4-Aryl-pyrimidin-2-yl tosylates as efficient reaction partners: application to the synthesis of pyrimidines functionalised with propargyloxy and 1,2,3-triazolo groups

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The 4-arylated pyrimidin-2-yl tosylate derivatives, easily prepared from cheap commercial materials, reacted efficiently with propargyl alcohol/NaOBu^t to give the corresponding 4-arylated 2-propargyloxy-pyrimidine derivatives which, in a one-pot reaction catalysed by $CuSO_4{\cdot}5H_2O$/sodium ascorbate, reacted with NaN_3 and hexyl or benzyl bromide to give a series of 2-(1-hexyl- or 1-benzyl-1,2,3-triazol-4-yl)methoxy-pyrimidine derivatives in good yields.

Keywords: 1,2,3-triazoles, Cu (I)-catalysed click reaction, C2-substituted pyrimidines, three-component reaction

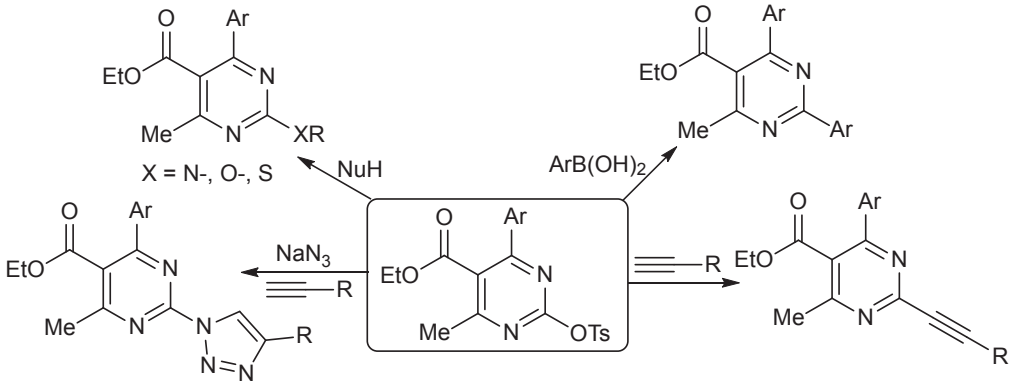
3,4-Dihydropyrimidinone (DHPM) is a simple heterocyclic scaffold exhibiting a wide range of pharmacological properties.[1,2] Among the DHPM derivatives, most of the pharmacologically important derivatives are N3-substituted- and C2-functionalised analogues.[3–8] Only a few methods have been developed to efficiently convert DHPM to 2-substituted pyrimidines.[9–15] In 2010, we reported the synthesis of 4-aryl-pyrimidin-2-yl tosylates and their utilisation in the formation of C2-substituted pyrimidines.[16] The 4-aryl-pyrimidin-2-yl tosylates were easily available from Biginelli 3,4-dihydropyrimidine-2(*1H*)-ones *via* oxidation and esterification under very mild conditions.[16] It has been shown that 4-aryl-pyrimidin-2-yl tosylates can be useful synthetic building blocks for important pyrimidine derivatives (Scheme 1). For example, they coupled with arylboronic acids and alkynes to deliver C–C coupling products[17] and reacted with phenols and anilines to construct C–O and C–N bonds.[18] We recently reported a multicomponent reaction (MCR) of 4-aryl-pyrimidin-2-yl tosylates with NaN_3 and alkynes[19] or active methylene ketones[20] for the synthesis of C2-(1,2,3-triazolo-subsituted)pyrimidines. In this context, we became interested in combining click chemistry (azide-alkyne cycloadditions) with MCR strategies. Here, we report the use of 4-aryl-pyrimidin-2-yl tosylates in the synthesis of pyrimidines functionalised with propargyloxy and 1,2,3-triazolo groups (Schemes 2 and 3).

It is well known that copper (I)-catalysed click chemistry of azide–alkyne cycloaddition proceed with high regioselectivity to deliver 1,4-disubstituted 1,2,3-triazoles as the major products.[21–23] Essentially, copper-catalysed three-component reactions of alkyl or aryl halides, terminal alkynes and safe-to-use sodium azide have been developed by several groups to produce 1,2,3-triazole derivatives.[24–29] We have also employed sodium azide in the work reported here.

