Fast, microwave-promoted one-pot synthesis of bicyclic pyrimidones from Baylis–Hillman adducts

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Two types of fused pyrimidones, 3-substituted-7-chloro-4*H*-pyrimido[1,2-*b*]pyridazin-4-ones and 6-substituted-5*H*-thiazolo-[3,2-*a*]pyrimidin-5-ones were easily prepared from Baylis–Hillman adduct acetates under microwave irritation in high yields.

Keywords: microwave irradiation, one-pot synthesis, bicyclic pyrimidones, Baylis–Hillman adducts

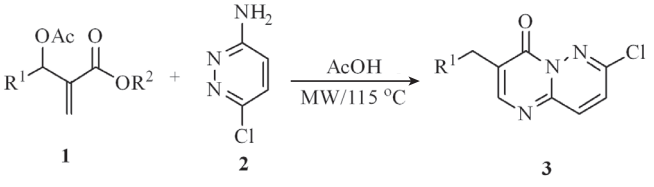
The pyrimidinone framework belongs to an important class of heterocyclic compounds possessing pharmacological properties such as anticancer, antihypertensive, antidepressant and anti-immune activities.[1–5] Because of the remarkable medicinal and pharmacological potential of pyrimidinone derivatives, development of simple and efficient methodologies for the synthesis of substituted fused pyrimidones has been and continues to be a challenging and attractive endeavour in organic and medicinal chemistry.

Microwave chemistry as a useful technique for a variety of applications in organic synthesis and transformations, has started to change the face of chemical reactions which offers several advantages over conventional homogeneous and heterogeneous reactions with respect to high reaction rates and yields.[6,7] The Baylis–Hillman reaction has proved to be a powerful tool for C–C bond-forming reactions, which are also atom economical, green and simple reaction and provide densely functionalised molecules, The Baylis–Hillman adducts have become valuable sources for making cyclic frameworks containing heteroatoms.[8–11] In pursuit of the interest in the synthesis of heterocyclic molecules,[12–15] we now report a one-pot, microwave-assisted fast protocol for facile transformation of the Baylis–Hillman adducts into bicyclic heterocyclic frameworks containing a pyrimidone moiety.

Results and discussion

Several approaches for the synthesis of 4*H*-pyrimido[1,2-*b*] pyridazin-4-ones **3** have been described in the literature,[16–24] and the classical method for the synthesis of 4*H*-pyrimido[1,2-*b*] pyridazin-4-ones, proposed by Svete and his co-workers, was by treatment of appropriately substituted 3-(dimethylamino) prop-2-enoates and 3-aminopyridazines in acetic acid.[16–20] However, most of these methods suffered from some drawbacks including difficultly accessible starting materials or the requirement for multistep synthetic transformations.

We now report a novel and simple method for the synthesis of compound **3** under microwave irritation from Baylis–Hillman adduct acetates **1** (Scheme 1).

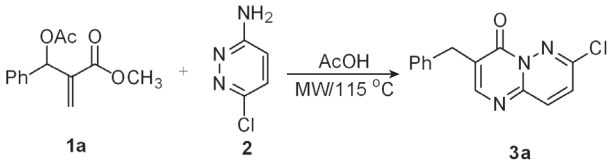


Scheme 1 Synthesis of various 3-substituted-7-chloro-4*H*-pyrimido[1,2-*b*] pyridazin-4-ones 3.

Initially, treatment of Baylis–Hillman adduct acetate **1a** and 6-chloropyridazin-3-amine **2** in refluxing toluene or acetic acid provided the desired product **3a** in 21% and 51% yields, respectively, even prolonging the reaction time and increasing the temperature (Table 1, entries 1–3) had little influence. Our previous studies indicated that solvent-free conditions may result in shortening the reaction time and improving the yield.[13,14] It was found that 81% yield of product can be obtained when the reaction was performed at 130 °C for 6 h under solvent-free conditions (Table 1, entry 4). However, with the aid of microwave irradiation, the reaction time could be shortened to 1 h with a slightly high yield (Table 1, entries 5). Fortunately, when the reaction mixture was performed in acetic acid under microwave irradiation at 115 °C, the yield of product **3a** could be increased up to 95% within 5 minutes (Table 1, entries 6 and 7).

