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Graphical Abstract

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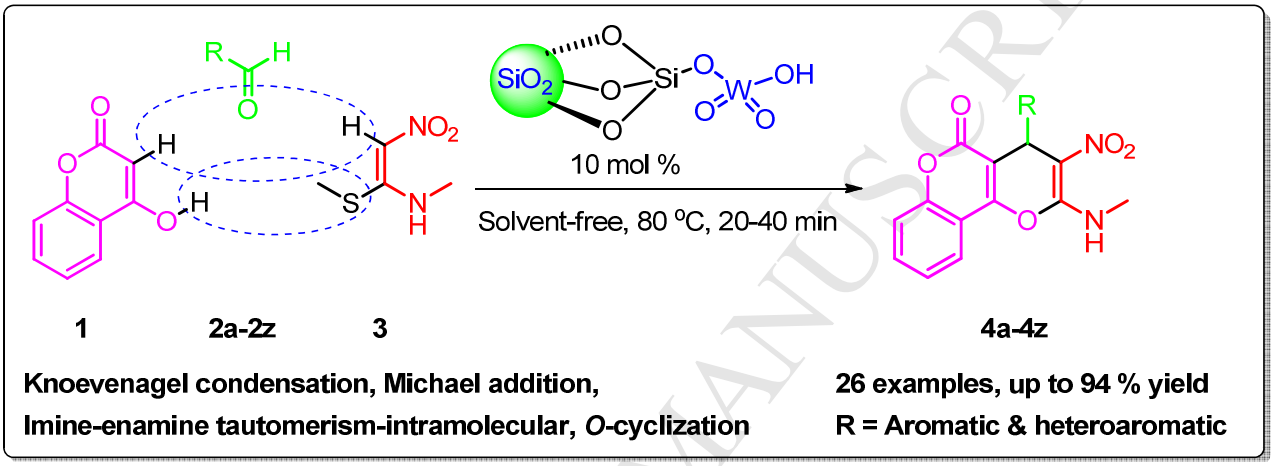

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ABSTRACT

A simple, efficient, green and solvent-free procedure for the synthesis of pyrano[3,2-*c*]chromen-5-ones has been developed by multi-component condensation of 4-hydroxycoumarin, aldehydes and (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine in the presence of a catalytic amount of silica-supported tungstic acid (STA). The reaction transformation presumably occurs via Knoevenagel condensation, Michael addition, imine-enamine tautomerism intramolecular, *O*-cyclization, elimination of MeSH. The present environmentally benign protocol offers several advantages such as shorter reaction times, a wide range of functional group tolerance, use of an inexpensive heterogeneous catalyst, and high yield of products via a simple experimental and work-up procedure. The catalyst can be recovered and reused for at least four runs without any significant impact on the product yields.

1. Introduction

Multicomponent reactions (MCRs) are special types of synthetically useful organic reactions in which three or more starting materials react to give a final product in a one-pot procedure.[1] MCRs have their inherent advantages such as short reaction times, low manpower requirement, high atom economy and simple purification processes. MCRs protocols can be used for fragment based drug design[2-4] and diversity-oriented synthesis of heterocyclic compounds because of their simplicity, efficiency, and high selectivity.[5]

Chemistry of heterocyclic compounds has been ubiquitous in natural products, biologically active agrochemicals, pharmaceutical agents, organic materials, and several well-designed molecules.[6] Therefore, the interest for developing new, versatile, and efficient synthesis of heterocyclic compounds have been important in synthetic organic and bio-organic chemistry. Pyrano[3,2-*c*]chromen-5-ones are a promising class of oxygen containing heterocyclic compounds are widely found in nature and gain much importance due to their broad series of biological activities.[7] For example, compound A has antibacterial, antituberculosis, antimalarial activities, compound B, and C also have antibacterial activity (Fig. 1).[8] Similarly, some pyran annulated heterocycles have a wide range of biological properties such as anti-coagulants,[9] anticancer agents,[10] anti-anaphylactics,[11] anti-tumoral,[12] anti-HIV etc.[13] Moreover, these compounds can be used as cognitive enhancers for the treatment of neurodegenerative diseases, including Alzheimer's disease, as well as for the treatment of schizophrenia and myoclonus.[14]

