The Synthesis of 6-Substituted Pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones Using Aminomethylene Malondialdehydes and 6-Aminouracils

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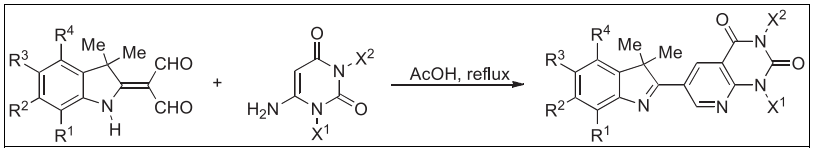

Variously substituted aminomethylene malondialdehydes (2-(3,3-dimethylindolin-2-ylidene)malondialdehydes) were reacted with some 6-aminouracils, to give 6-(3,3-dimethyl-3*H*-indol-2-yl)pyrido[2,3-*d*]pyrimidine-2,4-(1*H*,3*H*)-diones in good yields.

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INTRODUCTION

We have shown previously that the reaction of 2,3,3-trimethyl-3*H*-indoles (indolenines) with the Vilsmeier reagent formed from *N*,*N*-dimethylformamide and phosphorus oxychloride (phosphoric trichloride), producing aminomethylene malondialdehydes, e.g. **1**, is a general process, by demonstrating the transformation using variously substituted 2,3,3-trimethyl-3*H*-indoles [1–4]. Additionally, we have described a simple and straightforward preparation of 4-(3,3-dimethyl-3*H*-indol-2-yl)-substituted pyrazoles **2** by condensation of these aminomethylene malondialdehydes with hydrazine and aryl hydrazines [1,3,4] (Scheme 1).

Recently, we have been able to show that the principles embodied in transformations of simple indolenines *via* Vilsmeier formylations can be incorporated into more complex bisindolenine systems **3**,**5** and thus have prepared several bispyrazoles **4**,**6** in excellent yields [5] (Scheme 2).

Uracil and its annelated analogs occupy a unique place in the field of medicinal chemistry as useful anticancer and antiviral drugs [6]. The versatility of uracil derivatives for the synthesis of nitrogen-containing heterocycles of biological importance has been well documented in the literature [7]. Moreover, 6-aminouracils find wide applications as starting materials for the synthesis of a number of fused uracils of biological significance, for example, pyrano-, pyrido-, pyrazolo-, pyrimidino-, pyridazino-pyrimidines [8,9]. 6-Aminouracils are a very important class of functionalized uracils. We have now extended our studies of aminomethylene malondialdehydes and demonstrated the synthesis of new pyrido[2,3-*d*]pyrimidine-2,4-diones by condensations with various 6-aminouracils.

RESULTS AND DISCUSSION

2,3,3-Trimethyl-3*H*-indoles (indolenines) **8c–e** are new examples and were synthesized by the reaction of the relevant phenylhydrazine hydrochlorides **7c–e** with isopropyl methyl ketone in a Fischer reaction [10] (Scheme 3). The structures of the indolenines were evident from their molecular formulae, the six hydrogen singlets for the geminal groups at δ 1.26 (**8c**), δ 1.20 (**8d**), δ 1.39 (**8e**), and singlet signals for the imine-methyl groups, resonating at δ 2.28, δ 2.16, and δ 2.24 for **8c–e**, respectively. Each of the indolenines **8c–e** was now reacted with the Vilsmeier reagent and, aminomethylene malondialdehydes **9c–e** were obtained in excellent yields, according to our previously reported method [1,3,5]. The structures of the aminomethylene malondialdehydes rest on the observation of two one-hydrogen singlets at δ 9.74 and δ 9.77 for **9c**, δ 9.67 and δ 9.71 for **9d**, and δ 9.82 and δ 9.84 for **9e** corresponding to aldehyde protons. The presence of N–H groups was confirmed by ^{1}H-NMR one-hydrogen signals for the *N*-hydrogens appearing at δ 13.72 (**9c**), δ 13.70 (**9d**), and δ 13.55 (**9e**), respectively.

