Synthesis of Novel N,3-Substituted 3*H*-[1,2,3]Triazolo[4,5-*d*]pyrimidin-5-amines

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Abstract: Novel N,3-substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amines were prepared by an expedient method starting from 2-chloro-5-nitropyrimidin-4-yl thiocyanate via N^2,N^4-substituted 5-nitropyrimidine-2,4-diamines.

Key words: triazolopyrimidines, 5-nitropyrimidine-2,4-diamines, cyclization, hydrogenation, nucleophilic aromatic substitution

3-Substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidines have attracted considerable attention in medicinal chemistry. For example, 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7-amines (8-azaadenines) have been found to display anticonvulsive[1] and adenosine A_1 and A_3 receptor antagonistic activity.[2,3] Furthermore, N,3-substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amines are potent inhibitors of glycogen synthase kinase-3 (GSK-3)[4] (Figure 1).

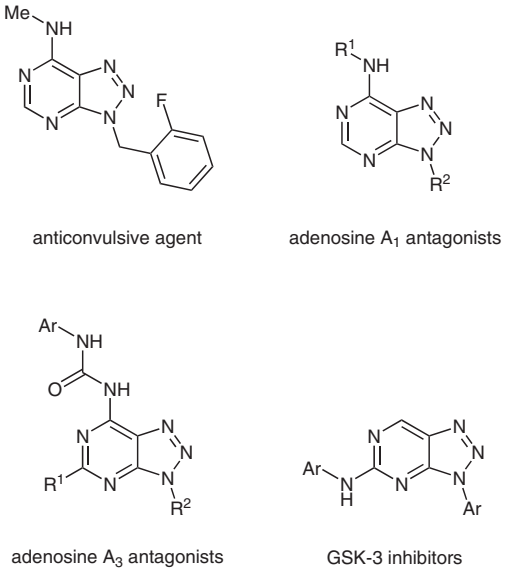
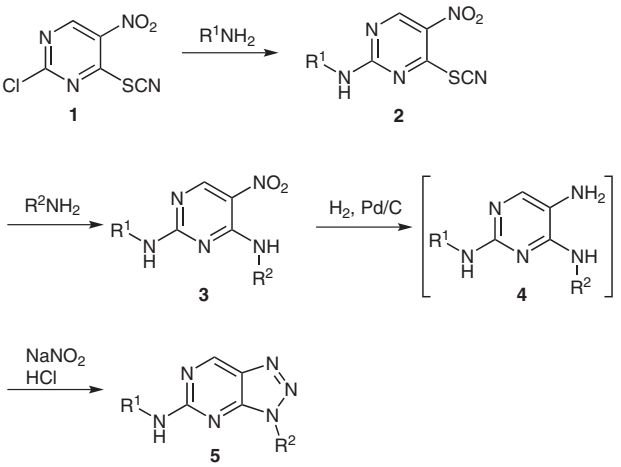


Figure 1 Selected biologically active 3-substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidines

The development of efficient methods for the preparation of new analogues of bioactive heterocyclic compounds represents an important challenge in organic and heterocyclic chemistry. Surprisingly, only few synthetic strategies for N,3-substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amines **5**, which suffer from broader scope, have been published.[4a,5] A method developed by Dille et al.[5] gives access only to compounds with identical N,3-substitution. The procedure described by Love et al.[4a] involves a complicated multistep protocol, with a regioselective monoaminolysis of 2,4-dichloro-5-nitropyrimidine at ring position 4 as the key step. Due to the high reactivity of both chlorine atoms this reaction is difficult to perform and is accompanied by side reactions causing low yields.[6]

As part of our research directed to bioactive 1,2,3-triazolo-condensed pyrimidine-amine derivatives, we here describe a straightforward synthetic method for a series of novel N,3-substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amines **5**, starting from 2-chloro-5-nitropyrimidin-4-yl thiocyanate[7] (**1**) as a precursor.

Reaction of 2-chloro-5-nitropyrimidin-4-yl thiocyanate (**1**) with two equivalents of primary amines at 0 °C provided the 2-amino-substituted 5-nitropyrimidin-4-yl thiocyanates **2a–d** in 91–98% yields (Scheme 1, Table 1), which were characterized by a sharp SCN absorption band at 2173–2184 cm^{-1} in the IR spectra. Without further purification, the crude starting materials **2** were converted into the N^2,N^4-substituted 5-nitropyrimidine-2,4-diamines **3a–g** by treatment with an excess of primary amines in DMF. A simple workup procedure, followed by recrystallization from methanol furnished **3a–g** as solid compounds in 83–93% yields (Scheme 1, Table 2).