Results and discussion

Initially, in order to optimise the first reaction of our proposed two-step synthesis, the base-catalysed reaction between the 4-phenyl-pyrimidin-2-yl tosylate derivative **1a** (Ar=Ph) and propargyl alcohol **2** was chosen as a model (Scheme 2). After several experiments we found that this reaction proceeded smoothly in the presence of 2 equiv. of NaOBu^t and 1 equiv. of K_3PO_4 at room temperature to form the desired 4-phenyl-2-propargyloxy-pyrimidine derivative **3a** (Ar=Ph) in a good yield of 83%. Other combinations of bases, for example NaOBu^t with K_2CO_3 or Et_3N gave lower yields (72% and 76%, respectively). Acetone, PEG-400 and dichloromethane (DCM) were tested as solvents, but only the latter gave a satisfactory yield. Applying these conditions to five other 4-aryl-pyrimidin-2-yl tosylate derivatives **1**, good yields (66–83%) of the desired products **3b–f** were obtained (Scheme 2). The reaction tolerated both electron-withdrawing group (Cl, Br and F) and electron-donating group (Me, MeO) on the phenyl ring to deliver the desired products.

For optimisation of the conditions for the second step of the synthesis (Scheme 3), a three-component Cu-catalysed reaction, the 4-phenyl-2-propargyloxy-pyrimidine derivative **3a** and benzyl bromide **4a** were chosen as model substrates to react with NaN_3. Recently, we reported that the Cu(I)



Scheme 1

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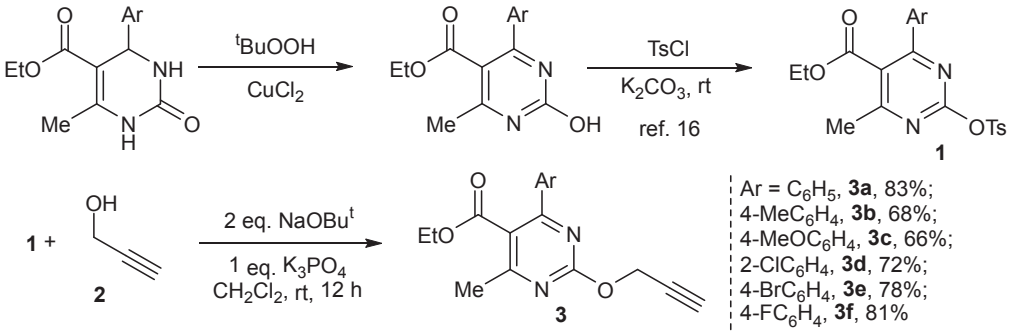
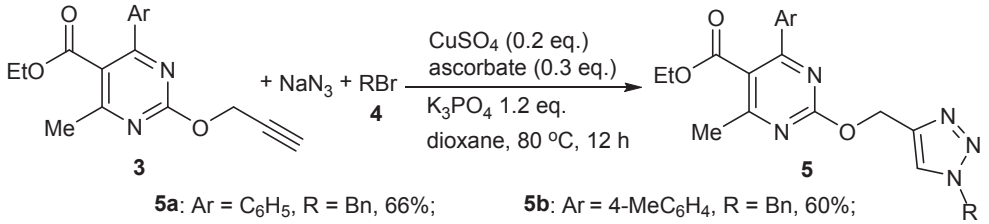


Scheme 2



5a: Ar = C_6H_5, R = Bn, 66%; **5b**: Ar = 4-MeC_6H_4, R = Bn, 60%;
5c: Ar = 2-ClC_6H_4, R = Bn, 64%; **5d**: Ar = 4-BrC_6H_4, R = Bn, 62%;
5e: Ar = 4-FC_6H_4, R = Bn, 68%; **5f**: Ar = C_6H_5, R = hexyl, 47%;
5g: Ar = 4-MeC_6H_4, R = hexyl 41%; **5h**: Ar = 2-ClC_6H_4, R = hexyl 44%;
5i: Ar = 4-BrC_6H_4, R = hexyl 44%; **5j**: Ar = 4-FC_6H_4, R = hexyl 46%;