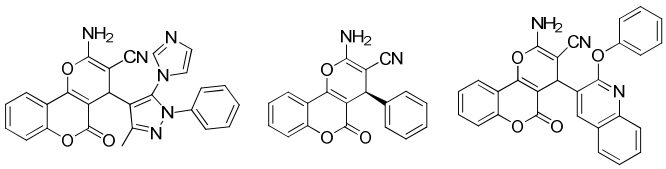

Figure 1 Examples of biologically active pyranocoumarin derivatives.

Therefore, there is a strong need to develop a quick and efficient synthetic method to access a biologically active pyranocoumarin molecule. But, a literature scan showed that, only one method has been developed so far for the synthesis of this skeleton.[15] However, these procedures suffer from relatively long reaction times, low yields, the use of toxic organic solvents and catalysts. Hence, the development of new and highly efficient, protocol for the synthesis of pyrano[3,2-*c*]chromen-5-ones derivatives is still highly desirable.

Currently, multi-component one-pot synthesis and solid supported catalysts have gained much interest because of their cost-effectiveness by reusability and ecological benefits.[16–18] Environmentally friendly and inexpensive solid acids are increasingly used due to their ease of handling and high catalytic activities. In the course of the last few years, particularly silica-

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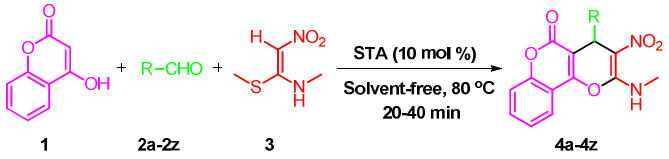
supported acid catalysts have established numerous applications in modern organic synthesis as they may be easily recovered and reused.[16] In this connection, silica-supported tungstic acid (STA) has attracted tremendous attention as a green and solid acid catalyst to construct carbon–carbon and carbon–heteroatom bonds in various organic trans-formations.[17,18] It has received significant notice due to its low cost, non-toxicity, air and water compatibility, ease of handling, greater selectivity, recyclability, enhanced reaction rates, experimental simplicity and ease of preparation.[17a]

As part of our ongoing research program on the development of clean protocols as well as our interest in applications of silica-supported catalysts[19-25] in organic reactions, herein, we report a green and convenient protocol for the synthesis of pyrano[3,2-*c*]chromen-5-ones via a multicomponent reaction of a 4-hydroxycoumarin, aldehydes and (*E*)-*N*-methyl-1-(methylthio)-2- nitroethenamine in the presence of catalytic amount of STA in solvent-free condition with excellent yields (**Scheme 1**).



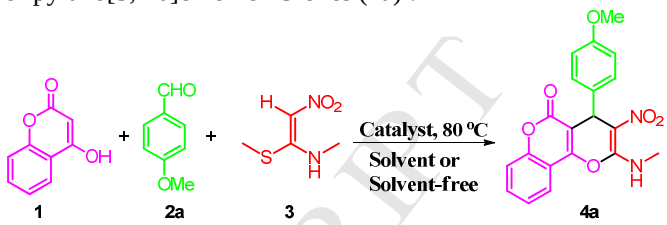
Scheme 1. Synthesis of pyrano[3,2-*c*]chromen-5-ones derivative catalyzed by STA under solvent free conditions.