Scheme 1 Synthesis of N,3-substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amines **5a–g**

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Table 1 2-Amino-Substituted 5-Nitropyrimidin-4-yl Thiocyanates **2a–d** Prepared

Product	R^1	Yield (%)[a]
2a	4-$FC_6H_4CH_2$	98
2b	*c*-Pr	91
2c	Et	94
2d	Ph	93

[a] Yield of crude product.

Table 2 N^2,N^4-Substituted 5-Nitropyrimidine-2,4-diamines **3a–g** Prepared

Product	R^1	R^2	Yield (%)
3a	Et	4-$FC_6H_4CH_2$	85
3b	*c*-Pr	2-$FC_6H_4CH_2$	92
3c	*c*-Pr	$PhCH_2CH_2$	88
3d	4-$FC_6H_4CH_2$	*c*-Pr	83
3e	4-$FC_6H_4CH_2$	Bn	85
3f	Ph	Bn	93
3g	*c*-Pr	Ph	89

The catalytic hydrogenation of 5-nitropyrimidine-2,4-diamines **3a–g** on 10% Pd/C in methanol provided the unstable pyrimidine-2,4,5-triamines **4**, which upon successive nitrosation with sodium nitrite in a mixture of hydrochloric acid and ethanol at 0 °C afforded the targeted N,3-substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amines **5a–g** in satisfactory yields of 51–75% (Scheme 1, Table 3).

Table 3 N,3-Substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amines **5a–g** Prepared

Product	R^1	R^2	Yield (%)
5a	Et	4-$FC_6H_4CH_2$	63
5b	*c*-Pr	2-$FC_6H_4CH_2$	66
5c	*c*-Pr	$PhCH_2CH_2$	68
5d	4-$FC_6H_4CH_2$	*c*-Pr	55
5e	4-$FC_6H_4CH_2$	Bn	59
5f	Ph	Bn	51
5g	*c*-Pr	Ph	75

In summary, we have developed an expedient four step preparation of N,3-substituted 3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amines **5a–g** starting from easily available 2-chloro-5-nitropyrimidin-4-yl thiocyanate (**1**). The described procedure is advantageous compared with literature methods with regard to performance and yields. Since the leaving groups of **1** can smoothly stepwise be replaced by amines, 2-chloro-5-nitropyrimidin-4-yl thiocyanate (**1**) can act as a powerful and efficient precursor for the synthesis of the target compounds **5**.

Melting points (uncorrected) were determined on a Mettler FP 62 apparatus. Elemental analyses were carried out with a Heraeus CHN-O-Rapid instrument. HRFAB-MS analyses were performed on a VG 70-250S spectrometer. IR spectra were recorded on a Varian 800 FT-IR spectrometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AMX 400 spectrometer using TMS as an internal standard and DMSO-d_6 or $CDCl_3$ as solvent. 2-Chloro-5-nitropyrimidin-4-yl thiocyanate[7a] (**1**), 2-(ethylamino)-5-nitropyrimidin-4-yl thiocyanate[8] (**2c**), and 5-nitro-2-(phenylamino)pyrimidin-4-yl thiocyanate[7b] (**2d**) were prepared according to literature procedures.

2-Amino-Substituted 5-Nitropyrimidin-4-yl Thiocyanates 2a,b; General Procedure

To a solution of 2-chloro-5-nitropyrimidin-4-yl thiocyanate (**1**; 2.17 g, 10 mmol) in benzene (20 mL) was added a solution of the appropriate primary amine (20 mmol) in EtOH (20 mL) dropwise under ice cooling. After stirring for 15 min at 0 °C, the solvent was removed under reduced pressure and EtOH (10 mL) was added. The separated solid was collected, washed with EtOH (2 × 5 mL), and dried. Products **2** were used for the synthesis of compounds **3** without further purification.

2-[(4-Fluorobenzyl)amino]-5-nitropyrimidin-4-yl Thiocyanate (2a)

Yield: 2.99 g (98%); yellow solid; mp 160 °C.