Encouraged by these results and the work-up operation, and with a view to understanding the generality of this reaction, we successfully extended the same strategy to a series of Baylis–Hillman adduct acetates with respect to steric and electronic effects (Table 2). As shown in Table 2, all reactions between aryl-substituted substrates **1** and 3-amino-6-chloropyridazine **2** went smoothly to provide the corresponding products in good to excellent yields and no obvious electronic and steric effect were observed (Table 2, entries 1–11). To further investigate the steric effect of the ester moiety, the ethyl ester substrates in substrates **1** gave lower yields and needed longer reaction times than those of methyl ester probably due to the greater steric effect of the former (Table 2, entries 1–4). Compared to aryl-substituted Baylis–Hillman adducts, alkyl-substituted ones provided the products in slightly lower yields (Table 2, entries 12 and 13).

Table 1 Optimisation of the synthesis of compound **3a**[a]



Entry	Solvent	Method[b]	Temp/°C	Time	Yield /%[c]
1	Toluene	T	reflux	24 h	21
2	Acetic acid	T	reflux	12 h	51
3	Acetic acid	T	reflux	24 h	52
4	–	T	130	6 h	81
5	–	MW	130	1 h	86
6	Acetic acid	MW	90	0.5 h	82
7	Acetic acid	MW	115	5 min	95

[a]The reaction was carried out on Baylis–Hillman adduct acetates **1a** (2 mmol) with 6-chloropyridazin-3-amine **2** (2 mmol) in solvent (10 mL) or solvent-free condition.
[b]T, traditional heating; MW, microwave irradiation (300W).
[c]Isolated yields based on **1a**.

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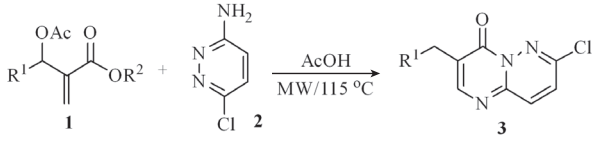
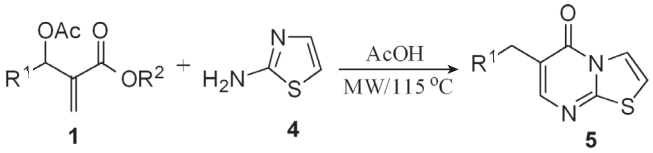
Table 2 Microwave assisted synthesis of **3** from Baylis–Hillman adducts **1**[a]



Entry	R^1	R^2	Time/min	Yield/%[b]
1	Ph	Me	5	95 (**3a**)
2	Ph	Et	15	89 (**3a**)
3	2-ClC_6H_4	Me	5	97 (**3b**)
4	2-ClC_6H_4	Et	15	91 (**3b**)
5	3-ClC_6H_4	Me	5	96 (**3c**)
6	4-ClC_6H_4	Me	5	93 (**3d**)
7	2-Cl-6-FC_6H_3	Me	5	98 (**3e**)
8	3-$NO_2C_6H_4$	Me	5	96 (**3f**)
9	3-$MeOC_6H_4$	Me	5	93 (**3g**)
10	4-FC_6H_4	Me	5	96 (**3h**)
11	2-Thiophenyl	Me	5	91 (**3i**)
12	Isopentyl	Me	10	83 (**3j**)
13	Pentyl	Me	10	85 (**3k**)

[a]The reaction was carried out on Baylis–Hillman adduct acetates **1** (2 mmol) with 6-chloropyridazin-3-amine **2** (2 mmol) in acetic acid (10 mL).
[b]Isolated yields based on **1**.

Zhong *et al.*[14] have reported 5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones **5** could be successfully prepared in satisfactory yields *via* treatment of Baylis–Hillman adduct acetate **1** and 2-aminothiazole **4** at 130 °C for 3–6 hours under solvent-free and base-free conditions. As the starting materials were similar, we thought the above, optimised, protocol was also suitable for the preparation of compounds **5**. To our surprise, compared with previous work,[14] the present method gave 5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones **5** in dramatically shorter reaction times and also in higher yields (Scheme 2, Table 3), especially for those substrates where R^1 is a heteroaryl or an alkyl group (Table 3, entries 5 and 6) or R^2 is an ethyl group (Table 3, entries 2 and 3).