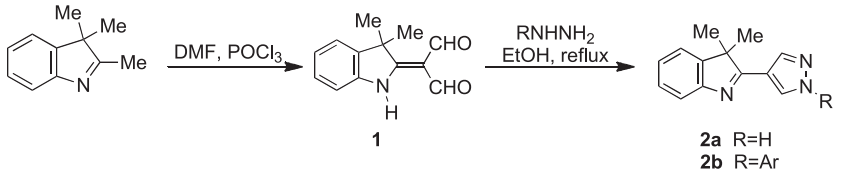
After some preliminary experiments, it was found that a mixture of aminomethylene malondialdehyde **9a** and 6-aminouracil **10a** afforded 6-(3,3-dimethyl-3*H*-indol-2-yl) pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione **11a** in 79% yield in refluxing acetic acid for 12 h (Scheme 4).

The ^{1}H-NMR spectrum of compound **11a** exhibited 2 one-hydrogen singlets at δ 8.84 and δ 9.32 for the newly-formed pyridine ring protons. The ^{13}C-NMR spectrum of compound **11a** showed 16 signals in agreement with the structure, and the mass spectrum showed the expected molecular ion peak. Encouraged by this success, we extended this reaction to various aminomethylene malondialdehydes **9b–e** and 6-aminouracils **10b–c** under similar conditions (acetic acid at reflux), furnishing the respective compounds **11b–k** in good yields.

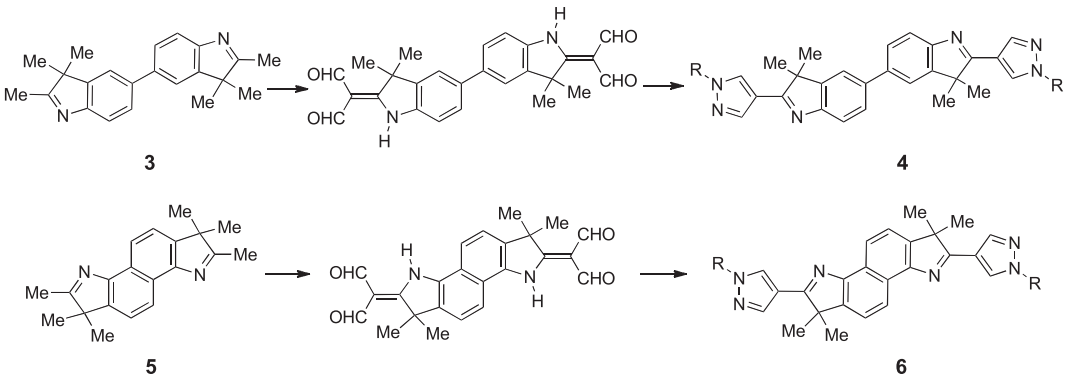
CONCLUSIONS

We have now extended our studies of aminomethylene malondialdehydes and demonstrated the synthesis of 6-

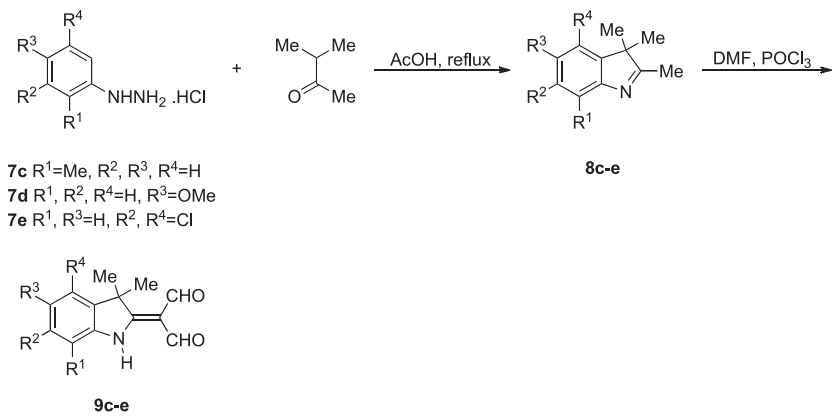
Scheme 1



Scheme 2



Scheme 3



(3,3-dimethyl-3*H*-indol-2-yl)pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **11** by condensations of 2-(3,3-dimethylindolin-2-ylidene)malondialdehydes with various 6-aminouracils.