Scheme 3

species generated *in situ* from $CuSO_4{\cdot}5H_2O$ (or $Cu(OAc)_2{\cdot}H_2O$) with sodium ascorbate (NaAsc) catalysed the reaction of an azide with an acetylene[30] and the amination of aryl halides with amines or amides.[31,32] So we tested the $CuSO_4{\cdot}5H_2O$ (20 mol%)/NaAsc (30 mol%) and $Cu(OAc)_2{\cdot}H_2O$ (20 mol%)/NaAsc (30 mol%) catalyst systems in the three-component model reaction. The results are shown in Table 1. We found that both catalyst systems gave a good yield of the product **5a** (Ar=Ph, R=Bn) in the presence of K_3PO_4 as a base (entries 1 and 2). The reaction was significantly affected by the base used. Although the inorganic bases K_3PO_4, K_2CO_3, and Cs_2CO_3 all delivered the desired product in 50–60% yield, Na_2CO_3 gave only a 30% yield and Et_3N resulted in only a trace of the product (entries 3–6). Among the solvents tested, acetone, DMSO, DMF, and dioxane gave satisfactory yields, the latter the best yield of 63% (entries 7–10). Cu (I) salts, for example, CuCl, CuBr, and CuI at 10 mol% also gave good yields in dioxane (entries 9–11). The best yield (63%) was realised using $CuSO_4{\cdot}5H_2O$/NaAsc in the presence of K_3PO_4 at 80 °C for 12 h in dioxane.

To test the scope of the second step of the synthesis, the 4-aryl-2-propargyloxypyrimidine derivatives **3a**–**b**, **3d**–**f** were reacted with sodium azide and benzyl bromide **4a** or hexyl bromide **4b** under the optimised conditions and the yields of the products obtained are shown in Scheme 3. In general, good yields (60–68%) of the desired products **5a**–**e** were obtained from benzyl bromide when the aryl group contained either an electron-withdrawing or an electron-donating group on the benzene ring. However, only moderate yields (41–47%) of the desired 1,2,3-triazole derivatives **5f**–**j** were obtained employing

Table 1 Optimisation of the reaction conditions (catalyst, base and solvent) for the one-pot reaction of **3a** with NaN_3 and benzyl bromide **4a** to form **5a** (Ar=Ph, R=Bn) (Scheme 3)[a]

Entry	Catalysis (mol %)	Solvent	Base	Yield/%[b]
1	$Cu(OAc)_2{\cdot}H_2O$ (20)/NaAsc (30)	EA	K_3PO_4	60
2	$CuSO_4{\cdot}5H_2O$ (20)/NaAsc (30)	EA	K_3PO_4	59
3	$CuSO_4{\cdot}5H_2O$ (20)/NaAsc (30)	EA	K_2CO_3	52
4	$CuSO_4{\cdot}5H_2O$ (20)/NaAsc (30)	EA	Na_2CO_3	30
5	$CuSO_4{\cdot}5H_2O$ (20)/NaAsc (30)	EA	Cs_2CO_3	55
6	$CuSO_4{\cdot}5H_2O$ (20)/NaAsc (30)	EA	Et_3N	Trace
7	$CuSO_4{\cdot}5H_2O$ (20)/NaAsc (30)	Acetone	K_3PO_4	47
8	$CuSO_4{\cdot}5H_2O$ (20)/NaAsc (30)	Dioxane	K_3PO_4	63
9	$CuSO_4{\cdot}5H_2O$ (20)/NaAsc (30)	DMSO	K_3PO_4	40
10	$CuSO_4{\cdot}5H_2O$ (20)/NaAsc (30)	DMF	K_3PO_4	35
9	CuI (10)	Dioxane	K_3PO_4	60
10	CuBr (10)	Dioxane	K_3PO_4	60
11	CuCl (10)	Dioxane	K_3PO_4	52

[a]Reaction conditions: **3a** (0.5 mmol), NaN_3 (0.75 mmol), **4a** (R=Bn) (0.6 mmol), base (0.6 mmol) and catalyst (10 or 30 mol%) were stirred in solvent (3 mL) at 80 °C for 12 h.
[b]Isolated yield.

hexyl bromide **4b**, again the yields not notably influenced by the nature of the aromatic substituent.