Scheme 2 Synthesis of various 5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones **5**.

Conclusions

In conclusion, we have developed a fast and efficient method for the synthesis of substituted fused pyrimidones from Baylis–Hillman adducts under MW irradiation in acetic acid. Future work will be aimed at investigating the scope of our procedure for the synthesis of other heterocyclic systems.

Experimental

Melting points were determined by Büchi B-540 melting point apparatus and are uncorrected. ^{1}H and ^{13}C spectra were recorded in DMSO-d_6 or $CDCl_3$ with tetramethylsilane (TMS, δ = 0) as an internal standard at ambient temperature on a Varian-400 MHz spectrometer at 400 and 100 MHz. Mass spectra were obtained on a Thermo Finnigan LCQ-Advantage spectrometer (ESI). HRMS was carried out on an APEX (Bruker) mass III spectrometer. The Baylis–Hillman adducts were prepared according to the literature procedure.[8] All microwave experiments were performed with the APEX Microwave Chemistry Workstation – Excel.

Table 3 Microwave assisted synthesis of **5**[a]

Entry	R^1	R^2	Time/min	Yield/%[b]
1	Ph	Me	5	**5a** 96 (92[c])
2	Ph	Et	15	**5a** 90 (73[c])
3	2-ClC_6H_4	Et	15	**5b** 89 (65[c])
4	3-$MeOC_6H_4$	Me	5	**5c** 95 (85[c])
5	2-Thiophenyl	Me	5	**5d** 86 (65[c])
6	Isopentyl	Me	10	**5e** 81 (30[c])

[a]The reaction was carried out on Baylis–Hillman adduct acetates **3** (2 mmol) with thiazol-2-amine **5** (2 mmol) in acetic acid (10 mL).
[b]Isolated yield based on **3**.
[c]The yields given in ref. 14.

*Synthesis of 3-substituted-7-chloro-4*H*-pyrimido[1,2-*b*]pyridazin-4-ones* (**3**) *and 6-substituted-5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones* (**5**)*; general procedure*

A magnetically stirred mixture of the appropriate Baylis–Hillman adduct acetate **1** (2 mmol) and 3-amino-6-chloropyridazine **2** or 2-aminothiazole **4** (2 mmol) was subjected to microwave irradiation (300 W) under an atmosphere of N_2 at 115 °C for 5–15 min in acetic acid (10 mL). After cooling, the mixture was poured into ice water (50 mL). The precipitate was filtered and washed with water (2 × 10 mL) and ethanol (2 × 5 mL), then dried under vacuum to afford **3** or **5**.

*3-Benzyl-7-chloro-4*H*-pyrimido[*1,2-b*]pyridazin-4-one* (**3a**): Grey powder; from methyl 2-[acetoxy(phenyl)methyl]acrylate to yield **3a** 516 mg (95%), or from ethyl 2-[acetoxy(phenyl)methyl]acrylate to yield **3a** 484 mg (89%); m.p. 219.5–221.1 °C; IR ν_{max} (KBr)/cm^{-1}: 3082, 3011, 1636, 1541, 1488, 1130, 1092, 832, 766.; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 3.76 (2H, s, CH_2), 7.21–7.34 (5H, m, ArH), 7.71 (1H, d, *J* = 9.6 Hz, CH=C*H*CCl), 7.74 (1H, d, *J* = 9.6 Hz, C*H*=CHCCl), 8.35 (1H, s, C=C*H*N); ^{13}C NMR (100 Hz, DMSO-d_6) δ_C 33.4, 126.3, 128.0, 128.3(2C), 128.9(2C), 130.2, 134.7, 138.5, 138.8, 145.6, 147.2, 167.1; MS (ESI): *m/z* (%): 272 (M^+ + 1, 100). HRMS calcd for $C_{14}H_{10}ClN_3O$ [M^+]: 271.0512; found: 271.0509.

