Trimethylsilyl Iodide as a Multifunctional Agent in the One-Pot Synthesis of 9-(1*H*-Indol-3-yl)xanthen-4-(9*H*)-ones from *O*-Methyl Protected Salicylaldehydes, Indoles, and β-Dicarbonyl Compounds

Ali Khalafi-Nezhad,* Maryam Nourisefat, Farhad Panahi*

Department of Chemistry, College of Sciences, Shiraz University, Shiraz, 71454, Iran
E-mail: khalafi@chem.susc.ac.ir; E-mail: panahi@shirazu.ac.ir; Fax +98(711)2280926

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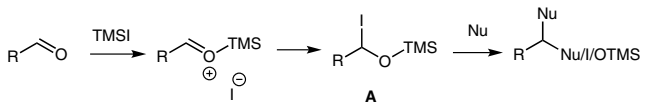
Abstract: Trimethylsilyl iodide (TMSI) is introduced as an efficient reagent for the one-pot synthesis of 9-(1*H*-indol-3-yl)xanthen-4-(9*H*)-ones using the reaction of 2-methoxybenzaldehydes (as *O*-methyl protected salicylaldehydes), indoles, and β-dicarbonyl compounds. In this protocol, a set of TMSI reactions involving silylation, silyl enol ether formation, methyl deprotection, and nucleophilic substitution/cyclization are performed to furnish the target product. The key step in this protocol is the deprotection of the methoxy group by TMSI.

Key words: trimethylsilyl iodide, xanthenes, salicylaldehydes, indoles, multicomponent reactions

Trimethylsilyl iodide (TMSI) is a proficient reagent that has been used for a range of specific organic transformations such as ring opening of cyclopropyl ketones,[1] spirocyclization of amines,[2] dealkylation of alkyl esters and alkyl ethers,[3] conversion of alkyl carbamates into amines,[4] and transformation of α,β-unsaturated sulfoxides into carbonyl compounds.[5] It has been widely applied for the silylation of alcohols and amines, and used for silyl enol ether formation of ketones or dicarbonyl compounds.[6] This reagent can also efficiently promulgate the methyl-deprotection of methoxy groups.[7] Furthermore, as a reducing agent, TMSI has been used for the reduction of unsaturated compounds and aldehydes.[8] Nucleophilic addition reaction of TMSI to aldehydes results in the production of a reactive intermediate (**A**), which undergoes subsequent reaction with other nucleophiles (Scheme 1).[9]

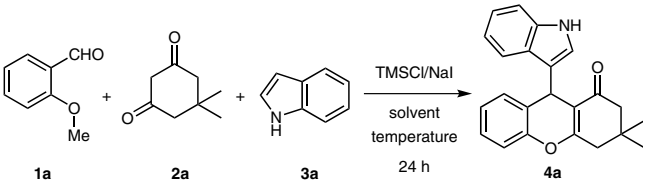


Scheme 1 Nucleophilic addition reaction of TMSI to aldehydes

Through the use of TMSI as a multifunctional agent[10] one can design a protocol in which all or a set of its transformations can be accomplished in a one-pot procedure. In fact, this protocol allows the preparation of a highly complex product in a single-step process. Recently, TMSI has been used to promote a reaction of salicylaldehydes and β-dicarbonyl compounds to prepare 4*H*-benzopyrans.[11] In another report, TMSI has been used to promote the reaction between salicylaldehydes and ketones for the construction of benzopyranic[2,3-*b*]ketals and spiroketals in a one-step procedure.[12]

In a continuation of our previous studies on multicomponent reactions,[13] herein, we report a novel and practical synthetic method for the synthesis of 9-(1*H*-indol-3-yl)xanthen-4-(9*H*)-ones through the reaction of *O*-methyl protected salicylaldehydes, indoles, and β-dicarbonyl compounds by using TMSI as a multifunctional agent. It is noteworthy that the 9-(1*H*-indol-3-yl)xanthen-4-(9*H*)-ones are a class of xanthenes with versatile biological activities.[14] Consequently, the synthesis of new derivatives and the development of new methodologies for the construction of this class of materials is of clear interest.[15]

Table 1 Optimization of the Reaction Conditions[a]



1a 2a 3a 4a

Entry	TMSCl/NaI (equiv)	Solvent	Temp (°C)	Yield of **4a** (%)[b]
1	0	MeCN	r.t.	0
2	1	MeCN	r.t.	trace
3	5	MeCN	r.t.	18
4	5	MeCN	50	55
5	5	MeCN	80	39
6	8	MeCN	50	78
7	10	MeCN	50	86
8	10	$CHCl_3$	50	63
9	10	THF	50	67
10	10	MeCN	r.t.	32
11	10	MeCN	50	0[c]

[a] Reaction conditions: 2-methoxybenzaldehyde (1 mmol), dimedone (1 mmol), indole (1 mmol).
[b] Isolated yield.
[c] Only TMSCl (10 equiv) was used.

