

## Supporting Information related to the article

# Identification of [1,2,3]triazolo[4,5-*d*]pyrimidin-7(6H)-ones as novel inhibitors of chikungunya virus replication

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| General synthetic procedures and analytical and<br>spectroscopic data of compounds <b>9b-m, 10b-m, 11b-n</b> and <b>15a,c-g</b> | S2-S9 |
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## Chemistry procedures

Melting points were obtained on a Reichert-Jung Kofler apparatus and are uncorrected. The elemental analysis was performed with a Heraeus CHN-O-RAPID instrument. The elemental compositions of the compounds agreed to within  $\pm 0.4\%$  of the calculated values. For all the tested compounds, satisfactory elemental analysis was obtained supporting  $>95\%$  purity. Electrospray mass spectra were measured on a quadrupole mass spectrometer equipped with an electrospray source (Hewlett-Packard, LC/MS HP 1100).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Varian INNOVA 300 operating at 299 MHz ( $^1\text{H}$ ) and 75 MHz ( $^{13}\text{C}$ ), respectively, a Varian INNOVA-400 operating at 399 MHz ( $^1\text{H}$ ) and 99 MHz ( $^{13}\text{C}$ ), respectively, and a VARIAN SYSTEM-500 operating a 499 MHz ( $^1\text{H}$ ) and 125 MHz ( $^{13}\text{C}$ ), respectively.

Analytical TLC was performed on silica gel 60 F<sub>254</sub> (Merck) precoated plates (0.2 mm). Spots were detected under UV light (254 nm) and/or charring with ninhydrin or phosphomolibdic acid. Separations on silica gel were performed by preparative centrifugal circular thin-layer chromatography (CCTLC) on a Chromatotron<sup>R</sup> (Kiesegel 60 PF<sub>254</sub> gipshaltig (Merck)), with layer thickness of 1 and 2 mm and flow rate of 4 or 8 mL/min, respectively. Flash column chromatography was performed in a Biotage Horizon instrument.

Microwave reactions were performed using the Biotage Initiator 2.0 single-mode cavity instrument from Biotage (Uppsala). Experiments were carried out in sealed microwave process vials utilizing the standard absorbance level (400 W maximum power). The temperature was measured with an IR sensor on the outside of the reaction vessel.

**General procedure for the reaction of 4,6-dichloropyrimidines with substituted anilines (9a-m).** A microwave vial was charged with the corresponding aniline (7, 1.0 mmol), the 4,6-dichloropyrimidine (8, 1.0 mmol), isobutanol (2.5 mL) and 37% aqueous HCl (0.07 mL/mmol). The reaction vessel was sealed and heated in a microwave reactor at 150 °C for 10-30 min. After cooling, the reaction mixture was worked up as indicated in each case.

**6-Chloro- $N^4$ -(3'-methoxyphenyl)-2-methylpyrimidine-4,5-diamine (9b).** Following the general procedure, a microwave vial was charged with 5-amino-4,6-dichloro-2-methylpyrimidine (200 mg, 1.12 mmol), 3-methoxyaniline (126  $\mu\text{L}$ , 1.12 mmol), isobutanol (2.8 mL) and 37% aqueous HCl (84  $\mu\text{L}$ ). After cooling, the product was isolated by filtration and dried to obtain 280 mg (95%) of **9b** as a beige solid. Mp: > 250 °C (decomposed). MS (ES, positive mode): m/z 265 (M+H)<sup>+</sup>.  $^1\text{H}$  NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  2.33 (s, 3H, CH<sub>3</sub>), 3.74 (s, 3H, OCH<sub>3</sub>), 5.49 (s, 2H, NH<sub>2</sub>), 6.62 (ddd, *J* = 8.2, 2.2, 0.8 Hz, 1H, H-4'), 7.21 (pt, *J* = 8.1 Hz, 1H, H-5'), 7.32 (ddd, *J* = 8.1, 2.0, 0.8 Hz, 1H, H-6'), 7.53 (pt, *J* = 2.2 Hz, 1H, H-2'), 9.13 (s, 1H, NH).

**6-Chloro- $N^4$ -(3'-chlorophenyl)-2-methylpyrimidine-4,5-diamine (9c).** Following the general procedure, a microwave vial was charged with 5-amino-4,6-dichloro-2-methylpyrimidine (200 mg, 0.48 mmol), 3-chloroaniline (50  $\mu\text{L}$ , 0.48 mmol), isobutanol (1.2 mL) and 37% aqueous HCl (36  $\mu\text{L}$ ). After cooling, the product was isolated by filtration and dried to obtain 120 mg (93%) of **9c** as a brown solid. Mp: 239-241 °C. MS (ES, positive mode): m/z 269 (M+H)<sup>+</sup>.  $^1\text{H}$  NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  2.33 (s, 3H, CH<sub>3</sub>), 6.38 (s, 2H, NH<sub>2</sub>), 7.05 (ddd, *J* = 8.0, 2.0, 0.8 Hz, 1H, H-4'), 7.33 (pt, *J* = 8.1 Hz, 1H, H-5'), 7.73 (ddd, *J* = 8.3, 2.0, 0.8 Hz, 1H, H-6'), 7.99 (pt, *J* = 2.1 Hz, 1H, H-2'), 9.11 (s, 1H, NH).

**6-Chloro- $N^4$ -(3'-benzoylphenyl)-2-methylpyrimidine-4,5-diamine (9d).** Following the general procedure, a microwave vial was charged with 5-amino-4,6-dichloro-2-methylpyrimidine (200 mg, 1.12 mmol), 3'-aminobenzophenone (221 mg, 1.12 mmol), isobutanol (2.8 mL) and 37% aqueous HCl (84  $\mu\text{L}$ ). After cooling, the product was isolated by filtration and dried to obtain 338 mg (89%) of **9d** as a dark solid, used as such for the next step. MS (ES, positive mode): m/z 260 (M+H)<sup>+</sup>.  $^1\text{H}$  NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  2.26 (s, 3H, CH<sub>3</sub>), 6.23 (s, 2H, NH<sub>2</sub>), 7.56 (m, 5H, H-4', H-5', H-3'', H-4''), 7.78 (d, *J* = 7.6 Hz, 2H, H-2''), 8.06 (d, *J* = 8.0 Hz, 1H, H-6'), 8.26 (s, 1H, H-2'), 9.13 (s, 1H, NH).

**6-Chloro- $N^4$ -(3'-isopropoxyphenyl)-2-methylpyrimidine-4,5-diamine (9e).** Following the general procedure, a microwave vial was charged with 5-amino-4,6-dichloro-2-methylpyrimidine (356 mg,

2.00 mmol), 3-isopropoxyaniline (300  $\mu$ L, 2.00 mmol), isobutanol (5.0 mL) and 37% aqueous HCl (150  $\mu$ L). The mixture was washed with saturated aqueous NaCO<sub>3</sub>. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated to dryness. The residue was purified by flash chromatography (dichloromethane/methanol, 30:1) to obtain 417 mg (71%) of **9e** as a solid. Mp: 144-146 °C. MS (ES, positive mode): m/z 293 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  1.28 (d, *J* = 6.0 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 2.30 (s, 3H, CH<sub>3</sub>), 4.53 (hept, *J* = 6.2 Hz, 1H, CH), 5.18 (s, 2H, NH<sub>2</sub>), 6.54 (m, 1H, H-4'), 7.17 (m, 2H, H-5', H-6'), 7.50 (d, *J* = 1.4 Hz, 1H, H-2'), 8.44 (s, 1H, NH).

