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{26}H_{32}N_5O$ 430.2601; Found 430.2598.

*9,9-Dimethyl-11-oxo-2,4,12-triphenyl-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11m**).* Yield 0.438 g (84%, *Method B*) of yellow crystals, mp 287−288 °C (from acetonitrile). IR (cm^{-1}): 3060, 2948, 2695, 1684, 1628, 1577, 1543, 1491, 1378, 1365, 1277, 1252, 1071, 844, 751. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.08 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 2.23 (d, J = 16.5 Hz, 1H, 10-CH_2), 2.35 (d, J = 16.5 Hz, 1H, 10-CH_2), 2.69−2.77 (m, 2H, 8-CH_2), 6.67 (s, 1H, H-12), 7.33−7.35 (m, 1H, Ar), 7.43−7.46 (m, 2H, Ar), 7.68−7.81 (m, 8H, Ar), 8.21−8.23 (m, 2H, Ar), 8.50−8.52 (m, 2H, Ar), 8.63 (s, 1H, H-3), 12.48 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 27.5, 28.6, 33.0, (signal of C-8 is overlapped by DMSO signal), 50.2, 55.7, 107.6, 111.8, 128.3, 128.9, 129.0, 129.3, 130.0, 130.8, 133.4, 133.8, 134.4, 138.6 (signals of carbons of benzene rings are partially overlapped), 145.8, 148.4, 149.7, 150.0, 163.3, 193.5. HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{32}H_{28}N_5O$ 498.2288; Found 498.2284.

*9,9-Dimethyl-11-oxo-12-phenyl-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11n**).* Yield 0.282 g (74%, *Method B*) of colorless crystals, mp 194−195 °C (from acetonitrile). IR (cm^{-1}): 3211, 3094, 2961, 2873, 1671, 1634, 1590, 1403, 1335, 1249, 1121, 1038, 920, 813, 767. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.03 (s, 3H, 9-CH_3), 1.11 (s, 3H, 9-CH_3), 2.20 (d, J = 16.4 Hz, 1H, 10-CH_2), 2.31 (d, J = 16.4 Hz, 1H, 10-CH_2), 2.68−2.77 (m, 2H, 8-CH_2), 6.54 (s, 1H, H-12), 7.29−7.38 (m, 3H, Ar), 7.50−7.52 (m, 2H, Ar), 7.88−7.90 (m, 1H, Ar), 9.11−9.12 (m, 1H, Ar), 9.69−9.70 (m, 1H, Ar), 12.42 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 27.4 (9-CH_3), 28.6 (9-CH_3), 32.9 (C-9), (signal of C-8 is overlapped by DMSO signal), 50.2 (C-10), 55.7 (C-12), 107.7 (C-11a), 116.8 (C-3), 128.6, 129.0, 129.3, 138.4 (carbons of Ph), 140.4 (C-4), 145.1 (C-13a), 149.0 (C-6a), 149.4 (C-7a), 158.9 (C-2), 193.5 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{20}H_{20}N_5O$ 346.1662; Found 346.1666.

*12-(4-Methoxyphenyl)-9,9-dimethyl-11-oxo-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium Perchlorate (**11o**).* Yield 0.392 g (70%, *Method B*) of colorless crystals, mp 201−202 °C (from AcOH/EtOAc 1:4). IR (cm^{-1}): 3261, 3206, 3159, 3082, 3032, 2954, 1669, 1633, 1585, 1512, 1404, 1244, 1104, 1171, 808, 764. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.03 (s, 3H, 9-CH_3), 1.09 (s, 3H, 9-CH_3), 2.18 (d, J = 16.3 Hz, 1H, 10-CH_2), 2.29 (d, J = 16.3 Hz, 1H, 10-CH_2), 2.65−2.74 (m, 2H, 8-CH_2), 3.70 (s, 3H, CH_3O), 6.48 (s, 1H, H-12), 6.88 (d, J = 7.3 Hz, 2H, Ar), 7.41 (d, J = 7.3 Hz, 2H, Ar), 7.85−7.87 (m, 1H, Ar), 9.09−9.10 (m, 1H, Ar), 9.65−9.66 (m, 1H, Ar), 12.34 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 26.9 (9-CH_3), 28.1 (9-CH_3), 32.4 (C-9), 39.5 (C-8), 49.7 (C-10), 54.7 (C-12), 55.1 (CH_3O), 107.3 (C-11a), 113.8 (C Ar), 116.2 (C-3), 129.5, 130.0, 139.9 (carbons of benzene ring), 144.6 (C-13a), 148.5 (C-6a), 148.6 (C-7a), 158.3 (C-2), 159.4 (CH_3O-$\underline{C}_{Ar}$), 193.0 (CO). HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{21}H_{22}N_5O_2$ 376.1768; Found 376.1761.