IR (KBr): 3221, 2173 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 4.64 (d, *J* = 6.3 Hz, 0.6 H, ArCH_2), 4.69 (d, *J* = 6.3 Hz, 1.4 H, ArCH_2), 7.10–7.52 (m, 4 H, ArH), 9.08 (s, 0.7 H, ArH), 9.15 (s, 0.3 H, ArH), 9.73 (t, *J* = 6.3 Hz, 0.3 H, NH), 9.85 (t, *J* = 6.4 Hz, 0.7 H, NH); due to existence of rotamers some signals appear twice.

^{13}C NMR (DMSO-d_6): δ = 43.3, 44.0, 107.9, 108.1, 115.1 (d, $^2J_{C,F}$ = 21.6 Hz), 115.1 (d, $^2J_{C,F}$ = 20.8 Hz), 129.5 (d, $^3J_{C,F}$ = 8.5 Hz), 129.9 (d, $^3J_{C,F}$ = 8.5 Hz), 130.8, 130.9, 134.1 (d, $^4J_{C,F}$ = 3.1 Hz), 134.1 (d, $^4J_{C,F}$ = 3.1 Hz), 157.1, 157.4, 160.1, 160.2, 160.5, 160.9, 161.3 (d, $^1J_{C,F}$ = 242.8 Hz), 161.4 (d, $^1J_{C,F}$ = 242.8 Hz); due to existence of rotamers some signals appear twice.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_8FN_5O_2S$: 306.0461; found: 306.0446.

2-(Cyclopropylamino)-5-nitropyrimidin-4-yl Thiocyanate (2b)

Yield: 2.16 g (91%); yellow solid; mp 196 °C (CH_2Cl_2–*n*-hexane).

IR (KBr): 3283, 2184 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 0.61–0.92 (m, 4 H, CH_2), 2.98–3.12 (m, 1 H, CH), 9.05 (s, 0.7 H, ArH), 9.18 (s, 0.3 H, ArH), 9.31 (d, *J* = 4.3 Hz, 0.3 H, NH), 9.46 (d, *J* = 3.8 Hz, 0.7 H, NH); due to existence of rotamers some signals appear twice.

^{13}C NMR (DMSO-d_6): δ = 6.0, 6.1, 24.7, 24.9, 107.7, 107.9, 130.7, 130.7, 156.5, 157.3, 159.6, 160.8, 161.4, 161.6; due to existence of rotamers some signals appear twice.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_8H_7N_5O_2S$: 238.0399; found: 238.0402.

N^2,N^4-Substituted 5-Nitropyrimidine-2,4-diamines 3a–g; General Procedure

To a solution of the respective crude thiocyanates **2** (3 mmol) in DMF (10 mL) was added the appropriate primary amine (15 mmol)

and the mixture was stirred at r.t. for 1.5 h. The reaction was quenched with H_2O (40 mL), the resulting precipitate filtered, and washed with H_2O (2 × 5 mL). The crude products were recrystallized from MeOH.

N^2-Ethyl-N^4-(4-fluorobenzyl)-5-nitropyrimidine-2,4-diamine (3a)

Yield: 743 mg (85%); yellow crystals; mp 177 °C.

IR (KBr): 3367, 3256, 2975, 1596 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.02 (t, *J* = 7.2 Hz, 2.4 H, $NHCH_2CH_3$), 1.12 (t, *J* = 7.2 Hz, 0.6 H, $NHCH_2CH_3$), 3.21–3.43 (m, 2 H, $NHCH_2CH_3$), 4.64–4.77 (m, 2 H, $ArCH_2$), 7.09–7.49 (m, 4 H, ArH), 8.09 (t, *J* = 5.6 Hz, 0.2 H, NH), 8.28 (t, *J* = 5.4 Hz, 0.8 H, NH), 8.85 (s, 0.8 H, ArH), 8.94 (s, 0.2 H, ArH), 9.03 (t, *J* = 5.8 Hz, 0.2 H, NH), 9.29 (t, *J* = 5.8 Hz, 0.8 H, NH); due to existence of rotamers some signals appear twice.