2. Results and discussion

For our initial investigation, the reaction of 4-hydroxycoumarin (**1**, 1 mmol), 4-methoxybenzaldehyde (**2a**, 1 mmol) and (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine (**3**, 1 mmol) was chosen as a model reaction to optimize the reaction conditions at 80 °C. The results are summarized in Table 1. The reaction was first carried out in ethanol in the absence and presence of several acid catalysts. The reaction did not proceed even after prolonged reaction time (18 hours) and no desired product was formed in the absence of catalyst at 80 °C in ethanol (Table 1, entry 1). After that, the model reaction was performed in the presence of 10 mol% of the tungstate sulfuric acid (TSA) in ethanol at 80 °C. The reaction provided the corresponding title product **4a**, which was isolated in 38% product yield (Table 1, entry 2) after 8 h. The product **4a** was confirmed by usual spectroscopic techniques. Therefore, our efforts focused on the search for a suitable catalyst, such as glucose sulfonic acid (GSA), phospho sulfonic acid (PSA), CAN.SiO_2, $FeCl_3$.SiO_2, $ZnCl_2$.SiO_2, *p*-TSA and STA can catalyze this reaction at 80 °C in ethanol (Table 1, entries 3–9). Among all the screened catalysts, STA was found superior for the desired product in MCR reaction, with these merits, like reaction time, product yield (Table 1, entry 9).

In addition, we investigated the influence of various organic solvents such as CH_2Cl_2, DMF, THF, H_2O, CH_3CN, and Toluene at different reaction temperatures on the model reaction with 10 mol% of STA (Table 1, entry 10-15). In these cases, product **4a** was formed in slightly lower yields. With respect to the solvent system, the best results were achieved using ethanol (Table 1, entry 9). In recent years, the syntheses of compounds under solvent-free conditions is an important task in heterocyclic synthesis, because such reactions are environmentally friendly, cost-effective and have easy workup procedures, fast reaction rates, and high yields.[26] Therefore, we decided to test a solvent-free version with STA catalyst (Table 1, entries 16–18). Most excitingly, when STA was used, the reaction proceeded very smoothly and gave the product 4a in 94% yield (Table 1, entry 16). Moreover, we found that the yields were obviously affected by the amount of STA loaded. When 5 mol%, 10 mol% and 20 mol% of STA were used the yields were 85, 94 and 93%, respectively (Table 1, entries 16-18). Therefore, 10 mol% of STA was sufficient and optimal quantity for the completion of the reaction.

Table 1 Optimization of reaction conditions for the synthesis of pyrano[3,2-*c*]chromen-5-ones (4a)[a].



Entry	Catalyst (mol %)	Solvent	Temp (^{0}C)	Time	Yield (%)[b]
1	-	EtOH	80	18 h	-
2	TSA (10%)	EtOH	80	8 h	38
3	GSA (10%)	EtOH	80	8 h	42
4	PSA (10%)	EtOH	80	7 h	29
5	CAN.SiO_2 (10%)	EtOH	80	5 h	52
6	$FeCl_3$.SiO_2 (10%)	EtOH	80	6 h	56
7	$ZnCl_2$.SiO_2 (10%)	EtOH	80	6 h	45
8	*p*-TSA (10%)	EtOH	80	3 h	78
9	STA (10%)	EtOH	80	2 h	88
10	STA (10%)	CH_2Cl_2	reflux	4 h	54
11	STA (10%)	DMF	120	3 h	60
12	STA (10%)	THF	reflux	4 h	46
13	STA (10%)	H_2O	reflux	6 h	-
14	STA (10%)	CH_3CN	reflux	4 h	65
15	STA (10%)	Toluene	reflux	4 h	52
16	STA (10%)	Neat	80	20 min	94
17	STA (5%)	Neat	80	40 min	85
18	STA (20%)	Neat	80	20 min	93

[a]Reaction of 4-hydroxycoumarin (**1**, 1 mmol), 4-methoxy benzaldehyde (**2a**, 1 mmol) and (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine (**3**, 1 mmol), STA (10 mol%) with solvent (5 mL) or solvent-free conditions. [b]Isolated yield.

