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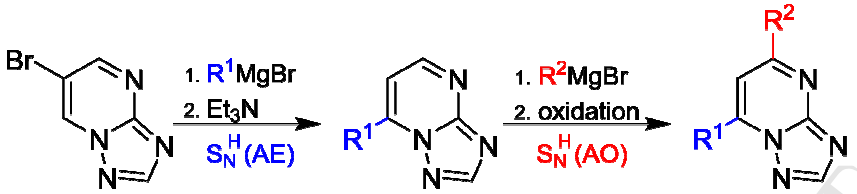

Direct (het)arylation of [1,2,4]triazolo[1,5-*a*]pyrimidines: both eliminative and oxidative pathways

Nikolay A. Rasputin,[a,*] Nadezhda S. Demina,[b] Roman A. Irgashev,[a,b] Gennady L. Rusinov,[a,b] Oleg N. Chupakhin,[a,b] and Valery N. Charushin[a,b]

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Abstract

(Hetero)arylation of [1,2,4]triazolo[1,5-*a*]pyrimidine through the direct nucleophilic C–H functionalization of the C-7 and C-5 positions has been implemented. The regioselective addition of a (het)aryl magnesium bromide to C-7 of 6-bromo-[1,2,4]triazolo[1,5-*a*]pyrimidine, followed by eliminative aromatization of the intermediate σ^H-adducts, has afforded 7-(hetero)aryl-substituted [1,2,4]triazolo[1,5-*a*]-pyrimidines (the S_N^H reaction, proceeding according to the "addition-elimination" scheme). A second treatment with a Grignard reagent has resulted in the C-5 σ^H-adducts, which have been oxidized while being *N*-magnesium salts into [1,2,4]triazolo[1,5-*a*]pyrimidines, bearing various combinations of (hetero)aromatic substituents at C-5 and C-7 (the S_N^H process, realizing *via* the "addition-oxidation" scheme). As a result of optical and electrochemical studies, the obtained compounds have proved to be promising luminescent dyes and push-pull systems.

Keywords

[1,2,4]Triazolo[1,5-*a*]pyrimidine, (het)aryl magnesium bromide, direct (het)arylation, Nucleophilic aromatic substitution of hydrogen (S_N^H)

1. Introduction

[1,2,4]Triazolo[1,5-*a*]pyrimidines (TAPs) (Figure 1) have gained great attention from organic chemists worldwide in recent years due to a wide range of applications, e.g., biological[1] or even mechanochromic[2] ones. At the same time, the pyrimidine ring, having a highly π-deficient character, is involved in many π-conjugated push-pull structures,[3] which form the basis for new materials for optical and optoelectronic applications. Pyrimidine-based push-pull molecules have been used as OLED basic components,[4] sensors,[5] liquid crystals[6] and dyes for organic solar cells.[7] In this context, azolo-annulated pyrimidines, including the TAP ring system, can also be regarded as promising subunits for the design of novel push-pull structures.

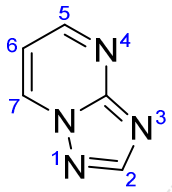


Figure 1. [1,2,4]Triazolo[1,5-a]pyrimidine (TAP) structure

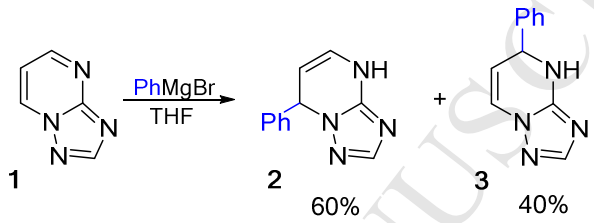
Generally, functional TAP derivatives are obtained either through annulation of a [1,2,4]triazole fragment to a pyrimidine ring, or by condensation of 3-amino-[1,2,4]triazoles with a variety of 1,3-dielectrophilic reagents, e.g., 1,3-dicarbonyl compounds and vinyl ketones.[8] The most common approach to 5,7-disubstituted-TAP synthesis is the reaction of 3-amino-[1,2,4]triazoles with chalcones,[9] however, this approach has a number of shortcomings: long reaction times up to three weeks at ambient temperature, or harsh reaction conditions, such as 120 °C for 24 hours, and a large percentage of various by-products.[10]

On the other hand, substituted TAPs can be synthesized through structural modification of the TAP core. Due to the electron-deficient character of TAP compounds, one main approach to modify their structures is based on the nucleophilic displacement of halogen (Cl, Br or I) atoms at the C-5 or C-7 position with *N*- , *C*- and *O*-nucleophiles.[11] However, there are only a few examples of the direct C-H functionalization of TAP.[12] To the best of our knowledge, no reports on the C-H functionalization of TAPs *via* nucleophilic aromatic substitution of hydrogen (S_N^H),[13] with the use of organomagnesium compounds as nucleophilic species are available in the literature. In this paper we wish to present a fast and simple way for (hetero)arylation of TAPs at the C-7 and C-5 positions using Grignard reagents.

2. Results and discussion

2.1 Synthesis

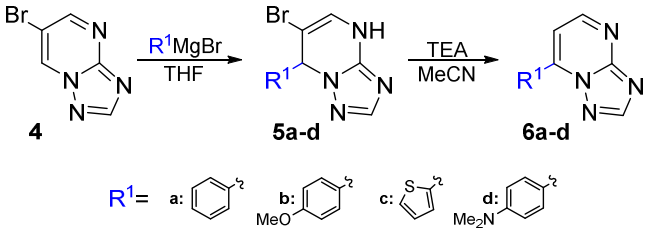
Taking into account the profound tendency of azaaromatic triazolopyrimidines to undergo nucleophilic additions, we have suggested using Grignard reagents for the direct functionalization of TAPs. The reaction of the parent TAP **1** with phenylmagnesium bromide proceeded smoothly in THF, but resulted in the formation of two isomeric adducts at both the C-7 and C-5 positions in the ratio 1.5:1, respectively, according to ^{1}H NMR spectroscopy and GC-MS data (Scheme 1).



Scheme 1. Unselective addition of phenylmagnesium bromide to TAP **1**.

We have failed to achieve the regioselectivity of phenylmagnesium bromide addition under various reaction conditions. Therefore, we have chosen 6-bromo-[1,2,4]triazolo[1,5-*a*]pyrimidine **4** (6-bromo-TAP) for further research, assuming that the C-6 bromine will increase the electrophilicity of the C-7 position. The increase is indirectly indicated by chemical shifts of H-7 in ^{1}H NMR spectra of TAP (9.43 ppm)[14] and 6-bromo-TAP (9.91 ppm).[15] In addition, this bromo-compound can easily be obtained by the direct bromination of TAP **1**.[16]

Indeed, 6-bromo-TAP **4** has reacted with Grignard reagents selectively at the C-7 position giving σ^{H}-adducts **5a-d** (Scheme 2), as evidenced by ^{1}H, ^{13}C NMR spectroscopy and X-ray diffraction analysis (Figure 2). However, the observed regioselectivity was only reached at – 78 °C.



Scheme 2. Selective addition of Grignard reagents at C-7 of TAP **4** followed by aromatization of the C-7 adducts.

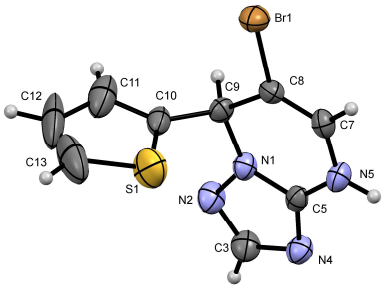
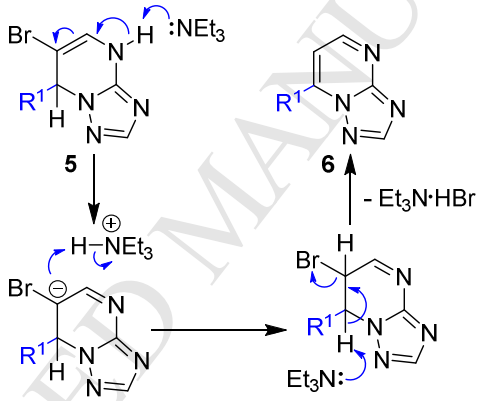


Figure 2. ORTEP diagram for the X-ray structure of **5c**.
Thermal ellipsoids of 50% probability are shown.

The σ^H-adducts **5a-d** transformed into aromatic compounds **6a-d** on treatment with triethylamine (TEA) (Scheme 2). A plausible mechanism involves hydrogen transfer from the N-4 position to C-6 by the imino-enamine tautomerism followed by 1,2-elemination of HBr (Scheme 3). Yields of compounds **5** and **6** are shown in Table 1.



Scheme 3. A possible mechanism for aromatization of σ^H-adducts **5** by action of TEA.

