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FULL-LENGTH PAPER

One-pot four-component synthesis of highly substituted [1,2,4]triazolo[1,5-*a*]pyrimidines

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Abstract A green one-pot four-component strategy has been developed for the synthesis of [1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide derivatives using an amine, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one, an aldehyde, and 3-amino-1,2,4-triazole in the presence of a catalytic amount of *p*-toluenesulfonic acid in water within 4–6 h.

Keywords Multicomponent reaction · MCRs · Triazolopyrimidine · Green chemistry · Water

Introduction

Fused triazole and pyrimidine ring systems have been studied for several years because of their medicinal and agricultural significance [1–3]. Among their important effects, some triazolopyrimidine derivatives are known as blood pressure regulators [4], antibacterial agents [5], selective serotonin 5-HT6 receptor antagonists [6], and cardiovascular vasodilators [7]. In addition, several triazolopyrimidine-2-sulfonamide derivatives with herbicidal activity such as florasulam, flumetsulam, and metosulam are produced commercially [8]. Some important structures containing fused triazole and pyrimidine scaffold and their associated biological activities are shown in Fig. 1 [9–11].

The use of water as a solvent in organic reactions has received considerable attention because it is inexpensive, non-flammable, has a high specific heat capacity and more importantly is not toxic [12,13]. Choice of solvent is one of the problems to face to perform eco-efficient processes.

In view of our interest in multicomponent reactions strategy and using water as a green solvent [14–25], herein we wish to report an efficient and green four-component procedure for the synthesis of a new class of [1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide derivatives **5** via a condensation reaction between an amine **1**, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one **2**, an aldehyde **3**, and 3-amino-1,2,4-triazole **4** in the presence of catalytic amounts of *p*-toluenesulfonic acid (*p*-TsOH · H_2O) as a catalyst in water (Scheme 1).

Results and discussion

N-alkyl-3-oxobutanamide **6** was synthesised from the nucleophilic reaction of benzyl amine with 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one **2** under solvent-free conditions at 150 °C for 30 min (Scheme 2). Then, the reaction of **6** with 4-nitrobenzaldehyde and 3-amino-1,2,4-triazole **4** was chosen as a model reaction for optimization of reaction conditions. The effect of solvents in reaction has been investigated in the presence of *p*-TsOH · H_2O as a catalyst under solvent–free conditions at 100 °C and in various solvents including water, ethanol, ethyl acetate, acetonitrile, DCM, and DMF under reflux conditions. As shown in Table 1, water provided the best results in terms of yield and ease of work up fulfilling green chemistry principles (Table 1, entries 2–8). To identify the optimal temperature for this reaction in water, the reaction was repeated at room temperature (25 °C), 60 and 80 °C for

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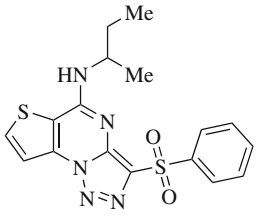
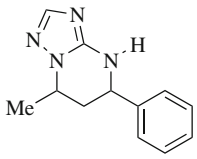
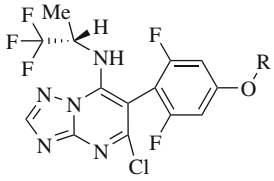
Fig. 1 Examples of biologically active triazolopyrimidine derivatives



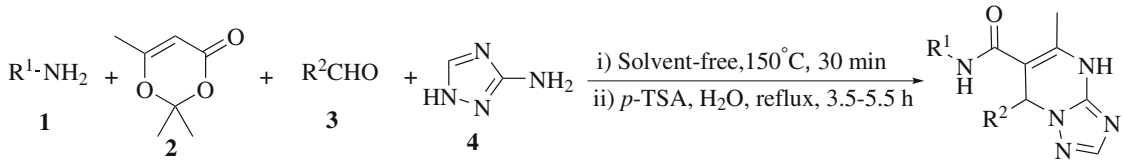
Anti-appetite [9]



Anticonvulsant [10]



Anticancer [11]