Compound **9f** has been previously described.<sup>1</sup>

Compound **9g** has been previously described.<sup>2</sup>

**3-((5-Amino-6-chloro-2-methylpyrimidin-4-yl)amino)benzonitrile (9h).** Following the general procedure, a microwave vial was charged with 5-amino-4,6-dichloro-2-methylpyrimidine (200 mg, 1.12 mmol), 3-aminobenzonitrile (133 mg, 1.12 mmol), isobutanol (2.8 mL) and HCl conc (84  $\mu$ L). After cooling, the product was isolated by filtration and dried to obtain 264 mg (91%) of **9h** as a brown solid. Mp: 235-237 °C. MS (ES, positive mode): m/z 260 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz)  $\delta$ : 2.35 (s, 3H, CH<sub>3</sub>), 5.75 (s, 2H, NH<sub>2</sub>), 7.50 (m, 2H, H-4', H-5'), 8.08 (d, *J* = 7.3 Hz, 1H, H-6'), 8.30 (s, 1H, H-2'), 9.28 (s, 1H, NH).

Compound **9i** and **9j** have been previously described.<sup>2</sup>

**6-Chloro-2-methyl-*N*<sup>4</sup>-(4'-propoxyphenyl)pyrimidine-4,5-diamine (9k).** Following the general procedure, a microwave vial was charged with 5-amino-4,6-dichloro-2-methylpyrimidine (356 mg, 2.00 mmol), 4-propoxylaniline (297  $\mu$ L, 2.00 mmol), isobutanol (5.0 mL) and 37% aqueous HCl (150  $\mu$ L). After cooling, the product was isolated by filtration and dried to obtain 493 mg (84%) of **9k** as a solid. Mp: 208-209 °C. MS (ES, positive mode): m/z 293 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  0.96 (t, *J* = 7.4 Hz, 3H, CH<sub>2</sub>CH<sub>3</sub>), 1.71 (h, *J* = 7.3 Hz, 2H, CH<sub>2</sub>CH<sub>3</sub>), 2.30 (s, 3H, CH<sub>3</sub>), 3.90 (t, *J* = 6.5 Hz, 2H, OCH<sub>2</sub>), 4.38 (s, 2H, NH<sub>2</sub>), 6.91 (d, *J* = 9.1 Hz, 2H, H-3'), 7.59 (d, *J* = 9.0 Hz, 2H, H-2'), 9.14 (s, 1H, NH).

**6-Chloro-*N*<sup>4</sup>-[3',4'-methylenedioxyphenyl]-2-methylpyrimidine-4,5-diamine (9l).** Following the general procedure, a microwave vial was charged with 5-amino-4,6-dichloro-2-methylpyrimidine (200 mg, 1.12 mmol), 3,4-(methylenedioxy)aniline (154 mg, 1.12 mmol), isobutanol (2.8 mL) and HCl conc (84  $\mu$ L). After cooling, the product was isolated by filtration and dried to obtain 278 mg (89%) of **9l** as a black solid, that was used as such for the next step. MS (ES, positive mode): m/z 279 (M+H)<sup>+</sup> with a Cl isotopic pattern. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  2.32 (s, 3H, CH<sub>3</sub>), 6.00 (s, 2H, CH<sub>2</sub>), 6.47 (s, 2H, NH<sub>2</sub>), 6.88 (d, *J* = 8.4 Hz, 1H, H-5'), 7.11 (dd, *J* = 8.4, 2.1 Hz, 1H, H-6'), 7.43 (d, *J* = 2.1 Hz, 1H, H-2'), 9.38 (s, 1H, NH).

**Ethyl 3-((5-amino-6-chloro-2-methylpyrimidin-4-yl)amino)benzoate (9m).** Following the general procedure, a microwave vial was charged with 5-amino-4,6-dichloro-2-methylpyrimidine (300 mg, 1.69 mmol), ethyl 3-aminobenzoate (247  $\mu$ L, 1.69 mmol), dioxane (4.2 mL) and HCl conc (127  $\mu$ L). After cooling, the product was isolated by filtration and dried to obtain 511 mg (98%) of **9m** as a solid used as such for the next step. MS (ES, positive mode): m/z 307 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  1.33 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>), 2.34 (s, 3H, CH<sub>3</sub>), 4.31 (q, *J* = 7.1 Hz, 2H, CH<sub>2</sub>), 5.84 (s, 2H, NH<sub>2</sub>), 7.46 (pt, *J* = 7.9 Hz, 1H, H-5'), 7.60 (m, 1H, H-4'), 8.12 (ddd, *J* = 8.0, 2.3, 1.1 Hz, 1H, H-6'), 8.46 (pt, *J* = 1.9 Hz, 1H, H-2'), 9.05 (s, 1H, NH).

#### General procedure for the synthesis of 7-chloro-3*H*-[1,2,3]triazolo[4,5-*d*] pyrimidines (10a-m) starting from 4,5-diaminopyrimidines.

To a suspension of the corresponding 4,5-diaminopyrimidine (**9a-m**, 1.00 mmol) in dichloromethane (3.5 mL/mmol), NaNO<sub>2</sub> (1.05 mmol) and 1 N HCl (3.5 mL/mmol) were added. The mixture was stirred at room temperature for 30 min. The reaction was diluted with dichloromethane. The organic layer was washed with saturated aqueous NaHCO<sub>3</sub>, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated to dryness.

**7-Chloro-3-(3'-methoxyphenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine (10b).** Following the general procedure, to a suspension of **9b** (296 mg, 1.12 mmol) in dichloromethane (3.9 mL), NaNO<sub>2</sub> (81 mg, 1.17 mmol) and 1 N HCl (3.9 mL) were added. After work-up, 233 mg (75%) of **10b** were obtained as a solid. Mp: > 110 °C (decomposed). MS (ES, positive mode): m/z 276

(M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  2.80 (s, 3H, CH<sub>3</sub>), 3.86 (s, 3H, OCH<sub>3</sub>), 7.17 (ddd, *J* = 8.3, 2.4, 1.1 Hz, 1H, H-4'), 7.52-7.70 (m, 3H, H-2', H-5', H-6').