*7-Chloro-3-(2-chlorobenzyl)-4*H*-pyrimido[1,2-*b*]pyridazin-4-one* (**3b**): Grey powder; from methyl 2-[acetoxy(phenyl)methyl] acrylate to yield **3b** 594 mg (95%), or from ethyl 2-(acetoxy(phenyl) methyl)acrylate to yield **3b** 556 mg (89%); m.p. 236.4–237.1 °C; IR ν_{max} (KBr)/cm^{-1}: 3036, 1632, 1481, 1259, 1125, 850, 741; ^{1}H NMR (400 Hz, DMSO-d_6) δ_H 3.86 (2H, s, CH_2), 7.28–7.35 (3H, m, ArH), 7.47–7.49 (1H, m, ArH), 7.74 (1H, d, *J* = 9.6 Hz, CH=C*H*CCl), 7.77 (1H, d, *J* = 9.6 Hz, C*H*=CHCCl), 8.08 (1H, s, C=C*H*N); ^{13}C NMR (100 Hz, DMSO-d_6) δ_C 31.3, 126.1, 127.2, 128.5, 129.3, 130.3, 130.9, 133.3, 134.8, 135.4, 139.1, 145.8, 147.4, 167.0; MS (ESI): *m/z* (%): 306 (M^+ + 1, 100). HRMS calcd for $C_{14}H_9Cl_2N_3O$ [M^+]: 305.0123; found: 305.0112.

*7-Chloro-3-(3-chlorobenzyl)-4*H*-pyrimido[1,2-*b*]pyridazin-4-one* (**3c**): Grey powder; yield 588 mg (96%); m.p. 230.3–231.7 °C; IR ν_{max} (KBr)/cm^{-1}: 3441, 1642, 1489, 1130, 791, 659; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 3.76 (2H, s, CH_2), 7.25–7.28 (1H, m, ArH), 7.29–7.32 (2H, m, ArH), 7.41 (1H, t, *J* = 0.4 Hz, ArH), 7.71 (1H, d, *J* = 9.6 Hz, CH=C*H*CCl), 7.74 (1H, d, *J* = 9.6 Hz, C*H*=CHCCl), 8.51 (1H, s, C=C*H*N); ^{13}C NMR (100 Hz, DMSO-d_6) δ_C 33.0, 126.2, 127.0, 127.6, 128.5, 130.0, 130.1, 132.8, 134.7, 139.1, 141.1, 145.6, 147.3, 167.0; MS (ESI): *m/z* (%): 306 (M^+ + 1, 100). HRMS calcd for $C_{14}H_9Cl_2N_3O$ [M^+]: 305.0123; found: 305.0114.

*7-Chloro-3-(4-chlorobenzyl)-4*H*-pyrimido[1,2-*b*]pyridazin-4-one* (**3d**): Grey powder; yield 569 mg (93%); m.p. 234.1–235.0 °C; IR ν_{max} (KBr)/cm^{-1}: 3052, 1625, 1486, 1130, 1016, 809, 657, 553; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 3.75 (2H, s, CH_2), 7.32–7.38 (4H, m, ArH), 7.71 (1H, d, *J* = 9.6 Hz, CH=C*H*CCl), 7.74 (1H, d, *J* = 9.6 Hz, C*H*=CHCCl), 8.45 (1H, s, C=C*H*N); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 32.7, 127.4, 128.1 (2C), 130.1, 130.7 (2C), 130.9, 134.7, 137.6, 138.9, 145.6, 147.3, 167.0; MS (ESI): *m/z* (%): 306 (M^+ + 1, 100). HRMS calcd for $C_{14}H_9Cl_2N_3O$ [M^+]: 305.0123; found: 305.0112.

*7-Chloro-3-(2-chloro-6-fluorobenzyl)-4*H-*pyrimido[1,2-*b*]pyridazin-4-one* (**3e**): Off-white powder; yield 635 mg (98%); m.p. 218.6–220.0 °C; IR ν_{max} (KBr)/cm^{-1}: 3033, 1633, 1478, 1249, 1125, 953, 852, 753, 559; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 3.90 (2H, s, CH_2), 7.26–7.31 (1H, m, ArH), 7.39–7.43 (2H, m, C*H*=*H*CCl), 7.62 (1H, s, ArH), 7.32 (1H, s, C=C*H*N); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 25.1 (d, *J*=3.0 Hz), 114.7 (d, *J*=22.8 Hz), 122.7 (d, *J*=18.2 Hz), 125.5 (d, *J*=25.8 Hz), 125.7, 129.9 (d, *J*=9.9 Hz), 130.4, 134.7, 134.8, 137.4, 145.9, 147.3, 161.1 (d, *J*=245.7 Hz), 166.7; MS (ESI): *m/z (%)*: 324 (M^++1, 100). HRMS calcd for $C_{14}H_8Cl_2FN_3O$ [M^+]: 323.0028; found: 323.0031.