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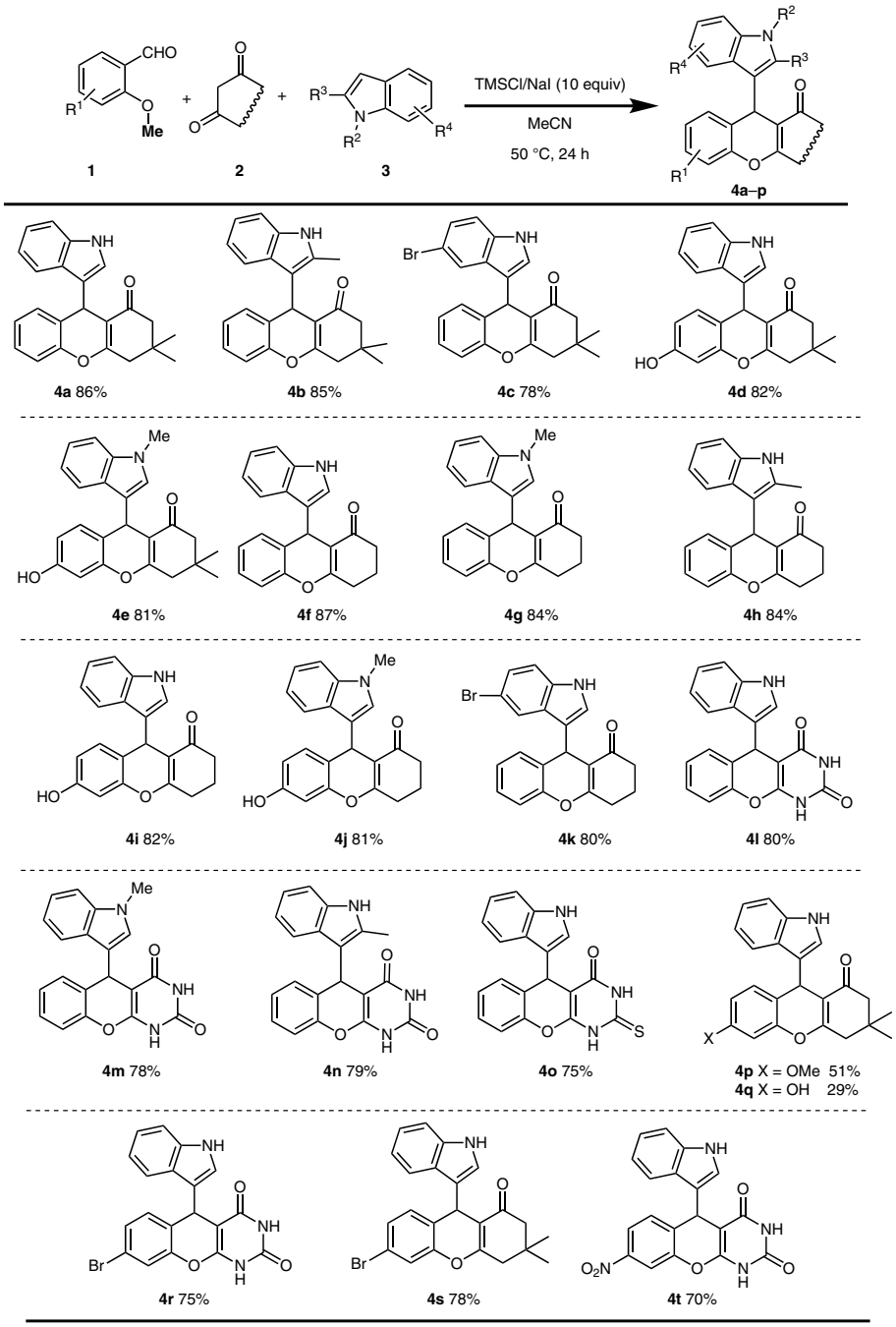
The current design of this study was based on the use of TMSI transformations to obtain the target product 9-(1*H*-indol-3-yl)xanthen-4-(9*H*)-ones in a single-step process. It was envisioned that the product could be obtained by silylation, silyl enol ether formation, methyl deprotection, and nucleophilic substitution and cyclization reactions, which are all promoted by TMSI.

To achieve appropriate conditions for the synthesis of 9-(1*H*-indol-3-yl)xanthen-4-(9*H*)-one derivatives using TMSI, we tested the reaction of 2-methoxybenzaldehyde (**1a**), dimedone (**2a**), and indole (**3a**) as a simple model substrate under a range of conditions. The results of the optimization study are summarized in Table 1.

When the reaction was conducted without any reagent in MeCN, no product was observed (Table 1, entry 1). When 5 equivalents of TMSI (generated in situ from TMSCl and NaI)[16] was used, 18% **4a** produced (Table 1, entry 3). The product yield was enhanced to 55% when the reaction was performed at 50 °C, however, upon increasing the temperature to 80 °C, the product yield decreased to 39%, demonstrating that temperature plays a significant role in the progress of the reaction (Table 1, entries 4 and 5). We also investigated the amount of TMSI required for the reac-



Scheme 2 Products of reaction between 2-methoxybenzaldehydes (1 mmol), indoles (1 mmol), and β-dicarbonyl compounds (1 mmol) in the presence of TMSI reagent. All yields are isolated yields.

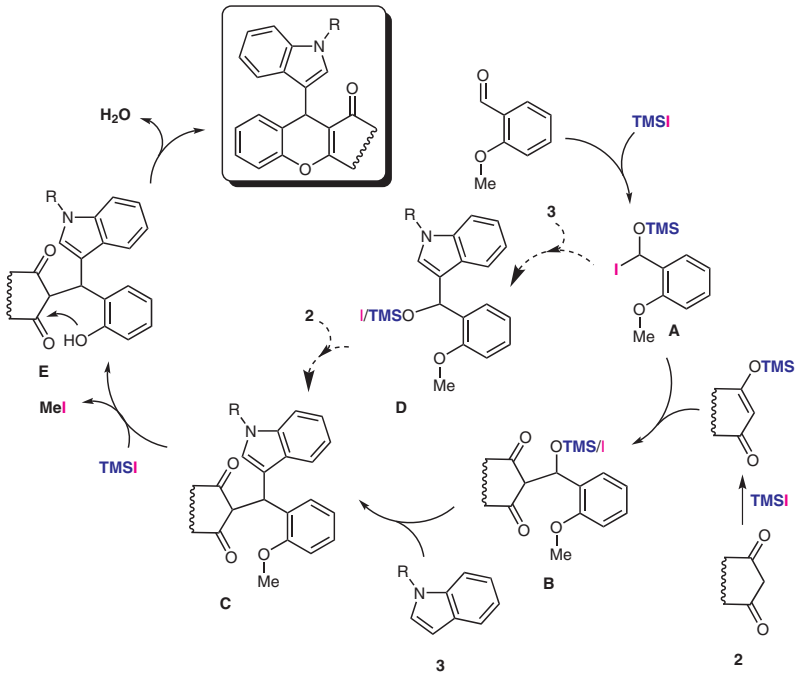
tion, and 10 equivalents of TMSI were established as optimal (Table 1, entries 4, 6, and 7). Subsequently, the effect of solvent was examined, however, $CHCl_3$ and tetrahydrofuran (THF) showed no superiority to MeCN (Table 1, entries 8 and 9). The reaction yield decreased significantly at r.t., which can be attributed to the methyl-deprotection step, because higher temperature is necessary for this stage (Table 1, entry 10).[16] In the absence of NaI (for the generation of TMSI in situ) no product was observed, suggesting TMSI is also a key reagent for this process. The result of this experiment also suggests that TMSCl does not promote this reaction alone (Table 1, entry 11). Thus, a simple system including TMSI (10 equiv) and MeCN at 50 °C was chosen as the optimized reaction conditions.