Table 1. Yields of σ^H-adducts **5** and S_N^H product **6** (Scheme 2).

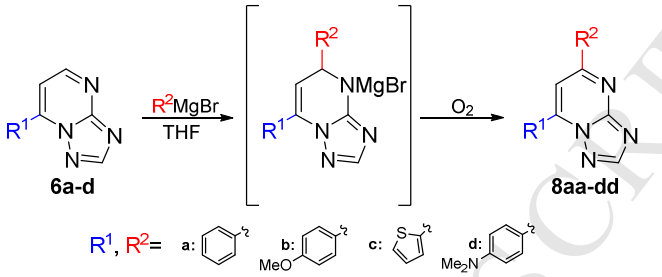
R^1	Entry	Yield (%)	Entry	Yield (%)
phenyl	**5a**	89	**6a**	71
4-methoxyphenyl	**5b**	74	**6b**	82
2-thienyl	**5c**	81	**6c**	85
4-(*N*,*N*-DMAP)[a]	**5d**	87	**6d**	77

[a] 4-(*N*,*N*-DMAP) is 4-(N,N-dimethylaminophenyl)

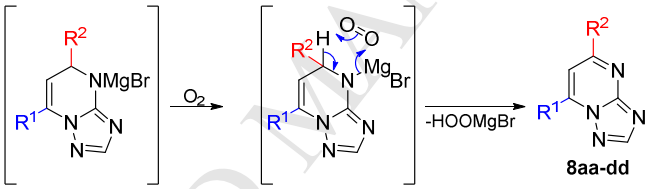
Compounds **6a-d** are susceptible to attack by a second Grignard reagent. The addition of organomagnesium nucleophiles to C-5 has afforded the σ^H-adducts, which have a tendency to undergo partial oxidation during the work-up and isolation procedure under air conditions. The reaction has resulted in the formation of a mixture of intermediate 4,5-dihydro-5,7-disubstituted-TAPs and aromatic products **8**.

We have suggested that the intermediate σ^H-adducts aromatize by the action of atmosphere oxygen in the form of the *N*-magnesium salts. To substantiate this assumption, we have carried

out experiments on the oxidation of *N*-magnesium salts with pure oxygen, and this hypothesis has proved to be correct (Scheme 4). The reaction appears to involve the formation of intermediate complexes of *N*-magnesium salts of dihydro-TAP with oxygen, which transform easily into aromatic compounds **8** (Scheme 5). The oxidation with pure oxygen has enabled us to obtain compounds **8** without any traces of dihydro-TAPs as impurities. Yields are shown in Table 2.



Scheme 4. One pot (het)arylation of TAP at the C-5 position using Grignard reagents.



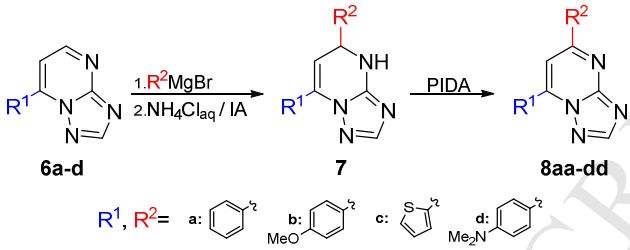
Scheme 5. A possible mechanism for oxidation of *N*-magnesium salts of σ^H-adducts with pure oxygen.

Table 2. Yields of compounds resulting from the second nucleophilic addition of a Grignard reagent followed by aromatization with pure oxygen (Scheme 4).

R^1	R^2	Entry	Yield (%)
phenyl	phenyl	**8aa**	86
phenyl	4-methoxyphenyl	**8ab**	64
phenyl	2-thienyl	**8ac**	53
phenyl	4-(*N*,*N*-DMAP)	**8ad**	70
4-methoxyphenyl	phenyl	**8ba**	65
4-methoxyphenyl	4-methoxyphenyl	**8bb**	67
4-methoxyphenyl	2-thienyl	**8bc**	41
4-methoxyphenyl	4-(*N*,*N*-DMAP)	**8bd**	51
2-thienyl	phenyl	**8ca**	64
2-thienyl	4-methoxyphenyl	**8cb**	85
2-thienyl	2-thienyl	**8cc**	73
2-thienyl	4-(*N*,*N*-DMAP)	**8cd**	60
4-(*N*,*N*-DMAP)	phenyl	**8da**	58
4-(*N*,*N*-DMAP)	4-(*N*,*N*-DMAP)	**8db**	49
4-(*N*,*N*-DMAP)	2-thienyl	**8dc**	46
4-(*N*,*N*-DMAP)	4-(*N*,*N*-DMAP)	**8dd**	40

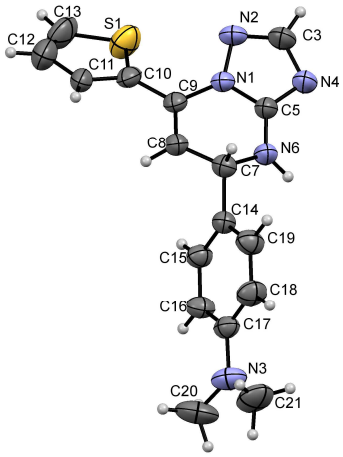
We have also used a similar approach to obtain pure 4,5-dihydro-TAP compounds **7**. The suggested method has involved neutralization of the *N*-magnesium salts through treatment of the reaction mixture with an aqueous solution of NH_4Cl under an inert atmosphere (IA) (Scheme 6).

By using this procedure, we have succeeded in obtaining intermediates **7aa**, **7ac**, **7ad**, **7ca**, **7cc**, **7cd** (Figure 3). The electron-donating character of the substituent R^1 plays a crucial role in stability of the σ^H-adducts **7**. Thus, we have been able to obtain and isolate only **7bc** in the series of 4,5-dihydro compounds, bearing such electron-donating substituents as 4-methoxyphenyl and 4-(*N*,*N*-dimethylaminophenyl groups at C-7.

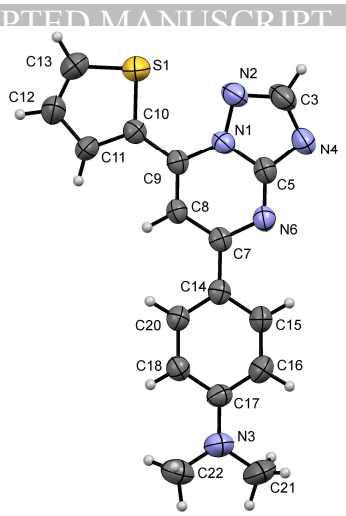


Scheme 6. Consecutive C-H Functionalization of TAP at C-5 by using Grignard reagents.

We have attempted to aromatize 4,5-dihydro derivatives **7** by using various oxidizing agents. However, the use of $Pb(OAc)_4$, $AgNO_3$, or $KMnO_4$ has resulted in rather complicated reaction mixtures, so we have failed to isolate any product. Neither $K_3[Fe(CN)_6]$, chloranil, nor DDQ reacted successfully with **7**, giving only starting materials. Treatment of **7** with perhydrol has given a significant amount of 6-hydroxylated products **8** according to GC-MS analysis. There are some literature examples of similar oxidations of adducts by the action of Br_2 or NBS, but this approach can not be applied in the case of 4-(*N*,*N*-dimethylaminophenyl) derivatives.[17]



Compound **7cd**



Compound **8cd**

Figure 3. The X-ray structure of 4,5-dihydro derivative **7cd** and its aromatic form **8cd**. Thermal ellipsoids of 50% probability are shown.

Finally, we have achieved good results in obtaining compounds **8** by using the hypervalent iodine compound - phenyliodonium diacetate (PIDA) (Scheme 6). In addition, the mixtures of dihydro-TAPs and aromatic compounds mentioned above have been treated with PIDA to afford pure aromatic compounds **8**. Yields are presented in Table 3. The oxidation procedure with PIDA can be regarded as an alternative synthetic route for the preparation of the target products **8**.

Table 3. Yields of adducts derived from the second addition of Grignard reagent followed by PIDA aromatization (Scheme 6).