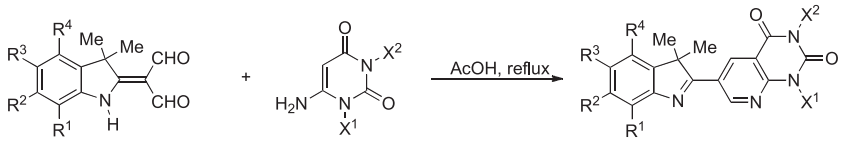
EXPERIMENTAL

General. Melting points were recorded on a Philip Harris C4954718 apparatus. ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker Avance AQS 300 MHz spectrometer, at 300 and 75 MHz, respectively. Chemical shifts δ are in parts per million (ppm) measured in $CDCl_3$ and DMSO-d_6 as solvents and relative to TMS as the internal standard. Infrared spectra were recorded on a Thermonicolet-Nexus 670 FT-IR instrument. High resolution mass spectra were recorded on an Agilent Technology (HP), MS Model: 5973 Network Mass, selective Detector Ion source: Electron Impact (EI) 70 eV, ion source temperature: 230°C, analyzer: quadrupole, and relative abundances of fragments are quoted in parentheses after the *m*/*z* values.

General procedure for synthesis of (8c–e). A mixture of an arylhydrazine hydrochloride **7c–e** (0.08 mol) and isopropyl methyl ketone (0.09 mol) was refluxed in acetic acid (50 mL) for 4–6 h and then cooled, diluted with water (50 mL), and neutralized with NaOH 2M, then extracted with EtOAc (4 × 100 mL). The organic layer was dried over Na_2SO_4, and solvent was evaporated to give **8c–e** as viscous oils.

***2,3,3,7-Tetramethyl-3H*-indole (8c).** (12.05 g, Yield 87%); FT-IR (KBr) ν_{max}/cm^{-1}: 3049, 3019, 2962, 2925, 1707, 1600, 1459, 764; ^{1}H-NMR ($CDCl_3$): δ 1.26 (s, 6H), 2.28 (s, 3H), 2.59 (s, 3H), 7.07–7.11 (m, 3H); ^{13}C-NMR ($CDCl_3$): δ 15.38, 16.95, 23.19, 53.66, 118.61, 125.04, 128.94, 129.39, 145.48, 152.06,

Scheme 4



9a R^1, R^2, R^3, R^4=H
9b R^1=Cl, R^2, R^3, R^4=H
9c R^1=Me, R^2, R^3, R^4=H
9d R^1, R^2, R^4=H, R^3=OMe
9e R^1, R^3=H, R^2, R^4=Cl

10a X^1, X^2=H
10b X^1=Me, X^2=H
10c X^1=Me, X^2=Me

11a-k

X^2	X^1	R^4	R^3	R^2	R^1	Product **11** (yield %)
H	H	H	H	H	H	**a** (79)
H	H	H	H	H	Cl	**b** (74)
H	H	H	H	H	Me	**c** (76)
H	H	H	OMe	H	H	**d** (67)
H	H	Cl	H	Cl	H	**e** (82)
H	Me	H	H	H	H	**f** (72)
H	Me	H	H	H	Cl	**g** (74)
H	Me	H	H	H	Me	**h** (77)
H	Me	H	OMe	H	H	**i** (79)
Me	Me	H	H	H	H	**j** (70)
Me	Me	H	H	H	Cl	**k** (78)

186.88; MS (EI, 70 eV): *m/z* (%) 173 (M^+, 82), 158 (100), 144 (27), 132 (13), 99 (8). Found: $[M]^+$ 173.1203, $C_{12}H_{15}N$ requires $[M]^+$ 173.1204.

