Fast and efficient synthesis of chromeno[*d*]pyrimidinediones catalysed by a TiO_2–SiO_2 nanocomposite in aqueous media

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A 1:1 TiO_2–SiO_2 nanocomposite was used as an efficient and green recyclable catalyst for the synthesis in water of 11 chromeno[*d*]pyrimidinediones, six of which are new. All reactions were carried out under very mild conditions to afford the corresponding products in excellent yields.

Keywords: aqueous media, chromeno[*d*]pyrimidinediones, recyclability of catalyst, TiO_2–SiO_2 nanocomposite

Chromene derivatives fused with N-containing heterocycles display a broad spectrum of bioactivities and have seen use as antioxidant,[1,2] anticancer,[3–6] antimicrobial,[7–10] and hypotensive agents,[11] and as a local anesthetic.[12] In addition, they can be used as cognitive enhancement drugs[13,14] for the treatment of neurodegenerative diseases, including Alzheimer's disease[15] and schizophrenia disorder.[16]

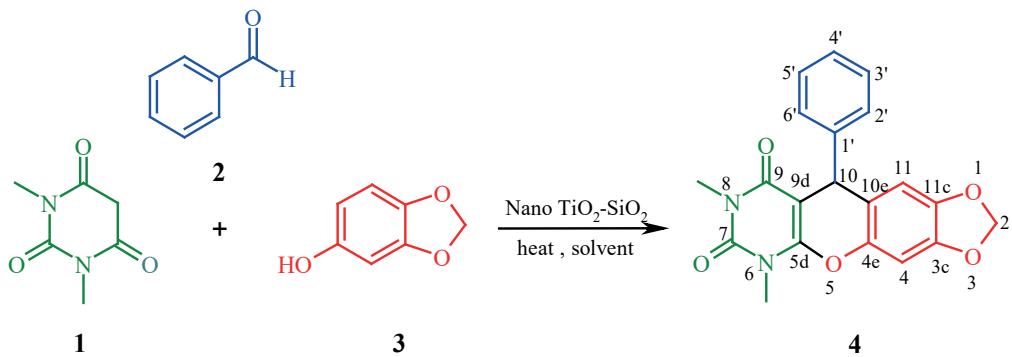
Currently, nanostructured metal oxides, which possess good physical and chemical abilities, promote numerous organic transformations. Titanium dioxide nanoparticles (TiO_2 NPs) are considered very close to ideal nanocatalysts due to their high efficiency and because they are non-toxic, inexpensive, moisture stable and reusable.[17] In view of these facts, we have already reported the use of TiO_2 NPs as an efficient heterogeneous catalyst in some organic transformations, *i.e.*, solvent-free synthesis of hexahydro-2-quinolinecarboxylic acid derivatives[18] and one-pot four-component coupling reactions for the preparation of indeno[1,2-*b*]quinolinediones,[19] and tetrahydrobenzo[*c*]acridinones,[20] in aqueous media. In addition, we have noted that TiO_2 NPs over silica shells (TiO_2–SiO_2 nanocomposite) improves their catalytic efficiency owing to an increase in surface area.[21]

In view of the abovementioned biological activities of substituted chromenes, we report herein a very simple route to synthesise some 6,8-dimethyl-10-aryl-6,10-dihydro-7*H*-[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-diones (**4a**–**k**) *via* a condensation reaction of 1,3-dimethylbarbituric acid **1**, an aromatic aldehyde (**2a**–**k**) and 3,4-methylenedioxyphenol **3** in aqueous media by using a TiO_2–SiO_2 nanocomposite with a molar ratio of 1:1 as an efficient and green catalyst (Scheme 1). Two previous reports used $Zr(HSO_4)_4$[22] and melamine trisulfonic acid[23] as acid catalysts and the same starting materials to prepare similar compounds in yields of 87–95% in solvent-free processes at 100–110 °C. Our hope was to conduct the process in water under less harsh conditions and exploit the impressive catalytic abilities of nanoparticles to prepare some of the same compounds in higher yield and some new ones. To the best of our knowledge, there have been no reports so far of the synthesis of these compounds using any nanocatalyst.