**7-Chloro-3-(3'-chlorophenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine (10c).** Following the general procedure, to a suspension of **9c** (300 mg, 1.11 mmol) in dichloromethane (3.9 mL), NaNO<sub>2</sub> (81 mg, 1.11 mmol) and 1 N HCl (3.9 mL) were added. After work-up, 203 mg (65%) of **10c** were obtained as a pale brown solid. Mp: 106-108 °C. MS (ES, positive mode): m/z 280 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz)  $\delta$ : 2.45 (s, 3H, CH<sub>3</sub>), 7.62 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H, H-4'), 7.68 (pt, *J* = 8.1 Hz, 1H, H-5'), 8.02 (ddd, *J* = 8.1, 2.0, 1.0 Hz, 1H, H-6'), 8.13 (pt, *J* = 2.0 Hz, 1H, H-2').

**7-Chloro-3-(3'-benzoylphenyl)-5-methyl-3*H*-[1,2,3]-triazolo[4,5-*d*]pyrimidine (10d).** Following the general procedure, to a suspension of **9d** (338 mg, 1.00 mmol) in dichloromethane (3.5 mL), NaNO<sub>2</sub> (73 mg, 1.05 mmol) and 1 N HCl (3.5 mL) were added. After work-up, 195 mg (56%) of **10d** were obtained as a pale brown solid. Mp: 136-138 °C. MS (ES, positive mode): 339 m/z (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz)  $\delta$ : 2.46 (s, 3H, CH<sub>3</sub>), 7.78 (m, 7H, H-4', H-5', H-2'', H-3'', H-4''), 8.43 (m, 1H, H-6'), 8.50 (s, 1H, H-2'), 9.13 (s, 1H, NH).

**7-Chloro-3-(3'-isopropoxyphenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine (10e).** Following the general procedure, to a suspension of **9e** (150 mg, 0.51 mmol) in dichloromethane (2.0 mL), NaNO<sub>2</sub> (69 mg, 0.56 mmol) and 1 N HCl (2.0 mL) were added. After work-up, the residue was purified by flash chromatography (hexane/ethyl acetate, 1:1) to obtain 152 mg (61%) of **10e** as a solid. Mp: 223-225 °C. MS (ES, positive mode): m/z 304 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  1.34 (d, *J* = 6.1 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 2.82 (s, 3H, CH<sub>3</sub>), 4.74 (hept, *J* = 6.0 Hz, 1H, CH), 7.16 (m, 1H, H-4'), 7.62 (m, 3H, H-2', H-5', H-6').

**N-(3-(7-Chloro-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-3-yl)phenyl)acetamide (10f).** A flask was charged with **9f** (150 mg, 0.51 mmol), in acetic acid (4 mL) and NaNO<sub>2</sub> (35 mg, 0.51 mmol) was slowly added. The vessel was stirred at room temperature for 30 min, dissolved in toluene (15 mL) and evaporated to dryness. The residue was purified by CCTLC in the Chromatotheron (dichloromethane/methanol, 20:1) to yield 108 mg (70%) of **10f** as a pale pink solid. Mp 296-298 °C. MS (ES, positive mode): m/z 303 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  2.09 (s, 3H, CH<sub>3</sub>), 2.45 (s, 3H, CH<sub>3</sub>), 7.53-8.36 (m, 4H, Ar), 12.75 (br s, 1H, NH).

**3-(7-Chloro-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-3-yl)-N,N-dimethylaniline (10g).** Following the general procedure, to a suspension of **9g** (312 mg, 1.12 mmol) in dichloromethane (4 mL), NaNO<sub>2</sub> (81 mg, 1.18 mmol) and HCl 1 N (4.0 mL) were added. After work-up, 87 mg (27%) of **10g** were obtained as a yellow solid. Mp 140-141 °C. MS (ES, positive mode): m/z 289 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  2.83 (s, 3H, CH<sub>3</sub>), 7.95 (pt, *J* = 8.0 Hz, 1H, H-5'), 8.09 (m, 1H, H-4'), 8.48 (ddd, *J* = 8.2 Hz, 2.2, 1.1 Hz, 1H, H-6'), 8.59 (pt, *J* = 1.8 Hz, 1H, H-2').

**3-(7-Chloro-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-3-yl)benzonitrile (10h).** Following the general procedure, to a suspension of **9h** (264 mg, 1.02 mmol) in dichloromethane (3.6 mL), NaNO<sub>2</sub> (74 mg, 1.05 mmol) and HCl 1 N (3.6 mL) were added. After work-up, 202 mg (73%) of **10h** were obtained as a brown solid. Mp: 136-138 °C. MS (ES, positive mode): m/z 271 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  2.83 (s, 3H, CH<sub>3</sub>), 7.95 (pt, *J* = 8.0 Hz, 1H, H-5'), 8.09 (m, 1H, H-6'), 8.48 (ddd, *J* = 8.2 Hz, 2.2, 1.1 Hz, 1H, H-4'), 8.59 (pt, *J* = 1.8 Hz, 1H, H-2').

Compound **10i** has been previously described.<sup>3</sup>

**(7-Chloro-3-(4'-acetylphenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine (10j).** Following the general procedure, to a suspension of **9j** (240 mg, 0.86 mmol) in dichloromethane (2.0 mL), NaNO<sub>2</sub> (66 mg, 0.95 mmol) and 1 N HCl (2.0 mL) were added. After work-up, 152 mg (61%) of **10j** were obtained as a solid. Mp: 195-197 °C. MS (ES, positive mode): m/z 288 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  2.45 (s, 3H, CH<sub>3</sub>), 2.65 (s, 3H, COCH<sub>3</sub>), 8.19-8.35 (m, 4H, Ar).

**7-Chloro-3-(4'-propoxyphenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine (10k).** Following the general procedure, to a suspension of **9k** (150 mg, 0.51 mmol) in dichloromethane (2.0 mL), NaNO<sub>2</sub> (40 mg, 0.46 mmol) and HCl 1 N (2.0 mL) were added. After work-up, 116 mg (75%) of **10k** were obtained as a solid. Mp: 222-224 °C. MS (ES, positive mode): m/z 304 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  1.00 (t, *J* = 7.4 Hz, 3H, CH<sub>2</sub>CH<sub>3</sub>), 1.77 (h, *J* = 7.3 Hz, 2H, CH<sub>2</sub>CH<sub>3</sub>), 2.78

(s, 3H, CH<sub>3</sub>), 4.03 (t, *J* = 6.6 Hz, 2H, OCH<sub>2</sub>), 7.22 (d, *J* = 9.1 Hz, 2H, H-3'), 7.92 (d, *J* = 9.1 Hz, 2H, H-2').

**7-Chloro-3(3',4'-methylenedioxyphenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine (10l).** Following the general procedure, to a suspension of **9l** (221 mg, 0.79 mmol) in dichloromethane (2.8 mL), NaNO<sub>2</sub> (57 mg, 0.83 mmol) and HCl 1 N (2.8 mL) were added. After work-up, 60 mg (26%) of **10l** were obtained as a beige solid. Mp: > 300 °C (decomposed). MS (ES, positive mode): m/z 290 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz): δ 2.42 (s, 3H, CH<sub>3</sub>), 6.17 (s, 2H, CH<sub>2</sub>), 7.17 (d, *J* = 8.3 Hz, 1H, H-5'), 7.42 (dd, *J* = 8.3, 2.0 Hz, 1H, H-6'), 7.49 (d, *J* = 2.0 Hz, 1H, H-2').