***5-Methoxy-2,3,3-trimethyl-3H*-indole (8d)**. (13.62 g, Yield 90%); FT-IR (KBr) ν_{max}/cm^{-1}: 2962, 2863, 2834, 1614, 1596, 1579, 1564, 1433, 1069, 824; ^{1}H-NMR ($CDCl_3$): δ 1.20 (s, 6H), 2.16 (s, 3H), 3.73 (s, 3H), 6.76 (dd, J_1 = 8.1 Hz, J_2 = 2.4 Hz, 1H), 7.09 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.1 Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ 15.16, 23.12, 53.65, 55.55, 108.04, 111.99, 119.96, 147.21, 147.33, 157.87, 185.60; MS (EI, 70 eV): *m/z* (%) 189 (M^+, 78), 174 (100), 160 (30), 148 (18), 115 (5). Found: $[M]^+$ 189.1154, $C_{12}H_{15}NO$ requires $[M]^+$ 189.1154.

4,6-Dichloro-2,3,3-trimethyl-3H-indole (8e). (14.78 g, Yield 81%); FT-IR (KBr) ν_{max}/cm^{-1}: 2971, 2930, 1700, 1580, 1451, 926, 799; ^{1}H-NMR ($CDCl_3$): δ 1.39 (s, 6H), 2.24 (s, 3H), 7.10 (s, 1H), 7.37 (s, 1H); ^{13}C-NMR ($CDCl_3$): δ 15.27, 19.77, 55.67, 119.13, 125.61, 129.61, 133.86, 139.67, 156.02, 191; MS (EI, 70 eV): *m/z* (%) 231 (6), 229 (48), 227 (M^+, 71), 212 (100), 198 (24), 186 (29), 138 (4). Found: $[M]^+$ 227.0268, $C_{11}H_{11}Cl_2N$ requires $[M]^+$ 227.0269.

General procedure for synthesis of (9c–e). To *N*,*N*-dimethylformamide (23 mL, 0.3 mol) cooled in an ice bath was added dropwise phosphorus oxychloride (13.7 mL, 0.15 mol) with stirring at below 5°C. After this addition, a solution of **8c–e** (0.05 mol) in DMF (11 mL, 0.15 mol) was added dropwise. The cooling bath was removed and the reaction mixture was stirred at 75°C for 6–8 h. The resulting solution was added to ice-cooled water and made alkaline with NaOH (aq.) solution. The resulting precipitate was collected by filtration after 12 h, dried in air, and recrystallized from ethanol, to give **9c-e**.

2-(3,3,7-Trimethylindolin-2-ylidene)malonaldehyde (9c). (10.31 g, Yield 90%); mp 118–120°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3124, 3031, 2973, 1648, 1611, 1179, 800; ^{1}H-NMR ($CDCl_3$): δ 1.73 (s, 6H), 2.43 (s, 3H), 7.09–7.27 (m, 3H), 9.74 (s, 1H), 9.77 (s, 1H), 13.72 (s, 1H); ^{13}C-NMR ($CDCl_3$): δ 16.28, 23.38, 51.67, 109.51, 119.58, 122.29, 125.81, 129.43, 138.21, 140.46, 179.29, 187.75, 192.52; MS (EI, 70 eV): *m/z* (%) 229 (M^+, 64), 202 (50), 186 (100), 171 (13), 158 (75), 143 (22), 130 (9), 115 (29), 91 (16), 77 (10). Found: $[M]^+$ 229.1103, $C_{14}H_{15}NO_2$ requires $[M]^+$ 229.1103.