Results and discussion

In preliminary experiments, we prepared the TiO_2–SiO_2 nanocomposite catalyst according to a known non-thermal sol-gel process.[24] The crystalline structure and purity of the synthesised nanocomposite was confirmed by X-ray diffraction (XRD) analysis. The XRD results confirmed the high crystallinity of the TiO_2–SiO_2 nanocomposite, which has a crystalline anatase phase of TiO_2 NPs in an amorphous silica matrix (Fig. 1 in the ESI).

The transmission electron microscopy (TEM) image of the TiO_2–SiO_2 nanocomposite (Fig. 2 in the ESI) also showed the typical grainy structure of nanoparticles with sizes of 5–9 nm. The chemical composition of the nanocomposite was determined by X-ray fluorescence (XRF) spectroscopy and the results showed that the molar ratio was 1:1.



2a, 4a Ar = C_6H_5, **2b**, **4b** Ar = 4-Br-C_6H_4, **2c**, **4c** Ar = 4-Cl-C_6H_4, **2d**, **4d** Ar = 2,4-Cl_2-C_6H_3, **2e**, **4e** Ar = 3-HO-C_6H_4, **2f**, **4f** Ar = 4-HO-C_6H_4, **2g**, **4g** Ar = 2-CH_3-C_6H_4, **2h**, **4h** Ar = 4-CH_3-C_6H_4, **2i**, **4i** Ar = 3-O_2N-C_6H_4, **2j**, **4j** Ar = Pyridine-4-yl, **2k**, **4k** Ar = Thiophen-2-yl

Scheme 1 Synthesis of chromeno[*d*]pyrimidinedione derivatives using a TiO_2–SiO_2 nanocomposite.

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Table 1 Synthesis of a pentacyclic compound (**4c**; Ar = 4-Cl-C_6H_4) from the reaction of 1,3-dimethylbarbituric acid **1**, 4-chlorobenzaldehyde (**2c**; Ar = 4-Cl-C_6H_4) and 3,4-methylenedioxyphenol **3** in the presence of a TiO_2–SiO_2 nanocomposite (1:1) under different conditions (Scheme 1)[a]

Entry	Nanocatalyst (mol% with respect to TiO_2)	Solvent	Temp. (°C)	Time (min)	Yield (%)[b]
1	no catalyst	H_2O	80	90	trace
2	TiO_2–SiO_2 (10%)	H_2O	80	60	80
3	TiO_2–SiO_2 (15%)	H_2O	80	45	96
4	TiO_2–SiO_2 (20%)	H_2O	80	45	96
5	nano TiO_2 (20%)	H_2O	80	60	79
6	nano SiO_2 (20%)	H_2O	80	80	74
7	TiO_2–SiO_2 (15%)	H_2O	70	50	78
8	TiO_2–SiO_2 (15%)	H_2O	90	45	95
9	TiO_2–SiO_2 (15%)	EtOH	80	45	77
10	TiO_2–SiO_2 (15%)	CH_3CN	80	45	74
11	TiO_2–SiO_2 (15%)	CH_2Cl_2	80	45	65

[a]Reaction conditions: a stirred mixture of 1,3-dimethylbarbituric acid **1** (1 mmol), 3,4-methylenedioxyphenol **3** (1 mmol), 4-chlorobenzaldehyde (**2c**; Ar = 4-Cl-C_6H_4) (1 mmol) and a TiO_2–SiO_2 nanocomposite (1:1) in solvent (5 mL) was heated at various temperatures and for various times.