The newly synthesised products **3a**–**f** and **5a**–**j** were fully characterised by their ^{1}H NMR, ^{13}C NMR spectra and elemental analyses. Some selected NMR data is discussed below. The formation of product **3a** was confirmed by observing two singlets at δ 5.09 and 2.48, which were assigned to methylene and alkyl protons of the prop-2-ynyloxy group. Formation of product **3a** was further confirmed by the ^{13}C NMR spectra showing singlets at δ 78.2, 74.7 and 55.1, which were assigned to methylene and alkyne carbons of the prop-2-ynyloxy group. The ^{1}H NMR spectrum of product **5a** exhibited a singlet at δ 5.50 attributed as the CH_2 of Bn group. This CH_2 appeared as a singlet at δ 61 in the ^{13}C NMR spectrum. Meanwhile the absence of alkyne protons and carbons in the ^{1}H NMR and ^{13}C NMR spectra confirmed the formation of **5a**.

Experimental

All starting materials and reagents were obtained commercially and used without further purification. Melting points were determined on an XT-4 electrothermal micromelting point apparatus and uncorrected. Mass-spectra were recorded on an Esquire 6000 instrument. NMR spectra were recorded at 400 (^{1}H) and 100 (^{13}C) MHz, respectively, on a Varian Mercury plus-400 instrument in $CDCl_3$ or DMSO-d_6 (for ^{13}C NMR of compound **5b**) and TMS as internal standard. TLC was performed on 5 × 10 cm aluminium plates coated with silica gel 60F-254 in an appropriate solvent. 4-Aryl-pyrimidin-2-yl tosylate derivatives **3a**–**f** were synthesised (Scheme 2) in accordance with our previously reported methods.[16]

Synthesis of 2-propargyloxy pyrimidines **3***; general procedure*

A mixture of pyrimidin-2-yl tosylate **1** (2 mmol), propargyl alcohol **2** (3 mmol), NaOBu^t (4 mmol), K_3PO_4 (2 mmol) in DCM (5 mL) was stirred at room temperature for 12 h. After completion (monitored by TLC), the reaction mixture was quenched into saturated aqueous NH_4Cl solution (15 mL). The aqueous phase was extracted with 3 × 15 mL of CH_2Cl_2 and the combined organic phases were dried over $MgSO_4$ and evaporated. The products were isolated by silica gel column chromatography eluting with EtOAc/petroleum ether (V/V = 1 : 15).

Ethyl 4-methyl-6-phenyl-2-(prop-2-ynyloxy)pyrimidine-5-carboxylate (**3a**): Yellow oil; ^{1}H NMR: δ 7.66 (d, J = 8.0 Hz, 2H), 7.47–7.27 (m, 3H), 5.09 (s, 2H), 4.16 (q, J = 8.0 Hz, 2H), 2.59 (s, 3H), 1.05 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 168.9, 168.0, 166.3, 163.0, 137.5, 130.2, 128.4, 128.3, 120.5, 78.2, 74.7, 61.7, 55.1, 22.7, 13.6; ESI-MS: 297.15 [M + 1]$^+$. Anal. calcd for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.45; found C, 69.21; H, 5.49; N, 9.60%.

*Ethyl 4-methyl-2-(prop-2-ynyloxy)-6-*p*-tolylpyrimidine-5-carboxylate* (**3b**): Yellow oil; ^{1}H NMR: δ 7.48 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 4.96 (s, 2H), 4.08 (q, J = 8.0 Hz, 2H), 2.45 (s, 3H), 2.27 (s, 3H), 0.98 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 168.3, 167.9, 165.8, 162.7, 140.3, 134.3, 128.8, 128.1, 120.0, 78.1, 74.5, 61.4, 54.8, 22.4, 21.1, 13.4; ESI-MS: 311.11 [M + 1]$^+$. Anal. calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03; found C, 69.88; H, 5.90; N, 9.12%.