The reaction was studied at different temperatures to find out the optimum reaction temperature for the preparation of **4a** in the presence of 10 mol% of STA under solvent free condition (Table 2). It was observed that the reaction did not proceed at room temperature, but in 40 °C reaction gives trace of product (Table 2, entry 2). The reaction proceeds smoothly at 60 °C but the yield of the product is not acceptable. On the other hand the reaction at 80 °C proceeded very effectively, with excellent yields (Table 2, entry 4). Further increase of temperature the

product yield was not increased. Therefore, the best reaction conditions were obtained by using 10 mol % of STA as the catalyst under solvent free condition at 80 °C to afford the desired product **4a** in 94% yield within 20 min (Table 2, entry 4).

A variety of substrates were submitted to the optimum reaction conditions and the desired products were obtained in excellent yields (Table 3). Various functional groups substituted at the aromatic ring of the aldehyde substrate, including electron withdrawing groups such as bromo, chloro, fluoro and nitro (Table 3, entries **4e**-**4h**, **4j**, **4o**, **4p**-**4t** and **4v**) and electron donating groups such as methyl, methoxy, ethoxy, and 4-*N*,*N*-dimethylamino (Table 3, entries **4a**-**4d**, **4i**, **4l**, **4m** and **4w**). In addition, heteroaryl aldehydes also participate in the multicomponent reaction to produce the desired products in good yields without affecting the heterocyclic moieties (Table 3, entries **4x**-**4z**). In general, the reactions were clean and no side products were detected. In all cases, the reactions proceeded efficiently at 80 ºC under solvent free conditions and with 10 mol% of the STA catalyst. Therefore, the present protocol has general applicability and accommodates a variety of substitution patterns.

Table 2: Temperature effect on the preparation of pyrano[3,2-*c*]chromen-5-ones[a].

Entry	Temp (°C)	Time (min)	Yield (%)[b]
1	Room temp	120	-
2	40	55	traces
3	60	45	65
4	80	20	94
5	100	20	93

[a]Reaction of 4-hydroxycoumarin (**1**, 1 mmol), benzaldehyde (**2a**, 1 mmol) and (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine (**3**, 1 mmol) catalyzed by STA (10 mol%) under solvent free condition. [b]Isolated yield.

Table 3 STA catalyzed multicomponent synthesis of pyrano[3,2-*c*]chromen-5-ones under solvent-free conditions[a].

Entry	R	Product	Time (min)	Yield (%)[b]	M.p (°C)
1	4-OMe-C_6H_4	**4a**	20	94	259-261
2	4-OC_2H_5-C_6H_4	**4b**	20	89	260-262
3	4-CH_3-C_6H_4	**4c**	20	94	258-260
4	3,4,5-OMe-C_6H_2	**4d**	22	90	266-268
5	3-Cl-C_6H_4	**4e**	30	87	256-258
6	4-F-C_6H_4	**4f**	35	89	265-267
7	4-NO_2-C6H4	**4g**	32	85	267-269
8	4-Br-C_6H_4	**4h**	36	86	265-267
9	3-OMe-C_6H_4	**4i**	20	90	267-269
10	2-NO_2-C_6H_4	**4j**	30	87	269-271
11	C_6H_5	**4k**	20	94	270-272
12	2,5-OMe-C_6H_3	**4l**	22	92	265-267
13	2-OMe-C_6H_4	**4m**	20	89	271-273
14	1-Napthaldehyde	**4n**	35	88	272-274
15	3-F-C_6H_4	**4o**	40	86	263-265
16	4-Cl-C_6H_4	**4p**	38	89	252-254
17	3-NO_2-C_6H_4	**4q**	36	85	265-267
18	2-Br-C_6H_4	**4r**	35	88	284-286
19	2-Cl,5-Br-C_6H_3	**4s**	37	90	282-284
20	2-OH,3-Br,5-Cl-C_6H_2	**4t**	40	87	245-247
21	2,3-OH-C_6H_3	**4u**	35	86	258-260
22	2-OH,3,5-Cl-C_6H_2	**4v**	36	90	247-249
23	4-*N*,*N*-Methyl- C_6H_4	**4w**	30	89	253-255
24	Pyridin-4-yl	**4x**	32	87	226-228
25	Furan-2-yl	**4y**	30	90	265-267
26	Thiophene-2-yl	**4z**	35	88	266-268