*9-(Ethoxycarbonyl)-2,3,4,8-tetramethyl-10-phenyl-7,10-dihydro-[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**11p**).* Yield 0.382 g (90%, *Method B*) of colorless crystals, mp 228−229 °C (from *i*-PrOH). IR (cm^{-1}): 3216, 3169, 3099, 3033, 2986, 1721,

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1672, 1635, 1598, 1535, 1386, 1247, 1109, 1075, 1055, 1003, 758. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.10 (t, J = 7.0 Hz, 3H, CH_2CH_3), 2.37 (s, 3H, CH_3), 2.55 (s, 3H, 8-CH_3), 2.67 (s, 3H, CH_3), 2.77 (s, 3H, CH_3), 4.03−4.06 (m, 2H, CH_2), 6.55 (s, 1H, H-10), 7.31−7.40 (m, 3H, Ar), 7.51−7.52 (m, 2H, Ar), 12.0 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.5 (CH_3), 13.6 (OCH_2CH_3), 13.8 (CH_3), 18.0 (CH_3), 23.9(CH_3), 55.7 (C-10), 59.9 (OCH_2CH_3), 99.7 (C-9), 123.4 (C-3), 127.7, 128.4, 128.7, 138.2 (carbons of Ph), 141.3 (C-11a), 144.8 (C-8), 147.0 (C-6a), 147.7 (C-4), 163.7 (COOEt), 167.5 (C-2). HRMS (ESI-TOF) m/z: [M − ClO_4]$^+$ Calcd for $C_{21}H_{24}N_5O_2$ 378.1925; Found 378.1921.

*3-Chloro-9-(ethoxycarbonyl)-2,4,8-trimethyl-10-phenyl-7,10-dihydro[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**11q**).* Yield 0.353 g (81%, *Method B*) of colorless crystals, mp 236−237 °C (from *i*-PrOH). IR (cm^{-1}): 3148, 3080, 1701, 1663, 1587, 1530, 1369, 1265, 1111, 1062, 1026, 1004, 757. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.09 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 2.55 (s, 3H, 8-CH_3), 2.76 (s, 3H, CH_3), 2.85 (s, 3H, CH_3), 4.02−4.05 (m, 2H, OCH_2CH_3), 6.57 (s, 1H, H-10), 7.33−7.40 (m, 3H, Ph), 7.51−7.52 (m, 2H, Ph), 12.16 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.7 (OCH_2CH_3), 15.1 (CH_3), 18.2 (CH_3), 24.1 (8-CH_3), 56.3 (C-10), 60.2 (OCH_2CH_3), 100.2 (C-9), 123.3 (C-3), 128.0, 128.6, 129.0, 138.0 (carbons of Ph), 141.7 (C-11a), 144.8 (C-8), 147.9 (C-6a), 148.7 (C-4), 163.8 (CO), 165.5 (C-2). HRMS (ESI-TOF) m/z: [M − ClO_4]$^+$ Calcd for $C_{20}H_{21}ClN_5O_2$ 398.1378; Found 398.1371.