R^1	R^2	Entry	Yield (%)	Entry	Yield (%)
phenyl	phenyl	**7aa**	71	**8aa**	79
phenyl	4-methoxyphenyl	**7ab**	-	**8ab**[a]	56
phenyl	2-thienyl	**7ac**	75	**8ac**	46
phenyl	4-(*N*,*N*-DMAP)	**7ad**	55	**8ad**	61
4-methoxyphenyl	phenyl	**7ba**	-	**8ba**[a]	58
4-methoxyphenyl	4-methoxyphenyl	**7bb**	-	**8bb**[a]	59
4-methoxyphenyl	2-thienyl	**7bc**	62	**8bc**	43
4-methoxyphenyl	4-(*N*,*N*-DMAP)	**7bd**	-	**8bd**[a]	47
2-thienyl	phenyl	**7ca**	46	**8ca**	56
2-thienyl	4-methoxyphenyl	**7cb**	-	**8cb**[a]	78
2-thienyl	2-thienyl	**7cc**	90	**8cc**	32
2-thienyl	4-(*N*,*N*-DMAP)	**7cd**	67	**8cd**	51
4-(*N*,*N*-DMAP)	phenyl	**7da**	-	**8da**[a]	48
4-(*N*,*N*-DMAP)	4-methoxyphenyl	**7db**	-	**8db**[a]	32
4-(*N*,*N*-DMAP)	2-thienyl	**7dc**	-	**8dc**[a]	35
4-(*N*,*N*-DMAP)	4-(*N*,*N*-DMAP)	**7dd**	-	**8dd**[a]	33

[a] Yields are based on compounds **6**.

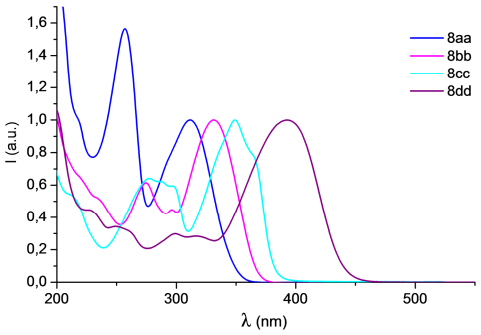
2.2 Optical and electrochemical studies

The UV-visible absorption and photoluminescence spectra of compounds **8** have been recorded at ambient temperature in acetonitrile solution ($2 \times 10^{-5} \mathrm{mol} \cdot \mathrm{L}^{-1}$), and the obtained results are summarized in Table 4 (also see Supplementary Data). Spectra of derivatives **8aa**, **8bb**, **8cc** and **8dd** are depicted in Figure 4.

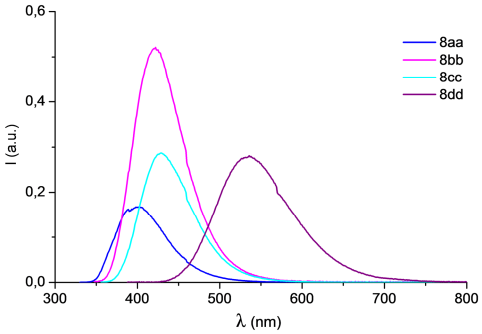
Compounds **8aa-dd** exhibit a very strong light absorption in violet and near UV regions of the spectrum. Compound **8aa** shows the most short-wave absorption band and fluorescence maximum in the visible spectral region (the blue light), but its relative fluorescence quantum yield is only 17%. The presence of the 4-methoxyphenyl substitutes in **8bb** provides the bathochromic shift of the absorption band, as well as the tiny bathofluoric shift of fluorescence due to the donor-acceptor interaction of the methoxy-group with the TAP ring system, the quantum yield also increases up to 52%. On the other hand, substantial bathochromic and bathofluoric effects are observed in the presence of the most electron-donating 4-(*N*,*N*-dimethylaminophenyl) substituent (**8dd**), however, the quantum yield is enhanced insignificantly, as comparing with **8bb**. The spectrum maxima of 2-thienyl-substituted compounds **8cc** are shifted bathochromically and bathofluorically relative to **8aa,** but their shifts are smaller than for **8dd** (Figure 3). The quantum yield of **8cc** is at the level of **8dd**.

Having studied compounds bearing various combinations of substituents, we have revealed some interesting optical effects. The compound **8cd** has the lowest quantum yield (2%), the largest Stokes shift and shows the greatest bathochromic and bathofluoric shifts. On the contrary, compound **8ba** has the highest quantum yield (55%), but one of the lowest Stokes shifts, small bathochromic and insignificant bathofluoric shifts. This pattern has possibly been observed because of an increase in the probability of nonradiating transitions.

The luminescence of compounds varies from blue (**8aa**, **8ab**, **8ac**, **8ba**, **8bb**, **8bc**, **8ca**, **8cb**, **8cc**) to green (**8bd**, **8da**, **8dc**, **8dd**) and orange (**8ad**, **8cd**). Compounds **8aa, 8bb, 8ca** may be good UV dyes with extinction coefficient $\varepsilon > 30000$, and compounds **8cd** and **8da-dd** may be used as dyes in the visible part of spectra.



(a)



(b)

Figure 4. UV-visible absorption (a) and emission (b) spectra of some 5,7-disubstituted TAPs in acetonitrile after normalization. Intensity of emission spectra is based on relative quantum yields.

Cyclic voltammetry (CV) measurements of compounds **8aa-dd** have been performed to study the electrochemical properties of compounds **8aa-dd**. All CV experiments were carried out in anhydrous acetonitrile at a concentration of ($1 \times 10^{-3}\text{mol} \cdot \text{L}^{-1}$) for the examined substances and tetrabutylammonium perchlorate (0.1 M) as the supporting electrolyte under an argon atmosphere. Reduction potentials have been out of the scan range in the current CV experiments. Compounds **8** containing only phenyl-, thienyl- and 4-methoxyphenyl- substitutes show two oxidation waves, while derivatives bearing a 4-(*N*,*N*-dimethylaminophenyl)- groups have more complicated curves and the least onset potentials ($E_{\text{ox}}^{\text{onset}}$) of the first oxidation peaks. The HOMO energy levels (E_{HOMO}) of these TAPs have been estimated from $E_{\text{ox}}^{\text{onset}}$ of the first oxidation peaks by the empirical equation: $E_{\text{HOMO}} = -\left[E_{\text{ox}}^{\text{onset}} - E_{1/2}(\text{Fc}/\text{Fc}^{+}) + 5.1\right]$. We have used a $+5.10$ eV value in the Fermi scale for the formal potential of the Fc/Fc^{+} redox couple instead of $+4.8$ eV in accordance with a recent discussion of Bazan et al.[18] The LUMO energy levels (E_{LUMO}) of these compounds have been calculated from their HOMO energy levels

(E_{HOMO}) and the optical band gaps ($E_{\mathrm{g}}^{\mathrm{opt}}$) using equation: $E_{\mathrm{LUMO}} = E_{\mathrm{HOMO}} + E_{\mathrm{g}}^{\mathrm{opt}}$. The obtained electrochemical data as well as the HOMO/LUMO energy levels are listed in Table 4.

For more information about the optical and electrochemical studies, see Supplementary Data.

Table 4. The optical and electrochemical properties of TAP-cored compounds **8**.

Compound	$^{abs}\lambda_{max}$ [a](nm)	$^{em}\lambda_{max}$ [a](nm)	E_{ox}^{onset} (V)	E_{HOMO} (eV)	E_{LUMO} (eV)	E_g^{opt} (eV)	Φ[b](%)	ε ($L \cdot cm^{-1} \cdot mol^{-1}$)
8aa	312	401	1.55	-6.55	-3.17	3.38	17	19646
8ab	324	435	1.35	-6.35	-3.35	3.00	39	23328
8ac	331	422	1.40	-6.40	-3.37	3.03	18	21665
8ad	389	582	0.56	-5.56	-3.00	2.56	3	23355
8ba	321	404	0.71	-5.71	-2.63	3.08	55	19137
8bb	332	421	1.29	-6.29	-3.15	3.14	52	34700
8bc	338	410	1.32	-6.32	-3.32	3.00	28	29729
8bd	387	556	0.51	-5.51	-2.94	2.57	15	25600
8ca	339	397	1.38	-6.38	-3.32	3.06	21	26903
8cb	345	450	1.25	-6.25	-3.28	2.97	37	29855
8cc	349	429	1.38	-6.38	-3.51	2.87	29	29731
8cd	400	602	0.49	-5.49	-3.07	2.42	2	20683
8da	394	518	0.53	-5.53	-2.96	2.57	33	26863
8db	390	499	0.49	-5.49	-2.95	2.54	52	29230
8dc	399	534	0.53	-5.53	-3.05	2.48	23	25147
8dd	393	535	0.44	-5.44	-2.92	2.52	28	44436

3. Conclusion

In conclusion, we have developed an elegant method for the direct (het)arylation of TAPs *via* the nucleophilic aromatic substitution of hydrogen (S_N^H) using Grignard reagents as nucleophiles. A variety of 7-(het)aryl- and 5,7-di(het)aryl-substituted TAPs have been prepared in two or three steps from readily available 6-bromo-TAP. The first addition of (het)arylmagnesium bromide to this bicyclic system followed by aromatization provided 7-substituted derivatives in 71-85 % yields. The second addition of a Grignard reagent with successive oxidation of the obtained σ^H-adducts in the form of the *N*-magnesium salts by pure oxygen has afforded 5,7-disubstituted-TAP derivatives in 41-86 % yields *via* the one pot procedure. Physicochemical measurements have been performed for the obtained series of 5,7-di(het)aryl-substituted TAPs to estimate their optical and redox properties. Some derivatives have appeared to be good dyes in the UV or visible regions.