*7-Chloro-3-(3-nitrobenzyl)-4*H-*pyrimido[1,2-*b*]pyridazin-4-one* (**3f**): Grey powder; yield 608 mg (96%); m.p. 277.2–279.1 °C; IR ν_{max} (KBr)/cm^{-1}: 3084, 1644, 1489, 1344, 1129, 1097; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 3.90 (2H, s, CH_2), 7.59 (1H, t, *J*=8.0 Hz, ArH), 7.71 (1H, d, *J*=9.6 Hz, CH=C*H*CCl), 7.76 (1H, d, *J*=9.6 Hz, C*H*=CHCCl), 7.84 (1H, d, *J*=8.0 Hz, ArH), 8.08 (1H, dq, J_1=1.2 Hz, J_2=8.0 Hz, ArH), 8.24 (1H, t, *J*=1.2 Hz, ArH), 8.63 (1H, s, C=C*H*N); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 33.0, 121.4, 123.4, 126.6, 129.6, 130.2, 134.8, 135.8, 139.4, 140.9, 145.7, 147.4, 147.7, 167.0; MS (ESI): *m/z* (%): 317 (M^++1, 100). HRMS calcd for $C_{14}H_9ClN_4O_3$ [M^+]: 316.0363; found: 316.0370.

*7-Chloro-3-(3-methoxybenzyl)-4*H-*pyrimido[1,2-*b*]pyridazin-4-one* (**3g**): Grey powder; yield 561 mg (93%); m.p. 205.3–207.1 °C; IR ν_{max} (KBr)/cm^{-1}: 3095, 1643, 1489, 1261, 1130, 1051, 817, 784; ^{1}H NMR (400 Hz, DMSO-d_6) δ_H 3.72 (5H, s, CH_2 and OCH_3), 6.78 (1H, dd, J_1=2.8 Hz, J_2=8.0 Hz, ArH), 6.89 (1H, s, ArH), 6.91 (1H, d, *J*=2.8 Hz, ArH), 7.20 (1H, t, *J*=8.0 Hz, ArH), 7.70 (1H, d, *J*=9.6 Hz, CH=C*H*CCl), 7.74 (1H, d, *J*=9.6 Hz, C*H*=CHCCl), 8.32 (1H, s, C=C*H*N); ^{13}C NMR (100 Hz, DMSO-d_6) δ_C 33.3, 54.9, 111.6, 114.7, 121.1, 127.8, 129.2, 130.1, 134.7, 138.7, 139.9, 145.5, 147.1, 159.2, 167.0; MS (ESI): *m/z* (%): 302 (M^++1, 100). HRMS calcd for $C_{15}H_{12}ClN_3O_2$ [M^+]: 301.0618; found: 301.0609.

*7-Chloro-3-(4-fluorobenzyl)-4*H-*pyrimido[1,2-*b*]pyridazin-4-one* (**3h**): Grey powder; yield 556 mg (96%); m.p. 237.3–239.0 °C, IR ν_{max} (KBr)/cm^{-1}: 3087, 1642, 1493, 1209, 1129, 806, 660, 558; ^{1}H NMR (400 Hz, DMSO-d_6) δ_H 3.74 (2H, s, CH_2), 7.11 (2H, t, *J*=8.8 Hz, ArH), 7.38 (2H, dd, J_1=5.6 Hz, J_2=8.8 Hz, ArH), 7.70 (1H, d, *J*=9.6 Hz, CH=C*H*CCl), 7.74 (1H, d, *J*=9.6 Hz, C*H*=CHCCl), 8.41 (1H, s, C=C*H*N); ^{13}C NMR (100 Hz, DMSO-d_6) δ_C 32.6, 114.9 (*J*=21.2 Hz, 2C), 127.8, 130.2, 130.7 (*J*=8.3 Hz, 2C), 134.6, 134.7, 138.8, 145.6, 147.2, 160.9 (*J*=240.4 Hz), 167.1; MS (ESI): *m/z* (%): 290 (M^++1, 100). HRMS calcd for $C_{14}H_9ClFN_3O$ [M^+]: 289.0418; found: 289.0413.