*3-Benzyl-9-(ethoxycarbonyl)-2,4,8-trimethyl-10-phenyl-7,10-dihydro[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**11r**).* Yield 0.366 g (76%, *Method B*) of colorless crystals, mp 156−157 °C (from *i*-PrOH). IR (cm^{-1}): 3213, 3161, 2926, 1706, 1660, 1593, 1527, 1455, 1383, 1271, 1248, 1107, 1057, 930, 739, 703. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.08 (t, J = 7.0 Hz, 3H, CH_2CH_3), 2.56 (s, 6H, $2CH_3$), 2.79 (s, 3H, CH_3), 4.02−4.04 (m, 2H, OCH_2CH_3), 4.28 (s, 2H, CH_2Ph), 6.55 (s, 1H, H-10), 7.13−7.14 (m, 2H, Ph), 7.21−7.24 (m, 1H, Ar), 7.28−7.34 (m, 3H, Ar), 7.37−7.40 (m, 2H, Ar), 7.52−7.54 (m, 2H, Ar), 12.05 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.8 (OCH_2CH_3), 14.2 (CH_3), 18.2 (CH_3), 23.8 (8-CH_3), 32.5 (CH_2Ph), 56.0 (C-10), 60.1 (OCH_2CH_3), 99.9 (C-9), 125.4 (C-3), 126.6, 127.9, 128.0, 128.6 (2C), 128.9, 136.8, 138.4 (carbons of 2Ph), 142.1 (C-11a), 145.1 (C-8), 147.4 (C-6a), 149.3 (C-4), 163.9 (COOEt), 168.1 (C-2). HRMS (ESI-TOF) m/z: [M − ClO_4]$^+$ Calcd for $C_{27}H_{28}N_5O_2$ 454.2238; Found 454.2230.

*9-(Ethoxycarbonyl)-8-methyl-10-phenyl-7,10-dihydro[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium Perchlorate (**11s**).* Yield 0.270 g (72%, *Method B*) of colorless crystals, mp 259−260 °C (from MeCN). IR (cm^{-1}): 3166, 3099, 2976, 1708, 1670, 1629, 1594, 1533, 1402, 1262, 1246, 1123, 1045, 1089, 767. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.09 (t, J = 7.0 Hz, 3H, OCH_2CH_3) 2.55 (s, 3H, 8-CH_3), 4.01−4.04 (m, 2H, OCH_2CH_3), 6.60 (s, 1H, H-10), 7.31−7.40 (m, 3H, Ph), 7.52−7.53 (m, 2H, Ph), 7.85−7.87 (m, 1H, H-3), 9.08 (d, J = 3.9 Hz, 1H, H-4), 9.65 (d, J = 6.5 Hz, 1H, H-2), 12.09 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.7 (OCH_2CH_3), 18.2 (CH_3), 56.5 (C-10), 60.2 (OCH_2CH_3), 100.2 (C-9), 116.2 (C-3), 128.2, 128.6, 128.9, 138.1 (carbons of Ph), 139.8 (C-2), 144.2 (C-11a), 144.6 (C-8), 148.4 (C-6a), 158.1 (C-4), 163.8 (COOEt). HRMS (ESI-TOF) m/z: [M − ClO_4]$^+$ Calcd for $C_{18}H_{18}N_5O_2$ 336.1455; Found 336.1452.

*12-(4-Bromophenyl)-2,3,4,9,9-pentamethyl-11-oxo-7,8,9,10,11,12-hexahydropyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]-quinazolin-5-ium Hydrogen Sulfate (**11t**).* Yield 0.265 g (57%, *Method B*) of yellowish crystals, mp 234−235 °C (from *i*-PrOH). IR (cm^{-1}): 3053, 2958, 2868, 2738, 1667, 1651, 1591, 1451, 1378, 1340, 1213, 1177, 1042, 894, 758. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.01 (s, 3H, 9-CH_3), 1.09 (s, 3H, 9-CH_3), 2.18 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.29 (d, J = 16.2 Hz, 1H, 10-CH_2), 2.35 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 2.69−2.71 (m, 2H, 8-CH_2), 2.77 (s, 3H, CH_3), 6.44 (s, 1H, H-12), 7.44 (d, J = 8.4 Hz, 2H, Ar), 7.54 (d, J = 8.4 Hz, 2H, Ar), 12.34 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.7, 13.9, 24.2, 27.0, 28.1, 32.4, (signal of C-8 is overlapped by DMSO signal), 49.6, 54.2, 106.5, 121.9, 123.7, 130.2, 131.3, 137.4, 142.0, 147.1, 147.9, 149.4, 167.9, 193.0. HRMS (ESI-TOF) m/z: [M − HSO_4]$^+$ Calcd for $C_{23}H_{25}BrN_5O$ 466.1237; Found 466.1216.