Ethyl 4-(4-methoxyphenyl)-6-methyl-2-(prop-2-ynyloxy)pyrimidine-5-carboxylate (**3c**): Yellow oil; ^{1}H NMR: δ 7.48 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 4.96 (s, 2H), 4.08 (q, J = 7.2 Hz, 2H), 2.45 (s, 3H), 2.27 (s, 3H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR: δ 168.3, 168.3, 165.1, 162.7, 161.36, 129.9, 129.4, 119.7, 113.6, 78.2, 74.5, 61.5, 55.1, 54.8, 22.5, 13.6; ESI-MS: 327.10 [M + 1]$^+$. Anal. calcd for $C_{18}H_{18}N_2O_4$: C, 66.25; H, 5.56; N, 8.58; found C, 66.40; H, 5.61; N, 8.49%.

Ethyl 4-(2-chlorophenyl)-6-methyl-2-(prop-2-ynyloxy)pyrimidine-5-carboxylate (**3d**): White solid, m.p. 113–114 °C (EtOH–H_2O (V/V = 10 : 1); ^{1}H NMR: δ 7.43 (d, J = 8.0 Hz, 1H), 7.38–7.32 (m, 3H), 5.06 (s, 2H), 4.05 (q, J = 8.0 Hz, 2H), 2.68 (s, 3H), 0.91 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 170.3, 166.6, 166.1, 162.9, 137.5, 131.9, 130.1, 129.9, 129.4, 126.5, 120.9, 77.9, 74.8, 61.3, 55.3, 23.6, 13.3; ESI-MS: 331.05 [M + 1]$^+$. Anal. calcd for $C_{17}H_{15}ClN_2O_3$: C, 61.73; H, 4.57; N, 8.47; found C, 61.91; H, 4.52; N, 8.55%.

Ethyl 4-(4-bromophenyl)-6-methyl-2-(prop-2-ynyloxy)pyrimidine-5-carboxylate (**3e**): Yellow oil; ^{1}H NMR: δ 7.58 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 5.08 (s, 2H), 4.20 (q, J = 8.0 Hz, 2H), 2.58 (s, 3H), 1.12 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 169.2, 167.8, 165.0, 163.0, 136.3, 131.6, 129.9, 124.9, 120.3, 78.1, 74.8, 61.8, 55.2, 22.7, 13.7; ESI-MS: 376.13 [M + 1]$^+$. Anal. calcd for $C_{17}H_{15}BrN_2O_3$: C, 54.42; H, 4.03; N, 7.47; found C, 54.63; H, 4.09; N, 7.55%.

Ethyl 4-(4-fluorophenyl)-6-methyl-2-(prop-2-ynyloxy)pyrimidine-5-carboxylate (**3f**): Yellow oil; ^{1}H NMR: δ 7.67 (q, J = 4.0 2H), 7.13 (t, J = 8.0 Hz, 2H), 5.07 (s, 2H), 4.19 (q, J = 8.0 Hz, 2H), 2.57 (s, 3H), 1.10 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 168.9, 167.9, 165.3, 164.9, 162.9, 162.8, 133.5, 130.5, 130.4, 120.3, 115.6, 115.4, 78.2, 74.723, 61.8, 55.1, 22.7, 13.7; ESI-MS: 315.21 [M + 1]$^+$. Anal. calcd for $C_{17}H_{15}FN_2O_3$: C, 64.96; H, 4.81; N, 8.91; found C, 65.12; H, 4.87; N, 8.80%.