The scope of the reaction was investigated with a selection of commercially available salicylaldehydes, indoles, and dicarbonyl compounds; the results are summarized in Scheme 2. A variety of dicarbonyl compounds and indoles were applicable to the reaction, affording the products in good to excellent yields.

The structural diversity of this process was increased by using different indoles, leading to the formation of new indole-based xanthene derivatives. Another important feature of this method is the use of different salicylaldehydes to generate the desired derivatives, however, the electronic properties of the substituents on the salicylic aldehydes had a significant influence on the reaction yield. The application of β-dicarbonyl compounds (dimedone, cyclohexane-1,3-dione, and barbituric acids) provided a handle with which to introduce other groups at the xanthene ring by using this multicomponent reaction. Under the optimized reaction conditions, barbituric acid having an amide group afforded **4l**, **4m**, and **4n** in good yields. A further extension of this new multicomponent coupling sequence was demonstrated by the preparation of 10-(1*H*-indol-3-yl)-2-thioxo-1,2,3,10-tetrahydro-9-oxa-1,3-diazaanthracen-4-one (**4o**) using thiobarbituric acid. Overall, the yield of barbituric acids was less than those of dimedone and cyclohexane-1,3-dione. Interestingly, the structural diversity of this process was further increased by using 2,4-dimethoxybenzaldehyde, which resulted in the formation of compound **4p** with 51% yield; this reaction was accompanied by the formation of 7-demethylated product **4q** in 29% yield.

Although, the reactions of salicyladehydes, 1,3-diketones, and indoles have been well established,[17] we developed an efficient strategy to improve the scope of this reaction by using 2-methoxybenzaldehydes as *O*-methyl protected salicylaldehydes. This protocol also demonstrated a new approach to TMSI-catalyzed multicomponent reactions containing more TMSI-transformations.

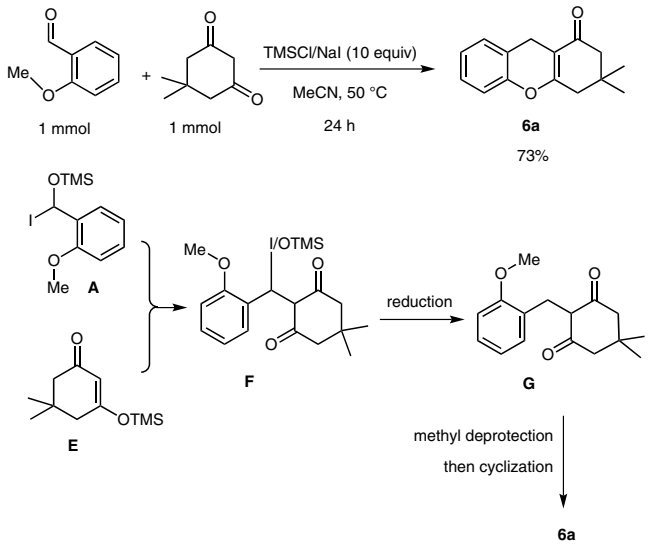
Although the mechanism of the current reaction has not been fully established at the present stage, a possible reaction pathway is shown in Scheme 3. Addition of TMSI to the C=O bond in the aldehyde results in the formation of intermediate **A**. TMSI can also convert the 1,3-diketone into the corresponding silyl enol ether. Nucleophilic attack of the silyl enol ether/enol form of 1,3-diketone on **A** resulted in the production of intermediate **B**. Subsequently, nucleophilic addition of indole to **B** with the elimination of TMSOH/HI affords intermediate **C**. It should be noted that the latter intermediate can also be generated through a second pathway (dashed line). In the latter pathway, the indole first adds to **A** to produce intermediate **D**, and then nucleophilic addition of β-dicarbonyl compound



Scheme 3 Proposed reaction mechanism for one-pot synthesis of 9-(1*H*-indol-3-yl)xanthen-4-(9*H*)-ones through reaction of salicyladehydes, indoles, and β-dicarbonyl compounds in the presence of TMSI

(either in the enol or silyl enol ether form) to **D** results in the production of **C**. Subsequently, methyl deprotection of intermediate **C** can be performed by TMSI to give intermediate **E**. Finally, intramolecular condensation of **E** gives the desired product.

Further experiments were conducted to obtain a deeper insight into the reaction mechanism. When 2-methoxybenzaldehyde and dimedone were used in the reaction, the prominent product was 4*H*-benzopyran **6a**[11] (Scheme 4). This experiment demonstrates that TMSI has three important roles in this reaction: (1) silyl enol ether formation,[18] (2) methyl deprotection, and (3) reduction. It is known that TMSI acts as a reducing agent through HI formation.[19]



Scheme 4 Synthesis of 4*H*-benzopyrans by using the reaction of 2-methoxybenzaldehyde and dimedone under the optimized conditions. Both the reduction and methyl-deprotection roles of TMSI are needed to form 4*H*-benzopyran product.

Interestingly, under the optimized reaction conditions, indole reacts with 2-methoxybenzaldehyde to produce bis(indolyl)methane[20] **7a** and **7a′**, suggesting that in the presence of indole (as a nucleophile) the reduction process is not accomplished (Scheme 5).