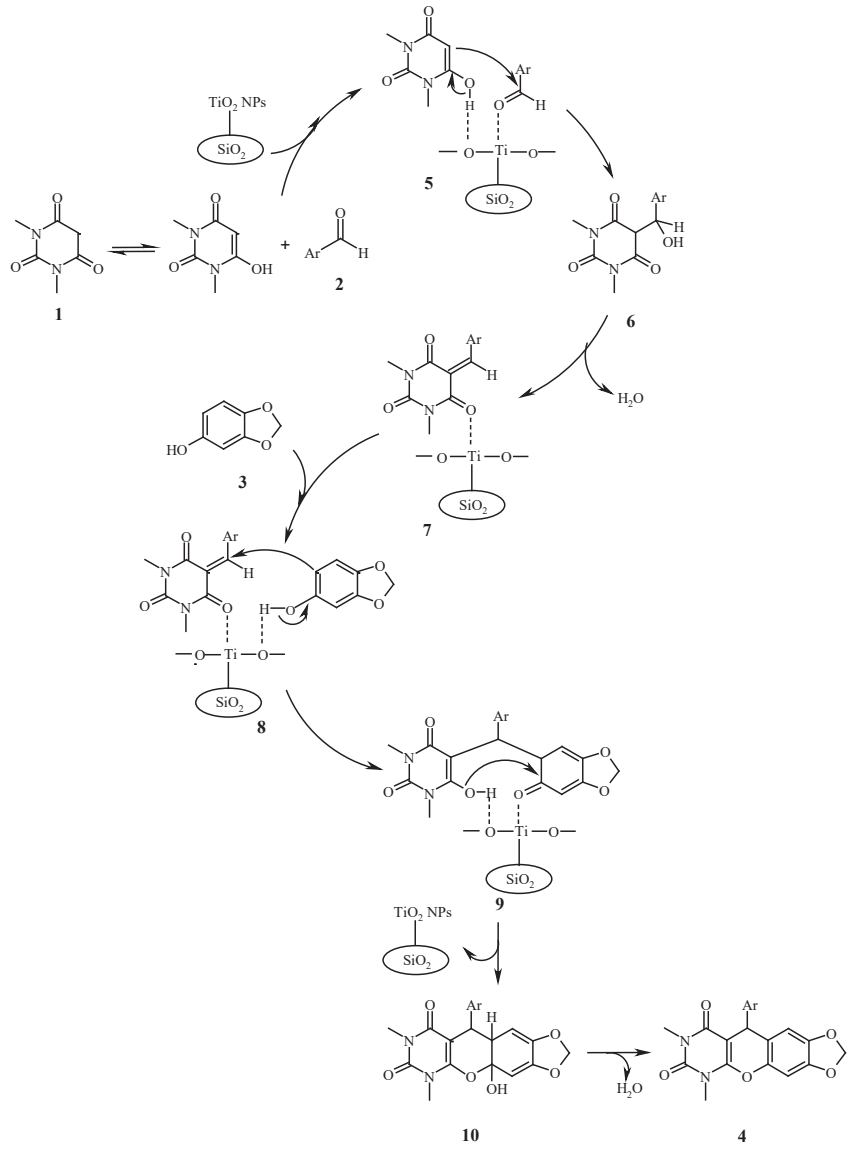
[b]Isolated yield.

Table 2 Yields of pentacyclic compounds (**4**; Ar = various) formed by heating a mixture of 1,3-dimethylbarbituric acid **1**, an araldehyde (**2**; Ar = various), 3,4-methylenedioxyphenol **3** and a TiO_2–SiO_2 nanocomposite in water at 80 °C for various times (Scheme 1)[a]

Product	Ar	Yield (%)[b]	Time (min)	M.p. (°C)	
				Observed	Literature
4a	C_6H_5	95	45	242–244	lit.[22] 245–246
4b	4-Br-C_6H_4	98	40	268–270	–
4c	4-Cl-C_6H_4	96	45	255–257	lit.[22] 254–255
4d	2,4-Cl_2-C_6H_3	94	55	277–279	lit.[22] 277–278
4e	3-HO-C_6H_4	96	50	265–267	–
4f	4-HO-C_6H_4	97	45	272–274	–
4g	2-CH_3-C_6H_4	94	50	236–238	–
4h	4-CH_3-C_6H_4	95	45	248–250	lit.[22] 248–249
4i	3-O_2N-C_6H_4	96	40	260–262	lit.[22] 262–263
4j	pyridine-4-yl	97	45	279–281	–
4k	thiophen-2-yl	96	40	276–278	–

[a]Reaction conditions: a stirred mixture of 1,3-dimethylbarbituric acid **1** (1 mmol), 3,4-methylenedioxyphenol **3** (1 mmol), an araldehyde (**2**; Ar = various) (1 mmol) and a TiO_2–SiO_2 nanocomposite (1:1, 15 mol%) in water (5 mL) was heated at 80 °C for various times.