Synthesis of C2-triazolomethoxypyrimidines **5***; general procedure*

A mixture of 2-propargyloxy pyrimidine derivatives **3** (0.5 mmol), NaN_3 (0.6 mmol), benzyl or hexyl bromide **4a**,**b** (0.6 mmol), $CuSO_4 \cdot 5H_2O$ (0.1 mmol), sodium ascorbate (0.15 mmol) and dioxane (3 mL) was stirred at 80 °C for 12 h. After completion (monitored by TLC), the reaction mixture was quenched into saturated aqueous NH_4Cl solution (10 mL). The aqueous phase was extracted with 3 × 15 mL of ethyl acetate and the combined organic phases were dried over $MgSO_4$ and evaporated. The products were separated by silica gel column chromatography eluting with EtOAc/petroleum ether (V/V = 1 : 3).

Ethyl 4-methyl-6-phenyl-2-[(1-phenyl-1H-1,2,3-triazol-4-yl)methoxy]-pyrimidine-5-carboxylate (**5a**): Yellow oil; ^{1}H NMR: δ 7.62 (d, J = 8.0 Hz, 3H), 7.43 (q, J = 8.0 Hz, 3H), 7.33 (d, J = 8.0 Hz, 3H), 7.24 (d, J = 4.0 Hz, 2H), 5.62 (s, 2H), 5.50 (s, 2H), 4.15 (q, J = 8.0 Hz, 2H), 2.56 (s, 3H), 1.03 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 168.6, 167.8, 166.2, 163.3, 143.5, 137.3, 134.2, 129.9, 128.9, 128.5, 128.2, 128.0, 127.9, 123.0, 120.1, 61.5, 61.1, 53.9, 22.5, 13.4. ESI-MS: 430.11 [M + 1]$^+$. Anal. calcd for $C_{24}H_{23}N_5O_3$: C, 67.12; H, 5.40; N, 16.31; found C, 67.33; H, 5.46; N, 16.41%.

*Ethyl 4-methyl-2-[(1-phenyl-1H-1,2,3-triazol-4-yl)methoxy]-6-*p*-tolyl-pyrimidine-5-carboxylate* (**5b**): Yellow oil; ^{1}H NMR: δ 7.59–7.53 (m, 3H), 7.35–7.34 (m, 3H), 7.27–7.22 (m, 4H), 5.61 (s, 2H), 5.50 (s, 2H), 4.19 (q, J = 8.0 Hz, 2H), 2.54 (s, 3H), 2.40 (s, 3H), 1.09 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 168.5, 168.2, 166.1, 163.3, 143.8, 140.4, 134.5, 134.3, 128.9, 128.9, 128.6, 128.1, 128.0, 122.9, 120.0, 77.3, 76.9, 76.7, 61.5, 61.2, 54.0, 22.5, 21.2, 13.6, 13.5. ESI-MS: 444.32 [M + 1]$^+$. Anal. calcd for $C_{25}H_{25}N_5O_3$: C, 67.70; H, 5.68; N, 15.79; found C, 67.52; H, 5.74; N, 15.91%.

Ethyl 4-(2-chlorophenyl)-6-methyl-2-[(1-phenyl-1H-1,2,3-triazol-4-yl) methoxy]pyrimidine-5-carboxylate (**5c**): Yellow oil; ^{1}H NMR: δ 7.69–7.24 (m, 10H), 5.58 (s, 2H), 5.50 (s, 2H), 4.04 (q, J = 8.0 Hz, 2H), 2.66 (s, 3H), 0.90 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 170.2, 166.4, 165.9, 163.2, 143.38, 137.4, 134.2, 129.9, 129.5, 129.2, 128.9, 128.5, 128.3, 128.2, 127.9, 123.2, 120.5, 61.3, 61.1, 53.9, 23.4, 13.2; ESI-MS: 464.95 [M + 1]$^+$. Anal. calcd for $C_{24}H_{22}ClN_5O_3$: C, 62.14; H, 4.78; N, 15.10; found C, 62.32; H, 4.72; N, 15.20%.