2-(5-Methoxy-3,3-dimethylindolin-2-ylidene)malonaldehyde (9d). (10.41 g, Yield 85%); mp 149–150°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3108, 3059, 2973, 1643, 1606, 1175, 801; ^{1}H-NMR ($CDCl_3$): δ 1.75 (s, 6H), 3.85 (s, 3H), 6.83 (dd, J_1 = 8.7 Hz, J_2 = 2.4 Hz, 1H), 6.89 (d, J = 2.4 Hz, 1H), 7.11 (d, J = 8.7 Hz, 1H), 9.67 (s, 1H), 9.71 (s, 1H), 13.70 (s, 1H); ^{13}C-NMR ($CDCl_3$): δ 23.07, 51.73, 55.84, 108.89, 109.25, 112.99, 113.30, 132.63, 142.66, 158.50, 178.92, 187.81, 192.40; MS (EI, 70 eV): *m/z* (%) 245 (M^+, 83), 217 (100), 202 (82), 187 (6), 174 (35), 159 (16), 144 (8), 131 (15), 115 (6), 103 (8), 77 (9). Found: $[M]^+$ 245.1052, $C_{14}H_{15}NO_3$ requires $[M]^+$ 245.1052.

2-(4,6-Dichloro-3,3-dimethylindolin-2-ylidene)malonaldehyde (9e). (11.51 g, Yield 81%); mp 197–199°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3093, 2984, 1664, 1609, 1329, 958, 833; ^{1}H-NMR ($CDCl_3$): δ 1.89 (s, 6H), 7.11 (d, J = 1.5 Hz, 1H), 7.16 (d, J = 1.5 Hz, 1H), 9.82 (s, 1H), 9.84 (s, 1H), 13.55 (s, 1H); ^{13}C-NMR ($CDCl_3$): δ 19.90, 52.69, 109.26, 111.80, 126.34, 130.62, 134.24, 134.90, 142.11, 179.72, 187.42, 192.80; MS (EI, 70 eV): *m/z* (%) 287 (4), 285 (26), 283 (M^+, 38), 268 (8), 255 (75), 240 (100), 212 (52), 177 (31), 151 (10), 140 (18), 115 (18), 90 (10). Found: $[M]^+$ 283.0167, $C_{13}H_{11}Cl_2NO_2$ requires $[M]^+$ 283.0167.

General procedure for synthesis of (11a-k). A mixture of an aminomethylene malondialdehyde **9a–e** (0.46 mmol) and a 6-aminouracil **10a–c** (0.46 mmol) in acetic acid (15 mL) was heated at reflux for 12–14 h. After this time, there was no trace of either of the starting materials in the crude product; the crude product showed just one spot on TLC. The solvent

was removed in vacuo, the residue was triturated with water, collected by filtration, and dried.

6-(3,3-Dimethyl-3H-indol-2-yl)pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11a). (0.111 g, Yield 79%); mp 209–212°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3168, 3062, 2852, 1692, 1613, 1520, 1449, 1352, 784; ^{1}H-NMR (DMSO-d_6): δ 1.53 (s, 6H), 7.29–7.38 (m, 2H), 7.54 (d, J = 7.2 Hz, 1H), 7.63 (d, J = 7.2 Hz, 1H), 8.84 (s, 1H), 9.32 (s, 1H), 11.63 (s, 1H), 12.01 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 24.25, 53.45, 110.42, 120.95, 121.95, 123.97, 126.65, 128.27, 135.42, 147.90, 150.78, 152.80, 153.70, 154.18, 162.58, 179.91; MS (EI, 70 eV): *m/z* (%) 306 (M^+, 100), 291 (71), 264 (4), 248 (5), 219 (7), 205 (12), 192 (16), 179 (6), 144 (31), 117 (55), 103 (39), 91 (21), 77 (28), 51 (9). Found: $[M]^+$ 306.1117, $C_{17}H_{14}N_4O_2$ requires $[M]^+$ 306.1117.