R^1 = benzyl, 4-Me-benzyl, allyl, *n*-propyl
R^2 = Ph, 4-ClPh, 3-NO_2Ph, 4-NO_2Ph, 4-MePh, 4-OMePh, 4-pyridine, *n*-Pr

Scheme 1 Synthesis of [1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamides **5a–k**

Scheme 2 Proposed mechanism for the formation of products **5a–k**

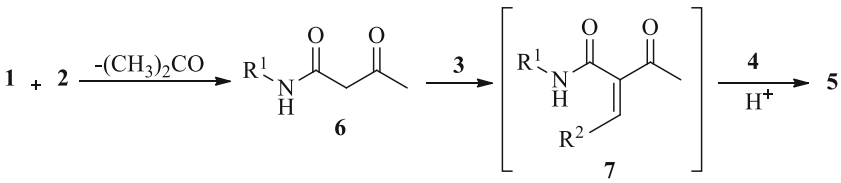


Table 1 Reaction optimization using **6**, 4-nitrobenzaldehyde and **4**

Entry	Conditions	Time (h)	Yield[a] (%)
1	H_2O/reflux	24	45
2	H_2O/reflux/10 mol% *p*-TsOH	4	87
3	EtOH/reflux/10 mol% *p*-TsOH	4	64
4	EtOAc/reflux/10 mol% *p*-TsOH	4	61
5	DCM/reflux/10 mol% *p*-TsOH	24	Trace
6	MeCN/reflux/10 mol% *p*-TsOH	8	76
7	DMF/reflux/10 mol% *p*-TsOH	24	45
8	Solvent-free/100 °C/ 10 mol% *p*-TsOH	24	38
9	H_2O/80 °C/10 mol% *p*-TsOH	24	43
10	H_2O/60 °C/10 mol% *p*-TsOH	24	Trace
11	H_2O/25 °C/10 mol% *p*-TsOH	24	Trace
12	H_2O/reflux/5 mol% *p*-TsOH	24	56
13	H_2O/reflux/7 mol% *p*-TsOH	16	64
14	H_2O/reflux/12 mol% *p*-TsOH	4	88
15	H_2O/reflux/15 mol% *p*-TsOH	4	88

[a] Isolated yield

24 h, too (Table1, entries 9–11). As indicated in Table 1, trace amounts of product were obtained at room temperature and 60 °C; however, the yield at 80 °C is 43 % after 24 h. After trying different amounts of the catalyst, the best result was obtained using 10 mol% (Table 1, entries 2 and 12–15). It is worth noting that in the absence of *p*-TsOH·H_2O, the desired product was obtained in low yield even at reflux conditions (Table 1, entry 1).

To explore the scope of this reaction, various amines **1** and aldehydes **3** were employed under the optimized reaction conditions. Various aryl aldehydes with different donor and acceptor substituents, heteroaromatic, and aliphatic aldehydes produced the corresponding products cleanly as shown in Table 2, and no undesirable side reactions were observed. Higher yields and short reaction times were noticed with electron-deficient aldehydes. The structures of these products (**5a–k**) are shown in Fig. 2.

All the products are new compounds, which were characterized from their elemental analysis, mass, IR, ^{1}H, and ^{13}C NMR spectra. For example, the ^{1}H NMR spectrum of **5a** exhibited a singlet for the methyl group ($\delta = 2.15$) and a multiplet at $\delta = 4.08 - 4.31$ for the methylene group. One singlet at 6.55 ppm was attributed to methine group (CHN). Ten aromatic hydrogens gave rise characteristic signals in the aromatic region of the spectrum. The spectrum also displays a broad singlet ($\delta = 8.35$) attributed to NHCO group, and a singlet at 10.26 ppm was recorded for the NH group. The ^{1}H-decoupled ^{13}C NMR spectrum of **5a** showed 16 distinct carbon signals in agreement with the expected product.