^{13}C NMR (DMSO-d_6): δ = 14.0, 14.8, 35.7, 35.9, 42.4, 42.9, 114.9 (d, $^2J_{C,F}$ = 21.2 Hz), 119.4, 120.4, 129.3 (d, $^3J_{C,F}$ = 8.8 Hz), 129.6 (d, $^3J_{C,F}$ = 8.8 Hz), 135.1 (d, $^4J_{C,F}$ = 2.9 Hz), 135.3 (d, $^4J_{C,F}$ = 2.9 Hz), 155.0, 155.3, 157.5, 158.0, 161.1 (d, $^1J_{C,F}$ = 242.2 Hz), 161.2, 161.5; due to existence of rotamers some signals appear twice.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{14}FN_5O_2$: 292.1210; found: 292.1213.

N^2-Cyclopropyl-N^4-(2-fluorobenzyl)-5-nitropyrimidine-2,4-diamine (3b)

Yield: 837 mg (92%); yellow crystals; mp 182 °C.

IR (KBr): 3382, 3211, 1593, 1564 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 0.41–0.72 (m, 4 H, CH_2), 2.70–2.97 (m, 1 H, CH), 4.78 (d, *J* = 6.1 Hz, 0. 5 H, $ArCH_2$), 4.83 (d, *J* = 6.1 Hz, 1.5 H, $ArCH_2$), 7.10–7.47 (m, 4 H, ArH), 8.15 (d, *J* = 4.0 Hz, 0.25 H, NH), 8.40 (d, *J* = 3.8 Hz, 0.75 H, NH), 8.84 (s, 0.75 H, ArH), 8.94 (t, *J* = 5.7 Hz, 0.25 H, NH), 9.00 (s, 0.25 H, ArH), 9.22 (t, *J* = 5.8 Hz, 0.75 H, NH); due to existence of rotamers some signals appear twice.

^{13}C NMR (DMSO-d_6): δ = 5.8, 6.1, 24.1, 24.2, 37.3 (d, $^3J_{C,F}$ = 3.7 Hz), 37.5 (d, $^3J_{C,F}$ = 4.4 Hz), 114.9 (d, $^2J_{C,F}$ = 21.2 Hz), 119.8, 120.9, 124.2 (d, $^4J_{C,F}$ = 3.7 Hz), 124.3, 125.7 (d, $^2J_{C,F}$ = 13.9 Hz), 128.7 (d, $^3J_{C,F}$ = 8.1 Hz), 128.9, 129.5 (d, $^3J_{C,F}$ = 4.4 Hz), 155.1, 155.3, 157.2, 158.0, 160.1 (d, $^1J_{C,F}$ = 243.7 Hz), 162.6, 162.8; due to existence of rotamers some signals appear twice.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{14}FN_5O_2$: 304.1210; found: 304.1217.

N^2-Cyclopropyl-5-nitro-N^4-(2-phenylethyl)pyrimidine-2,4-diamine (3c)

Yield: 790 mg (88%); yellow crystals; mp 176 °C.

IR (KBr): 3380, 1619, 1589, 1561 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 0.55–0.79 (m, 4 H, CH_2), 2.84–3.00 (m, 3 H, CH and $NHCH_2CH_2Ph$), 3.66–3.85 (m, 2 H, $NHCH_2CH_2Ph$), 7.17–7.35 (m, 5 H, ArH), 8.18 (d, *J* = 4.3 Hz, 0.25 H, NH), 8.43 (d, *J* = 4.0 Hz, 0.75 H, NH), 8.56 (t, *J* = 5.4 Hz, 0.25 H, NH), 8.75–8.89 (m, 1.5 H, NH and ArH), 8.96 (s, 0.25 H, ArH); due to existence of rotamers some signals appear twice.

^{13}C NMR (DMSO-d_6): δ = 6.0, 6.2, 24.2, 34.5, 34.7, 41.4, 41.8, 119.6, 120.6, 126.1, 128.3, 128.6, 128.6, 139.2, 154.8, 155.3, 157.2, 157.9, 162.7; due to existence of rotamers some signals appear twice.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{17}N_5O_2$: 300.1461; found: 300.1462.

N^4-Cyclopropyl-N^2-(4-fluorobenzyl)-5-nitropyrimidine-2,4-diamine (3d)

Yield: 756 mg (83%); yellow solid; mp 195 °C.