Reaction of 5,7-Dimethyl-[1,2,4]triazolo[1,5-*a*]pyrimidin-2-amine (3c), Dimedone (12), and Benzaldehyde. A magnetically stirred mixture of amine **3c** (0.326 g, 2 mmol), compound **12** (0.308 g, 2.2 mmol), benzaldehyde (0.233 g, 2.2 mmol), a 70% aqueous solution of $HClO_4$ (0.302 g, 2.1 mmol), and AcOH (1.0 mL) was heated at 90 °C for 1 h, then diluted with ethanol (5 mL) and cooled to 40 °C. The precipitate formed was collected by filtration and washed with ethanol to give *3,3,6,6-tetramethyl-9-phenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione* (**14**). Yield 0.392 g (73%) of colorless crystals, mp 201−203 °C (lit.[27] 202−204 °C). IR (cm^{-1}): 2959, 2915, 2871, 1679, 1625, 1360, 1198, 1140, 1002, 699. ^{1}H NMR (500 MHz, DMSO-d_6): δ 0.91 (s, 6H, $2CH_3$), 1.04 (s, 6H, $2CH_3$), 2.08 (d, J = 16.2 Hz, 2H, CH_2), 2.27 (d, J = 16.2 Hz, 2H, CH_2), 2.51−2.60 (m, 4H, CH_2), 4.53 (s, 1H, CH), 7.08−7.24 (m, 5H, Ph). MS (EI, 70 eV), m/z (%): 350 (71) [M]$^+$, 273 (100), 265 (11), 217 (15), 161 (10), 133 (4), 77 (6).

The solution after separation of **14** was evaporated to a volume of ∼2 mL and cooled to 20 °C. The precipitate formed was collected by filtration and recrystallized from EtOH to give *5,7-dimethyl-[1,2,4]-triazolo[1,5-a]pyrimidin-2-amine perchlorate* (**13**). Yield 0.368 g (70%) of colorless crystals, mp 256−258 °C. IR (cm^{-1}): 3333, 3148, 3002, 2764, 1654, 1563, 1538, 1421, 1360, 1204, 1116, 1028, 775. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.45 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 6.25 (br s, 2H, NH_2), 6.84 (s, 1H, H-6). ^{13}C NMR (125 MHz, DMSO-d_6): δ 17.0, 24.5, 109.0, 145.3, 154.7, 161.8, 166.5. HRMS (ESI-TOF) m/z: [M − ClO_4]$^+$ Calcd for $C_7H_{10}N_5$ 164.0931, found 164.0931.

*10,10-Dimethyl-8-oxo-7-phenyl-7,8,9,10,11,12-hexahydropyrimido[1′,2′:2,3][1,2,4]triazolo[5,1-b]quinazolin-6-ium Perchlorate (**16n**).* A mixture of compound **5a** (1 mmol), tetramethoxypropane **6h** (1.3 mmol), a 70% aqueous solution of $HClO_4$ (0.152 g, 1.05 mmol), and AcOH (0.5 mL) was stirred at room temperature for 10 min and then diluted with acetone (3 mL). The precipitate formed was collected by filtration and dried in vacuum at room temperature. Yield 0.231 g (52%) of colorless crystals, mp 197−198 °C. IR (cm^{-1}): 3217, 3137, 3088, 2959, 2895, 1659, 1626, 1566, 1538, 1497, 1412, 1331, 1274, 1109, 1039, 908, 799. ^{1}H NMR (500 MHz, DMSO-d_6): δ 0.99 (s, 3H, 10-CH_3), 1.11 (s, 3H, 10-CH_3), 2.21 (d, J = 16.2 Hz, 1H, 9-CH_2), 2.36 (d, J = 16.2 Hz, 1H, 9-CH_2), 2.68−2.75 (m, 2H, 11-CH_2), 7.08 (s, 1H, H-7), 7.34−7.41 (m, 3H, Ar), 7.59−7.60 (m, 2H, Ar), 7.74 (dd, J = 6.9, 4.6 Hz, 1H, Ar), 9.15−9.16 (m, 1H, Ar), 9.48−9.49 (m, 1H, Ar), 12.81 (br s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 27.2 (10-CH_3), 28.5 (10-CH_3), 32.9 (C-10), 39.7 (C-11), 50.0 (C-9), 57.7 (C-7), 109.8 (C-7a), 114.0 (C-3), 128.7, 129.4, 130.1, 134.9 (carbons of benzene ring), 135.7 (C-2 or C-4), 148.7 (C-11a), 150.4 (C-12a), 152.2 (C-13a), 161.6 (C-2 or C-4), 193.6 (CO). HRMS (ESI-TOF) m/z: [M − ClO_4]$^+$ Calcd for $C_{20}H_{20}N_5O$ 346.1662; Found 346.1658.