We propose a mechanism for the formation of [1,2,4]triazolo[1,5 -*a*]pyrimidine-6-carboxamides **5** in Scheme 2. Compound **7** results from the initial addition of an aldehyde **3** to *N*-alkyl-3-oxobutanamide **6**, which derived from

Table 2 Synthesis of [1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamides **5a–k**

Entry	Amine	Aldehyde	Product	Time (h)	Yield[a] (%)
1	Benzylamine	4-Nitrobenzaldehyde	**5a**	4	87
2	Benzylamine	4-Chlorobenzaldehyde	**5b**	4.5	85
3	Benzylamine	Benzaldehyde	**5c**	5	86
4	Benzylamine	4-Methoxybenzaldehyde	**5d**	5	82
5	Benzylamine	Propionaldehyde	**5e**	5.5	81
6	Benzylamine	4-Pyridinecarbaldehyde	**5f**	5	85
7	4-Methylbenzylamine	3-Nitrobenzaldehyde	**5g**	4	91
8	4-Methylbenzylamine	4-Methylbenzaldehyde	**5h**	6	85
9	4-Methylbenzylamine	4-Chlorobenzaldehyde	**5i**	5.4	90
10	Allylamine	3-Nitrobenzaldehyde	**5j**	5	83
11	n-Propylamine	4-Chlorobenzaldehyde	**5k**	5	88

[a] Isolated yield

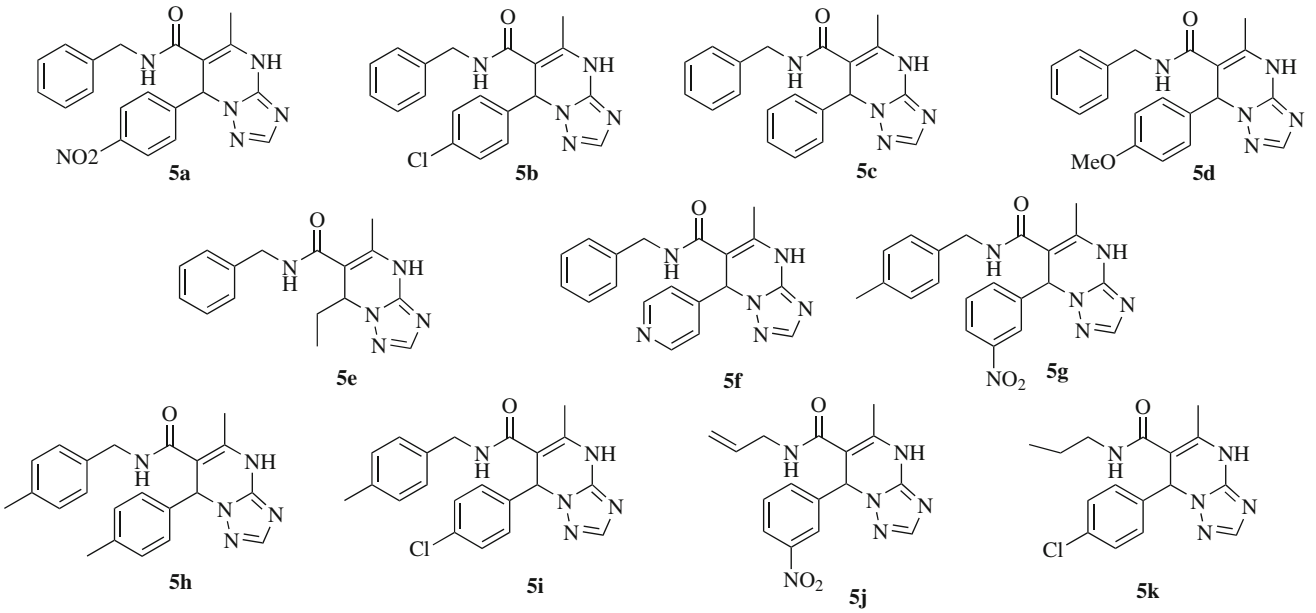


Fig. 2 Products **5a–k**

the addition of an amine **1** to 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one **2**. Then, a subsequent Michael-type addition of the 3-amino-1,2,4-triazole **4** to **7** followed by an intramolecular condensation reaction produces product **5**.