Ethyl 4-(4-bromophenyl)-6-methyl-2-[(1-phenyl-1H-1,2,3-triazol-4-yl) methoxy]pyrimidine-5-carboxylate (**5d**): Yellow oil; ^{1}H NMR: δ 7.57–7.49 (m, 6H), 7.36–7.25 (m, 4H), 5.60 (s, 2H), 5.51 (s, 2H), 4.18 (q, J = 8.0 Hz, 2H), 2.55 (s, 3H), 1.10 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 169.1, 167.8, 165.1, 163.5, 143.7, 136.4, 134.3, 131.6, 131.6, 129.9, 129.1, 128.8, 128.1, 124.8, 123.0, 120.1, 61.8, 61.4, 54.2, 22.7, 13.6; ESI-MS: 509.35 [M + 1]$^+$. Anal. calcd for $C_{24}H_{22}BrN_5O_3$: C, 56.70; H, 4.36; N, 13.78; found C, 56.87; H, 4.40; N, 13.72%.

Ethyl 4-(4-fluorophenyl)-6-methyl-2-[(1-phenyl-1H-1,2,3-triazol-4-yl) methoxy]pyrimidine-5-carboxylate (**5e**): Yellow oil; ^{1}H NMR: δ 7.56 (q, J = 4.0 Hz, 3H), 7.26 (d, J = 4.0 Hz, 3H), 7.18 (q, J = 4.0 Hz, 2H), 7.03 (t, J = 8.0 Hz, 2H), 5.53 (s, 2H), 5.42 (s, 2H), 4.10 (q, J = 8.0 Hz,

2H), 2.47 (s, 3H), 1.01 (t, J = 8.0 Hz, 3H); ^{13}C NMR: δ 168.8, 167.9, 165.0, 163.3, 143.6, 134.2, 130.3, 130.3, 128.9, 128.7, 128.0, 123.0, 115.5, 115.3, 61.7, 61.3, 54.1, 22.6, 13.6; ESI-MS: 448.35 $[M+1]^+$. Anal. calcd for $C_{24}H_{22}FN_5O_3$: C, 64.42; H, 4.96; N, 15.65; found C, 64.60; H, 5.01; N, 15.58%.

Ethyl 2-[(1-hexyl-1H-1,2,3-triazol-4-yl)methoxy]-4-methyl-6-phenyl-pyrimidine-5-carboxylate (**5f**): Yellow oil; ^{1}H NMR: δ 7.66 (t, J = 8.0 Hz, 3H), 7.46 (d, J = 8.0 Hz, 3H), 5.66 (s, 2H), 4.34 (q, J = 4.0 Hz, 2H), 4.15 (q, J = 8.0 Hz, 2H), 2.60 (s, 3H), 1.87 (d, J = 4.0 Hz, 2H), 1.30 (s, 6H), 1.04 (t, J = 8.0 Hz, 3H), 0.88 (s, 3H); ^{13}C NMR: δ 168.8, 168.1, 166.5, 163.5, 143.4, 137.6, 130.1, 128.4, 128.3, 122.8, 120.3, 61.7, 61.5, 50.3, 31.1, 30.2, 26.1, 22.7, 22.3, 13.9, 13.6; ESI-MS: 424.18 $[M+1]^+$. Anal. calcd for $C_{23}H_{29}N_5O_3$: C, 65.23; H, 6.90; N, 16.54; found C, 65.41; H, 6.97; N, 16.63%.

*Ethyl 4-methyl-2-[(1-hexyl-1H-1,2,3-triazol-4-yl)methoxy]-6-*p*-tolyl-pyrimidine-5-carboxylate* (**5g**): Yellow oil; ^{1}H NMR: δ 7.58 (s, 1H), 7.51 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 5.59 (s, 2H), 4.27 (t, J = 8.0 Hz, 2H), 4.12 (t, J = 8.0 Hz, 2H), 2.50 (s, 3H), 2.37 (s, 3H), 1.81 (t, J = 4.0 Hz, 2H), 1.23 (s, 6H), 1.04 (t, J = 8.0 Hz, 3H), 0.81 (t, J = 4.0 Hz, 3H); ^{13}C NMR: δ 168.6, 168.3, 166.2, 163.5, 143.5, 140.5, 134.6, 129.1, 128.3, 122.8, 120.1, 61.6, 61.4, 50.3, 31.1, 30.1, 26.1, 22.7, 22.3, 21.3, 13.8, 13.6; ESI-MS: 438.32 $[M+1]^+$. Anal. calcd for $C_{24}H_{31}N_5O_3$: C, 65.88; H, 7.14; N, 16.01; found C, 65.99; H, 7.10; N, 16.06%.