[b]Yields refer to those of pure isolated products characterised by IR, ^{1}H NMR and ^{13}C NMR spectral data and by elemental analyses.



Scheme 2 Suggested mechanism for the reaction of 1,3-dimethylbarbituric acid **1**, aromatic aldehydes **2** and 3,4-methylenedioxyphenol **3** catalysed by a TiO_2–SiO_2 nanocomposite.

Using TiO_2–SiO_2 as a catalyst, we chose the model reaction of 1,3-dimethylbarbituric acid **1**, 4-chlorobenzaldehyde (**2c**; Ar = 4-Cl-C_6H_4) and 3,4-methylenedioxyphenol **3** (Scheme 1) in water to optimise the reaction conditions. The results are shown in Table 1. Using 10 mol% TiO_2–SiO_2 at 80 °C, the expected product (**4c**; Ar = 4-Cl-C_6H_4) was formed in 80% yield in 60 min (entry 2). In the absence of a catalyst, only a trace of product was obtained even after 90 min (entry 1). We investigated the optimum catalyst loading and the results indicated that 15 mol% of catalyst was sufficient (entries 2–4). The catalytic efficiency of two commercial nanopowders, TiO_2 NPs (10–30 nm, anatase TiO_2) and SiO_2 NPs (20 nm, non-porous) was tested, but 20 mol% of each produced the desired product **4c** in only 79 and 74% yields, respectively (entries 5 and 6). To find the optimum reaction temperature, the model reaction was carried out at different temperatures. The results showed that the yield was not affected by the temperature increasing above 80 °C (entries 7 and 8). Then, we tested other solvents. We found that the best yield of product is obtained in aqueous media (entries 3 and 9–11).

We then applied the optimised procedure to determine yields when various substituted aromatic aldehydes were in reaction with 1,3-dimethylbarbituric acid and 3,4-methylenedioxyphenol (Table 2). The isolated compounds (**4a**–**k**) were characterised by IR, ^{1}H NMR and ^{13}C NMR spectroscopic data and also by elemental analyses.

A suggested mechanism for the formation of product **4** is given in Scheme 2. It is feasible that the TiO_2 NPs participate in two catalytic steps. In the initial step, the formation of alkene **7** is the result of a Knoevenagel condensation between metal-activated aromatic aldehyde **2** and enolised 1,3-dimethylbarbituric acid **1**, *via* intermediates **5** and **6**. 3,4-Methylenedioxyphenol **3** then adds to metal-activated alkene **7** to generate the Michael adduct **9** *via* intermediate **8**. Further cyclisation of **9** gives product **4**, after dehydration.

Also, we evaluated the recycling of the TiO_2–SiO_2 nanocomposite catalyst using the model reaction, which yielded **4c**. However, there was no significant loss of activity after four runs (product yields: 96, 95, 93 and 91%).

Experimental

All of the chemical materials used in this work were purchased from Merck and Sigma-Aldrich and used without further purification. Melting points were determined on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were obtained on an ABB FTIR (FTLA 2000) spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-500 Avance at 500 and 125 MHz, respectively, using TMS as an internal standard and DMSO-d_6 as the solvent. Elemental analyses were carried out using a Foss-Heraeus CHN-O-rapid analyser. The TEM image of the catalyst was obtained on a Philips EM208 transmission electron microscope under acceleration. Powder XRD data were determined on a Philips, X'Pert diffractometer using Cu Kα radiation (λ = 1.54 Å). The composition analysis of catalyst was carried out by XRF spectroscopy using Oxford ED 2000 equipment.

Preparation of TiO_2–SiO_2 nanocomposite catalyst

Titanium tetrachloride (2 mL) was added dropwise to deionised water (200 mL) in an ice-water bath with strong magnetic stirring. After the hydrolysis was completed, the released HCl was neutralised with dilute NH_4OH to pH 7. The solid produced was filtered off and washed with distilled water and then dispersed into a 0.3 M HNO_3 aqueous solution (200 mL) to remove all the chloride ions. The mixture was then refluxed under strong stirring at 70 °C for 16 h to yield a titania sol. Tetraethylorthosilicate (25 mL) was added dropwise into the above sol and stirred at 70 °C for about 0.5 h. Finally, the TiO_2–SiO_2 nanocomposite powder was filtered and washed with distilled water and then air dried at ambient temperature.[24] The synthesised catalyst was fully characterised by XRD, TEM and XRF techniques.