6-(7-Chloro-3,3-dimethyl-3H-indol-2-yl)pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11b). (0.116 g, Yield 74%); mp 232–233°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3173, 3062, 2825, 1694, 1615, 1527, 1457, 1368, 790; ^{1}H-NMR (DMSO-d_6): δ 1.56 (s, 6H), 7.30 (t, J = 7.8 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H), 8.89 (d, J = 2.1 Hz, 1H), 9.31 (d, J = 2.1 Hz, 1H), 11.66 (s, 1H), 12.06 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 24.07, 55.05, 110.62, 120.91, 123.64, 125.02, 128.16, 128.51, 135.94, 149.26, 150.11, 150.76, 153.99, 154.21, 162.55, 181.30; MS (EI, 70 eV): *m/z* (%) 342 (34), 340 (M^+, 100), 325 (35), 306 (6), 264 (4), 239 (4), 192 (8), 178 (16), 164 (10), 115 (28), 102 (10), 75 (7). Found: $[M]^+$ 340.0726, $C_{17}H_{13}ClN_4O_2$ requires $[M]^+$ 340.0727.

6-(3,3,7-Trimethyl-3H-indol-2-yl)pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11c). (0.112 g, Yield 76%); mp 221–224°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3165, 3023, 2851, 1709, 1613, 1516, 1445, 1359, 1270, 757; ^{1}H-NMR (DMSO-d_6): δ 1.52 (s, 6H), 2.56 (s, 3H), 7.16–7.18 (m, 2H), 7.32 (d, J = 7.5 Hz, 1H), 8.86 (s, 1H), 9.30 (s, 1H), 11.62 (s, 1H), 11.97 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 16.96, 24.32, 53.64, 110.47, 119.26, 124.25, 126.65, 129.31, 130.28, 135.46, 147.76, 150.76, 151.29, 153.59, 154.01, 162.63, 178.66; MS (EI, 70 eV): *m/z* (%) 320 (M^+, 100), 305 (25), 264 (5), 229 (27), 219 (5), 201 (60), 186 (75), 168 (10), 158 (42), 143 (14), 125 (14), 115 (34), 97 (35), 83 (31), 69 (33), 57 (39). Found: $[M]^+$ 320.1273, $C_{18}H_{16}N_4O_2$ requires $[M]^+$ 320.1273.

6-(5-Methoxy-3,3-dimethyl-3H-indol-2-yl)pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11d). (0.104 g, Yield 67%); mp 236–237°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3169, 3059, 2837, 1700, 1613, 1525, 1461, 1369, 1281, 794; ^{1}H-NMR (DMSO-d_6): δ 1.52 (s, 6H), 3.77 (s, 3H), 6.89 (d, J = 8.4 Hz, 1H), 7.17 (s, 1H), 7.53 (d, J = 8.4 Hz, 1H), 8.78 (s, 1H), 9.27 (s, 1H), 11.62 (s, 1H), 11.99 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 24.36, 53.61, 56.03, 108.15, 110.33, 113.56, 121.51, 124.26, 134.91, 146.40, 149.75, 150.77, 153.38, 153.86, 158.95, 162.62, 177.71; MS (EI, 70 eV): *m/z* (%) 336 (M^+, 100), 321 (81), 305 (8), 293 (29), 278 (12), 264 (3), 235 (7), 207 (9), 174 (9), 147 (8), 117 (10), 103 (11), 90 (8), 77 (13), 63 (6). Found: $[M]^+$ 336.1222, $C_{18}H_{16}N_4O_3$ requires $[M]^+$ 336.1222.