*7-Chloro-3-(thiophen-2-ylmethyl)-4*H-*pyrimido[1,2-*b*]pyridazin-4-one* (**3i**): Grey powder; yield 505 mg (91%); m.p. 215.5–217.1 °C; IR ν_{max} (KBr)/cm^{-1}: 3082, 1641, 1490, 1133, 837; ^{1}H NMR (400 Hz, DMSO-d_6) δ_H 3.96 (2H, s, CH_2), 6.94–6.98 (2H, m, ArH), 7.34 (1H, dd, J_1=0.8 Hz, J_2=4.8 Hz, ArH), 7.71 (1H, d, *J*=9.6 Hz, CH=C*H*CCl), 7.75 (1H, d, *J*=9.6 Hz, C*H*=CHCCl), 8.39 (1H, s, C=C*H*N); ^{13}C NMR (100 Hz, DMSO-d_6) δ_C 27.6, 124.6, 126.1, 126.8, 127.3, 130.2, 134.7, 138.7, 140.3, 145.7, 147.2, 166.8; MS (ESI): *m/z* (%): 278 (M^++1, 100). HRMS calcd for $C_{12}H_8ClN_3OS$ [M^+]: 277.0077; found: 277.0079.

*7-Chloro-3-isopentyl-4*H-*pyrimido[1,2-*b*]pyridazin-4-one* (**3j**): Purple powder; yield 418 mg (83%); m.p. 166.6–168.2 °C; IR ν_{max} (KBr)/cm^{-1}: 3140, 2951, 1634, 1482, 1139, 849, 657, 552; ^{1}H NMR (400 Hz, DMSO-d_6) δ_H 0.90 (3H, s, CH_3), 0.92 (3H, s, CH_3), 1.40–1.46 (2H, m, $CHCH_2CH_2$), 1.52–1.59 (1H, m, CH), 2.42 (2H, t, *J*=7.2 Hz, $CHCH_2CH_2$), 7.70 (1H, d, *J*=9.6 Hz, CH=C*H*CCl), 7.74 (1H, d, *J*=9.6 Hz, C*H*=CHCCl), 8.37 (1H, s, C=C*H*N); ^{13}C NMR (100 Hz, DMSO-d_6) δ_C 22.3 (2C), 25.7, 27.3, 36.1, 129.1, 130.0, 134.7, 137.9, 145.4, 146.9, 167.4; MS (ESI): *m/z* (%): 252 (M^++1, 100). HRMS calcd for $C_{12}H_{14}ClN_3O$ [M^+]: 251.0825; found: 251.0819.

*7-Chloro-3-pentyl-4*H-*pyrimido[1,2-*b*]pyridazin-4-one* (**3k**): Light pink powder; yield 428 mg (85%); m.p. 173.1–175.1 °C; IR ν_{max} (KBr)/cm^{-1}: 3034, 2953, 1635, 1481, 1139, 850, 760, 551; ^{1}H NMR (400 Hz, DMSO-d_6) δ_H 0.91 (3H, t, *J*=6.8 Hz, CH_3), 1.26–1.39 (4H, m, $CH_3CH_2CH_2CH_2CH_2C$), 1.62–1.67 (2H, m, $CH_3CH_2(CH_2)_3C$), 2.58 (2H, t, *J*=7.6 Hz, $CH_3(CH_2)_3CH_2C$), 7.34 (1H, d, *J*=9.6 Hz, CH=C*H*CCl), 7.60 (1H, d, *J*=9.6 Hz, C*H*=CHCCl), 7.92 (1H, s, C=C*H*N); ^{13}C NMR (100 Hz, DMSO-d_6) δ_C 13.9, 21.9, 26.6, 27.7, 31.0, 128.9, 130.0, 134.7, 137.9, 145.4, 146.9, 167.4; MS (ESI): *m/z* (%): 252 (M^++1, 100). HRMS calcd for $C_{12}H_{14}ClN_3O$ [M^+]: 251.0825; found: 251.0821.