Conclusion

In conclusion, the present procedure provides an example of a green chemistry approach for the one-pot four-component synthesis of [1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide derivative via the cyclocondensation reaction of primary aliphatic or aromatic amines, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one, 3-amino-1,2,4-triazole and aliphatic or aromatic aldehydes catalyzed by *p*-TsOH · H_2O in water within 4–6 h. This procedure offers several notable advantages including operational simplicity, use of a low-cost and readily available catalyst, easy workup, improved yields, and little environmental impact due to the use of water as solvent.

Experimental

General experimental

All chemicals and solvents were purchased from Merck and Fluka and used without further purification. Melting points were measured on an Electrothermal 9200 apparatus and are uncorrected. Mass spectra were recorded on a Finnigan-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H NMR spectra were recorded on a Bruker

DRX-300 Avance spectrometer at 300.13 MHz and ^{13}C NMR spectra were recorded on a Bruker DRX-400 Avance spectrometer at 100.65 MHz using DMSO-d_6 and TMS as solvent and reference, respectively; chemical shifts (δ scale) are reported in parts per million (ppm). ^1H NMR spectra are reported in order: number of protons, multiplicity, and approximate coupling constant (J value) in hertz (Hz); signals were characterized as singlet (s), doublet (d), triplet (t), multiplet (m), broad signal (br s), and aryl (Ar). Elemental analyses were performed with an Elementar Analysensysteme GmbH VarioEL. All the products are new compounds, which were characterized by IR, ^1H NMR, ^{13}C NMR, mass spectra, and elemental analyses data.

Typical procedure for the synthesis of *N*-benzyl-4,7-dihydro-5-methyl-7-(4-nitrophenyl)-[1,2,4] triazolo[1,5-a]pyrimidine-6-carboxamide (5a)

A mixture of benzylamine (0.11 g, 1.0 mmol) and 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (0.14 g, 1.0 mmol) was heated under solvent-free conditions at 150 °C for 30 min, and then 4-nitrobenzaldehyde (0.15 g, 1.0 mmol), 3-amino-1,2,4-triazole (0.08 g, 1.0 mmol) and *p*-TsOH · H_2O (0.02 g, 10 mol%) in 5 mL H_2O were added simultaneously. The resulting mixture was stirred under reflux conditions for 3.5 h. After completion of the reaction, as indicated by TLC (EtOAc:*n*-hexane, 1:2), the reaction mixture was filtered off and the residue washed with ethanol to give **5a** as a pure product. Yellow powder (0.33 g, 85 %): dec. 288–290 °C. IR (KBr) cm^{-1}: 3295, 3027, 2918, 1665, 1603, 1517. ^1H NMR (300.13 MHz, DMSO-d_6) δ: 2.15 (3H, s, CH_3), 4.08–4.31 (2H, m, CH_2), 6.55 (1H, s, CH), 6.86 (2H, d, $^3J_{HH}$ = 5.8Hz, H–Ar), 7.07–7.14 (3H, m), 7.45 (2H, d, $^3J_{HH}$ = 8.1Hz), 7.65 (1H, s, N = CH), 8.15 (2H, d, $^3J_{HH}$ = 8.1Hz), 8.35 (1H, br s, NHCO), 10.26 (1H, s, NH). ^{13}C NMR (100.64 MHz, DMSO-d_6) δ: 13.6(CH_3), 38.3(CH_2), 55.9(CH), 98.4, 119.9, 122.8, 123.2, 124.1, 125.0, 132.4, 135.5, 143.4, 143.8, 144.0, 146.4 (C–Ar, C=C, C=N), 161.9 (CO). MS m/z : 391 (M^+ + 1, 10), 390 (M^+, 23), 284 (45), 258 (40), 163 (21), 135 (24), 107 (60), 91 (100), 65 (12). Anal. Calcd for $C_{20}H_{18}N_6O_3$: C, 61.53; H, 4.65; N, 21.53; found C, 61.59; H, 4.69; N, 21.46.