Rearrangement of Compound 16n to Compound 11n. A magnetically stirred mixture of compound **16n** (0.446 g, 1 mmol) and AcOH (0.5 mL) was heated at 90 °C for 1 h and then diluted with ethanol (2 mL). The precipitate formed after cooling to room temperature was collected by filtration to yield perchlorate **11n** (0.405 g, 91%).

*2-Amino-5,7-diphenyl-4,5,6,7-tetrahydro-3H-[1,2,4]triazolo[1,5-a]pyrimidin-8-ium Perchlorate (**19**).* A solution of compound **8b** (0.456 g, 1 mmol) in EtOH (5.0 mL) or DMF (2.0 mL) was refluxed (or heated at 90 °C in case of DMF) for 24 h. The precipitate formed after cooling to room temperature was collected by filtration and recrystallized from ethanol to give compound **19** as colorless crystals. Yield 0.265 g (68%, from EtOH), 0.202 g (52%, from DMF), mp 203−204 °C. IR (cm^{-1}): 3447, 3363, 3184, 3090, 2970, 1656, 1458, 1074, 753, 699, 622. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.25−2.33 (m, 1H, CH_2), 2.46−2.55 (m, 1H, CH_2), 4.86−4.90 (m, 1H, H-5), 5.26−5.30 (m, 1H, H-7), 7.32−7.58 (m, 10H, 2Ph), 8.92 (br s, 1H, NH) (signals of NH_2 and NH are broadened and merged into the background). ^{13}C NMR (125 MHz, DMSO-d_6): δ 39.8, 53.5, 58.5, 126.8, 127.7, 128.2, 128.4, 128.6, 137.6, 139.7 (signals of two aromatic carbons are overlapped), 148.0, 150.8. Anal. Calcd for $C_{17}H_{18}ClN_5O_4$: C, 52.11; H, 4.63; N, 17.87. Found: C, 51.92; H, 4.74; N, 17.80.

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HRMS (ESI-TOF) m/z: $[M - ClO_4]^+$ Calcd for $C_{17}H_{18}N_5$ 292.1557; Found 292.1555.

General Procedure for the Synthesis of Compounds 20a–c. A suspension of the appropriate perchlorate **8b,e,g** (1 mmol) in 5% ethanol solution of KOH (5 mL) was stirred for 15 min and then diluted with water (5 mL). The precipitate formed was collected by filtration, washed with water, and recrystallized from $CHCl_3$/$CH_3COOC_2H_5$ (1:3).

*8,10-Dimethyl-2,4-diphenyl-3,4-dihydro-2H-[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidine (**20a**).* Yield 0.263 g (74%) of orange-red crystals, mp 206–207 °C. IR (cm^{-1}): 3057, 3029, 2962, 2873, 2837, 1655, 1634, 1563, 1528, 1299, 1281, 1181, 746. ^1H NMR (500 MHz, DMSO-d_6): δ 1.64–1.71 (m, 1H, H-3), 2.23 (s, 3H, CH_3), 2.46–2.48 (m, 1H, H-3), 2.81 (s, 3H, CH_3), 4.71–4.73 (m, 1H, H-2), 5.29 (dd, J = 10.6, 4.6 Hz, 1H, H-4), 6.15 (s, 1H, H-9), 7.17–7.33 (m, 8H, Ar), 7.45–7.46 (m, 2H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6): δ 18.4, 25.2, 41.9, 56.7, 59.4, 107.5, 126.7, 126.9, 127.8, 128.0, 128.4, 128.7, 140.8, 145.9, 147.1, 147.2, 149.1, 168.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{22}N_5$ 356.1870; Found 356.1867.