IR (KBr): 3345, 3248, 1591, 1565 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 0.60–0.85 (m, 4 H, CH_2), 2.95–3.11 (m, 1 H, CH), 4.54 (d, *J* = 6.3 Hz, 1.6 H, $ArCH_2$), 4.57 (d, *J* = 6.3 Hz, 0.4 H, $ArCH_2$), 7.00–7.48 (m, 4 H, ArH), 8.31 (d, *J* = 4.5 Hz, 0.2 H, NH), 8.44 (d, *J* = 4.0 Hz, 0.8 H, NH), 8.68 (t, *J* = 6.4 Hz, 0.2 H, NH), 8.81–8.89 (m, 1.6 H, NH and ArH), 8.91 (s, 0.2 H, ArH); due to existence of rotamers some signals appear twice.

^{13}C NMR (DMSO-d_6): δ = 6.4, 6.5, 23.9, 23.9, 43.5, 43.9, 114.9 (d, $^2J_{C,F}$ = 20.8 Hz), 114.9 (d, $^2J_{C,F}$ = 21.6 Hz), 119.8, 120.8, 129.2 (d, $^3J_{C,F}$ = 7.7 Hz), 129.6 (d, $^3J_{C,F}$ = 8.5 Hz), 135.3 (d, $^4J_{C,F}$ = 3.1 Hz), 135.5 (d, $^4J_{C,F}$ = 3.1 Hz), 156.5, 156.7, 157.4, 157.7, 161.2 (d, $^1J_{C,F}$ = 242.0 Hz), 161.4, 161.7; due to existence of rotamers some signals appear twice.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{14}FN_5O_2$: 304.1210; found: 304.1216.

N^4-Benzyl-N^2-(4-fluorobenzyl)-5-nitropyrimidine-2,4-diamine (3e)

Yield: 899 mg (85%); yellow solid; mp 166 °C.

IR (KBr): 3361, 1591, 1561 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 4.38–4.77 (m, 4 H, $ArCH_2$), 6.98–7.41 (m, 9 H, ArH), 8.58 (t, *J* = 6.3 Hz, 0.2 H, NH), 8.78 (t, *J* = 6.3 Hz, 0.8 H, NH), 8.82–8.95 (m, 1 H, ArH), 9.04 (t, *J* = 6.0 Hz, 0.2 H, NH), 9.25 (t, *J* = 6.2 Hz, 0.8 H, NH); due to existence of rotamers some signals appear twice.

^{13}C NMR (DMSO-d_6): δ = 42.8, 43.2, 43.4, 43.7, 114.9 (d, $^2J_{C,F}$ = 21.2 Hz), 114.9 (d, $^2J_{C,F}$ = 21.2 Hz), 119.8, 120.7, 126.7, 126.8, 127.1, 127.5, 128.2, 128.2, 129.0 (d, $^3J_{C,F}$ = 8.1 Hz), 129.2 (d, $^3J_{C,F}$ = 8.1 Hz), 135.1 (d, $^4J_{C,F}$ = 2.9 Hz), 135.5 (d, $^4J_{C,F}$ = 2.9 Hz), 138.8, 138.9, 155.1, 155.3, 157.7, 158.0, 161.1 (d, $^1J_{C,F}$ = 242.2 Hz), 161.2 (d, $^1J_{C,F}$ = 242.2 Hz), 161.4, 161.7; due to existence of rotamers some signals appear twice.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{16}FN_5O_2$: 354.1366; found: 354.1351.

N^4-Benzyl-5-nitro-N^2-phenylpyrimidine-2,4-diamine (3f)

Yield: 897 mg (93%); yellow crystals; mp 193 °C.

IR (KBr): 3376, 1592, 1552 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 4.79 (d, *J* = 6.1 Hz, 2 H, $ArCH_2$), 6.99–7.62 (m, 10 H, ArH), 9.02 (s, 1 H, ArH), 9.44 (s, 1 H, NH), 10.34 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 43.9, 120.1, 123.2, 126.7, 128.2, 128.4, 138.6, 138.7, 155.4, 157.3, 159.4.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{15}N_5O_2$: 322.1304; found: 322.1295.

N^2-Cyclopropyl-5-nitro-N^4-phenylpyrimidine-2,4-diamine (3g)

Yield: 727 mg (89%); yellow crystals; mp 228 °C.