6-(4,6-Dichloro-3,3-dimethyl-3H-indol-2-yl)pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11e). (0.142 g, Yield 82%); mp 254–256°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3177, 3075, 2800,1692, 1604, 1516, 1436, 1370, 854; ^{1}H-NMR (DMSO-d_6): δ 1.67 (s, 6H), 7.45 (d, J = 1.5 Hz, 1H), 7.73 (d, J = 1.5 Hz, 1H), 8.85 (s, 1H), 9.31 (s, 1H), 11.67 (s, 1H), 12.09 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 20.61, 55.55, 110.56, 120.46, 122.86, 126.53, 129.09, 133.83, 136.16, 141.58, 150.77, 154.18, 154.51, 155.71, 162.45, 182.87; MS (EI, 70 eV): *m/z* (%) 378 (12), 376 (56), 374 (M^+, 100), 359 (35), 347 (13), 332 (22), 320 (12), 289 (9), 226 (13), 212 (17), 198 (10), 173 (12), 136 (13), 115 (36), 99 (10). Found: $[M]^+$ 374.0338, $C_{17}H_{12}Cl_2N_4O_2$ requires $[M]^+$ 374.0337.

6-(3,3-Dimethyl-3H-indol-2-yl)-1-methylpyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11f). (0.106 g, Yield 72%); mp 229–231°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3173, 3055, 2972, 2840, 1709, 1688, 1603, 1487, 762; ^{1}H-NMR (DMSO-d_6): δ 1.53 (s, 6H), 3.52 (s, 3H), 7.28–7.34 (m, 2H), 7.53 (d, J = 7.2 Hz, 1H), 7.62 (d, J = 7.2 Hz, 1H), 8.92 (s, 1H), 9.38 (s, 1H), 11.89 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 24.17, 28.93, 53.46, 111.80, 121, 121.97, 123.76, 126.72, 128.28, 135.79, 147.93. 150.99, 152.76, 153.26, 153.31, 161.48, 179.80; MS (EI, 70 eV): *m/z* (%) 320 (M^+, 100), 305 (46), 264 (4), 218 (9), 205 (18), 192 (21), 164 (11), 144 (27), 128 (10), 115 (82), 103 (88), 91 (55), 77 (91), 63 (25), 51 (35). Found: $[M]^+$ 320.1273, $C_{18}H_{16}N_4O_2$ requires $[M]^+$ 320.1273.

6-(7-Chloro-3,3-dimethyl-3H-indol-2-yl)-1-methylpyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11g). (0.120 g, Yield 74%); mp 242–244°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3174, 3054, 2848, 1719, 1691, 1610, 1502, 1334, 753; ^{1}H-NMR (DMSO-d_6): δ 1.57 (s, 6H), 3.54 (s, 3H), 7.31 (t, J = 7.8 Hz, 1H), 7.41 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 8.99 (s, 1H), 9.4 (s, 1H), 11.92 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 24, 28.97, 55.06, 112, 120.93, 123.44, 125.07, 128.33, 128.52, 136.29, 149.23, 150.15, 150.99, 153.37, 153.53, 161.47, 181.19; MS (EI, 70 eV): *m/z* (%) 356 (33), 354 (M^+, 100), 339 (31), 319 (4), 239 (8), 205 (10), 192 (12), 178 (35), 164 (19), 137 (14), 115 (92), 102 (35), 89 (27), 75 (30). Found: $[M]^+$ 354.0885, $C_{18}H_{15}ClN_4O_2$ requires $[M]^+$ 354.0884.

1-Methyl-6-(3,3,7-trimethyl-3H-indol-2-yl)pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11h). (0.118 g, Yield 77%); mp 233–234°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3170, 3043, 2924, 2855, 1695, 1611, 1505, 1462, 758; ^{1}H-NMR (DMSO-d_6): δ 1.52 (s, 6H), 2.54 (s, 3H), 3.53 (s, 3H), 7.16–7.18 (m, 2H), 7.32 (d, J = 7.5 Hz, 1H), 8.95 (s, 1H), 9.38 (s, 1H), 11.90 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 16.93, 24.25, 28.91, 53.65, 111.83, 119.27, 124.04, 126.72, 129.31, 130.33, 135.83, 147.80, 150.97, 151.26, 153.13, 153.19, 161.52, 178.54; MS (EI, 70 eV): *m/z* (%) 334 (M^+, 100), 319 (59), 278 (8), 235 (10), 219 (14), 158 (18), 144 (12), 115 (31), 91 (27), 77 (8). Found: $[M]^+$ 334.1429, $C_{19}H_{18}N_4O_2$ requires $[M]^+$ 334.1429.