*6-Benzyl-5*H-*thiazolo[3,2-*a*]pyrimidin-5-one* (**5a**) Pale yellow crystals; from methyl 2-(acetoxy(phenyl)methyl)acrylate to yield **5a** 465 mg (96%), from ethyl 2-(acetoxy(phenyl)methyl)acrylate to yield **5a** 436 mg (90%); m.p. 227.9–230.1 °C (lit.[14] 229.9–227.5 °C), ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 3.87 (2H, s, CH_2), 7.21–7.98 (6H, m, ArH), 7.73 (1H, d, *J*=4.4 Hz, SCH=C*H*N), 8.16 (1H, s, COC=C*H*N); MS(ESI): *m/z* (%): 243 (M^++1, 100).

*6-(2-Chlorobenzyl)-5*H-*thiazolo[3,2-*a*]pyrimidin-5-one* (**5b**): Colourless crystals; yield 492 mg (89%); m.p. 201.7–202.5 °C (lit.[14] 201.5–202.2 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 3.77 (2H, s, CH_2), 7.26 (1H, d, *J*=4.8 Hz, NC=C*H*S), 7.29–7.32 (2H, m, ArH), 7.37 (1H, dd, J_1=3.6 Hz, J_2=6.0 Hz, ArH), 7.47 (1H, dd, J_1=3.6 Hz, J_2=5.6 Hz, ArH), 7.75 (1H, d, *J*=4.8 Hz, SCH=C*H*N), 7.99 (1H, s, COC=C*H*N); MS(ESI): *m/z* (%): 277 (M^++1, 100).

*6-(3-Methoxybenzyl)-5*H-*thiazolo[3,2-*a*]pyrimidin-5-one* (**5c**): Grey powder; yield 517 mg (95%); m.p. 204.1–205.1 °C (lit.[14] 204.0–204.8 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 3.65 (2H, s, CH_2), 3.73 (3H, s, OCH_3), 6.79 (1H, dd, J_1=2.8 Hz, J_2=8.4 Hz, ArH), 6.82 (1H, d, *J*=9.2 Hz, ArH), 6.87 (1H, s, ArH), 7.21 (1H, t, *J*=7.2 Hz, ArH), 7.26 (1H, d, *J*=4.4 Hz, NCH=C*H*S), 7.73 (1H, d, *J*=4.4 Hz, SCH=C*H*N), 8.13 (1H, s, COC=C*H*N); MS(ESI): *m/z* (%): 273 (M^++1) (100).

*6-(2-Thienylmethyl)-5*H-*thiazolo[3,2-*a*]pyrimidin-5-one* (**5d**): Grey power; yield 427 mg (86%); m.p. 192.6–193.2 °C (lit.[14] 192.5–193.2 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 3.89 (2H, s, CH_2), 6.96 (2H, m, NCH=C*H*S, SC=C*H*), 7.28 (1H, d, *J*=4.8 Hz, SCH=CH), 7.34 (1H, t, *J*=3.6 Hz, SCH=C*H*), 7.76 (1H, d, *J*=4.4 Hz, SCH=C*H*N), 8.27 (1H, s, COC=C*H*N); MS(ESI): *m/z* (%): 249 (M^++1) (100).

*6-Isopentyl-5*H-*thiazolo[3,2-*a*]pyrimidin-5-one* (**5e**): Brown crystals; yield 360 mg (81%); m.p. 145.7–146.9 °C (lit.[14] 145.8–146.4 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.88 (6H, s, 2×CH_3), 1.43 (2H, q, *J*=8 Hz, $(CH_3)_2CHCH_2$), 1.55–1.60 (1H, m, $(CH_3)_2CH$), 2.46 (2H, t, *J*=8 Hz, CH_2), 6.84 (1H, d, *J*=4.8 Hz, NCH=C*H*S), 7.41 (1H, d, *J*=4.8 Hz, SCH=C*H*N), 7.86 (1H, s, COC=C*H*N); MS(ESI): *m/z* (%): 223 (M^++1) (100).

Electronic Supplementary Information

Spectral characterisation data (^{1}H and ^{13}C NMR spectra and MS) for new compounds described in this paper are available through: stl.publisher.ingentaconnect.com/content/stl/jcr/supp-data

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