Synthesis of chromeno[d]pyrimidinediones (**4a**–**k**)*; general procedure*

A mixture of 1,3-dimethylbarbituric acid **1** (156 mg, 1 mmol), an aromatic aldehyde **2a**–**k** (1 mmol), 3,4-methylenedioxyphenol **3** (138 mg, 1 mmol) and the TiO_2–SiO_2 nanocomposite (21 mg, 15 mol%) in H_2O (5 mL) was stirred at 80 °C for 40–55 min. After reaction completion, as indicated by TLC, the reaction mixture was filtered and the residue was treated with hot ethanol (5 mL) and then centrifuged at 2000–3000 rpm for 10 min to recover the catalyst. The recovered catalyst was then washed with ethanol for reuse and air dried at ambient temperature for several hours. The pure product was obtained by cooling the ethanol solution to room temperature, dilution with H_2O (1 mL) and crystallisation.

*6,8-Dimethyl-10-phenyl-6,10-dihydro-7*H*-[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4a**): White powder; m.p. 242–244 °C (lit.[34] 245–246 °C); yield 346 mg (95%); IR (KBr) (ν_{max} cm^{-1}): 3077, 2967, 2874, 1708, 1686, 1653, 1590, 1487, 1434, 1378, 1295; ^{1}H NMR: δ 3.26 (s, 3H, N6CH_3), 3.57 (s, 3H, N8CH_3), 5.02 (s, 1H, H10), 5.89 (d, *J* = 1.3 Hz, 1H, H2), 5.94 (d, *J* = 1.3 Hz, 1H, H2′), 6.52 (s, 1H, C11H), 6.66 (s, 1H, C4H), 7.21 (m, 5H, ArH); ^{13}C NMR: δ 28.0, 29.2, 40.1, 90.1, 97.7, 101.6, 109.7, 116.8, 127.9, 129.2, 129.3, 140.2, 145.0, 146.7, 146.9, 150.8, 152.4, 161.8. Anal. calcd for $C_{20}H_{16}N_2O_5$ (364.36): C, 65.93; H, 4.43; N, 7.69; found: C, 66.04; H, 4.59; N, 7.57%.

*6,8-Dimethyl-10-(4-bromophenyl)-6,10-dihydro-7*H*-[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4b**): White powder; m.p. 268–270 °C; yield 434 mg (98%); IR (KBr) (ν_{max} cm^{-1}): 3041, 2965, 2887, 1710, 1670, 1656, 1601, 1488, 1431, 1381, 1301; ^{1}H NMR: δ 3.28 (s, 3H, N6CH_3), 3.55 (s, 3H, N8CH_3), 5.01 (s, 1H, H10), 5.91 (d, *J* = 0.9 Hz, 1H, H2), 5.95 (d, *J* = 0.9 Hz, 1H, H2′), 6.50 (s, 1H, C11H), 6.65 (s, 1H, C4H), 7.37 (d, *J* = 8.0 Hz, 2H, C2′H, C6′H), 7.47 (d, *J* = 8.0 Hz, 2H, C3′H, C5′H); ^{13}C NMR: δ 28.2, 29.6, 38.2, 89.7, 98.1, 101.5, 109.7, 117.7, 122.5, 124.2, 136.4, 140.2, 146.5, 146.8, 147.3, 150.3, 152.4, 162.6. Anal. calcd for $C_{20}H_{15}BrN_2O_5$ (443.25): C, 54.20; H, 3.41; N, 6.32; found: C, 54.03; H, 3.53; N, 6.46%.