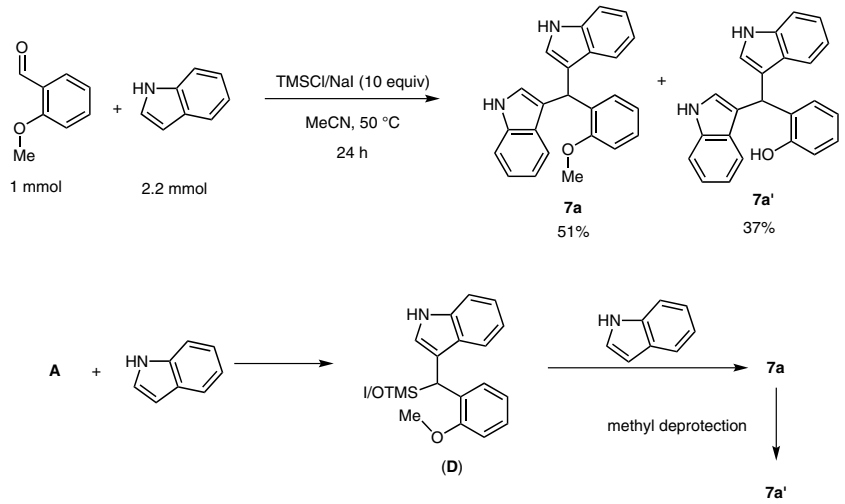
It is worth mentioning that this protocol is highly dependent on the strength of the nucleophile used. For example, by the use of 5-nitro-1*H*-indole the obtained product was **6a**, demonstrating that, in the presence of a weak nucleophile, reduction is the prominent process (Scheme 6).

In summary, we have developed a new and efficient method for the synthesis of 9-(1*H*-indol-3-yl)xanthen-4-(9*H*)-one derivatives in high yields by using TMSI as a multifunctional agent. A set of reactions involving, silylation, silyl enol ether formation, methyl deprotection, and nucleophilic substitution/cyclization are proposed to be mediated by the TMSI reagent to furnish the target product. Further studies on this reaction are expected to lead to new multicomponent reactions for the synthesis of new compounds using TMSI as a multifunctional agent.

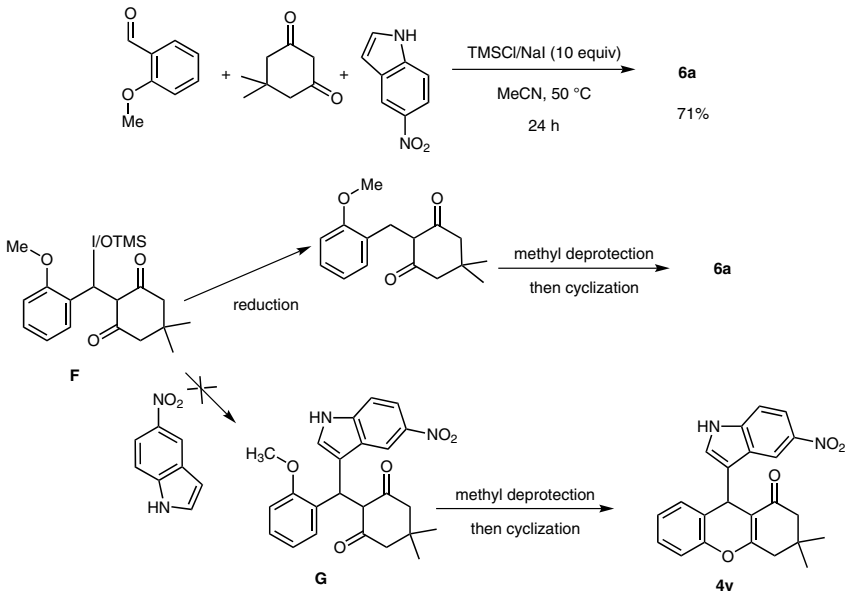
Chemicals were purchased from Fluka and Aldrich and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Avance 250 MHz spectrometer in DMSO solution with TMS as internal standard. Chemical shifts are given in the δ scale in parts per million (ppm) and the bonds are assigned as singlet (s), doublet (d), triplet (t), and multiplet (m). FTIR spectroscopy (Shimadzu FT-IR 8300 spectrophotometer) was employed for the characterization of compounds. Melting points were determined in open capillary tubes in a Barnstead Electrothermal 9100 BZ circulating oil melting point apparatus. The reactions were monitored by TLC on silica gel PolyGram SILG/UV254 plates.

General Procedure

To a stirring solution of 2-methoxybenzaldehydes (1 mmol) in MeCN (5 mL) containing TMSCl (10 mmol) and NaI (10 mmol) were added diketone (1 mmol) and indole (1 mmol), and the resulting mixture was vigorously stirred for 24 h at 50 °C (reaction monitored by TLC). The mixture was then extracted with EtOAc (3 × 10 mL), the combined extract was washed with brine (2 × 3 mL) and dried (Na_2SO_4). Removal of the solvent under reduced pressure



Scheme 5 Reaction of indole with 2-methoxybenzaldehyde in the presence of TMSI under optimized conditions results in the production of bis(indolyl)methanes **7a** and **7a′**. This reaction confirms the nucleophilic addition of indole to intermediate **A** and **D**.



Scheme 6 Reaction of 2-methoxybenzaldehyde, dimedone, and 5-nitro-1*H*-indole under the optimized conditions resulted in the production of 4*H*-benzopyran **6a**. This reaction confirms that TMSI acts as a reducing agent in the presence of weak nucleophiles.

gave almost pure products, which were further purified by recrystallization from EtOH.

9-(1*H*-Indol-3-yl)-3,3-dimethyl-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4a)
Yield: 0.29 g (86%); white solid; mp 190–193 °C.

IR (KBr): 3410, 2878, 1643, 1373, 1227, 1180, 741 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 0.91 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3), 2.03–2.29 (m, 2 H, CH_2), 2.61 (s, 2 H, CH_2), 5.17 (s, 1 H, CH), 6.87 (t, *J* = 7.5 Hz, 1 H, ArH), 6.94–7.02 (m, 2 H, ArH), 7.13 (s, 3 H, ArH), 7.24 (t, *J* = 5.0 Hz, 2 H, ArH), 7.41 (d, *J* = 7.7 Hz, 1 H, ArH), 10.81 (br s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 31.9, 33.8, 34.0, 36.8, 55.4, 116.7, 117.2, 121.3, 123.5, 123.6, 124.8, 126.0, 127.8, 129.9, 130.4, 131.0, 132.6, 135.0, 141.6, 154.2, 169.4, 201.2.

MS: *m*/*z* (%) = 343 (36) $[M]^+$, 344 (28) [M + 1].