IR (KBr): 3224, 1585, 1551 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 0.56–0.80 (m, 4 H, CH_2), 2.72–2.80 (m, 0.75 H, CH), 2.92–3.00 (m, 0.25 H, CH), 7.12–7.95 (m, 5 H, ArH), 8.39 (d, *J* = 4.3 Hz, 0.25 H, NH), 8.72 (d, *J* = 3.5 Hz, 0.75 H, NH), 8.97 (s, 0.75 H, ArH), 9.09 (s, 0.25 H, ArH), 10.18 (s, 0.25 H, NH), 10.40 (s, 0.75 H, NH); due to existence of rotamers some signals appear twice.

^{13}C NMR (DMSO-d_6): δ = 6.1, 6.1, 24.3, 24.4, 119.8, 122.2, 122.7, 124.4, 124.5, 128.5, 128.6, 137.4, 153.5, 157.7, 158.4, 162.8; due to existence of rotamers some signals appear twice.

HRMS-FAB: *m/z* $[M + H]^+$ calcd for $C_{13}H_{13}N_5O_2$: 272.1148, found: 272.1145.

N,3-Substituted 3*H*-[1,2,3]Triazolo[4,5-*d*]pyrimidin-5-amines; 5a–g; General Procedure

A suspension of the respective diamine **3** (2 mmol) in MeOH (20 mL) was hydrogenated using a catalytic amount of 10% Pd/C (2 h/ 2 bar). Afterwards, the suspension was filtered through an SPE tube RP-18 purchased from Supelco (Sigma-Aldrich, Munich, Germany) in order to remove the catalyst. The filtrate was evaporated to dryness and the residue dissolved in a mixture of EtOH (20 mL) and aq 1 M HCl (20 mL). To this mixture, was added a solution of $NaNO_2$ (2 mmol) in H_2O (3 mL) dropwise at 0 °C and stirred at r.t. for 1 h. Next, 20–30 mL of the solvent was removed under reduced pressure and the suspension was stored at 5–8 °C for 5 h. The precipitate was filtered and recrystallized from MeOH to afford compounds **5a–g** as solid products.

***N*-Ethyl-3-(4-fluorobenzyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine (5a)**

Yield: 343 mg (63%); colorless solid; mp 131 °C.

IR (KBr): 3256, 2966, 1618 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.29 (t, *J* = 7.3 Hz, 3 H, $NHCH_2CH_3$), 3.48–3.59 (m, 2 H, $NHCH_2CH_3$), 5.61 (s, 2 H, $ArCH_2$), 5.73 (s, 1 H, NH), 6.97–7.50 (m, 4 H, ArH), 9.00 (s, 1 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 14.4, 36.6, 48.9, 115.7 (d, $^2J_{C,F}$ = 21.4 Hz), 130.4 (d, $^3J_{C,F}$ = 8.4 Hz), 130.9 (d, $^4J_{C,F}$ = 3.1 Hz), 131.2, 150.9, 152.6, 161.3, 162.6 (d, $^1J_{C,F}$ = 247.2 Hz).

Anal. Calcd for $C_{13}H_{13}FN_6$: C, 57.35; H, 4.81; N, 30.86. Found: C, 57.17; H, 5.15; N, 30.72.

***N*-Cyclopropyl-3-(2-fluorobenzyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine (5b)**

Yield: 376 mg (66%); colorless solid; mp 132 °C.

IR (KBr): 3236, 1614 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.55–0.92 (m, 4 H, CH_2), 2.81–2.89 (m, 1 H, CH), 5.76 (s, 2 H, $ArCH_2$), 5.89 (s, 1 H, NH), 7.05–7.43 (m, 4 H, ArH), 9.05 (s, 1 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 7.3, 24.3, 43.1 (d, $^3J_{C,F}$ = 5.4 Hz), 115.6 (d, $^2J_{C,F}$ = 20.8 Hz), 122.2 (d, $^2J_{C,F}$ = 14.6 Hz), 124.3 (d, $^4J_{C,F}$ = 3.9 Hz), 130.3 (d, $^3J_{C,F}$ = 8.5 Hz), 130.6, 131.4, 151.2, 152.5, 160.6 (d, $^1J_{C,F}$ = 248.9 Hz), 162.4.

Anal. Calcd for $C_{14}H_{13}FN_6$: C, 59.15; H, 4.61; N, 29.56. Found: C, 59.11; H, 4.89; N, 29.64.