Ethyl 4-(2-chlorophenyl)-2-[(1-hexyl-1H-1,2,3-triazol-4-yl)methoxy]-6-methylpyrimidine-5-carboxylate (**5h**): Yellow oil; ^{1}H NMR: δ 7.67 (s, 1H), 7.45 (d, J = 7.2 Hz, 1H), 7.36 (d, J = 7.2 Hz, 3H), 5.62 (s, 2H), 4.34 (t, J = 7.2 Hz, 2H), 4.05 (q, J = 7.2 Hz, 2H), 2.69 (s, 3H), 1.88 (s, 2H), 1.28 (s, 6H), 1.06 (t, J = 8.0 Hz, 3H), 0.90 (d, 7.2 Hz, 3H); ^{13}C NMR: δ 170.4, 166.7, 166.2, 163.5, 143.2, 137.7, 131.9, 130.1, 129.8, 129.4, 126.6, 123.1, 120.8, 61.7, 61.3, 50.4, 31.1, 30.2, 26.1, 23.7, 22.4, 13.9, 13.4; ESI-MS: 459.02 $[M+1]^+$. Anal. calcd for $C_{23}H_{28}ClN_5O_3$: C, 60.32; H, 6.16; N, 15.29; found C, 60.11; H, 6.20; N, 15.41%.

Ethyl 4-(4-bromophenyl)-2-[(1-hexyl-1H-1,2,3-triazol-4-yl)methoxy]-6-methylpyrimidine-5-carboxylate (**5i**): Yellow oil; ^{1}H NMR: δ 7.58 (s, 1H), 7.51 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H), 5.57 (s, 2H), 4.27 (t, J = 8.0 Hz, 2H), 4.12 (q, J = 8.0 Hz, 2H), 2.51 (s, 3H), 1.81 (t, J = 8.0 Hz, 2H), 1.22 (s, 6H), 1.04 (t, J = 8.0 Hz, 3H), 0.80 (d, J = 4.0 Hz, 3H); ^{13}C NMR: δ 169.0, 167.8, 165.1, 163.5, 143.2, 136.4, 131.6, 129.9, 124.8, 122.8, 120.1, 61.8, 61.4, 50.3, 31.0, 30.1, 26.0, 22.7, 22.3, 13.8, 13.6; ESI-MS: 503.22 $[M+1]^+$. Anal. calcd for $C_{23}H_{28}BrN_5O_3$: C, 54.99; H, 5.62; N, 13.94; found C, 55.19; H, 5.68; N, 14.04%.

Ethyl 4-(4-fluorophenyl)-2-[(1-hexyl-1H-1,2,3-triazol-4-yl)methoxy]-6-methylpyrimidine-5-carboxylate (**5j**): Yellow oil; ^{1}H NMR: δ 7.66 (s, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 5.66 (s, 2H), 4.35 (s, 2H), 4.20 (q, J = 8.0 Hz, 2H), 2.59 (s, 3H), 1.89 (s, 2H), 1.31 (s, 6H), 1.11 (t, J = 8.0 Hz, 3H), 0.88 (d, J = 4.0 Hz, 3H); ^{13}C NMR: δ 168.9, 168.1, 165.2, 163.5, 162.8, 143.4, 133.7, 130.5, 130.4, 122.8, 120.2, 115.7, 115.4, 61.8, 61.5, 50.4, 31.1, 30.2, 26.1, 22.8, 22.4, 13.9; ESI-MS: 442.17 $[M+1]^+$. Anal. calcd for $C_{23}H_{28}FN_5O_3$: C, 62.57; H, 6.39; N, 15.86; found C, 62.72; H, 6.44; N, 15.77%.

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