The described approach allows access to a wide range of novel TAPs, thus designing new useful compounds for material science applications.

4. Experimental

All reagents and solvents were purchased from commercial sources and dried by using standard procedures before use. [1,2,4]Triazolo[1,5-a]pyrimidine 1, 6-bromo[1,2,4]triazolo[1,5-a]pyrimidine and phenyliodinium diacetate were prepared according to the earlier reported procedures.[19] Melting points were determined on Boetius combined heating stages and are

uncorrected. Elemental analysis was carried on a Eurovector EA 3000 automated analyzer. ^{1}H and ^{13}C NMR spectra were recorded on AVANCE-400 and AVANCE-500 instruments in DMSO-d_6 or $CDCl_3$ with TMS as an internal standard. The GC-MS analysis of all samples was carried out using an Agilent GC 7890A MS 5975C Inert XL EI/CI GC-MS spectrometer with a quadrupole mass-spectrometric detector with electron ionization (70 eV), and scan over the total ionic current in the range m/z 20÷1000 and a quartz capillary column HP-5MS (30 m×0.25 mm, film thickness 0.25 mm). Column chromatography was carried out using Alfa Aesar silica gel 0.040–0.063 mm (230–400 mesh), eluting with ethyl acetate – hexane (1:1) or ethyl acetate containing 0.5% of triethylamine. The progress of the reactions and the purity of compounds were checked by TLC on Sorbfil plates (Russia), in which the spots were visualized with UV light (λ 254 or 365 nm). X-ray diffraction analysis was performed on an automated X-ray diffractometer "Xcalibur E" on standard procedure.

Optical spectra were obtained using a Shimadzu UV-2600 double-beam UV-Vis spectrophotometer, a Varian Cary Eclipse fluorescence spectrophotometer and a Hêllma QS-101 high precision quartz cell in acetonitrile solution. Solutions of compounds with 4-(N,N-dimethylaminophenyl) substituents were made with the addition of Me_4NOH base. Bi-quinine sulfate was used as the standard for relative quantum yield measuring.[20] Cyclic voltammetry was carried out on a Metrohm Autolab PGSTAT128N potentiostat with a standard three-electrode configuration. Typically, a three electrode cell equipped with a platinum working electrode, a $Ag/AgNO_3$ (0.01M) reference electrode, and a glass carbon rod counter electrode was employed. The measurements were done in anhydrous acetonitrile with tetrabutylammonium perchlorate (0.1 M) as the supporting electrolyte under an argon atmosphere at a scan rate of 100 mV/s. The potential of the $Ag/AgNO_3$ reference electrode was calibrated using the ferrocene/ferrocenium redox couple (Fc/Fc^+).

1. General procedure for the synthesis of 6-bromo-7-substituted-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidines.

Magnesium powder (36 mg, 1.5 mmol) was immersed in abs. THF (10 ml) under argon or nitrogen, and the appropriate bromo(het)arene (1.5 mmol) was added. The reaction mixture was stirred at room temperature until formation of a clear solution, cooled to – 78 °C and charged with 6-bromo-[1,2,4]triazolo[1,5-*a*]pyrimidine (**4**) (200 mg, 1 mmol). After 1 hour the bath temperature was elevated to 50 °C. Two hours later the flask was cooled, and cold water (3 ml) and ammonium chloride (107 mg, 2 mmol) were added to the reaction mixture. After that, the

solvent was distilled off *in vacuo*, the precipitate was filtered off, washed with cold water and ethyl acetate, dried and recrystallized from isopropanol or acetonitrile to give compounds **5a-d**.

*1.1 6-Bromo-7-phenyl-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine (**5a**).*

Yield: 246 mg (89 %); white solid; m.p. 161-163 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.16 (d, J = 4.9 Hz, 1H, NH), 7.57 (s, 1H, N=CH-N), 7.42 – 7.30 (m, 3H, Ph), 7.28 – 7.22 (m, 2H, Ph), 6.97 (dd, J = 5.0, 0.8 Hz, 1H, HN-CH=C), 6.14 (d, J = 0.8 Hz, 1H, CH-N). ^{13}C NMR (126 MHz, DMSO-d6) δ 149.9, 147.4, 139.2, 128.6, 128.5, 127.6, 125.8, 92.3, 64.9; Anal. Calcd for $C_{11}H_9BrN_4$ (277.13): C, 47.68; H, 3.27; N, 20.22 Found: C, 47.79; H, 3.34; N, 20.19

*1.2 6-Bromo-7-(4-methoxyphenyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine (**5b**).*

Yield: 227 mg (74 %); white solid; m.p. 160-162 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.13 (s, 1H, NH), 7.56 (s, 1H, N=CH-N), 7.21 – 7.14 (m, 2H, CH=C-CH), 6.95 (s, 1H, HN-CH=C), 6.94 – 6.89 (m, 2H, CH-C(OMe)=CH), 6.08 (s, 1H, CH-N), 3.74 (s, 3H, OMe). ^{13}C NMR (126 MHz, DMSO-d_6) δ 159.4, 149.7, 147.3, 131.3, 128.8, 125.6, 113.9, 92.6, 64.4, 55.1; Anal. Calcd for $C_{12}H_{11}BrN_4O$ (307.15): C, 46.93; H, 3.61; N, 18.24 Found: C, 46.97; H, 3.59; N, 18.19

*1.3 6-Bromo-7-(2-thienyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine (**5c**).*

Yield: 229 mg (81 %); light brown solid; m.p. 156-157 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.26 (s, 1H, NH), 7.62 (s, 1H, N=CH-N), 7.54 (d, J = 5.2 Hz, 1H, CH=CH-S), 7.20 (d, J = 3.6 Hz, 1H, C=CH-CH), 7.03 – 6.96 (m, 2H, CH=CH-S, HN-CH=C), 6.52 (s, 1H, CH-N). ^{13}C NMR (126 MHz, DMSO-d_6) δ 149.9, 146.9, 142.9, 127.8, 127.2, 126.7, 125.9, 91.7, 60.1; Anal. Calcd for $C_9H_7BrN_4S$ (283.15): C, 38.18; H, 2.49; N, 19.79 Found: C, 38.25; H, 2.41; N, 19.71

*1.4 6-Bromo-7-(4-(N,N-dimethylaminophenyl))-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine (**5d**).*

Yield: 278 mg (87 %); light yellow solid; m.p. 166-167 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.06 (s, 1H, NH), 7.54 (s, 1H, N=CH-N), 7.05 (d, J = 8.1 Hz, 2H, CH=C-CH), 6.92 (d, J = 4.4 Hz, 1H, HN-CH=C), 6.67 (d, J = 8.3 Hz, 2H, CH-C(NMe_2)=CH), 5.97 (s, 1H, CH-N), 2.88 (s, 6H, NMe_2). ^{13}C NMR (126 MHz, DMSO-d_6) δ 150.4, 149.6, 147.2, 128.3, 126.5, 125.4, 112.0, 93.2, 64.6, 39.6; Anal. Calcd for $C_{13}H_{14}BrN_5$ (320.19): C, 48.77; H, 4.41; N, 21.87 Found: C, 48.82; H, 4.46; N, 21.80

2. General procedure for the synthesis of 7-substituted [1,2,4]triazolo[1,5-a]pyrimidines.

The relevant 6-bromo-7-substituted 4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidine **5a-d** (1 mmol) and triethylamine (TEA) (0.216 ml, 1.5 mmol) were immersed in acetonitrile and refluxed until the initial substance completely disappeared (the reaction progress was monitored by TLC).
The reaction mixture was diluted with water, cooled, then the precipitate was filtered off, washed with water, dried and recrystallized from isopropanol to afford the desired products **6a-d**.