***N*-Cyclopropyl-3-(2-phenylethyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine (5c)**

Yield: 382 mg (68%); colorless solid; mp 112 °C.

IR (KBr): 3236, 1610 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.55–0.92 (m, 4 H, CH_2), 2.79–2.88 (m, 1 H, CH), 3.34 (t, *J* = 7.7 Hz, 2 H, $NHCH_2CH_2Ph$), 4.70–4.80 (m, 2 H, $NHCH_2CH_2Ph$), 5.88 (s, 1 H, NH), 7.16–7.32 (m, 5 H, ArH), 9.03 (s, 1 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 7.3, 24.3, 35.4, 47.3, 126.9, 128.7, 128.7, 131.5, 137.4, 151.2, 152.4, 162.2.

Anal. Calcd for $C_{15}H_{16}N_6$: C, 64.27; H, 5.75; N, 29.98. Found: C, 64.31; H, 5.75; N, 30.18.

3-Cyclopropyl-*N*-(4-fluorobenzyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine (5d)

Yield: 313 mg (55%); colorless solid; mp 130 °C.

IR (KBr): 3249, 1612 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.15–1.49 (m, 4 H, CH_2), 3.72–3.84 (m, 1 H, CH), 4.68 (d, *J* = 5.6 Hz, 2 H, $ArCH_2$), 6.19 (s, 1 H, NH), 6.94–7.42 (m, 4 H, ArH), 8.96 (s, 1 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 6.5, 28.4, 45.6, 115.9 (d, $^2J_{C,F}$ = 21.4 Hz), 129.8 (d, $^3J_{C,F}$ = 7.6 Hz), 134.6, 152.3, 153.2, 161.7, 162.6 (d, $^1J_{C,F}$ = 246.4 Hz).

Anal. Calcd for $C_{14}H_{13}FN_6$: C, 59.15; H, 4.61; N, 29.56. Found: C, 59.21; H, 4.91; N, 29.30.

3-Benzyl-*N*-(4-fluorobenzyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine (5e)

Yield: 448 mg (59%); colorless solid; mp 192 °C.

IR (KBr): 3246, 1614 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.66 (d, *J* = 5.6 Hz, 2 H, $ArCH_2$), 5.63 (s, 2 H, $ArCH_2$), 6.05 (s, 1 H, NH), 6.96–7.41 (m, 9 H, ArH), 9.01 (s, 1 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 45.2, 49.8, 115.5 (d, $^2J_{C,F}$ = 21.1 Hz), 128.4, 128.4, 128.8, 129.3 (d, $^3J_{C,F}$ = 8.3 Hz), 135.0, 152.9.

Anal. Calcd for $C_{18}H_{15}FN_6$: C, 64.66; H, 4.52; N, 25.13. Found: C, 64.49; H, 4.80; N, 25.04.

3-Benzyl-*N*-phenyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine (5f)

Yield: 309 mg (51%); colorless solid; mp 194 °C.

IR (KBr): 3248, 1618, 1547 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.72 (s, 2 H, $ArCH_2$), 7.10–7.69 (m, 10 H, ArH), 7.72 (s, 1 H, NH), 9.14 (s, 1 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 50.3, 119.6, 123.5, 128.5, 128.5, 128.9, 129.0, 132.0, 134.8, 138.7, 150.4, 152.7, 158.6.

Anal. Calcd for $C_{17}H_{14}N_6$: C, 67.54; H, 4.67; N, 27.80. Found: C, 67.15; H, 4.74; N, 27.60.

***N*-Cyclopropyl-3-phenyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine (5g)**

Yield: 379 mg (75%); colorless solid; mp 184 °C.

IR (KBr): 3229, 1617, 1560 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.61–0.96 (m, 4 H, CH_2), 2.86–2.95 (m, 1 H, CH), 6.00 (s, 1 H, NH), 7.39–7.61 (m, 3 H, ArH), 8.32 (s, 2 H, ArH), 9.13 (s, 1 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 7.3, 24.4, 120.5, 127.7, 129.4, 132.4, 136.6, 150.6, 152.9, 162.6.

Anal. Calcd for $C_{13}H_{12}N_6$: C, 61.89; H, 4.79; N, 33.31. Found: C, 61.87; H, 4.88; N, 33.14.

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