*2,4,8,10-Tetraphenyl-3,4-dihydro-2H-[1,2,4]triazolo[1,5-a:4,3-a′]-dipyrimidine (**20b**).* Yield 0.402 g (84%) of violet crystals, mp 207–208 °C. IR (cm^{-1}): 3064, 3033, 2965, 2920, 1653, 1617, 1599, 1516, 1490, 1360, 1297, 1282, 1184, 1132, 1016. ^1H NMR (500 MHz, DMSO-d_6): δ 1.70–1.80 (m, 1H, H-3), 2.50–2.54 (m, 1H, H-3), 4.62–4.64 (m, 1H, H-2), 5.33–5.35 (m, 1H, H-4), 7.07–7.58 (m, 17H, Ar), 7.86–7.87 (m, 2H, Ar), 8.19–8.21 (d, J = 7.0 Hz, 2H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6): δ 41.5 (C-3), 56.2 (C-2), 59.3 (C-4), 105.2 (C-9), 125.9, 126.4, 126.8, 127.39, 127.43, 127.5, 127.6, 128.2, 128.8, 129.9, 130.0, 130.5, 131.6, 135.5, 140.2, 145.1, 145.2, 146.9, 149.4, 162.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{26}N_5$ 480.2183; Found 480.2177.

*9-Chloro-8,10-dimethyl-2,4-diphenyl-3,4-dihydro-2H-[1,2,4]-triazolo[1,5-a:4,3-a′]dipyrimidine (**20c**).* Yield 0.296 g (76%) of red crystals, mp 193–194 °C. IR (cm^{-1}): 3026, 2911, 2836, 1659, 1617, 1564, 1517, 1494, 1429, 1319, 1367, 1269, 1187, 1028, 733. ^1H NMR (500 MHz, DMSO-d_6): δ 1.65–1.72 (m, 1H, H-3), 2.37 (s, 3H, CH_3), 2.51–2.53 (m, 1H, H-3), 3.03 (s, 3H, CH_3), 4.72–4.74 (m, 1H, H-2), 5.32 (dd, J = 10.8, 4.7 Hz, 1H, H-4), 7.18–7.34 (m, 8H, H Ar), 7.45–7.46 (m, 2H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6): δ 15.0, 24.7, 41.6, 56.8, 59.7, 113.8, 126.7, 126.9, 127.8, 128.0, 128.4, 128.7, 140.6, 145.0, 145.8, 146.4, 147.1, 165.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{21}ClN_5$ 390.1480; Found 390.1469.

*5,7-Diphenyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-a]pyrimidin-2-amine (**2b**).* A suspension of compound **8b** (0.456 g, 1 mmol) in 5% ethanol solution of KOH (5 mL) was refluxed for 24 h. The precipitate formed after cooling to room temperature was collected by filtration and washed with ethanol to give amine **2b**. Yield 0.279 g (87%), mp 279–280 °C (lit.[16] mp 279–280 °C). ^1H NMR (500 MHz, DMSO-d_6): δ 1.99 (m, 1H, 6-CH_2), 2.33 (m, 1H,6-CH_2), 4.60 (m, 1H, H-5), 4.85 (2H, NH_2), 5.12 (m, 1H, H-7), 7.03 (s, 1H, NH), 7.18–7.37 (m, 8H, Ar.), 7.42 (m, 2H, Ar). Anal. Calcd for $C_{17}H_{17}N_5$: C, 70.08; H, 5.88; N, 24.04. Found: C, 70.15; H, 5.90; N, 23.94. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{18}N_5$ 292.1557; Found 292.1555. Spectral characteristics and physical properties of the compound obtained are identical to the authentic sample of **2b**.

General Procedure for the Synthesis of Compounds 21a–c. A suspension of the appropriate perchlorate **11a,c,i** in a saturated aqueous solution of CH_3COONa (5 mL) was stirred for 15 min. The precipitate formed was collected by filtration, washed with water, and recrystallized from EtOH/H_2O (1:3).