6-(5-Methoxy-3,3-dimethyl-3H-indol-2-yl)-1-methylpyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11i). (0.128 g, Yield 79%); mp 249–252°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3186, 3067, 2968, 1710, 1681, 1604, 1480, 1283, 826; ^{1}H-NMR (DMSO-d_6): δ 1.52 (s, 6H), δ 3.51 (s, 3H), δ 3.78 (s, 3H), 6.89 (d, J = 8.4 Hz, 1H), 7.16 (s, 1H), 7.52 (d, J = 8.4 Hz, 1H), 8.87 (s, 1H), 9.34 (s, 1H), 11.87 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 24.29, 28.90, 53.61, 56.02, 108.18, 111.73, 113.51, 121.56, 124.03, 135.30, 146.37, 149.80, 150.99, 152.92, 152.98, 158.97, 161.52, 177.56; MS (EI, 70 eV): *m/z* (%) 350 (M^+, 100), 335 (60), 307 (24), 292 (9), 221 (5), 174 (9), 126 (8), 103 (11), 77 (12). Found: $[M]^+$ 350.1379, $C_{19}H_{18}N_4O_3$ requires $[M]^+$ 350.1379.

6-(3,3-Dimethyl-3H-indol-2-yl)-1,3-dimethylpyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (11j). (0.107 g, Yield 70%); mp 237–241°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3053, 2978, 1667, 1611, 1503, 1335, 1290, 778; ^{1}H-NMR (DMSO-d_6): δ 1.54 (s, 6H), 3.31 (s, 3H), 3.60 (s, 3H), 7.28–7.35 (m, 2H), 7.54 (d, J = 7.2 Hz,

1H), 7.64 (d, $J = 7.2$ Hz, 1H), 8.98 (s, 1H), 9.40 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 24.19, 28.70, 29.86, 53.50, 111.02, 121.05, 122, 124.03, 126.77, 128.31, 136.18, 147.95, 151.35, 151.93, 152.78, 153.34, 161.17, 179.81; MS (EI, 70 eV): *m/z* (%) 334 (M^+, 100), 319 (55), 262 (5), 234 (7), 205 (15), 144 (20), 117 (25), 103 (21), 91 (11), 77 (16). Found: $[M]^+$ 334.1429, $C_{19}H_{18}N_4O_2$ requires $[M]^+$ 334.1429.

6-(7-Chloro-3,3-dimethyl-3H-indol-2-yl)-1,3-dimethylpyrido [2,3-d]pyrimidine-2,4(1H,3H)-dione (11k). (0.132 g, Yield 78%); mp 248–249°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3050, 2980, 1714, 1674, 1607, 1493, 1295, 750; ^{1}H-NMR (DMSO-d_6): δ 1.58 (s, 6H), 3.33 (s, 3H), 3.62 (s, 3H), 7.31 (t, $J = 7.5$ Hz, 1H), 7.43 (d, $J = 7.5$ Hz, 1H), 7.54 (d, $J = 7.5$ Hz, 1H), 9.04 (s, 1H), 9.42 (s, 1H); ^{13}C-NMR (DMSO-d_6): δ 23.99, 28.72, 29.90, 55.07, 112.01, 120.84, 123.49, 125.08, 128.37, 128.54, 136.30, 149.23, 150.12, 150.89, 153.32, 153.52, 161.46, 181.19; MS (EI, 70 eV): *m/z* (%) 370 (35), 368 (M^+, 100), 353 (36), 333 (5), 239 (8), 204 (7), 191 (12), 178 (20), 164 (8), 115 (20), 102 (12). Found: $[M]^+$ 368.1041, $C_{19}H_{17}ClN_4O_2$ requires $[M]^+$ 368.1040.

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