*2.1 7-Phenyl-[1,2,4]triazolo[1,5-a]pyrimidine (**6a**).*

Yield: 139 mg (71 %); white solid; m.p. 140-141 °C (lit. 146 °C);[21] ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.96 (d, *J* = 4.6 Hz, 1H, N=C<u>H</u>-CH), 8.74 (s, 1H, N=C<u>H</u>-N), 8.24 – 8.17 (m, 2H, Ph), 7.71 – 7.61 (m, 4H, Ph, N=CH-C<u>H</u>). ^{13}C NMR (126 MHz, DMSO-d_6) δ 155.7, 155.5, 155.0, 147.3, 131.7, 129.6, 129.5, 128.7, 109.7; Anal. Calcd for $C_{11}H_8N_4$ (196.21): C, 67.34; H, 4.11; N, 28.55 Found: C, 67.41; H, 4.16; N, 28.46

*2.2 7-(4-Methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**6b**).*

Yield: 185 mg (82 %); white solid; m.p. 194-195 °C (lit. 197-198 °C);[21] ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, *J* = 4.7 Hz, 1H, N=C<u>H</u>-CH), 8.73 (s, 1H, N=C<u>H</u>-N), 8.32 – 8.25 (m, 2H, C<u>H</u>=C-C<u>H</u>), 7.61 (d, *J* = 4.7 Hz, 1H, N=CH-C<u>H</u>), 7.24 – 7.17 (m, 2H, C<u>H</u>-C(OMe)=C<u>H</u>), 3.89 (s, 3H, OMe). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.0, 155.9, 155.4, 154.7, 147.0, 131.5, 121.5, 114.2, 108.6, 55.6; Anal. Calcd for $C_{12}H_{10}N_4O$ (226.24): C, 63.71; H, 4.46; N, 24.76 Found: C, 63.65; H, 4.43; N, 24.82

*2.3 7-(2-Thienyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**6c**).*

Yield: 172 mg (85 %); off-white solid; m.p. 179-180 °C (lit. 209-211 °C);[22] ^{1}H NMR (500 MHz, DMSO-*d6*) δ 8.90 (d, *J* = 4.9 Hz, 1H, N=C<u>H</u>-CH), 8.84 (s, 1H, N=C<u>H</u>-N), 8.59 (dd, *J* = 3.9, 1.2 Hz, 1H, C=C<u>H</u>-CH), 8.21 (dd, *J* = 5.0, 1.2 Hz, 1H, CH=C<u>H</u>-S), 8.00 (d, *J* = 4.9 Hz, 1H, N=CH-C<u>H</u>), 7.44 (dd, *J* = 5.0, 3.9 Hz, 1H, C<u>H</u>=CH-S). ^{13}C NMR (126 MHz, DMSO-*d6*) δ 155.5, 155.4, 154.3, 141.1, 135.5, 133.1, 129.7, 128.3, 106.0; Anal. Calcd for $C_9H_6N_4S$ (202.23): C, 53.45; H, 2.99; N, 27.70 Found: C, 53.53; H, 3.05; N, 27.63

*2.4 7-(4-(N,N-dimethylaminophenyl))-[1,2,4]triazolo[1,5-a]pyrimidine (**6d**).*

Yield: 184 mg (77 %); yellow solid; m.p. 209-211 °C (lit. 198-200 °C);[23] ^{1}H NMR (500 MHz, DMSO-*d6*) δ 8.78 (d, *J* = 4.9 Hz, 1H, N=C<u>H</u>-CH), 8.69 (s, 1H, N=C<u>H</u>-N), 8.35 – 8.28 (m, 2H, C<u>H</u>=C-C<u>H</u>), 7.57 (d, *J* = 4.9 Hz, 1H, N=CH-C<u>H</u>), 6.91 – 6.88 (m, 2H, C<u>H</u>-C(NMe_2)=C<u>H</u>), 3.07 (s, 6H, NMe_2). ^{13}C NMR (126 MHz, DMSO-*d6*) δ 156.1, 155.2, 154.1, 152.3, 147.4, 131.0,

115.1, 111.2, 106.7, 39.6; Anal. Calcd for $C_{13}H_{13}N_5$ (239.28): C, 65.25; H, 5.48; N, 29.27 Found: C, 65.33; H, 5.45; N, 29.24

3. General procedure for the synthesis of 5,7-disubstituted 4,5-dihydro[1,2,4]triazolo[1,5-a]pyrimidines.

Grignard reagent solution was prepared from magnesium powder (36 mg, 1.5 mmol) and the appropriate bromo(het)arene (1.5 mmol) in THF (10 ml). It was cooled to – 78 °C and the corresponding 7-substituted-TAP **6 (**1 mmol) was added. After 1 hour the bath temperature was elevated to 50 °C, and the reaction mixture was stirred for an additional 2 hours. When the reaction was completed, the flask was cooled, and the reaction mixture was charged with cold water (2-3 ml) and ammonium chloride (107 mg, 2 mmol) under an inert atmosphere. Next the THF was distilled off *in vacuo*, the residue was filtered off, washed with cold water, dried and recrystallized from acetonitrile.

*3.1 5,7-Diphenyl-4,5-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine (**7aa**).*

Yield: 195 mg (71 %); white crystals; m.p. 177-178 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.18 (t, *J* = 2.0 Hz, 1H, NH), 7.66 – 7.58 (m, 2H, Ph), 7.53 (s, 1H, N=CH-N), 7.45 – 7.35 (m, 7H, Ph), 7.36 – 7.27 (m, 1H, Ph), 5.52 (dd, *J* = 5.0, 1.7 Hz, 1H, NH-CH-CH), 5.46 (dd, *J* = 5.0, 2.0 Hz, 1H, NH-CH-CH). ^{13}C NMR (126 MHz, DMSO-d_6) δ 153.4, 149.3, 143.6, 134.4, 131.8, 129.0, 128.7, 128.3, 128.0, 127.7, 126.2, 107.8, 54.1. Anal. Calcd for $C_{17}H_{14}N_4$ (274.33): C, 74.43; H, 5.14; N, 20.42 Found: C, 74.23; H, 5.16; N, 20.63

*3.2 7-Phenyl-5-(2-thienyl)-4,5-dihydro-[1,2,4]triazolo[1,5-a] pyrimidine (**7ac**).*

Yield: 210 mg (75 %); pale brown crystalls; m.p. 169-170 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.36 (t, *J* = 2.0 Hz, 1H, NH), 7.66 – 7.59 (m, 2H, Ph), 7.55 (s, 1H, N=CH-N), 7.47 (dd, *J* = 5.0, 1.3 Hz, 1H, CH=CH-S), 7.46 – 7.40 (m, 3H, Ph), 7.08 (dt, *J* = 3.4, 0.9 Hz, 1H, C=CH-CH), 7.02 (dd, *J* = 5.0, 3.5 Hz, 1H, CH=CH-S), 5.71 (dd, *J* = 5.3, 2.1 Hz, 1H, NH-CH-CH), 5.60 (dd, *J* = 5.2, 1.7 Hz, 1H, NH-CH-CH). ^{13}C NMR (126 MHz, DMSO-d_6) δ 152.9, 149.4, 147.7, 134.8, 131.7, 129.2, 128.4, 128.1, 127.1, 125.8, 124.3, 107.2, 49.4. Anal. Calcd for $C_{15}H_{12}N_4S$ (280.35): C, 64.26; H, 4.31; N, 19.99; S, 11.44 Found: C, 64.20; H, 4.35; N, 20.03; S, 11.20

*3.3 7-Phenyl-5-(4-(N,N-dimethylaminophenyl))-4,5-dihydro-[1,2,4]triazolo[1,5-a] pyrimidine (**7ad**).*

Yield: 96 mg (55 %); lustrous yellow solid; m.p. 180-182 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.00 (d, *J* = 2.0 Hz, 1H, NH), 7.61 (ddd, *J* = 6.9, 3.9, 2.1 Hz, 2H, Ph), 7.50 (s, 1H, N=CH-N), 7.42 (dt, *J* = 4.4, 1.2 Hz, 3H, Ph), 7.19 – 7.12 (m, 2H, CH=C-CH), 6.76 – 6.68 (m, 2H, CH-C(NMe_2)=CH), 5.44 (dd, *J* = 5.0, 1.7 Hz, 1H, NH-CH-CH), 5.30 (dd, *J* = 4.9, 1.8 Hz, 1H, NH-CH-CH), 2.87 (s, 6H, NMe_2). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.7, 156.0, 155.4, 152.3, 146.6, 131.3, 130.2, 129.7, 129.1, 128.5, 122.7, 111.6, 105.6, 39.2; Anal. Calcd for $C_{19}H_{19}N_5$ (317.40): C, 71.90; H, 6.03; N, 22.07 Found: C, 71.83; H, 5.97; N, 22.15

*3.4 7-(4-Methoxyphenyl)-5-(2-thienyl)-4,5-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine (**7bc**).*

Yield: 191 mg (62 %); light brown solid; m.p. 147-148 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.31 (t, *J* = 2.0 Hz, 1H, NH), 7.62 – 7.51 (m, 2H, CH=C-CH), 7.54 (s, 1H, N=CH-N), 7.46 (dd, *J* = 5.0, 1.3 Hz, 1H, CH=CH-S), 7.10 – 7.03 (m, 1H, C=CH-CH), 7.05 – 6.95 (m, 3H, CH-C(OMe)=CH, CH=CH-S), 5.67 (dd, *J* = 5.2, 2.1 Hz, 1H, NH-CH-CH), 5.51 (dd, *J* = 5.2, 1.7 Hz, 1H, NH-CH-CH), 3.80 (s, 3H, OMe). ^{13}C NMR (126 MHz, DMSO-d_6) δ 159.9, 152.9, 149.3, 147.9, 134.5, 129.8, 127.1, 125.7, 124.3, 124.0, 113.5, 105.9, 55.2, 49.3; Anal. Calcd for $C_{16}H_{14}N_4OS$ (310.38): C, 61.92; H, 4.55; N, 18.05 Found: C, 61.86; H, 4.57; N, 18.12