**Ethyl 3-(7-chloro-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-3-yl)benzoate (10m).** Following the general procedure, to a suspension of **9m** (511 mg, 1.67 mmol) in dichloromethane (5.8 mL), NaNO<sub>2</sub> (121 mg, 1.75 mmol) and HCl 1 N (5.8 mL) were added. After work-up, 367 mg (69%) of **10m** were obtained as a white solid. Mp: 109-110 °C. MS 318 (ES, positive mode): m/z (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz): δ 1.36 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>), 2.82 (s, 3H, CH<sub>3</sub>), 4.39 (q, *J* = 7.1 Hz, 2H, CH<sub>2</sub>), 7.87 (pt, *J* = 8.0 Hz, 1H, H-5'), 8.15 (m, 1H, H-6'), 8.42 (m, 1H, H-4'), 8.70 (pt, *J* = 1.9 Hz, 1H, H-2').

**General procedure for the synthesis of [1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-ones (11a-m).**

To a solution of the corresponding 7-chloro-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine (**10**) (1.00 mmol) in anhydrous DMF (4.5 mL/mmol), sodium acetate (3.00 mmol) was added. The reaction was microwave-irradiated at 120 °C for 1 hour. The mixture was dissolved in dichloromethane and washed with brine. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated to dryness. The residue was purified as indicated in each case..

**3-(3'-Methoxyphenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (11b).** Following the general procedure, to a solution of **10b** (167 mg, 0.61 mmol) in anhydrous DMF (2.7 mL), sodium acetate (151 mg, 1.82 mmol) was added. After work-up, the residue was purified by precipitation with dichloromethane to yield 84 mg (54%) of **11b** as a beige solid. Mp: 280-282 °C. MS (ES, positive mode): m/z 258 (M+H)<sup>+</sup>. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ 2.42 (s, 3H, CH<sub>3</sub>), 3.84 (s, 3H, OCH<sub>3</sub>), 7.10 (ddd, *J* = 8.3, 2.3, 1.2 Hz, 1H, H-4'), 7.54 (pt, *J* = 8.3, 1H, H-5'), 7.61 (m, 2H, H-2', H-6'), 12.74 (s, 1H, NH). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 22.4 (CH<sub>3</sub>), 56.0 (OCH<sub>3</sub>), 108.3, 114.5, 114.7 (Ar), 129.3 (C-7a), 131.0, 136.8 (Ar), 149.3 (C-3a), 156.9 (C-5), 160.3 (C-7), 161.5 (Ar). Anal. (C<sub>12</sub>H<sub>11</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**3-(3'-Chlorophenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (11c).** Following the general procedure, to a solution of **10c** (150 mg, 0.54 mmol) in anhydrous DMF (2.4 mL), sodium acetate (133 mg, 1.61 mmol) was added. After work-up, the residue was purified by precipitation with dichloromethane/hexane to yield 109 mg (77%) of **11c** as a beige solid. Mp: 255-257 °C. MS (ES, positive mode): m/z 262 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ 2.45 (s, 3H, CH<sub>3</sub>), 7.62 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H, H-4'), 7.68 (pt, *J* = 8.1 Hz, 1H, H-5'), 8.03 (ddd, *J* = 8.0, 2.0, 1.1 Hz, 1H, H-6'), 8.13 (pt, *J* = 2.0 Hz, 1H, H-2'), 12.79 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 22.1 (CH<sub>3</sub>), 121.1, 122.1, 129.2 (Ar), 129.3 (C-7a), 131.9, 134.3, 136.9 (Ar), 149.3 (C-3a), 156.1 (C-5), 161.4 (C-7). Anal. (C<sub>11</sub>H<sub>8</sub>ClN<sub>5</sub>O<sub>2</sub>): C, H, N.

**3-(3'-Benzoylphenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (11d).** Following the general procedure, to a solution of **4e** (195 mg, 0.56 mmol) in anhydrous DMF (2.5 mL), sodium acetate (139 mg, 1.67 mmol) was added and the mixture was irradiated at 120 °C for 1 h. The residue was purified by precipitation with dichloromethane and hexane to yield 140 mg (75%) of **5e** as a yellow solid. Mp: 281-283 °C. MS (ES, positive mode): m/z 332 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ 2.41 (s, 3H, CH<sub>3</sub>), 7.74 (m, 7H, H-4', H-5', H-2'', H-3'', H-4''), 8.31 (ddd, *J* = 7.8, 2.1, 1.3 Hz, 1H, H-6'), 8.39 (pt, *J* = 1.6 Hz, 1H, H-2'), 12.76 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 22.3 (CH<sub>3</sub>), 123.5, 129.4 (Ar), 129.6 (C-7a), 130.5, 126.4, 130.4, 131.0, 133.8, 136.0, 137.1, 138.7 (Ar), 149.5 (C-3a), 156.4 (C-5), 161.5 (C-7), 195.2 (CO). Anal. (C<sub>18</sub>H<sub>13</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**3-(3'-Isopropoxyphenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (11e).**

Following the general procedure, to a solution of **10e** (60 mg, 0.19 mmol) in anhydrous DMF (1.0 mL) sodium acetate (75 mg, 0.57 mmol) was added. The residue was purified by flash chromatography (dichloromethane/methanol) to yield 38 mg (71%) of **10e** as a solid. Mp: 224-225

°C. MS (ES, positive mode): m/z 286 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ 1.33 (d, *J* = 6.0 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 2.45 (s, 3H, CH<sub>3</sub>), 4.71 (hept, *J* = 5.7 Hz, 1H, CH), 7.10 (m, 1H, H-4'), 7.54 (m, 3H, H-2', H-5', H-6'), 12.75 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 22.1 (CH(CH<sub>3</sub>)<sub>2</sub>), 22.7 (CH<sub>3</sub>), 70.2 (CH), 109.5, 114.1, 116.0 (Ar), 129.3 (C-7a), 131.0, 137.0 (Ar), 157.5 (C-5), 158.4 (Ar), 161.8 (C-7). Anal. (C<sub>14</sub>H<sub>15</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**N-(3-(5-Methyl-7-oxo-6,7-dihydro-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-3-yl)phenyl)acetamide (11f).**

Following the general procedure, a microwave vial was charged with **10f** (90 mg, 0.30 mmol) and sodium acetate (75 mg, 0.90 mmol) in anhydrous DMF (1.5 mL) and was irradiated at 120 °C for 1 h. After work-up, the residue was purified by CCTLC in the Chromatotheron (dichloromethane/methanol, 30:1) to yield 30 mg (35%) of **11f** as a white solid. Mp 287-289 °C. MS (ES, positive mode): m/z 285 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz): δ 2.09 (s, 3H, COCH<sub>3</sub>), 2.45 (s, 3H, CH<sub>3</sub>), 7.53-8.35 (m, 4H, Ar), 10.29 (br s, 1H, NH), 12.74 (br s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 22.1 (CH<sub>3</sub>), 24.5 (CH<sub>3</sub>), 112.9, 117.0, 119.5 (Ar), 129.3 (C-7a), 130.4, 135.9, 140.8 (Ar) 149.1 (C-3a), 156.2 (C-5), 161.0 (C-7) 169.2 (CO). Anal. (C<sub>13</sub>H<sub>12</sub>N<sub>6</sub>O<sub>2</sub>): C, H, N.