*6,8-Dimethyl-10-(4-chlorophenyl)-6,10-dihydro-7*H*-[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4c**): White powder; m.p. 255–257 °C (lit.[34] 254–255 °C); yield 383 mg (96%); IR (KBr) (ν_{max} cm^{-1}): 3085, 2958, 2862, 1707, 1675, 1660, 1576, 1478, 1430, 1352, 1298; ^{1}H NMR: δ 3.27 (s, 3H, N6CH_3), 3.54 (s, 3H, N8CH_3), 5.01 (s, 1H, H10), 5.92 (d, *J* = 1.0 Hz, 1H, H2), 5.97 (d, *J* = 1.0 Hz, 1H, H2′), 6.47 (s, 1H, C11H), 6.67 (s, 1H, C4H), 7.19 (d, *J* = 7.0 Hz, 2H, C2′H, C6′H), 7.22 (d, *J* = 7.0 Hz, 2H, C3′H, C5′H); ^{13}C NMR: δ 28.1, 29.0, 39.6, 89.6, 98.1, 101.9, 108.0, 116.1, 128.1, 128.8, 132.7, 143.0, 143.6, 145.7, 147.4, 150.6, 152.8, 161.7. Anal. calcd for $C_{20}H_{15}ClN_2O_5$ (398.80): C, 60.24; H, 3.79; N, 7.02; found: C, 60.07; H, 3.66, N, 6.83%.

*6,8-Dimethyl-10-(2,4-dichlorophenyl)-6,10-dihydro-7*H*-[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4d**): White powder; m.p. 277–279 °C (lit.[34] 277–278 °C); yield 407 mg (94%); IR (KBr) (ν_{max} cm^{-1}): 3080, 2969, 2875, 1700, 1668, 1647, 1568, 1477, 1433, 1388, 1291; ^{1}H NMR: δ 3.27 (s, 3H, N6CH_3), 3.57 (s, 3H, N8CH_3), 5.12 (s, 1H, H10), 5.92 (d, *J* = 1.2 Hz, 1H, H2), 5.96 (d, *J* = 1.2 Hz, 1H, H2′), 6.55 (s, 1H, C11H), 6.63 (s, 1H, C4H), 7.12 (m, 2H, C5′H, C6′H), 7.36 (m, 1H, C3′H); ^{13}C NMR: δ 28.1, 29.0, 38.6, 88.2, 98.0, 101.9, 107.5, 115.1, 127.6, 129.7, 131.2, 133.2, 133.5, 141.0, 142.7, 145.6, 147.5, 150.7, 153.1, 161.7. Anal. calcd for $C_{20}H_{14}Cl_2N_2O_5$ (433.25): C, 55.45; H, 3.26; N, 6.47; found: C, 55.63; H, 3.12; N, 6.31%.

*6,8-Dimethyl-10-(3-hydroxyphenyl)-6,10-dihydro-7*H*-[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4e**): Yellow powder; m.p. 265–267 °C; yield 363 mg (96%); IR (KBr) (ν_{max} cm^{-1}): 3181, 3064, 2925, 2851, 1709, 1688, 1651, 1600, 1532, 1362, 1292; ^{1}H NMR: δ 3.27 (s, 3H, N6CH_3), 3.53 (s, 3H, N8CH_3), 4.99 (s, 1H, H10), 5.92 (d, *J* = 1.2 Hz, 1H, H2), 5.97 (d, *J* = 1.2 Hz, 1H, H2′),

6.49 (s, 1H, C11H), 6.67 (s, 1H, C4H), 7.14 (m, 1H, C4′H), 7.40 (m, 3H, C2′H, C5′H, C6′H), 9.41 (s, 1H, OH); ^{13}C NMR: δ 28.7, 30.0, 39.6, 90.2, 97.7, 101.5, 109.0, 114.6, 116.4, 116.9, 119.3, 120.1, 140.2, 145.5, 146.9, 147.5, 150.8, 152.3, 158.1, 163.2. Anal. calcd for $C_{20}H_{16}N_2O_6$ (380.35): C, 63.16; H, 4.24; N, 7.36; found: C, 63.04; H, 4.33; N, 7.57%.