[a]Reaction of 4-hydroxycoumarin (**1**, 1 mmol), benzaldehyde (**2a-2z**, 1 mmol) and (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine (**3**, 1 mmol) (**3**, mmol) catalyzed by STA (10 mol%) under solvent free. [b]Isolated yield.

All the structure of synthesized compounds (**4a-4z**) have been ascertained on the basis of ^{1}H NMR, ^{13}C NMR, IR and HRMS data.

The reusability of catalysts is an important factor for commercial uses. The reusability of the catalyst was also examined in the synthesis of **4a** (pyrano[3,2-*c*]chromen-5-ones). The catalyst was easily recovered after each run from the reaction medium, washed with ethyl acetate and acetone, dried under vacuum at 120 °C and tested for its activity in subsequent runs. It was found that the catalyst could be reused four times without loss of activity (Table 4, entry 1–4).

Table 4: A study of the reusability of STA in the model reaction[a]

Entry	Reaction cycle	Yield (%)[b]
1	First (fresh run)	94
2	Second cycle	92
3	Third cycle	88
4	Fourth cycle	88

[a]Model reaction run with 4-hydroxycoumarin (**1**, 1 mmol), 4-methoxybenzaldehyde (**2a**, 1 mmol) and (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine (**3**, 1 mmol), STA (10 mol%) under solvent-free conditions. [b]Isolated yield.

The possible reaction sequences taking place in the synthesis of pyrano[3,2-*c*]chromen-5-ones derivatives **(4a-4z)** is shown in (Figure 2). The first step is the Knoevenagel condensation between 4-hydroxycoumarin **1** and aldehyde **2** in the presence of STA afforded intermediate **5**, which acts as Michael acceptor. The adduct **5** immediately undergoes Michael type addition with (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine **3** to affords the iminol **6**. This iminol **6** apparently tautomerizes to aminol **7** followed by intramolecular *O*-cyclization to give the pyrano[3,2-*c*]chromen-5-ones derivatives **(4a-4z)** in good yield through the elimination of MeSH.

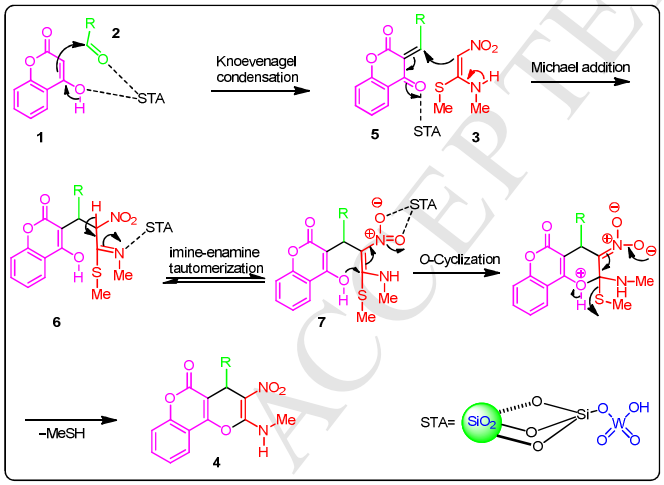


Figure 2: Possible Mechanism for the synthesis of pyrano[3,2-*c*]chromen-5-ones derivatives

3. Conclusion

In conclusion, we demonstrated a facile and environmentally benign method for the synthesis of highly functionalized pyrano[3,2-*c*]chromen-5-ones by a one-pot three-component condensation reaction of 4-hydroxycoumarin, aldehydes, and (*E*) -*N*-methyl-1-(methylthio)-2-nitroethenamine in the presence of an inexpensive and reusable silica-supported tungstic acid (STA) as a heterogeneous catalyst under solvent-free conditions. The advantages of this method over other existing ones are reduced reaction times, excellent yields, simple experimental procedure, low cost, easy handling, and economic viability of the catalyst. The procedures provide access to compounds that are useful in heterocyclic synthesis.