**3-(3-(Dimethylamino)phenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (11g).**

Following the general procedure, to a solution of **10g** (50 mg, 0.17 mmol) in DMF (0.8 mL), sodium acetate (43 mg, 0.52 mmol) was added. After work-up, the precipitate was isolated by filtration and washed with water to yield 38 mg (81%) of **11g** as a yellow solid. Mp 319-321 °C. MS (ES, positive mode): m/z 272 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ: 2.42 (s, 3H, CH<sub>3</sub>), 2.97 (s, 3H, NMe<sub>2</sub>), 6.86 (dd, *J* = 8.4, 2.2 Hz, 1H, H-6'), 7.21 (dd, *J* = 8.0, 1.2 Hz, 1H, H-4'), 7.27 (pt, *J* = 2.2 Hz, 1H, H-2'), 7.40 (pt, *J* = 8.1 Hz, 1H, H-5'), 12.68 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 22.1 (CH<sub>3</sub>), 40.4 (NMe<sub>2</sub>), 106.2 (C-2'), 110.0 (C-4'), 113.0 (C-6'), 129.2 (C-7a), 130.3 (C-5'), 136.6 (C-1'), 149.1 (C-3a), 151.4 (C-3'), 156.3 (C-5), 160.8 (C-7). Anal. (C<sub>13</sub>H<sub>14</sub>N<sub>6</sub>O): C, H, N.

**3-(5-Methyl-7-oxo-6,7-dihydro-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-3-yl)benzonitrile (11h).**

Following the general procedure, to a solution of **10h** (170 mg, 0.63 mmol) in anhydrous DMF (2.8 mL), sodium acetate (153 mg, 1.88 mmol) was added. After work-up, the residue was washed with ether and the resulting solid was purified by precipitation with dichloromethane/methanol to yield 104 mg (65%) of **11h** as a beige solid. Mp: > 280 °C (decomposed). MS (ES, positive mode): m/z 253 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ 2.46 (s, 3H, CH<sub>3</sub>), 7.87 (pt, *J* = 8.0 Hz, 1H, H-5'), 8.03 (m, 1H, H-6'), 8.39 (ddd, *J* = 8.3, 2.1, 1.0 Hz, 1H, H-4'), 8.50 (pt, *J* = 1.8 Hz, 1H, H-2'), 12.82 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 22.0 (CH<sub>3</sub>), 112.9 (C-3'), 118.3 (CN), 125.7, 127.3 (Ar), 129.2 (C-7a), 131.7, 133.1, 136.1 (Ar), 149.4 (C-3a), 156.3 (C-5), 161.4 (C-7). Anal. (C<sub>12</sub>H<sub>8</sub>N<sub>6</sub>O): C, H, N.

**3-(3'-Acetylphenyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (11i).** Following the general procedure, to a solution of **10i** (90 mg, 0.33 mmol) in anhydrous DMF (1.5 mL), sodium acetate (82 mg, 0.99 mmol) was added. After work-up, the residue was purified by flash chromatography (dichloromethane/methanol) to yield 50 mg (59%) of **11i** as a beige solid. Mp 262-264 °C. MS (ES, positive mode): m/z 256 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ 2.65 (s, 3H, CH<sub>3</sub>), 7.80 (pt, *J* = 7.9 Hz, 1H, H-5'), 8.13 (d, *J* = 7.8 Hz, 1H, H-6'), 8.28 (d, *J* = 8.0 Hz, 1H, H-4'), 8.37 (s, 1H, H-5), 8.55 (s, 1H, H-2'), 12.94 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 27.6 (CH<sub>3</sub>), 121.7, 127.0 (Ar), 129.6 (C-7a), 131.0, 131.2, 136.2, 138.6 (Ar), 149.1 (C-3a), 151.4 (C-7), 155.9 (C-5), 197.7 (CO). Anal. (C<sub>12</sub>H<sub>9</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**3-(4'-Acetylphenyl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (11j).** Following the general procedure, to a solution of **10j** (86 mg, 0.29 mmol) in anhydrous DMF (2.0 mL) sodium acetate (75 mg, 0.87 mmol) was added. After work-up, the residue was purified by flash chromatography (dichloromethane/methanol) to yield 54 mg (62%) of **11j** as a solid. Mp: 286-287 °C. MS (ES, positive mode): 270 m/z (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz): δ 2.45 (s, 3H, CH<sub>3</sub>), 2.64 (s, 3H, COCH<sub>3</sub>), 8.24 (d, *J* = 9.0 Hz, 4H, H-2', H-3'), 12.75 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 22.1 (CH<sub>3</sub>), 27.3 (CH<sub>3</sub>), 122.0 (Ar), 129.5 (C-7a), 130.2, 136.8, 139.1 (Ar), 149.4 (C-3a), 156.1 (C-5), 161.4 (C-7), 197.5 (CO). Anal. (C<sub>13</sub>H<sub>11</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**5-Methyl-3-(4'-propoxyphenyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (11k).** Following the general procedure, to a solution of **10k** (60 mg, 0.19 mmol) in anhydrous DMF (2.0 mL), sodium

acetate (50 mg, 0.57 mmol) was added. After work-up, the residue was purified by flash chromatography (dichloromethane/methanol) to yield 35 mg (65%) of **11k** as a solid. Mp: 267-268 °C. MS (ES, positive mode): m/z 286 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ: 1.01 (t, *J* = 7.4 Hz, 3H, CH<sub>2</sub>CH<sub>3</sub>), 1.78 (h, *J* = 7.1 Hz, 2H, CH<sub>2</sub>CH<sub>3</sub>), 2.43 (s, 3H, CH<sub>3</sub>), 4.03 (t, *J* = 6.5 Hz, 2H, OCH<sub>2</sub>), 7.18 (d, *J* = 9.0 Hz, 2H, H-3'), 7.85 (d, *J* = 9.0 Hz, 2H, H-2'), 12.69 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 11.1 (CH<sub>2</sub>CH<sub>3</sub>), 22.2 (CH<sub>3</sub>), 22.6 (CH<sub>2</sub>CH<sub>3</sub>), 70.1 (OCH<sub>2</sub>), 115.8, 124.8, 128.7 (Ar), 129.2 (C-7a), 149.2 (C-3a), 156.5 (C-5), 159.6 (C-7), 160.9 (Ar). Anal. (C<sub>14</sub>H<sub>15</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**3-(Benzo[*d*][1,3]dioxol-5-yl)-5-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (11l).** Following the general procedure, to a solution of **10l** (32 mg, 0.11 mmol) in anhydrous DMF (0.5 mL), sodium acetate (28 mg, 0.33 mmol) was added. The resulting precipitate was filtered and washed with water to yield 15 mg (50%) of **11l** as a beige solid. Mp: > 290 °C (decomposed). MS (ES, positive mode): m/z 272 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ: 2.30 (s, 3H, CH<sub>3</sub>), 6.12 (s, 2H, CH<sub>2</sub>), 7.10 (d, *J* = 8.4 Hz, 1H, H-5'), 7.57 (dd, *J* = 8.4, 2.0 Hz, 1H, H-6'), 7.63 (d, *J* = 1.9 Hz, 1H, H-2'); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 24.0 (CH<sub>3</sub>), 102.3 (CH<sub>2</sub>), 103.3, 108.9, 115.3 (Ar), 129.3 (C-7a), 131.1, 147.0, 148.1 (Ar), 150.3 (C-3a), 165.1 (C-5), 173.9 (C-7). Anal. (C<sub>12</sub>H<sub>9</sub>N<sub>5</sub>O<sub>3</sub>): C, H, N.