3.5 *7-(2-Thienyl)-5-phenyl-4,5-dihydro-[1,2,4]triazolo[1,5-a] pyrimidine (**7ca**).*

Yield: 129 mg (46 %); light brown crystalls; m.p. 176-178 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.26 (t, *J* = 2.0 Hz, 1H, NH), 7.73 (dd, *J* = 3.8, 1.2 Hz, 1H, C=CH-CH), 7.64 (dd, *J* = 5.1, 1.2 Hz, 1H, CH=CH-S), 7.62 (s, 1H, N=CH-N), 7.43 – 7.34 (m, 4H, Ph), 7.33 – 7.27 (m, 1H, Ph), 7.11 (dd, *J* = 5.1, 3.7 Hz, 1H, CH=CH-S), 5.76 (dd, *J* = 5.2, 1.7 Hz, 1H, NH-CH-CH), 5.48 (dd, *J* = 5.1, 2.0 Hz, 1H, NH-CH-CH). ^{13}C NMR (126 MHz, DMSO-d_6) δ 153.3, 149.4, 143.5, 132.5, 128.8, 128.5, 128.0, 127.9, 127.8, 127.2, 126.1, 105.6, 54.2. Anal. Calcd for $C_{15}H_{12}N_4S$ (280.35): C, 64.26; H, 4.31; N, 19.99; S, 11.44 Found: C, 64.19; H, 4.37; N, 20.04; S, 11.17

*3.6 5,7-Di(2-thienyl)-4,5-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine (**7cc**).*

Yield: 257 mg (90 %); off-white solid; m.p. 204-206 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.44 (s, 1H, NH), 7.75 (d, *J* = 3.7 Hz, 1H, C=CH-CH), 7.67 (d, *J* = 5.1 Hz, 1H, CH=CH-S), 7.63 (s, 1H, N=CH-N), 7.47 (d, *J* = 5.0 Hz, 1H, CH=CH-S), 7.13 (t, *J* = 4.4 Hz, 1H, CH=CH-S), 7.06 (d, *J* = 3.5 Hz, 1H, C=CH-CH), 7.01 (t, *J* = 4.4 Hz, 1H, CH=CH-S), 5.83 (d, *J* = 5.3 Hz, 1H, NH-CH-CH), 5.73 (d, *J* = 5.5 Hz, 1H, NH-CH-CH). ^{13}C NMR (126 MHz, DMSO-d_6) δ 152.8, 149.5, 147.5, 132.3, 129.0, 128.3, 128.2, 127.3, 127.1, 125.8, 124.3, 105.0, 49.5; Anal. Calcd for $C_{13}H_{10}N_4S_2$ (286.37): C, 54.52; H, 3.52; N, 19.56 Found: C, 54.44; H, 3.48; N, 19.60

*3.7 7-(2-Thienyl)-5-(4-(N,N-dimethylaminophenyl))-4,5-dihydro-[1,2,4]triazolo[1,5-a]pyrimi-dine (**7cd**).*

Yield: 216 mg (67 %); dark yellow crystals; m.p. 170-172 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.09 (s, 1H, NH), 7.72 (dd, *J* = 3.7, 1.2 Hz, 1H, C=CH-CH), 7.63 (dd, *J* = 5.1, 1.2 Hz, 1H, CH=CH-S), 7.58 (s, 1H, N=CH-N), 7.16 – 7.08 (m, 3H, CH=C-CH, CH=CH-S), 6.75 – 6.68 (m, 2H, CH-C(NMe$_2$)=CH), 5.68 (dd, *J* = 5.1, 1.7 Hz, 1H, NH-CH-CH), 5.31 (dd, *J* = 5.1, 1.8 Hz, 1H, NH-CH-CH), 2.86 (s, 6H, NMe$_2$). ^{13}C NMR (126 MHz, DMSO-d_6) δ 153.3, 150.2, 149.3, 132.8, 131.0, 128.1, 127.8, 127.7, 127.2, 127.0, 112.5, 106.1, 53.7, 40.1; Anal. Calcd for $C_{17}H_{17}N_5S$ (323.42): C, 63.13; H, 5.30; N, 21.65 Found: C, 63.18; H, 5.27; N, 21.61

4. General procedure for the synthesis of 5,7-disubstituted [1,2,4]triazolo[1,5-a]pyrimidines.

*General procedure **A***. Grignard reagent solution was prepared from magnesium powder (36 mg, 1.5 mmol) and the appropriate bromo(het)arene (1.5 mmol) in THF (10 ml). It was cooled to – 78 °C and the corresponding 7-substituted-TAP **6 (**1 mmol) was added. After 1 hour the bath temperature was elevated to 50 °C, and the reaction mixture was stirred for another 2 hours. Then the oxygen atmosphere was created and kept for 2 hours. When the reaction was completed, the flask was cooled, and the reaction mixture was charged with cold water (2-3 ml) and ammonium chloride (107 mg, 2 mmol). The THF was then distilled off *in vacuo*, the residue was filtered off, washed with cold water and hexane, dried and recrystallized from isopropanol, acetonitrile or ethyl acetate – hexane (1:1) to afford the desired products **8aa-dd**.

*General procedure **B***. The 5,7-substituted 4,5-dihydro-TAP (**7aa-dd**) (1 mmol) and phenyliodinium diacetate (PIDA) (0.320 g, 1 mmol) were immersed in acetonitrile and gently stirred at room temperature for 6 hours until the starting material had disappeared (the reaction progress was checked by TLC). Then the residue was purified by flash column chromatography eluting with either ethyl acetate, or ethyl acetate – hexane (1:1) or ethyl acetate containing 0.5% of trimethylamine and after that recrystallized from isopropanol, acetonitrile or ethyl acetate – hexane (1:1) to afford the desired products **8aa-dd**.

*4.1 5,7-Diphenyl-[1,2,4]triazolo[1,5-a]pyrimidine (**8aa**).*

Recrystallized from isopropanol. Yield: A. 234 mg (86 %) B. 215 mg (79%); off-white solid; m.p. 165-166 °C (lit. 151-152 °C);[24] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.72 (s, 1H, N=C-CH), 8.46 – 8.37 (m, 2H, Ph), 8.34 – 8.26 (m, 2H, Ph), 8.17 (s, 1H, N=CH-N), 7.74 – 7.56 (m, 6H, Ph). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.6, 156.0, 155.8, 147.5, 136.1, 131.6, 131.3, 129.9,

129.8, 129.0, 128.5, 127.8, 106.8; Anal. Calcd for $C_{17}H_{12}N_4$ (272.31): C, 74.98; H, 4.44; N, 20.58 Found: C, 75.02; H, 4.40; N, 20.61

*4.2 7-Phenyl-5-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**8ab**).*

Purified by flash column chromatography eluting with ethyl acetate, recrystallized from ethyl acetate. Yield: A. 193 mg (64 %), B. 169 mg (56 %); pale yellow solid; m.p. 173-175 °C (lit. 166 °C);[25] ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.66 (s, 1H, N=C-C<u>H</u>), 8.43 – 8.36 (m, 2H, C<u>H</u>=C-C<u>H</u>), 8.31 – 8.24 (m, 2H, Ph), 8.10 (s, 1H, N=C<u>H</u>-N), 7.77 – 7.55 (m, 3H, Ph), 7.18 – 7.11 (m, 2H, C<u>H</u>-C(OMe)=C<u>H</u>), 3.88 (s, 3H, OMe). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.0, 155.8, 147.2, 131.5, 130.0, 129.8, 129.6, 128.5, 114.4, 106.2, 55.5; Anal. Calcd for $C_{18}H_{14}N_4O$ (302.34): C, 71.51; H, 4.67; N, 18.53 Found: C, 71.56; H, 4.63; N, 18.59

*4.3 7-Phenyl-5-(2-thienyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**8ac**).*