Compounds characterization data

N-Benzyl-7-(4-chlorophenyl)-4,7-dihydro-5-methyl-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide (5b)

White powder (0.33 g, 87 %): mp 295–297 °C. IR (KBr) cm^{-1}: 3290, 3034, 2915, 1672, 1610, 1530. ^1H NMR (300.13 MHz, DMSO-d_6) δ: 2.14 (3H, s, CH_3), 4.11–4.29 (2H, m, CH_2), 6.41 (1H, s, CH), 6.81 (2H, br s, H–Ar), 7.16 (3H, s, H–Ar), 7.23 (2H, d, $^3J_{HH}$ = 6.9 Hz), 7.38 (2H, d, $^3J_{HH}$ = 7.3 Hz), 7.62 (1H, s, N=CH), 8.32 (1H, br s, NHCO), 10.13 (1H, s, NH). ^{13}C NMR (100.64 MHz, DMSO-d_6) δ: 13.5 (CH_3), 38.1 (CH_2), 55.9(CH), 98.9, 122.7, 122.9, 124.1, 124.7, 125.6, 129.0, 131.8, 135.5, 135.8, 143.9, 146.1, (C–Ar, C=C, C=N), 162.1 (CO). MS m/z: 382 (M^++1, ^{37}Cl, 18), 381 (M^+, ^{37}Cl, 30), 380 (M^+ + 1, ^{35}Cl, 54), 379 (M^+, ^{35}Cl, 56), 364 (23), 337 (11), 288 (52), 273 (40), 247 (40), 163 (28), 135 (20), 109 (30), 91 (100), 65 (23). Anal. Calcd for $C_{20}H_{18}ClN_5O$: C, 63.24; H, 4.78; N, 18.44; found C, 63.29; H, 4.72; N, 18.49.

N-Benzyl-4,7-dihydro-5-methyl-7-phenyl-[1,2,4] triazolo[1,5-*a*]pyrimidine-6-carboxamide (5c)

White powder (0.30 g, 86 %): mp 293–295 °C. IR (KBr) cm^{-1}: 3392, 3282, 3051, 2905, 1664, 1609, 1530. ^1H NMR (300.13 MHz, DMSO-d_6) δ: 2.13 (3H, s, CH_3), 4.19 (2H, br s, CH_2), 6.40 (1H, br s, CH), 6.80-7.30 (10H, m, H–Ar), 7.59 (1H, br s, N=CH), 8.30 (1H, br s, NHCO), 10.06 (1H, br s, NH).^{13}C NMR (100.64 MHz, DMSO-d_6) δ: 18.1 (CH_3), 42.6 (CH_2), 54.5 (CH), 104.1, 127.4, 127.6, 127.8, 128.2, 128.9, 129.2, 136.3, 140.2, 140.5, 141.6, 148.7 (C–Ar, C=C, C=N), 166.9 (CO). MS m/z: 346 (M^++1, 21), 345 (M^+, 25), 239 (67), 212(55), 163 (23), 135 (20), 109 (10), 91 (100), 65 (12). Anal. Calcd for $C_{20}H_{19}N_5O$: C, 69.55; H, 5.54; N, 20.28; found C, 69.49; H, 5.60; N, 20.21.

N-Benzyl-4,7-dihydro-7-(4-methoxyphenyl)-5-methyl-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide (5d)

White powder (0.31 g, 82 %): mp 293–295 °C. IR (KBr) cm^{-1}: 3319, 3027, 2918, 1664, 1609, 1520. ^1H NMR (300.13 MHz, DMSO-d_6) δ: 2.14 (3H, s, CH_3), 3.33 (3H, s, OCH_3), 4.17 (1H, d of ABq, J_{AB} = 15.3 Hz, $^3J_{HH}$ = 5.3 Hz, CH_2), 4.26 (1H, d of ABq, J_{AB} = 15.3 Hz, $^3J_{HH}$ = 6.4 Hz, CH_2), 6.36 (1H, s, CH), 6.80–6.90 (4H, m, H–Ar), 7.11–7.18 (5H, m, H–Ar), 7.58 (1H, s, N=CH), 8.27 (1H, t, $^3J_{HH}$ = 5.7 Hz, NHCO), 10 (1H, s, NH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ: 18.1 (CH_3), 42.9 (CH_2), 56.0 (CH), 60.6 (OMe), 104.2, 114.6, 127.3, 127.6, 128.8, 129.0, 129.5, 133.8, 136.1, 140.2, 148.5, 150.5, 160.0 (C–Ar, C=C, C=N), 167.0 (CO). MS m/z: 377 (M^+ + 2, 3), 376 (M^+ + 1, 12), 375 (M^+, 21), 284 (17), 269 (40), 243 (40), 134 (14), 91 (100), 65 (24). Anal. Calcd for $C_{21}H_{21}N_5O_2$: C, 67.18; H, 5.64; N, 18.65; found C, 67.12; H, 5.60; N, 18.58.