**Ethyl 3-(5-methyl-7-oxo-6,7-dihydro-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-3-yl) benzoate (11m).** Following the general procedure, to a solution of **10m** (170 mg, 0.63 mmol) in anhydrous DMF (2.8 mL), sodium acetate (153 mg, 1.88 mmol) was added. After work-up, the residue was washed with ether and the resulting solid was purified by precipitation with dichloromethane/methanol to yield 104 mg (65%) of **11m** as a beige solid. Mp: 245-247 °C. MS (ES, positive mode): m/z 253 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ 2.46 (s, 3H, CH<sub>3</sub>), 7.87 (pt, *J* = 8.0 Hz, 1H, H-5'), 8.03 (m, 1H, H-6'), 8.39 (ddd, *J* = 8.3, 2.1, 1.0 Hz, 1H, H-4'), 8.50 (pt, *J* = 1.8 Hz, 1H, H-2'), 12.82 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 14.6 (CH<sub>2</sub>CH<sub>3</sub>), 22.1 (CH<sub>3</sub>), 61.8 (CH<sub>2</sub>CH<sub>3</sub>), 122.6, 126.7 (Ar), 129.4 (C-7a), 129.7, 130.8, 131.7, 136.1 (Ar), 149.3 (C-3a), 156.2 (C-5), 161.3 (C-7), 165.2 (CO). Anal. (C<sub>14</sub>H<sub>13</sub>N<sub>5</sub>O<sub>3</sub>): C, H, N.

**3-(5-Methyl-7-oxo-6,7-dihydro-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-3-yl)benzoic acid (11n).** To a solution of **11m** (500 mg, 1.67 mmol) in anhydrous DMF (11.0 mL/mmol), KOH 20% (4.3 mL) was added. The reaction was microwave-irradiated at 100 °C for 30 min. After cooling, the reaction was concentrated to dryness. The residue was dissolved in water, acidified by addition of HCl 1 N and the precipitate thus formed was isolated by filtration to yield 419 mg (92%) of **11n** as a yellow solid. Mp: > 290 °C (decomposed). MS (ES, positive mode): m/z 272 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ 2.45 (s, 3H, CH<sub>3</sub>), 7.79 (pt, *J* = 8.0 Hz, 1H, H-5'), 8.08 (m, 1H, H-6'), 8.29 (ddd, *J* = 8.0, 2.2, 1.0 Hz, 1H, H-4'), 8.58 (pt, *J* = 1.7 Hz, 1H, H-2'), 12.78 (s, 1H, NH), 13.42 (s, 1H, COOH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz): δ 22.1 (CH<sub>3</sub>), 122.9, 126.5 (Ar), 129.4 (C-7a), 129.9, 130.7, 132.7, 136.0 (Ar), 149.3 (C-3a), 156.2 (C-5), 161.3 (C-7), 166.8 (COOH). Anal. (C<sub>12</sub>H<sub>9</sub>N<sub>5</sub>O<sub>3</sub>): C, H, N.

**General procedure for the synthesis of [1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-ones (15a-g) from the 5-amino-1*H*-1,2,3-triazole-4-carboxamide 13.** To a solution of Na (5.00 mmol) in ethanol (10 mL/mmol), the carboxamide **13** (1.00 mmol) and the appropriate ester (4.00 mmol) were added. The reaction mixture was heated at reflux for 1 to 8 hours. After cooling, the reaction was concentrated to dryness. The residue was dissolved in water, acidified by addition of acetic acid and the precipitate thus formed was isolated by filtration and purified as specified.

**3-(3'-Isopropoxyphenyl)-5-trifluoromethyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (15a).** Following the general procedure, to a solution of Na (43 mg, 1.85 mmol) in ethanol (3.7 mL), **13** (96 mg, 0.37 mmol) and ethyl trifluoroacetate (175  $\mu$ L, 1.47 mmol) were added. The reaction mixture was refluxed for 1 hour. After work-up, **15a** (84 mg, 67%) was isolated as a white solid. Mp: 214-216 °C. MS (ES, positive mode): m/z 340 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ 1.32 (d, *J* = 6.0 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 4.69 (hept, *J* = 6.2 Hz, 1H, CH), 7.13 (ddd, *J* = 7.8, 2.5, 1.6, 1H, H-4'), 7.55 (m, 3H, H-2', H-5', H-6'); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ 22.0 (CH<sub>3</sub>), 70.4 (CH), 109.8, 114.5, 117.1 (Ar), 122.1 (q ap, CF<sub>3</sub>), 131.2 (C-7a), 131.3, 136.2 (Ar), 147.5 (C-3a), 148.0 (d, *J* = 39.3 Hz, C-5), 156.7 (C-7), 158.6 (Ar). Anal. (C<sub>14</sub>H<sub>12</sub>F<sub>3</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**5-Cyanoethyl-3-(3'-isopropoxypyhenyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (15c).**

Following the general procedure, to a solution of Na (38 mg, 1.65 mmol) in ethanol (3.3 mL), **13** (90 mg, 0.33 mmol) and ethyl cyanoacetate (140  $\mu$ L, 1.31 mmol) were added. The reaction mixture was refluxed for 8 hours. After cooling, a precipitate was obtained that was purified by CCTLC (dichloromethane/methanol, 20:1) to yield 23 mg (23%) of **15c** as a beige solid. Mp: 242-244  $^{\circ}$ C. MS (ES, positive mode): m/z 311 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.30 (d, *J* = 6.0 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 4.31 (s, 2H, CH<sub>2</sub>), 4.73 (hept, *J* = 6.0 Hz, 1H, CH), 7.07 (ddd, *J* = 8.3, 2.5, 0.9, 1H, H-4'), 7.52 (pt, *J* = 8.2 Hz, 1H, H-5'), 7.60 (ddd, *J* = 8.0, 1.9, 0.9 Hz, 1H, H-6'), 7.73 (pt, *J* = 2.1 Hz, 1H, H-2'), 13.05 (s, 1H, NH); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  22.2 (CH<sub>3</sub>), 25.0 (CH<sub>2</sub>), 70.4 (CH), 108.8, 113.8 (Ar), 115.6 (CN), 117.2 (Ar), 129.8 (C-7a), 131.2, 136.7 (Ar), 148.3 (C-3a), 154.8 (C-5), 155.7 (C-7), 158.6 (Ar). Anal. (C<sub>15</sub>H<sub>14</sub>N<sub>6</sub>O<sub>2</sub>): C, H, N.