*6,8-Dimethyl-10-(4-hydroxyphenyl)-6,10-dihydro-7*H-*[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4f**): White powder; m.p. 272–274 °C; yield 369 mg (97%); IR (KBr) (ν_{max} cm^{-1}): 3188, 3085, 2931, 2866, 1711, 1689, 1636, 1570, 1475, 1430, 1386, 1297; ^{1}H NMR: δ 3.25 (s, 3H, N6CH$_3$), 3.54 (s, 3H, N8CH$_3$), 4.97 (s, 1H, H10), 5.88 (d, *J* = 1.0 Hz, 1H, H2), 5.95 (d, *J* = 1.0 Hz, 1H, H2′), 6.50 (s, 1H, C11H), 6.66 (s, 1H, C4H), 7.54 (d, *J* = 8.4 Hz, 2H, C2′H, C6′H), 7.88 (d, *J* = 8.4 Hz, 2H, C3′H, C5′H), 9.38 (s, 1H, OH); ^{13}C NMR: δ 28.8, 29.4, 38.9, 90.0, 98.4, 101.4, 109.0, 114.5, 116.3, 124.6, 139.2, 146.5, 147.0, 148.0, 151.8, 153.1, 157.3, 163.5. Anal. calcd for $C_{20}H_{16}N_2O_6$ (380.35): C, 63.16; H, 4.24; N, 7.36; found: C, 63.28; H ,4.34; N, 7.29%.

*6,8-Dimethyl-10-(2-methylphenyl)-6,10-dihydro-7*H-*[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4g**): White powder; m.p. 236–238 °C; yield 356 mg (94%); IR (KBr) (ν_{max} cm^{-1}): 3049, 2955, 2871, 1712, 1672, 1639, 1594, 1490, 1428, 1375, 1260; ^{1}H NMR: δ 2.29 (s, 3H, C2'CH$_3$), 3.28 (N6CH$_3$), 3.57 (s, 3H, N8CH$_3$), 5.01 (s, 1H, H10), 5.90 (d, *J* = 1.0 Hz, 1H, H2), 5.96 (d, *J* = 1.0 Hz, 1H, H2′), 6.47 (s, 1H, C11H), 6.68 (s, 1H, C4H), 7.15 (m, 3H, C3′H, C4′H, C5′H), 7.23 (m, 1H, C6′H); ^{13}C NMR: δ 20.8, 27.9, 28.7, 39.5, 89.8, 98.5, 102.4, 108.9, 115.7, 126.2, 127.6, 130.1, 131.0, 135.6, 141.2, 146.1, 146.8, 148.5, 151.3, 152.9, 162.8. Anal. calcd for $C_{21}H_{18}N_2O_5$ (378.38): C, 66.66; H, 4.79; N, 7.40; found: C, 66.51; H, 4.50; N, 7.64%.

*6,8-Dimethyl-10-(4-methylphenyl)-6,10-dihydro-7*H-*[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4h**): White powder; m.p. 248–250 °C (lit.[34] 248–249 °C); yield 359 mg (95%); IR (KBr) (ν_{max} cm^{-1}): 3075, 2956, 2870, 1705, 1672, 1642, 1603, 1476, 1434, 1396, 1273; ^{1}H NMR: δ 2.25 (s, 3H, C4′C*H*$_3$), 3.28 (s, 3H, N6CH$_3$), 3.54 (s, 3H, N8CH$_3$), 4.99 (s, 1H, H10), 5.90 (d, *J* = 0.9 Hz, 1H, H2), 5.95 (d, *J* = 0.9 Hz, 1H, H2′), 6.52 (s, 1H, C11H), 6.67 (s, 1H, C4H), 7.07 (d, *J* = 8.0 Hz, 2H, C3′H, C5′H), 7.15 (d, *J* = 8.0 Hz, 2H, C2′H, C6′H); ^{13}C NMR: δ 20.9, 28.1, 29.0, 38.9, 90.1, 98.0, 101.8, 108.3, 116.6, 127.7, 129.3, 136.5, 142.3, 143.0, 145.5, 147.1, 150.7, 152.5, 161.9. Anal. calcd for $C_{21}H_{18}N_2O_5$ (378.38): C, 66.66; H, 4.79; N, 7.40; found: C, 66.75; H, 4.81; N, 7.33%.