N-Benzyl-7-etyhl-4,7-dihydro-5-methyl-[1,2,4] triazolo[1,5-*a*]pyrimidine-6-carboxamide (5e)

White powder (0.24 g, 81 %): mp 223–225 °C. IR (KBr) cm^{-1}: 3324, 3034, 2915, 1671, 1615, 1524. ^1H NMR (300.13

MHz, DMSO-d_6) δ: 0.61 (3H, t, $^3J_{HH}$ = 7.2Hz, CH_3), 1.45–1.56 (1H, m, CH_2), 1.85–1.97 (1H, m, CH_2), 2.03 (3H, s, CH_3), 4.343 (2H, d, $^3J_{HH}$ = 5.8Hz, NCH_2), 5.41 (1H, s, CH), 7.21–7.36 (5H, m, H–Ar), 7.65 (1H, s, CH), 8.42 (1H, t,$^3J_{HH}$ = 5.5 Hz, NHCO), 9.72 (1H, s, NH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ: 8.1, 17.9, 27.7, 43.2 (CH_3, CH_2), 57.9 (CH), 102.7, 127.6, 128.1, 129.1, 136.8, 140.6, 149.6, 150.4 (C–Ar, C=C, C=N), 167.5 (CO). 298 ($M^+ + 1$, 23), 297 (M^+, 7), 268 (85), 163 (60), 91 (100), 65 (22). Anal. Calcd for $C_{16}H_{19}N_5O$: C, 64.63; H, 6.44; N, 23.55; found C, 64.57; H, 6.40; N, 23.62.

N-Benzyl-4,7-tetrahydro-5-methyl-7-(pyridin-4-yl)-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide (5f)

White powder (0.30 g, 85 %): mp 287–290 °C. IR (KBr) cm^{-1}: 3293, 3076, 2905, 1659, 1592, 1540. ^{1}H NMR (300.13 MHz, DMSO-d_6) δ: 2.14 (3H, s, CH_3), 4.17 (1H, d of ABq, J_{AB} = 15.1 Hz, $^3J_{HH}$ = 5.2 Hz, CH_2), 4.28 (1H, d of ABq, J_{AB} = 15.2 Hz, $^3J_{HH}$ = 6.3 Hz, CH_2), 6.42 (1H, s, CH), 6.87-6.92 (2H, m, H–Ar), 7.10–7.23 (5H, m, H–Ar), 7.65 (1H, s, N=CH), 8.36 (1H, t, $^3J_{HH}$ = 5.5 Hz, NHCO), 8.48–8.53 (2H, m, H–Ar), 10.21 (1H, s, NH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ: 18.2 (CH_3), 43.0 (CH_2), 60.2 (CH), 102.9, 123.0, 127.4, 127.8, 128.9, 137.2, 140.1, 148.9, 149.5, 150.7, 151.0 (C–Ar, C=C, C=N), 166.7 (CO). 346 ($M^+ + 1$, 19), 345 (M^+, 14), 268 (17), 240 (47), 213(50), 163 (30), 135 (20), 109 (30), 91 (100), 65 (19). Anal. Calcd for $C_{19}H_{18}N_6O$: C, 65.88; H, 5.24; N, 24.26; found C, 65.81; H, 5.18; N, 24.31.