**3-(3'-Isopropoxypyhenyl)-5-propyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (15d).**

Following the general procedure, to a solution of Na (36 mg, 1.55 mmol) in ethanol (3.1 mL), compound **13** (80 mg, 0.31 mmol) and ethyl butyrate (139  $\mu$ L, 1.22 mmol) were added. The reaction was microwave-irradiated at 90  $^{\circ}$ C for 2 hours. After work-up, a precipitate was obtained that was purified by CCTLC (dichloromethane/methanol, 20:1) to yield **15d** (23 mg, 24%) as a white solid. Mp: 216-218  $^{\circ}$ C. MS (ES, positive mode): m/z 314 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  0.93 (t, *J* = 7.4 Hz, 3H, CH<sub>3</sub>), 1.31 (d, *J* = 6.0 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 1.74 (d, *J* = 7.4 Hz, 2H, CH<sub>2</sub>), 2.66 (h, *J* = 7.4 Hz, 2H, CH<sub>2</sub>), 4.68 (hept, *J* = 5.6 Hz, 1H, CH), 7.07 (d, *J* = 8.2 Hz, 1H, H-4'), 7.51 (pt, *J* = 8.1 Hz, 1H, H-5'), 7.57 (d, *J* = 8.1 Hz, 1H, H-6'), 7.62 (s, 1H, H-2'), 12.70 (s 1H, NH); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  13.8 (CH<sub>3</sub>), 20.6 (CH<sub>2</sub>), 22.1 (CH(CH<sub>3</sub>)<sub>2</sub>), 36.5 (CH<sub>2</sub>), 70.3 (CH), 109.3, 114.1, 116.6 (Ar), 129.4 (C-7a), 131.1, 136.9 (Ar), 149.1 (C-3a), 156.4 (C-7), 158.5 (Ar), 164.0 (C-5). Anal. (C<sub>16</sub>H<sub>19</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**3-(3'-Isopropoxypyhenyl)-5-isopropyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (15e).**

Following the general procedure, to a solution of Na (36 mg, 1.55 mmol) in ethanol (3.1 mL), **13** (80 mg, 0.31 mmol) and ethyl isobutyrate (140  $\mu$ L, 1.22 mmol) were added. The reaction was microwave-irradiated at 90  $^{\circ}$ C for 2 hour. After work-up, a precipitate was obtained that was purified by CCTLC (dichloromethane/methanol, 20:1) to yield **15e** (8 mg, 8%) as a white solid. Mp: 246-247  $^{\circ}$ C. MS (ES, positive mode): m/z 314 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.25 (d, *J* = 6.8 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 1.32 (d, *J* = 6.0 Hz, 6H, CH<sub>3</sub>), 3.00 (hept, *J* = 6.8 Hz, 1H, CH), 4.69 (hept, *J* = 6.0 Hz, 1H, OCH), 7.05 (ddd, *J* = 8.3, 2.5, 0.9 Hz, 1H, H-4'), 7.52 (pt, *J* = 8.1 Hz, 1H, H-5'), 7.60 (ddd, *J* = 8.1, 2.0, 0.9 Hz, 1H, H-6'), 7.68 (pt, *J* = 2.2 Hz, 1H, H-2'), 12.69 (s 1H, NH); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  21.1 (CH(CH<sub>3</sub>)<sub>2</sub>), 22.4 (CH(CH<sub>3</sub>)<sub>2</sub>), 33.9 (CH), 70.5 (CH), 109.0, 114.1, 117.1 (Ar), 129.7 (C-7a), 131.4, 137.2 (Ar), 149.2 (C-3a), 156.7 (C-7), 158.7 (Ar), 168.5 (C-5). Anal (C<sub>16</sub>H<sub>19</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**3-(3'-Isopropoxypyhenyl)-5-phenyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (15f).**

Following the general procedure, to a solution of Na (33 mg, 1.45 mmol) in ethanol (2.9 mL), **13** (80 mg, 0.31 mmol) and ethyl phenylacetate (145  $\mu$ L, 1.16 mmol) were added. The reaction mixture was refluxed for 8 hours to obtain a precipitate that was purified by CCTLC (dichloromethane/methanol, 20:1) to yield 44 mg (41%) of **15f** as a white solid. Mp: 245-246  $^{\circ}$ C. MS (ES, positive mode): m/z 348 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.33 (d, *J* = 6.0 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 4.73 (hept, *J* = 6.0 Hz, 1H, CH), 7.09 (m, 1H, H-4'), 7.62 (m, 6H, H-3'', H-4'', H-2', H-5', H-6'), 8.14 (d, *J* = 7.8 Hz, 2H, H-2''), 13.05 (s, 1H, NH); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  22.3 (CH<sub>3</sub>), 70.6 (CH), 109.5, 114.5, 117.2, 129.2, 129.5 (Ar), 129.8 (C-7a), 131.4, 132.3, 133.1, 137.1 (Ar), 149.3 (C-3a), 156.9 (C-7), 158.4 (Ar), 158.8 (C-5). Anal. (C<sub>19</sub>H<sub>17</sub>N<sub>5</sub>O<sub>2</sub>): C, H, N.

**3-(3'-Isopropoxypyhenyl)-5-(4''-pyridyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (15g).**

Following the general procedure, to a solution of Na (33 mg, 1.45 mmol) in ethanol (2.9 mL), **13** (80 mg, 0.31 mmol) and methyl 4-pyridylacetate (159  $\mu$ L, 1.16 mmol) were added. The reaction mixture was refluxed for 5 hours to yield 85 mg (79%) of **15g** as a beige solid. Mp: 259-260  $^{\circ}$ C. MS (ES, positive mode): m/z 349 (M+H)<sup>+</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.33 (d, *J* = 6.0 Hz, 6H, CH(CH<sub>3</sub>)<sub>2</sub>), 4.73 (hept, *J* = 6.0 Hz, 1H, CH), 7.11 (d, *J* = 8.7 Hz, 1H, H-4'), 7.56 (pt, *J* = 8.3 Hz, 1H, H-5'), 7.66 (m, 2H, H-2', H-6'), 8.05 (d, *J* = 5.9 Hz, 2H, H-2''), 8.83 (d, *J* = 5.7 Hz, 2H, H-3''); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  22.2 (CH<sub>3</sub>), 70.4 (CH), 109.4, 114.4, 117.0, 122.5 (Ar), 130.1 (C-

7a), 131.2, 136.7, 139.5 (Ar), 148.7 (C-3a), 150.9, 156.4 (Ar), 156.6 (Ar, C-7), 158.6 (C-5). Anal. (C<sub>18</sub>H<sub>16</sub>N<sub>6</sub>O<sub>2</sub>): C, H, N.