*6,8-Dimethyl-10-(3-nitrophenyl)-6,10-dihydro-7*H-*[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4i**): Pale yellow powder; m.p. 260–262 °C (lit.[34] 262–263 °C); yield 393 mg (96%); IR (KBr) (ν_{max} cm^{-1}): 3056, 2943, 2850, 1702, 1666, 1659, 1529, 1486, 1351, 1224; ^{1}H NMR: δ 3.27 (s, 3H, N6CH$_3$), 3.57 (s, 3H, N8CH$_3$), 5.15 (s, 1H, H10), 5.94 (d, *J* = 1.0 Hz, 1H, H2), 5.98 (d, *J* = 1.0 Hz, 1H, H2′), 6.44 (s, 1H, C11H), 6.77 (s, 1H, C4H), 7.47 (m, 3H, C4′H, C5′H, C6′H), 7.96 (m, 1H, C2′H); ^{13}C NMR: δ 28.1, 29.0, 39.1, 88.8, 98.4, 102.1, 107.9, 115.0, 122.8, 128.4, 129.3, 134.5, 143.0, 145.9, 147.1, 147.8, 148.5, 150.5, 152.8, 161.8. Anal. calcd for $C_{20}H_{15}N_3O_7$ (409.35): C, 58.68; H, 3.69; N, 10.27; found: C, 58.61; H, 3.54; N, 10.14%.

*6,8-Dimethyl-10-(pyridin-4-yl)-6,10-dihydro-7*H-*[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4j**): Pale yellow powder; m.p. 279–281 °C; yield 343 mg (97%); IR (KBr) (ν_{max} cm^{-1}): 3066, 2974, 2846, 1704, 1670, 1661, 1587, 1478, 1432, 1364, 1287; ^{1}H NMR: δ 3.27 (s, 3H, N6CH$_3$), 3.56 (s, 3H, N8CH$_3$), 5.11 (s, 1H, H10), 5.93 (d, *J* = 1.1 Hz, 1H, H2), 5.97 (d, *J* = 1.1 Hz, 1H, H2′), 6.50 (s, 1H, C11H), 6.67 (s, 1H, C4H), 7.36 (d, *J* = 8.1 Hz, 2H, C2′H, C6′H), 8.43 (d, *J* = 8.1 Hz, 2H, C3′H, C5′H); ^{13}C NMR: δ 28.1, 29.3, 40.1, 90.6, 99.2, 102.8, 108.5, 116.1, 126.7, 146.6, 147.7, 148.3, 150.1, 150.9, 151.2, 153.1, 163.7. Anal. calcd for $C_{19}H_{15}N_3O_5$ (365.34): C, 62.46; H, 4.14; N, 11.5; found: C, 62.56; H, 4.01; N, 11.42%.

*6,8-Dimethyl-10-(thiophen-2-yl)-6,10-dihydro-7*H-*[1,3]dioxolo[4′,5′:6,7]chromeno[2,3-*d*]pyrimidine-7,9(8*H*)-dione* (**4k**): White powder; m.p. 276–278 °C; yield 359 mg (96%); IR (KBr) (ν_{max} cm^{-1}): 3074, 2969, 2851, 1709, 1682, 1655, 1571, 1484, 1429, 1366, 1275; ^{1}H NMR: δ 3.26 (s, 3H, N6CH$_3$), 3.55 (s, 3H, N8CH$_3$), 4.98 (s, 1H, H10), 5.87 (d, *J* = 0.9 Hz, 1H, H2), 5.94 (d, *J* = 0.9 Hz, 1H, H2′), 6.45 (s, 1H, C11H), 6.64 (s, 1H, C4H), 7.05 (m, 3H, ArH); ^{13}C NMR: δ 28.2, 29.1, 39.4, 88.9, 98.0, 101.7, 109.4, 115.4, 122.6, 127.5, 138.9, 145.8, 146.5, 147.4, 150.1, 151.8, 152.6, 162.1. Anal. calcd for $C_{18}H_{14}N_2O_5S$ (370.38): C, 58.37; H, 3.81; N, 7.56; found: C, 58.42; H, 3.92; N, 7.48%.

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