4. Experimental

4.1 Material and methods

Chemicals were purchased from Aldrich and Alfa Aesar Chemical Companies and used without further purification. NMR spectra were recorded in parts per million (ppm) in DMSO-d_6 on a Jeol JNM ECP 600 NMR instrument using TMS as internal standard. Standard abbreviations were used to denote signal multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Mass spectra were recorded on a Jeol JMS-700 mass spectrometer. The IR spectra were recorded on a perkin elmer (U.S.A), spectrum X instrument. All melting points were determined using open capillaries on an Electrothermal-9100 (Japan) instrument and are uncorrected.

4.2 Synthesis of 4-(4-methoxyphenyl) -2-(methylamino) -3-nitro-4*H*,5*H*-pyrano [3,2-*c*]chromen-5-one (4a).

A mixture of 4-hydroxycoumarin (**1**, 1 mmol), 4-methoxybenzaldehyde (**2a**, 1 mmol), (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine (**3**, 1 mmol) and silica-supported tungstic acid (STA) (10 mol %) was stirred at 80 ^{o}C under solvent-free conditions. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was washed with ethanol. The residue dissolved in DCM, and the insoluble STA was separated by simple filtration and washed with DCM. The solvent was evaporated under reduced pressure and the obtained crude was recrystallized from ethanol to afford the pure yellow product **4a.** The recovered catalyst was washed with ethyl acetate and acetone, dried and reused. Compounds **4b**-**4z** were also synthesized by adopting this procedure.

4.2.1. 4-(4-methoxyphenyl) -2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one **(4a)**. Yield 94%; yellow solid; Mp: 259-261 ^{o}C; IR (ν_{max}) cm^{-1}: 3211 (N-H$_{str}$), 2941 & 2854 (C-H$_{str}$), 1722 (C=O$_{str}$), 1265 & 1121 (C-O$_{str}$), 1640 & 1435 (C=C$_{str}$), 1013 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.38 (d, J = 5.0 Hz, 1H), 8.00 (d, J = 7.9 Hz, 1H), 7.75 – 7.72 (m, 1H), 7.50 (dd, J = 16.4, 8.0 Hz, 2H), 7.23 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 5.02 (s, 1H), 3.69 (s, 3H), 3.31 (d, J = 4.9 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.25, 158.31, 156.76, 151.99, 151.67, 133.28, 133.14, 129.57, 125.05, 122.84, 116.63, 113.49, 112.68, 107.99, 106.90, 55.06, 36.62, 28.73; HRMS (ESI, m/z): calcd for $C_{20}H_{16}N_2O_6$ (M+H^{+}) 380.1008, found: 380.1010.

4.2.2. 4-(4-ethoxyphenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one **(4b)**. Yield 89%; yellow solid; Mp: 260-262 ^{o}C; IR (ν_{max}) cm^{-1}: 3220 (N-H$_{str}$), 2935 & 2812 (C-H$_{str}$), 1700 (C=O$_{str}$), 1236 & 1102 (C-O$_{str}$), 1632 & 1404 (C=C$_{str}$), 1018 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.36 (d, J = 5.1 Hz, 1H), 7.98 (d, J = 7.9 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.21 (d, J = 8.8 Hz, 2H), 6.79 (d, J = 8.7 Hz, 2H), 5.01 (s, 1H), 3.94 (q, J = 7.0 Hz, 2H), 3.31 (d, J = 4.8 Hz, 3H), 1.27 (dd, J = 7.3, 6.7 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.19, 157.57, 156.75, 151.95, 151.63, 133.08, 129.47, 124.99, 122.77, 116.57, 113.93, 112.64, 107.97, 106.90, 62.96, 36.55, 28.66, 14.62; HRMS (ESI, m/z): calcd for $C_{21}H_{18}N_2O_6$ (M+H^{+}) 394.1165, found: 394.1166.