## References

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## ANALYTICAL DATA

| Comp.      | Formula  | Calculated (%) |      |       | Found (%) |      |       |
|------------|--|----------------|------|-------|-----------|------|-------|
|            |  | C              | H    | N     | C         | H    | N     |
| <b>2</b>   | C <sub>13</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub>                | 57.99          | 4.12 | 26.01 | 57.67     | 3.98 | 25.75 |
| <b>3a</b>  | C <sub>13</sub> H <sub>12</sub> N <sub>6</sub> O                             | 58.20          | 4.51 | 31.33 | 57.96     | 4.68 | 31.09 |
| <b>3b</b>  | C <sub>14</sub> H <sub>14</sub> N <sub>6</sub> O                             | 59.56          | 5.00 | 29.77 | 59.46     | 4.85 | 29.58 |
| <b>3c</b>  | C <sub>14</sub> H <sub>13</sub> N <sub>5</sub> O <sub>2</sub>                | 59.36          | 4.63 | 24.72 | 59.60     | 4.62 | 24.53 |
| <b>4</b>   | C <sub>14</sub> H <sub>13</sub> N <sub>5</sub> O <sub>2</sub>                | 59.36          | 4.63 | 24.72 | 59.65     | 4.59 | 24.68 |
| <b>6a</b>  | C <sub>14</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub>                | 62.68          | 4.51 | 20.88 | 62.52     | 4.85 | 20.79 |
| <b>6b</b>  | C <sub>15</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub>                | 63.82          | 5.00 | 19.85 | 63.58     | 5.06 | 19.98 |
| <b>11a</b> | C <sub>12</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub>                | 56.03          | 4.31 | 27.22 | 55.92     | 3.97 | 26.90 |
| <b>11b</b> | C <sub>12</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub>                | 56.03          | 4.31 | 27.22 | 55.96     | 4.10 | 27.12 |
| <b>11c</b> | C <sub>11</sub> H <sub>8</sub> ClN <sub>5</sub> O <sub>2</sub>               | 50.49          | 3.08 | 26.76 | 50.79     | 2.91 | 26.58 |
| <b>11d</b> | C <sub>18</sub> H <sub>13</sub> N <sub>5</sub> O <sub>2</sub>                | 65.25          | 3.95 | 21.14 | 64.98     | 3.81 | 20.89 |
| <b>11e</b> | C <sub>14</sub> H <sub>15</sub> N <sub>5</sub> O <sub>2</sub>                | 58.94          | 5.30 | 24.55 | 58.75     | 5.60 | 24.25 |
| <b>11f</b> | C <sub>13</sub> H <sub>12</sub> N <sub>6</sub> O <sub>2</sub>                | 54.93          | 4.25 | 29.56 | 54.82     | 4.36 | 29.65 |
| <b>11g</b> | C <sub>13</sub> H <sub>14</sub> N <sub>6</sub> O                             | 57.77          | 5.22 | 31.09 | 57.51     | 5.02 | 30.78 |
| <b>11h</b> | C <sub>12</sub> H <sub>8</sub> N <sub>6</sub> O                              | 57.14          | 3.20 | 33.32 | 57.02     | 3.25 | 33.45 |
| <b>11i</b> | C <sub>12</sub> H <sub>9</sub> N <sub>5</sub> O <sub>2</sub>                 | 56.47          | 3.55 | 27.44 | 56.28     | 3.69 | 27.25 |
| <b>11j</b> | C <sub>13</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub>                | 57.99          | 4.12 | 26.01 | 57.84     | 4.28 | 25.95 |
| <b>11k</b> | C <sub>14</sub> H <sub>15</sub> N <sub>5</sub> O <sub>2</sub>                | 58.94          | 5.30 | 24.55 | 58.84     | 5.55 | 24.36 |
| <b>11l</b> | C <sub>12</sub> H <sub>9</sub> N <sub>5</sub> O <sub>3</sub>                 | 53.14          | 3.34 | 25.82 | 53.02     | 3.68 | 25.77 |
| <b>11m</b> | C <sub>14</sub> H <sub>13</sub> N <sub>5</sub> O <sub>3</sub>                | 56.18          | 4.38 | 23.42 | 56.02     | 4.62 | 23.33 |
| <b>11n</b> | C <sub>12</sub> H <sub>9</sub> N <sub>5</sub> O <sub>3</sub>                 | 53.14          | 3.34 | 25.82 | 52.95     | 3.28 | 25.75 |
| <b>13</b>  | C <sub>12</sub> H <sub>15</sub> N <sub>5</sub> O <sub>2</sub>                | 55.16          | 5.79 | 26.80 | 55.30     | 5.80 | 26.78 |
| <b>14</b>  | C <sub>12</sub> H <sub>15</sub> N <sub>5</sub> O <sub>2</sub>                | 55.16          | 5.79 | 26.28 | 54.68     | 5.87 | 26.61 |
| <b>15a</b> | C <sub>14</sub> H <sub>12</sub> F <sub>3</sub> N <sub>5</sub> O <sub>2</sub> | 49.56          | 3.57 | 20.64 | 49.29     | 3.33 | 20.38 |
| <b>15b</b> | C <sub>15</sub> H <sub>17</sub> N <sub>5</sub> O <sub>2</sub>                | 60.19          | 5.72 | 23.40 | 60.21     | 6.01 | 23.62 |
| <b>15c</b> | C <sub>15</sub> H <sub>14</sub> N <sub>6</sub> O <sub>2</sub>                | 58.06          | 4.55 | 27.08 | 57.96     | 4.52 | 26.98 |
| <b>15d</b> | C <sub>16</sub> H <sub>19</sub> N <sub>5</sub> O <sub>2</sub>                | 61.33          | 6.11 | 22.35 | 61.08     | 6.23 | 22.46 |
| <b>15e</b> | C <sub>16</sub> H <sub>19</sub> N <sub>5</sub> O <sub>2</sub>                | 61.33          | 6.11 | 22.35 | 61.02     | 6.18 | 22.50 |
| <b>15f</b> | C <sub>19</sub> H <sub>17</sub> N <sub>5</sub> O <sub>2</sub>                | 65.69          | 4.93 | 20.16 | 64.99     | 4.95 | 20.07 |
| <b>15g</b> | C <sub>18</sub> H <sub>16</sub> N <sub>6</sub> O <sub>2</sub>                | 62.06          | 4.63 | 24.12 | 61.70     | 4.61 | 23.78 |
| <b>16</b>  | C <sub>13</sub> H <sub>13</sub> N <sub>5</sub> O <sub>3</sub>                | 54.35          | 4.56 | 24.38 | 54.22     | 4.65 | 24.21 |
| <b>20</b>  | C <sub>15</sub> H <sub>17</sub> N <sub>5</sub> O <sub>2</sub>                | 60.19          | 5.72 | 23.40 | 60.24     | 6.01 | 23.68 |