Anal. Calcd for $C_{23}H_{21}NO_2$ (343.4): C, 80.44; H, 6.16; N, 4.08. Found: C, 80.52; H, 6.19; N, 4.14.

3,3-Dimethyl-9-(2-methyl-1*H*-indol-3-yl)-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4b)
Yield: 0.30 g (85%); white solid; mp 247–250 °C.

IR (KBr): 3294, 2962, 2322, 1632, 1458, 1380, 1226, 1180, 1149, 1018, 933, 871, 632.6 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 0.80 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 1.96–2.25 (m, 2 H, CH_2), 2.47–2.60 (m, 5 H, CH_2, CH_3), 5.10 (s, 1 H, CH), 6.73 (t, *J* = 7.5 Hz, 1 H, ArH), 6.84 (t, *J* = 7.5 Hz, 1 H, ArH), 6.93–7.15 (m, 6 H, ArH), 10.74 (br s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 11.5, 26.4, 27.6, 28.8, 31.4, 50.1, 110.4, 111.6, 114.9, 115.8, 117.0, 118.0, 119.5, 124.6, 125.2, 126.3, 127.3, 130.0, 131.4, 135.0, 148.9, 163.4, 196.0.

MS: *m*/*z* (%) = 357 (23) $[M]^+$.

Anal. Calcd for $C_{24}H_{23}NO_2$ (357.45): C, 80.64; H, 6.49; N, 3.92. Found: C, 81.68; H, 6.49; N, 4.81.

9-(5-Bromo-1*H*-indol-3-yl)-3,3-dimethyl-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4c)
Yield: 0.32 g (78%); white solid; mp 205–208 °C.

IR (KBr): 3463, 3193, 2954, 2869, 2360, 1643, 1589, 1488, 1380, 1311, 1234, 1149, 1026, 756, 655, 578, 478 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 0.89 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 2.02–2.29 (m, 2 H, CH_2), 2.50–2.67 (m, 2 H, CH_2), 5.16 (s, 1 H, CH), 7.00–7.25 (m, 7 H, ArH), 7.57 (s, 1 H, ArH), 11.03 (br s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 26.3, 28.2, 28.7, 31.5, 50.0, 111.1, 111.8, 113.5, 116.1, 119.5, 120.6, 123.2, 124.3, 124.8, 125.3, 126.9, 127.5, 129.72, 134.8, 148.8, 164.3, 196.2.

MS: *m*/*z* (%) = 422 (31) $[M]^+$.

Anal. Calcd for $C_{23}H_{20}BrNO_2$ (422.3): C, 65.41; H, 4.77; N, 3.32. Found: C, 65.47; H, 4.81; N, 3.39.

6-Hydroxy-9-(1*H*-indol-3-yl)-3,3-dimethyl-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4d)
Yield: 0.29 g (82%); white solid; mp 126–129 °C.

IR (KBr): 3818, 3749, 3386, 2692, 1627, 1458, 1373, 1218, 1172, 1095, 1033, 964.3, 840.9, 740.6, 424.3 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 0.64 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 1.77–2.02 (m, 2 H, CH_2), 2.23–2.33 (m, 2 H, CH_2), 4.81 (s, 1 H, CH), 6.25 (s, 2 H, ArH), 6.62–6.86 (m, 4 H, ArH), 7.00 (s, 1 H, ArH), 7.11 (s, 1 H, ArH), 9.30 (s, 1 H, OH), 10.51 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 26.6, 27.9, 28.7, 31.5, 50.1, 102.**?**, 111.4, 112.2, 112.3, 116.0, 118.2, 118.3, 119.9, 120.6, 122.3, 125.2, 130.2, 136.3, 149.4, 156.4, 163.9, 196.0.

MS: *m*/*z* (%) = 359 (27) $[M]^+$.

Anal. Calcd for $C_{23}H_{21}NO_3$ (359.4): C, 76.86; H, 5.89; N, 3.90. Found: C, 76.91; H, 5.92; N, 3.96.

6-Hydroxy-3,3-dimethyl-9-(1-methyl-1*H*-indol-3-yl)-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4e)
Yield: 0.30 g (81%); white solid; mp 272–275 °C.

IR (KBr): 3155, 3055, 2954, 2360, 1627, 1589, 1512, 1473, 1373, 1218, 1141, 1095, 1033, 964, 856, 732 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 0.88 (s, 3 H, CH_3), 1.00 (s, 3 H, CH_3), 2.02–2.26 (m, 2 H, CH_2), 2.55 (s, 2 H, CH_2), 3.63 (s, 3 H, CH_3), 5.06 (s, 1 H, CH), 6.46–6.55 (m, 2 H, ArH), 6.89–7.10

(m, 4 H, ArH), 7.27 (d, J = 8.0 Hz, 1 H, ArH), 7.40 (d, J = 7.7 Hz, 1 H, ArH), 9.67 (br s, 1 H, OH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 26.6, 27.8, 28.7, 31.5, 32.0, 50.2, 102.3, 109.5, 112.1, 112.4, 115.9, 118.3, 118.5, 119.2, 120.7, 125.5, 126.7, 130.2, 136.6, 149.42, 156.5, 163.9, 196.1.

MS: m/z (%) = 373 (25) $[M]^+$, 374 (23) [M + 1], 375 (8) [M + 2].

Anal. Calcd for $C_{24}H_{23}NO_3$ (373.4): C, 77.19; H, 6.21; N, 3.75. Found: C, 77.24; H, 6.23; N, 3.78.

9-(1*H*-Indol-3-yl)-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4f)
Yield: 0.27 g (87%); white solid; mp 255–258 °C.

IR (KBr): 3749, 3332, 3055, 2947, 2360, 1766, 1635, 1581, 1481, 1458, 1427, 1380, 1226, 1180, 1134, 1091, 995, 918, 864, 794, 748, 624, 555.5, 424 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 1.62–1.71 (m, 2 H, CH_2), 2.01–2.02 (m, 2 H, CH_2), 2.36–2.56 (m, 2 H, CH_2), 4.98 (s, 1 H, CH), 6.63–6.78 (m, 3 H, ArH), 6.89 (s, 3 H, ArH), 7.04 (d, J = 8.0 Hz, 2 H, ArH), 7.24 (d, J = 7.5 Hz, 1 H, ArH), 10.58 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 20.0, 27.0, 28.4, 36.5, 111.5, 113.1, 116.0, 118.2, 118.4, 119.5, 120.7, 122.6, 124.6, 125.2, 125.8, 127.3, 129.6, 136.4, 148.96, 166.0, 196.1.