Purified by flash column chromatography eluting with ethyl acetate – hexane (1:1), recrystallized from ethyl acetate – hexane (1:1). Yield: A. 147 mg (53 %), B. 128 mg (46 %); off-white solid; m.p. 115-120 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.48 (s, 1H, N=C-C<u>H</u>), 8.13 – 8.05 (m, 2H, Ph), 7.88 (dd, *J* = 3.7, 1.2 Hz, 1H, C=C<u>H</u>-CH), 7.68 – 7.58 (m, 4H, Ph, CH=C<u>H</u>-S), 7.50 (s, 1H, N=C<u>H</u>-N), 7.19 (dd, *J* = 5.0, 3.8 Hz, 1H, C<u>H</u>=CH-S). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 156.5, 156.1, 147.9, 142.1, 131.8, 131.6, 130.0, 129.2, 128.9, 128.8, 128.5, 105.5, 77.2; Anal. Calcd for $C_{15}H_{10}N_4S$ (278.33): C, 64.73; H, 3.62; N, 20.13 Found: C, 64.69; H, 3.66; N, 20.17

*4.4 7-Phenyl-5-(4-(N,N-dimethylaminophenyl))-[1,2,4]triazolo[1,5-a]pyrimidine (**8ad**).*[22]

Purified by flash column chromatography eluting with ethyl acetate, recrystallized from acetonitrile. Yield: A. 220 mg (70 %), B. 192 mg (61 %); lustrous dark yellow crystals; m.p. 213-214 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 (s, 1H, N=C-C<u>H</u>), 8.31 – 8.26 (m, 2H, C<u>H</u>=C-C<u>H</u>), 8.25 – 8.21 (m, 2H, Ph), 7.98 (s, 1H, N=C<u>H</u>-N), 7.70 – 7.60 (m, 3H, Ph), 6.89 – 6.81 (m, 2H, C<u>H</u>-C(NMe_2)=C<u>H</u>), 3.05 (s, 6H, NMe_2). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.6, 155.8, 154.8, 152.0, 146.3, 130.9, 129.3, 128.9, 128.1, 122.8, 111.3, 105.3, 95.5, 39.6; Anal. Calcd for $C_{19}H_{17}N_5$ (315.38): C, 72.36; H, 5.43; N, 22.21 Found: C, 72.45; H, 5.41; N, 22.18

*4.5 7-(4-Methoxyphenyl)-5-phenyl-[1,2,4]triazolo[1,5-a]pyrimidine (**8ba**).*[26]

Purified by flash column chromatography eluting with ethyl acetate, recrystallized from isopropanol. Yield:A. 196 mg (65 %), B. 175 mg (58 %); white solid; m.p. 174-175 °C; ^{1}H NMR

(500 MHz, DMSO-d_6) δ 8.71 (s, 1H, N=C-CH), 8.44 – 8.35 (m, 4H, Ph, CH=C-CH), 8.12 (s, 1H, N=CH-N), 7.61 (tt, *J* = 3.3, 2.1 Hz, 3H, Ph), 7.24 – 7.17 (m, 2H, CH-C(OMe)=CH), 3.90 (s, 3H, OMe). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.9, 160.4, 155.95, 155.93, 147.2, 136.3, 131.7, 131.2, 128.9, 127.8, 121.8, 114.0, 105.7, 55.6; Anal. Calcd for $C_{18}H_{14}N_4O$ (302,34): C, 71.51; H, 4.67; N, 18.53 Found: C, 71.48; H, 4.71; N, 18.51

*4.6 5,7-Di(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**8bb**).*

Purified by flash column chromatography eluting with ethyl acetate and recrystallized from isopropanol. Yield: A. 222 mg (67 %), 196 mg (59 %); pale yellow solid; m.p. 183-184°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.65 (s, 1H, N=C-CH), 8.41 – 8.31 (m, 4H, CH=C-CH, CH=C-CH), 8.03 (s, 1H, N=CH-N), 7.23 – 7.16 (m, 2H, CH-C(OMe)=CH), 7.16 – 7.09 (m, 2H, CH-C(OMe)=CH), 3.90 (s, 3H, OMe), 3.87 (s, 3H, OMe).^{13}C NMR (126 MHz, DMSO-d_6) δ 161.9, 161.8, 160.0, 156.0, 155.7, 146.9, 131.7, 129.5, 128.6, 121.9, 114.3, 114.0, 105.1, 55.5, 55.4; Anal. Calcd for $C_{19}H_{16}N_4O_2$ (332.36): C, 68.66; H, 4.85; N, 16.86 Found: C, 68.67; H, 4.90; N, 16.88

*4.7 7-(4-Methoxyphenyl)-5-(2-thienyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**8bc**).*

Purified by flash column chromatography eluting with ethyl acetate – hexane (1:1), recrystallized from ethyl acetate – hexane (1:1). Yield: A. 126 mg (41 %), B. 132 mg (43 %); beige solid; m.p. 154-155 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.65 (s, 1H, N=C-CH), 8.37 – 8.29 (m, 3H, CH=C-CH, C=CH-CH), 8.10 (s, 1H, N=CH-N), 7.92 (dd, *J* = 5.0, 1.1 Hz, 1H, CH=CH-S), 7.30 (dd, *J* = 5.0, 3.7 Hz, 1H, CH=CH-S), 7.24 – 7.17 (m, 2H, CH-C(OMe)=CH), 3.90 (s, 3H, OMe). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.9, 155.9, 155.7, 155.6, 147.0, 142.2, 132.2, 131.7, 130.5, 129.0, 121.7, 114.0, 104.5, 55.6; Anal. Calcd for $C_{16}H_{12}N_4OS$ (308.36): C, 62.32; H, 3.92; N, 18.17 Found: C, 62.40; H, 3.95; N, 18.21

*4.8 7-(4-Methoxyphenyl)-5-(4-(N,N-dimethylaminophenyl))-[1,2,4]triazolo[1,5-a] pyrimidine (**8bd**).*

Purified by flash column chromatography eluting with ethyl acetate, recrystallized from a minimal amount of isopropanol. Yield: A. 176 mg (51 %), B. 162 mg (47 %); bright yellow solid; m.p. 174-175 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 (s, 1H, N=C-CH), 8.30 (d, *J* = 8.4 Hz, 2H, CH=C-CH), 8.23 (d, *J* = 8.5 Hz, 2H, CH=C-CH), 7.89 (s, 1H, N=CH-N), 7.17 (d, *J* = 8.4 Hz, 2H, CH-C(OMe)=CH), 6.80 (d, *J* = 8.6 Hz, 2H, CH-C(NMe_2)=CH), 3.89 (s, 3H, OMe), 3.03 (s, 6H, NMe_2). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.6, 160.5, 156.1, 155.3, 152.2,

146.2, 131.5, 129.0, 122.8, 122.1, 113.9, 111.5, 104.4, 55.5, 39.6; Anal. Calcd for $C_{20}H_{19}N_5O$ (345.41): C, 69.55; H, 5.54; N, 20.28 Found: C, 69.61; H, 5.52; N, 20.31

*4.9 7-(2-Thienyl)-5-phenyl-[1,2,4]triazolo[1,5-a]pyrimidine (**8ca**).*

Purified by flash column chromatography eluting with ethyl acetate, recrystallized from isopropanol. Yield: A. 178 mg (64 %), B. 156 mg (56 %); off-white solid; m.p. 180-183 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.84 – 8.79 (m, 2H, N=C-CH, C=CH-CH), 8.51 (s, 1H, N=CH-N), 8.42 (dd, *J* = 6.7, 3.0 Hz, 2H, Ph), 8.22 (dd, *J* = 5.0, 1.1 Hz, 1H, CH=CH-S), 7.62 (dd, *J* = 4.9, 1.9 Hz, 3H, Ph), 7.46 (dd, *J* = 5.0, 3.9 Hz, 1H, CH=CH-S). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.1, 155.9, 141.3, 136.3, 135.6, 133.3, 131.2, 130.0, 128.9, 128.1, 127.8, 102.9; Anal. Calcd for $C_{15}H_{10}N_4S$ (278.33): C, 64.73; H, 3.62; N, 20.13 Found: C, 64.66; H, 3.58; N, 20.20

*4.10 7-(2-Thienyl)-5-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**8cb**).*

Recrystallized from isopropanol. Yield: A. 262 mg (85 %), B. 240 mg (78 %); light yellow solid; m.p. 182-183°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.81 – 8.74 (m, 2H, N=C-CH, CH=CH-S), 8.44 (s, 1H, N=CH-N), 8.42 – 8.36 (m, 2H, CH=C-CH), 8.20 (dd, *J* = 5.0, 1.2 Hz, 1H, C=CH-CH), 7.46 (dd, *J* = 5.0, 3.9 Hz, 1H, CH=CH-S), 7.19 – 7.12 (m, 2H, CH-C(OMe)=CH), 3.89 (s, 3H, OMe). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.9, 159.8, 155.7, 155.6, 141.0, 135.3, 133.1, 130.1, 129.5, 128.5, 128.1, 114.3, 102.2, 55.4; Anal. Calcd for $C_{16}H_{12}N_4OS$ (308.36): C, 62.32; H, 3.92; N, 18.17 Found: C, 62.38; H, 3.93; N, 18.11