*2,4,9,9-Tetramethyl-11-oxo-12-phenyl-8,10,11,12-tetrahydro-9H-pyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]quinazolin-5-ium-7-ide (**21a**).* Yield 0.313 g (85%) of yellow crystals, mp > 300 °C. IR (cm^{-1}): 3272, 3145, 3076, 3025, 2964, 2870, 1670, 1658, 1608, 1436, 1381, 1336, 1247, 1118, 1050, 930, 741. ^1H NMR (500 MHz, DMSO-d_6): δ 0.94 (s, 3H, 9-CH_3), 1.02 (s, 3H, 9-CH_3), 2.10 (d, J = 16.1, 1H, 10-CH_2), 2.21 (d, J = 16.1, 1H, 10-CH_2), 2.54–2.63 (m, 5H, 10-CH_2 + CH_3), 2.67 (s, 3H, CH_3), 6.40 (s, 1H, H-12), 7.21–7.39 (m, 5H, Ph), 7.59 (s, 1H, H-3). ^{13}C NMR (125 MHz, DMSO-d_6): δ 16.7 (CH_3), 25.0 (CH_3), 27.5 (9-CH_3), 28.7 (9-CH_3), 32.9 (C-9), 41.0 (C-8), 50.3 (C-10), 55.1 (C-12), 107.1 (C-11a), 116.4 (C-3), 128.3, 129.0, 129.1, 139.0 (Ph), 144.5 (C-13a), 149.2 (C-6a), 150.5 (C-4), 151.9 (C-7a), 168.6 (C-2), 193.1 (CO). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{24}N_5O$ 374.1975; Found 374.1977.

*9-(Ethoxycarbonyl)-2,4,8-trimethyl-10-phenyl-7,10-dihydro-[1,2,4]triazolo[1,5-a:4,3-a′]dipyrimidin-5-ium-7-ide (**21b**).* Yield 0.323 g (89%) of yellow crystals, mp 208–209 °C. IR (cm^{-1}): 3210, 3173, 3074, 2979, 2941, 1707, 1667, 1639, 1596, 1531, 1439, 1378, 1245, 1106, 1067, 753, 706. ^1H NMR (500 MHz, DMSO-d_6): δ 1.09 (t, J = 7.1 Hz, 3H, $OCH_2C\underline{H}_3$), 2.53 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 2.73 (s, 3H, CH_3), 4.0–4.04 (m, 2H, $OC\underline{H}_2CH_3$), 6.53 (s, 1H, H-10), 7.29–7.39 (m, 3H, Ph), 7.48–7.50 (m, 2H, Ph), 7.66 (s, 1H, H-3). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.8, 16.2, 18.9, 24.4, 56.0, 59.9, 99.3, 115.9, 127.9, 128.6, 128.8, 138.7, 143.6, 146.6, 148.2, 150.1, 164.0, 168.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{22}N_5O_2$ 364.1768; Found 364.1762.

*12-(2,4-Dichlorophenyl)-2,3,4,9,9-pentamethyl-11-oxo-8,10,11,12-tetrahydro-9H-pyrimido[1′,2′:1,5][1,2,4]triazolo[3,4-b]-quinazolin-5-ium-7-ide (**21c**).* Yield 0.333 g (73%) of yellow crystals, mp > 300 °C. IR (cm^{-1}): 2950, 2920, 2865, 1633, 1566, 1528, 1494, 1381, 1355, 1265, 1199, 1124, 1090, 851. ^1H NMR (500 MHz, DMSO-d_6): δ 0.92 (s, 3H, 9-CH_3), 1.00 (s, 3H, 9-CH_3), 1.90 (d, J = 15.9 Hz, 1H, 10-CH_2), 2.10 (d, J = 15.9 Hz, 1H, 10-CH_2), 2.21 (s, 3H, CH_3), 2.35–2.43 (m, 2H, 8-CH_2), 2.45 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 6.65 (s, 1H, H-12), 7.19–7.39 (m, J = 16.0 Hz, 2H, Ar), 7.42 (br s, 1H, Ar). ^{13}C NMR (125 MHz, DMSO-d_6): δ 14.1, 14.3, 24.3, 27.7, 29.8, 32.5, (signal of C-8 is overlapped by DMSO signal), 47.1, 50.9, 102.9, 122.1, 127.8, 128.9, 132.4, 133.2, 134.1, 138.6, 142.8, 146.2, 155.0, 163.9, 165.9, 191.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{24}Cl_2N_5O$ 456.1352; Found 456.1342.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01908.

Crystallographic data for **8h**, **9a**, **11b**, **11c**, **11p**, **16n**, and **20a** (ZIP)

B3LYP 6-311++G(2d,2p) fully optimized geometries, given in standard XYZ format (XYZ)

Detailed results of quantum chemical calculations, copies of NMR and IR spectra, and HRMS data (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: chern13@yandex.ru.

Notes

The authors declare no competing financial interest.

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