MS: m/z (%) = 315 (43) $[M]^+$, 316 (29) [M + 1].

Anal. Calcd for $C_{21}H_{17}NO_2$ (315.4): C, 79.98; H, 5.43; N, 4.44. Found: C, 80.02; H, 5.45; N, 4.49.

9-(1-Methyl-1*H*-indol-3-yl)-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4g)
Yield: 0.27 g (84%); white solid; mp 212–215 °C.

IR (KBr): 3340, 2877, 2360, 1643, 1488, 1373, 1326, 1234, 1134, 1064, 995, 748, 555 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 1.87–1.95 (m, 2 H, CH_2), 2.26–2.31 (m, 2 H, CH_2), 2.71–2.72 (m, 2 H, CH_2), 3.64 (s, 3 H, CH_3), 5.18 (s, 1 H, CH), 6.93–7.13 (m, 6 H, ArH), 7.26 (s, 2 H, ArH), 7.45–7.51 (m, 1 H, ArH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 20.0, 27.0, 28.1, 32.1, 36.5, 109.6, 113.0, 116.0, 118.5, 118.5, 118.8, 120.8, 124.6, 125.5, 125.7, 126.9, 127.8, 129.58, 136.6, 148.8, 166.1, 196.1.

MS: m/z (%) = 329 (32) $[M]^+$, 330 (16) [M + 1].

Anal. Calcd for $C_{22}H_{19}NO_2$ (329.4): C, 80.22; H, 5.81; N, 4.25. Found: C, 80.28; H, 5.83; N, 4.29.

9-(2-Methyl-1*H*-indol-3-yl)-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4h)
Yield: 0.27 g (84%); white solid; mp 237–240 °C.

IR (KBr): 3355, 2877, 2360, 1635, 1581, 1458, 1373, 1234, 1180, 1118, 995, 918, 864, 748, 617, 570, 524 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 1.72–1.97 (m, 2 H, CH_2), 2.17–2.32 (m, 2 H, CH_2), 2.53 (s, 3 H, CH_3), 2.67–2.69 (m, 2 H, CH_2), 5.12 (s, 1 H, CH), 6.77 (t, J = 7.5 Hz, 1 H, ArH), 6.87 (t, J = 7 Hz, 1 H, ArH), 6.93–7.17 (m, 6 H, ArH), 10.74 (br s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 11.5, 20.1, 26.9, 27.6, 36.5, 110.4, 112.6, 114.9, 115.8, 116.8, 118.2, 119.5, 124.6, 125.2, 126.4, 127.3, 129.9, 131.50, 134.9, 148.8, 165.4, 196.2.

MS: m/z (%) = 329 (35) $[M]^+$.

Anal. Calcd for $C_{22}H_{19}NO_2$ (329.4): C, 80.22; H, 5.81; N, 4.25. Found: C, 80.17; H, 5.79; N, 4.32.

6-Hydroxy-9-(1*H*-indol-3-yl)-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4i)
Yield: 0.27 g (82%); yellow solid; mp >300 °C (dec.).

IR (KBr): 3755, 3379, 3301, 2569, 1635, 1589, 1512, 1373, 1226, 1180, 1002, 856, 786, 756, 524, 424 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 1.83–1.92 (m, 2 H, CH_2), 2.23 (s, 2 H, CH_2), 2.67 (s, 2 H, CH_2), 5.06 (s, 1 H, CH), 6.42–6.48 (m, 2 H, ArH), 6.86–7.08 (m, 4 H, ArH), 7.24 (s, 1 H, ArH), 7.39 (s, 1 H, ArH), 9.54 (s, 1 H, OH), 10.76 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 20.0, 27.0, 27.8, 36.5, 102.2, 111.4, 112.3, 113.4, 116.1, 118.3, 119.9, 120.9, 122.4, 125.2, 130.1, 136.3, 149.4, 156.46, 156.9, 196.2.

MS: m/z (%) = 331 (18) $[M]^+$.

Anal. Calcd for $C_{21}H_{17}NO_3$ (331.4): C, 76.12; H, 5.17; N, 4.23. Found: C, 76.07; H, 5.13; N, 4.29.

6-Hydroxy-9-(1-methyl-1*H*-indol-3-yl)-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4j)
Yield: 0.27 g (81%); yellow solid; mp >300 °C (dec.).

IR (KBr): 3433, 3155, 2931, 2823, 2707, 1627, 1581, 1512, 1458, 1380, 1226, 1180, 1134, 1095, 1064, 1002, 964, 848, 740 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 1.88–1.89 (m, 2 H, CH_2), 2.22 (s, 2 H, CH_2), 2.65 (s, 2 H, CH_2), 3.62 (s, 3 H, CH_3), 5.05 (s, 1 H, CH), 6.47 (s, 2 H, ArH), 7.03 (s, 4 H, ArH), 7.25 (s, 1 H, ArH), 7.42 (s, 1 H, ArH), 9.55 (br s, 1 H, OH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 20.0, 27.0, 27.6, 32.0, 36.5, 102.2, 109.5, 112.3, 113.4, 116.0, 118.4, 118.5, 120.7, 122.8, 126.7, 130.0, 136.5, 149.27, 156.4, 165.9, 196.1.

MS: m/z (%) = 345 (29) $[M]^+$.

Anal. Calcd for $C_{22}H_{19}NO_3$ (345.4): C, 76.50; H, 5.54; N, 4.06. Found: C, 76.44; H, 5.57; N, 4.14.

9-(5-Bromo-1*H*-indol-3-yl)-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4k)
Yield: 0.31 g (80%); white solid; mp 244–247 °C.