*4.11 5,7-Di(2-thienyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**8cc**).*

Purified by flash column chromatography eluting with ethyl acetate, recrystallized from isopropanol. Yield: A. 207 mg (73%), B. 91 mg (32 %); brown solid; m.p. 186-188 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.75 (s, 1H, N=C-CH), 8.74 (dd, *J* = 3.9, 1.2 Hz, 1H, C=CH-CH), 8.47 (s, 1H, N=CH-N), 8.39 (dd, *J* = 3.8, 1.1 Hz, 1H, C=CH-CH), 8.21 (dd, *J* = 5.0, 1.1 Hz, 1H, CH=CH-S), 7.92 (dd, *J* = 5.1, 1.0 Hz, 1H, CH=CH-S), 7.46 (dd, *J* = 5.0, 3.9 Hz, 1H, CH=CH-S), 7.33 (dd, *J* = 5.0, 3.8 Hz, 1H, CH=CH-S). ^{13}C NMR (126 MHz, DMSO-d_6) δ 155.64, 155.61, 155.2, 142.2, 141.1, 135.6, 133.2, 132.2, 130.3, 129.8, 128.9, 128.1, 101.7; Anal. Calcd for $C_{13}H_8N_4S_2$ (284.36): C, 54.91; H, 2.84; N, 19.70 Found: C, 54.94; H, 2.79; N, 19.72

*4.12 7-(2-Thienyl)-5-(4-(N,N-dimethylaminophenyl))-[1,2,4]triazolo[1,5-a]pyrimidine (**8cd**).*

Purified by flash column chromatography eluting with ethyl acetate containing 0.5 % of trimethylamine, recrystallized from ethyl acetate, then from isopropanol. Yield: A. 193 mg (60

%), B. 164 mg (51 %); lustrous brown solid; m.p. 189-191 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.75 (dd, *J* = 4.0, 1.2 Hz, 1H, C=C<u>H</u>-CH), 8.68 (s, 1H, N=C-C<u>H</u>), 8.34 (s, 1H, N=C<u>H</u>-N), 8.33 – 8.27 (m, 2H, C<u>H</u>=C-C<u>H</u>), 8.17 (dd, *J* = 5.0, 1.2 Hz, 1H, CH=C<u>H</u>-S), 7.44 (dd, *J* = 5.1, 3.9 Hz, 1H, C<u>H</u>=CH-S), 6.86 (d, *J* = 9.0 Hz, 2H, C<u>H</u>-C(NMe$_2$)=C<u>H</u>), 3.06 (s, 6H, NMe$_2$). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.3, 155.7, 155.3, 152.3, 140.5, 134.8, 132.7, 130.3, 129.1, 128.0, 122.8, 111.5, 101.6, 39.1; Anal. Calcd for $C_{17}H_{15}N_5S$ (321.40): C, 63.53; H, 4.70; N, 21.79 Found: C, 63.57; H, 4.67; N, 21.82

*4.13 7-(4-(N,N-dimethylaminophenyl))-5-phenyl-[1,2,4]triazolo[1,5-a]pyrimidine (**8da**).*

Purified by flash column chromatography eluting with ethyl acetate containing 0.5 % of trimethylamine, recrystallized from isopropanol. Yield: A. 183 mg (58 %), B. 151 mg (48%); bright yellow solid; m.p. 177-179 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.68 (s, 1H, N=C-C<u>H</u>), 8.43 – 8.34 (m, 4H, Ph, C<u>H</u>=C-C<u>H</u>), 8.02 (s, 1H, N=C<u>H</u>-N), 7.59 (dd, *J* = 5.0, 1.9 Hz, 3H, Ph), 6.90 – 6.83 (m, 2H, C<u>H</u>-C(NMe$_2$)=C<u>H</u>), 3.06 (s, 6H, NMe$_2$). ^{13}C NMR (126 MHz, DMSO-d_6) δ 159.9, 155.7, 152.3, 147.5, 136.6, 131.2, 130.9, 128.9, 127.7, 115.5, 111.1, 103.7; Anal. Calcd for $C_{19}H_{17}N_5$ (315.38): C, 72.36; H, 5.43; N, 22.21 Found: C, 72.42; H, 5.46; N, 22.27

*4.14 7-(4-(N,N-dimethylaminophenyl))-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**8db**).*

Purified by flash column chromatography eluting with ethyl acetate containing 0.5 % of trimethylamine, recrystallized from acetonitrile. Yield: A. 169 mg (49 %), B. 110 mg (32%); yellow solid; m.p. 190-193 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.63 (s, 1H, N=C-C<u>H</u>), 8.41 – 8.33 (m, 4H, C<u>H</u>=C-C<u>H</u>, C<u>H</u>=C-C<u>H</u>), 7.98 (s, 1H, N=C<u>H</u>-N), 7.16 – 7.09 (m, 2H, C<u>H</u>-C(OMe)=C<u>H</u>), 6.92 – 6.85 (m, 2H, C<u>H</u>-C(NMe$_2$)=C<u>H</u>), 3.87 (s, 3H, OMe), 3.07 (s, 6H, NMe$_2$). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.7, 159.6, 156.2, 155.5, 152.2, 147.3, 131.2, 129.4, 128.9, 115.7, 114.3, 111.1, 103.2, 55.4, 39.6; Anal. Calcd for $C_{20}H_{19}N_5O$ (345.41): C, 69.55; H, 5.54; N, 20.28 Found: C, 69.59; H, 5.50; N, 20.33

*4.15 7-(4-(N,N-dimethylaminophenyl))-5-(2-thienyl)-[1,2,4]triazolo[1,5-a]pyrimidine (**8dc**).*

Purified by flash column chromatography eluting with ethyl acetate containing 0.5 % of trimethylamine, recrystallized from isopropanol. Yield: A. 148 mg (46 %), B. 112 mg (35 %); dark yellow solid; m.p. 205-206 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.62 (s, 1H, N=C-C<u>H</u>), 8.39 – 8.34 (m, 2H, C<u>H</u>=C-C<u>H</u>), 8.32 (dd, *J* = 3.8, 1.1 Hz, 1H, C=C<u>H</u>-CH), 8.03 (s, 1H, N=C<u>H</u>-N), 7.89 (dd, *J* = 5.0, 1.1 Hz, 1H, CH=C<u>H</u>-S), 7.29 (dd, *J* = 5.0, 3.8 Hz, 1H, C<u>H</u>=CH-S), 6.92 –

6.84 (m, 2H, C<u>H</u>-C(NMe$_2$)=C<u>H</u>), 3.07 (s, 6H, NMe$_2$). ^{13}C NMR (126 MHz, DMSO-d_6) δ 155.9, 155.5, 155.4, 152.3, 147.4, 142.5, 131.7, 131.2, 129.9, 128.8, 115.4, 111.1, 102.5, 39.2; Anal. Calcd for $C_{17}H_{15}N_5S$ (321.40): C, 63.53; H, 4.70; N, 21.79 Found: C, 63.57; H, 4.73; N, 21.85

*4.16 5,7-Di(4-(N,N-dimethylaminophenyl))-[1,2,4]triazolo[1,5-a]pyrimidine (**8dd**).*

Purified by flash column chromatography eluting with ethyl acetate containing 0.5 % of trimethylamine, recrystallized from isopropanol. Yield: A. 143 mg (40 %), B. 118 mg (33 %); dark yellow solid; m.p. 219-221 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H, N=C-C<u>H</u>), 8.36 – 8.29 (m, 2H, C<u>H</u>=C-C<u>H</u>), 8.28 – 8.21 (m, 2H, C<u>H</u>=C-C<u>H</u>), 7.87 (s, 1H, N=C<u>H</u>-N), 6.92 – 6.87 (m, 2H, C<u>H</u>-C(NMe$_2$)=C<u>H</u>), 6.86 – 6.80 (m, 2H, C<u>H</u>-C(NMe$_2$)=C<u>H</u>), 3.06 (s, 6H, NMe$_2$), 3.04 (s, 6H, NMe$_2$). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.1, 156.4, 155.2, 152.13, 152.11, 146.8, 131.0, 128.9, 123.12, 116.1, 111.6, 111.1, 102.6, 39.6, 39.3; Anal. Calcd for $C_{21}H_{22}N_6$ (358.45): C, 70.37; H, 6.19; N, 23.45 Found: C, 70.35; H, 6.22; N, 23.49

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Supporting Information

Supplementary data associated with this article can be found, in the online version, at

Copies of ^{13}C and ^{1}H NMR spectra for all new compounds; absorption, excitation and emission spectra for **8** compounds; data of UV-visible and electrochemical studies.

X-ray crystallographic data for **5c** (CCDC: 1516469)

X-ray crystallographic data for **7cd (**CCDC: 1510810)

X-ray crystallographic data for **8cd (**CCDC: 1510811)

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