5-Methyl-*N*-(4-methylbenzyl)-7-(3-nitrophenyl)-4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide (5g)

White powder (0.36 g, 91 %): dec 297–299 °C. IR (KBr) cm^{-1}: 3295, 3027, 2918, 1664, 1590, 1532. ^{1}H NMR (300.13 MHz, DMSO-d_6) δ: 2.16 (3H, s, CH_3), 2.20 (3H, s, CH_3), 4.14 (2H, s, CH_2), 6.57 (1H, s, CH), 6.68 (2H, d, $^3J_{HH}$ = 6.6Hz, H–Ar), 6.88 (2H, d, $^3J_{HH}$ = 6.9Hz, H–Ar), 7.64 (2H, s, H–Ar), 8.00 (1H, s, N=CH), 8.18 (1H, m, H–Ar), 8.31 (1H, br s, NHCO), 10.25 (1H, s, NH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ: 18.2, 21.4 (CH_3), 42.7 (CH_2), 60.5 (CH), 103.1, 122.8, 124.0, 127.7, 129.3, 131.0, 134.9, 136.4, 137.0, 137.3, 143.5, 148.5, 148.6, 151.0 (C–Ar, C=C, C=N), 166.5 (CO). MS m/z: 405 ($M^+ + 1$, 5), 404 (M^+, 3), 285 (12), 268 (24), 238 (10), 210 (10), 163 (11), 135 (19), 120 (75),105 (100), 77 (25). Anal. Calcd for $C_{21}H_{20}N_6O_3$: C, 62.37; H, 4.98; N, 20.78; found C, 62.31; H, 4.90; N, 20.83.

5-Methyl-*N*-(4-methylbenzyl)-7-*p*-tolyl-4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide (5h)

White powder (0.32 g, 85 %): mp 290–293 °C. IR (KBr) cm^{-1}: 3319, 3039, 2905, 1664, 1615, 1529. ^{1}H NMR (300.13 MHz, DMSO-d_6) δ: 2.12 (3H, s, CH_3), 2.23 (3H, s, CH_3), 2.30 (3H, s, CH_3), 4.12–4.18 (2H, m, CH_2), 6.36 (1H, s, CH), 6.75 (2H, d, $^3J_{HH}$ = 6.8 Hz, H–Ar), 6.95 (2H, d, $^3J_{HH}$ = 6.9 Hz, H–Ar),7.10 (4H, m, H–Ar), 7.59 (1H, s, N=CH), 8.25 (1H, br s, NHCO), 10.02 (1H, s, NH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ: 18.1, 21.5, 21.6 (CH_3), 42.6 (CH_2), 60.8 (CH), 104.2, 127.7, 128.1, 129.3, 129.7, 136.1, 136.3, 137.1, 138.1, 138.7, 148.6, 150.5 (C–Ar, C=C, C=N), 166.9 (CO). MS m/z: 375 ($M^+ + 2$, 3), 374 ($M^+ + 1$, 11), 373 (M^+, 30), 253 (40), 227 (40), 197 (19), 135 (21), 105 (100), 91 (40). Anal. Calcd for $C_{22}H_{23}N_5O$: C, 70.76; H, 6.21; N, 18.75; found C, 70.71; H, 6.28; N, 18.81.

7-(4-Chlorophenyl)-5-methyl-*N* -(4-methylbenzyl)-4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide (5i)

White powder (0.35 g, 90 %): mp 297–299 °C. IR (KBr) cm^{-1}: 3319, 3039, 2918, 1665, 1615, 1531. ^{1}H NMR (300.13 MHz, DMSO-d_6) δ: 2.13 (3H, s, CH_3), 2.24 (3H, s, CH_3), 4.07-4.22 (2H, m, CH_2), 6.40 (1H, s, CH), 6.72 (2H, d, $^3J_{HH}$ = 7.0 Hz, H–Ar), 6.96 (2H, d, $^3J_{HH}$ = 6.7 Hz, H–Ar), 7.21 (2H, d, $^3J_{HH}$ = 7.2 Hz, H–Ar), 7.36 (2H, d, $^3J_{HH}$ = 6.9 Hz, H–Ar), 7.61 (1H, s, N=CH), 8.25 (1H, br s, NHCO), 10.10 (1H, s, NH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ: 18.1, 21.5 (CH_3), 42.6 (CH_2), 60.5 (CH), 103.7, 127.7, 129.2, 129.4, 130.1, 133.6, 136.3, 136.4, 137.1, 140.4, 148.6, 150.7 (C–Ar, C=C, C=N), 166.7 (CO). MS m/z: 395 ($M^+ + 2$, 5), 394 ($M^+ + 1$, 6), 393 (M^+, 12), 288 (20), 273 (25), 247 (28), 163 (11), 135 (15), 105 (100), 77 (29). Anal. Calcd for $C_{21}H_{20}ClN_5O$: C, 64.04; H, 5.12; N, 17.78; found C, 64.09; H, 5.18; N, 17.85.