IR (KBr): 3379, 2885, 2360, 1643, 1581, 1450, 1337, 1234, 1180, 1103, 995, 918, 879, 794, 756, 624, 424 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 1.85–1.99 (m, 2 H, CH_2), 2.20–2.31 (m, 2 H, CH_2), 2.67–2.76 (m, 2 H, CH_2), 5.21 (s, 1 H, CH), 6.98–7.05 (m, 1 H, ArH), 7.10–7.15 (m, 4 H, ArH),7.24–7.28 (m, 2 H, ArH), 7.69 (s, 1 H, ArH), 11.08 (br s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 20.0, 27.0, 28.0, 36.4, 111.2, 113.1, 113.4, 116.0, 119.7, 120.6, 123.2, 124.5, 124.7, 125.6, 127.1, 1275, 129.6, 134.91, 148.9, 166.1, 196.1.

MS: m/z (%) = 394 (65) $[M]^+$, 395 (80) [M + 1], 396 (35) [M + 2].

Anal. Calcd for $C_{21}H_{16}BrNO_2$ (394.3): C, 63.97; H, 4.09; N, 3.55. Found: C, 63.91; H, 4.13; N, 3.42.

5-(1*H*-Indol-3-yl)-1*H*-chromeno[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4l)
Yield: 0.26 g (80%); white solid; mp 247–250 °C.

IR (KBr): 3818, 3749, 3502, 3402, 3278, 3224, 3031, 2862, 2515, 1697, 1651, 1581, 1519, 1488, 1458, 1380, 1280, 1226, 1103, 1041, 887, 763, 663, 594, 540, 509 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 4.69 (s, 1 H, CH), 6.52 (s, 1 H, ArH), 6.74–7.34 (m, 8 H, ArH), 10.98 (s, 1 H, NH), 11.18 (s, 1 H, NH), 11.97 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 33.5, 53.2, 85.1, 116.4, 120.7, 125.5, 127.9, 129.1, 149.0, 149.4, 150.4, 155.3, 163.4, 168.8, 169.5.

MS: *m*/*z* (%) = 331 (37) [M]$^+$, 332 (22) [M + 1], 333 (9) [M + 2].

Anal. Calcd for $C_{19}H_{13}N_3O_3$ (331.3): C, 68.88; H, 3.95; N, 12.68. Found: C, 68.94; H, 3.88; N, 12.72.

5-(1-Methyl-1*H*-indol-3-yl)-1*H*-chromeno[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4m)
Yield: 0.26 g (78%); white solid; mp 219–222 °C.

IR (KBr): 3494, 3224, 2862, 2360, 1697, 1651, 1519, 1496, 1458, 1380, 1326, 1280, 1226, 1064, 871, 748, 663, 424 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 3.65 (s, 3 H, CH_3), 4.70 (s, 1 H, CH, ArH), 6.61–7.35 (m, 9 H, ArH), 10.99 (s, 1 H, NH), 11.97 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 32.1, 33.5, 85.1, 109.4, 116.4, 117.2, 118.1, 119.0, 120.8, 125.5, 127.7, 127.9, 129.1, 136.8, 149.5, 150.5, 163.4, 168.9, 169.5.

MS: *m*/*z* (%) = 345 (30) [M]$^+$.

Anal. Calcd for $C_{20}H_{15}N_3O_3$ (345.4): C, 69.56; H, 4.38; N, 12.17. Found: C, 69.48; H, 4.32; N, 12.09.

5-(2-Methyl-1*H*-indol-3-yl)-1*H*-chromeno[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4n)
Yield: 0.27 g (79%); white solid; mp >300 °C (dec.).

IR (KBr): 3294, 2831, 2360, 1712, 1674, 1519, 1458, 1342, 1257, 1041, 756, 671, 547, 439.7 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 2.52 (s, 3 H, CH_3), 5.15 (s, 1 H, CH), 6.74 (t, *J* = 7.5 Hz, 1 H, ArH), 6.86 (t, *J* = 7.5 Hz, 1 H, ArH), 6.95–7.23 (m, 6 H, ArH), 10.78 (br s, 1 H, NH), 10.90 (br s, 1 H, NH), 11.90 (br s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 11.5, 27.9, 87.9, 110.6, 113.9, 115.7, 116.4, 118.2, 119.6, 124.7, 125.3, 126.2, 127.8, 130.1, 132.0, 134.9, 148.2, 149.6, 153.2, 163.1.

MS: *m*/*z* (%) = 345 (44) [M]$^+$.

Anal. Calcd for $C_{20}H_{15}N_3O_3$ (345.3): C, 69.56; H, 4.38; N, 12.17. Found: C, 69.64; H, 4.46; N, 12.26.

5-(1*H*-Indol-3-yl)-2-thioxo-2,3-dihydro-1*H*-chromeno[2,3-*d*]pyrimidin-4(5*H*)-one (4o)
Yield: 0.26 g (75%); yellow solid; mp >300 °C (dec.).

IR (KBr): 3494, 3402, 3016, 2908, 2360, 1681, 1589, 1458, 1334, 1265, 1234, 1134, 1080, 1041, 941, 817, 748.3, 671.2, 594, 547, 416 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 4.69 (s, 1 H, CH), 6.08 (s, 1 H), 6.51–6.55 (m, 2 H, ArH), 6.77 (t, *J* = 7.2 Hz, 1 H, ArH), 6.88–6.97 (m, 3 H, ArH), 7.24 (t, *J* = 7.5 Hz, 2 H, ArH), 10.44 (s, 1 H, NH), 11.18 (s, 1 H, NH), 11.97 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 33.5, 53.2, 110.8, 111.0, 115.2, 117.9, 118.2, 119.1, 120.2, 125.7, 126.9, 129.4, 130.2, 136.8, 136.8, 154.4.

MS: *m*/*z* (%) = 347 (22) [M]$^+$.

Anal. Calcd for $C_{19}H_{13}N_3O_2S$ (347.4): C, 65.69; H, 3.77; N, 12.10. Found: C, 65.75; H, 3.82; N, 12.17.

6-Methoxy-9-(1*H*-indol-3-yl)-3,3-dimethyl-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4p)
Yield: 0.19 g (51%); white solid; mp 192–198 °C.

IR (KBr): 3309, 2962, 2353, 1627, 1496, 1373, 1218, 740 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 0.90 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 2.03–2.28 (m, 2 H, CH_2), 2.59 (s, 2 H, CH_2), 3.68 (s, 3 H, CH_3), 5.11 (s, 1 H, CH), 6.59 (d, *J* = 8.2 Hz, 1 H, ArH), 6.71 (s, 1 H, ArH), 6.87 (t, *J* = 7.2 Hz, 1 H, ArH), 6.98 (t, *J* = 7.7 Hz, 1 H, ArH), 7.09–7.13 (m, 2 H, ArH), 7.27 (d, *J* = 8 Hz, 1 H, ArH), 7.39 (d, *J* = 7.7 Hz, 1 H, ArH), 10.79 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 26.6, 28.0, 28.7, 31.5, 50.2, 55.2, 100.9, 111.3, 111.4, 112.2, 117.6, 118.2, 119.7, 120.6, 122.4, 125.1, 130.2, 136.3, 149.5, 158.3, 163.8, 196.0.

MS: *m*/*z* (%) = 373 (38) [M]$^+$.

Anal. Calcd for $C_{24}H_{23}NO_3$ (373.5): C, 77.19; H, 6.21; N, 3.75. Found: C, 77.11; H, 6.15; N, 3.68.

6-Hydroxy-9-(1*H*-indol-3-yl)-3,3-dimethyl-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4q)
Yield: 0.10 g (29%); white solid; mp 126–129 °C.

IR (KBr): 3818, 3749, 3386, 2692, 1627, 1458, 1373, 1218, 1172, 1095, 1033, 964.3, 840.9, 740.6, 424.3 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 0.64 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 1.77–2.02 (m, 2 H, CH_2), 2.23–2.33 (m, 2 H, CH_2), 4.81 (s, 1 H, CH), 6.25 (s, 2 H, ArH), 6.62–6.86 (m, 4 H, ArH), 7.00 (s, 1 H, ArH), 7.11 (s, 1 H, ArH), 9.30 (s, 1 H, OH), 10.51 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 26.6, 27.9, 28.7, 31.5, 50.1, 102., 111.4, 112.2, 112.3, 116.0, 118.2, 118.3, 119.9, 120.6, 122.3, 125.2, 130.2, 136.3, 149.4, 156.4, 163.9, 196.0.

MS: *m*/*z* (%) = 359 (42) [M]$^+$, 360 (25) [M + 1], 361 (12) [M + 2].

Anal. Calcd for $C_{23}H_{21}NO_3$ (359.4): C, 76.86; H, 5.89; N, 3.90. Found: C, 76.92; H, 5.93; N, 3.97.

8-Bromo-5-(1*H*-indol-3-yl)-1*H*-chromeno[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4r)
Yield: 0.31 g (75%); yellow solid; mp 341–345 °C (dec.).

IR (KBr): 3494, 3402, 3016, 2908, 2360, 1681, 1589, 1458, 1334, 1265, 1234, 1134, 1080, 1041, 941, 817, 748.3, 671.2, 594, 547, 416 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 4.69 (s, 1 H, CH), 6.52 (s, 1 H, ArH), 6.74–7.34 (m, 7 H, ArH), 9.85 (s, 1 H, NH), 10.18 (s, 1 H, NH), 10.90 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 23.0, 27.8, 45.4, 58.9, 80.1, 88.89, 150.0, 151.0, 152.7, 165.2, 165.3, 170.5.

MS: *m*/*z* (%) = 410 (21) [M]$^+$.

Anal. Calcd for $C_{19}H_{12}BrN_3O_3$ (410.23): C, 55.63; H, 2.95; N, 10.24. Found: C, 55.54; H, 2.88; N, 10.18.

6-Bromo-9-(1*H*-indol-3-yl)-3,3-dimethyl-3,4-dihydro-2*H*-xanthen-1(9*H*)-one (4s)
Yield: 0.33 g (78%); white solid; mp 269–273 °C.

IR (KBr): 3463, 3193, 2954, 2869, 2360, 1643, 1589, 1488, 1380, 1311, 1234, 1149, 1026, 756, 655, 578, 478 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 0.71 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 1.80–2.09 (m, 2 H, CH_2), 2.25–2.31 (m, 2 H, CH_2), 4.78 (s, 1 H, CH), 6.46–6.55 (m, 2 H, ArH), 6.89–7.10 (m, 4 H, ArH), 7.27 (d, *J* = 8 Hz, 1 H, ArH), 7.40 (d, *J* = 7.7 Hz, 1 H), 10.34 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 25.1, 26.0, 27.5, 29.1, 31.5, 50.2, 110.3, 115.3, 117.6, 128.2, 129.6, 130.5, 148.8, 164.3, 195.5.

MS: *m*/*z* (%) = 422 (27) [M]$^+$.

Anal. Calcd for $C_{23}H_{20}BrNO_2$ (422.32): C, 65.41; H, 4.77; N, 3.32. Found: C, 65.32; H, 4.71; N, 3.25.

5-(1*H*-Indol-3-yl)-8-nitro-1*H*-chromeno[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4t)
Yield: 0.26 g (70%); white solid; mp 219–222 °C.

IR (KBr): 3818, 3749, 3502, 3402, 3278, 3224, 3031, 2862, 2515, 1697, 1651, 1581, 1519, 1488, 1458, 1380, 1280, 1226, 1103, 1041, 887, 763, 663, 594, 540, 509 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, TMS): δ = 4.97 (s, 1 H, CH), 6.56–6.66 (m, 2 H, ArH), 6.77 (t, J = 7 Hz, 1 H, ArH), 6.94–7.08 (m, 3 H, ArH), 7.64–7.89 (m, 2 H, ArH), 9.74 (s, 1 H, NH), 10.03 (s, 1 H, NH), 10.60 (s, 1 H, NH).

^{13}C NMR (62.5 MHz, DMSO-d_6, TMS): δ = 23.3, 28.3, 45.2, 59.7, 88.9, 117.9, 118.0, 118.5, 123.8, 125.1, 135.8, 137.0, 149.9, 165.3, 170.0.

MS: m/z (%) = 376 (16) $[M]^+$.

Anal. Calcd for $C_{19}H_{12}N_4O_5$ (376.33): C, 60.64; H, 3.21; N, 14.89. Found: C, 60.55; H, 3.16; N, 14.80.

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