N-Allyl-4,7-dihydro-5-methyl-7-(3-nitrophenyl)-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide (5j)

White powder (0.28 g, 83 %): dec. 289–291 °C. IR (KBr) cm^{-1}: 3282, 3027, 2918, 1666, 1597, 1533. ^{1}H NMR (300.13 MHz, DMSO-d_6) δ: 2.15 (3H, s, CH_3), 3.62 (2H, br s, CH_2), 4.74 (1H, d, $^3J_{HH(trans)}$ = 17.0 Hz, CH=CH_2), 4.85 (1H, d, $^3J_{HH(cis)}$ = 10.4Hz, CH=CH_2), 5.52–5.65 (1H, m, CH=CH_2) 6.57 (1H, s, CH), 7.63-7.67 (3H, m, H–Ar), 8.02 (2H, m, H–Ar, N=CH), 7.24–7.37 (5H, m, H–Ar), 7.94 (1H, br s, NHCO), 10.12 (1H, s, NH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ: 18.1 (CH_3), 41.8 (CH_2), 60.4 (CH), 103.1, 115.6, 122.6, 123.9, 131.0, 134.7, 135.9, 137.1, 143.6, 148.6, 148.8, 151.1 (C–Ar, C=C, C=N), 166.4 (CO). MS m/z: 341

(M^++1, 8), 340 (M^+, 9), 323 (100), 284 (24), 252 (68), 218 (20), 161 (50), 135 (20), 109 (18), 41 (29). Anal. Calcd for $C_{16}H_{16}N_6O_3$: C, 56.47; H, 4.74; N, 24.69; found C, 56.53; H, 4.79; N, 24.63.

7-(4-Chlorophenyl)-4,7-dihydro-5-methyl-*N*-propyl-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxamide (5k)

White powder (0.29 g, 88 %): mp 287–289 °C. IR (KBr) cm^{-1}: 3282, 2966, 2918, 1670, 1609, 1536. ^{1}H NMR (300.13 MHz, DMSO-d_6) δ: 0.65 (3H, t, $^3J_{HH}$ = 6.4Hz, CH_3), 1.22-1.25 (2H, m, CH_2), 2.10 (3H, s, CH_3), 2.93 (2H, m, CH_2), 6.37 (1H, s, CH), 7.18 (2H, d, $^3J_{HH}$ = 7.2Hz, H–Ar), 7.37 (2H, d, $^3J_{HH}$ = 7.4 Hz, H–Ar), 7.61 (1H, s, N=CH), 7.78 (1H, br s, NHCO), 10.05 (1H, s, NH). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ: 12.0,18.0, 23.0 (CH_3), 41.2 (CH_2), 60.5 (CH), 104.1, 129.2, 129.9, 133.5, 135.9, 140.5, 148.8, 150.7 (C–Ar, C=C, C=N), 166.6 (CO).MS m/z: 334 (M^+ + 1,^{37}Cl, 12), 333 (M^+,^{37}Cl, 18), 332 (M^++1,^{35}Cl, 42), 331 (M^+,^{35}Cl, 42), 288 (34), 273 (100), 246 (75), 220 (50), 161 (65), 127 (23), 109 (23), 67 (34). Anal. Calcd for $C_{16}H_{18}ClN_5O$: C, 57.92; H, 5.47; N, 21.11; found C, 57.88; H, 5.53; N, 21.07.

Supporting Information Available

IR, ^{1}H NMR, ^{13}C NMR and mass spectra for compounds **5a–k**.

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