4.2.3. 2-(methylamino)-3-nitro-4-(p-tolyl)-4H,5H-pyrano[3,2-c]chromen-5-one (**4c**). Yield 94%; yellow solid; Mp: 258-260 ^{o}C; IR (ν_{max}) cm^{-1}: 3196 (N-H$_{str}$), 2988 & 2836 (C-H$_{str}$), 1712 (C=O$_{str}$), 1289 & 1095 (C-O$_{str}$), 1628 & 1410 (C=C$_{str}$), 1014 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.38 (d, J = 5.1 Hz, 1H), 7.99 (dd, J = 7.9, 1.5 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.51 – 7.46 (m, 2H), 7.20 (d, J = 8.1 Hz, 2H), 7.06 (d, J = 7.9 Hz, 2H), 5.03 (s, 1H), 3.31 (d, J = 5.0 Hz, 3H), 2.22 (s, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.15, 156.75, 151.96, 151.72, 138.28, 136.24, 133.09, 128.62, 128.30, 124.98, 122.78, 116.56, 112.61, 107.86, 106.80, 36.99, 28.66, 20.58; HRMS (ESI, m/z): calcd for $C_{20}H_{16}N_2O_5$ (M+H$^+$) 364.1059, found: 364.1059.

4.2.4. 2-(methylamino)-3-nitro-4-(3,4,5-trimethoxyphenyl)-4H,5H-pyrano[3,2-c]chromen-5-one (**4d**). Yield 90%; yellow solid; Mp: 266-268 ^{o}C; IR (ν_{max}) cm^{-1}: 3224 (N-H$_{str}$), 2952 & 2851 (C-H$_{str}$), 1698 (C=O$_{str}$), 1273 & 1114 (C-O$_{str}$), 1636 & 1430 (C=C$_{str}$), 1025 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.38 (d, J = 5.1 Hz, 1H), 8.00 (d, J = 7.9 Hz, 1H), 7.74 – 7.71 (m, 1H), 7.49 (dd, J = 14.9, 7.9 Hz, 2H), 6.57 (s, 2H), 5.08 (s, 1H), 3.71 (s, 6H), 3.60 (s, 3H), 3.32 (d, J = 5.0 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.33, 156.92, 152.54, 152.03, 136.91, 136.70, 133.12, 124.95, 122.89, 116.58, 112.72, 107.48, 106.46, 106.01, 59.90, 56.00, 37.56, 28.72; HRMS (ESI, m/z): calcd for $C_{22}H_{20}N_2O_8$ (M+H$^+$) 440.1220, found: 440.1222.

4.2.5. 4-(3-chlorophenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4e**). Yield 87%; yellow solid; Mp: 256-258 ^{o}C; IR (ν_{max}) cm^{-1}: 3188 (N-H$_{str}$), 2978 & 2834 (C-H$_{str}$), 1731 (C=O$_{str}$), 1242 & 1125 (C-O$_{str}$), 1606 & 1426 (C=C$_{str}$), 1028 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.42 (d, J = 5.1 Hz, 1H), 8.00 (dd, J = 7.9, 1.4 Hz, 1H), 7.75 – 7.72 (m, 1H), 7.52 – 7.47 (m, 2H), 7.40 (t, J = 1.6 Hz, 1H), 7.30 (ddt, J = 13.9, 6.5, 1.7 Hz, 3H), 5.06 (s, 1H), 3.32 (d, J = 5.0 Hz, 3H),^{13}C NMR (151 MHz, DMSO-d_6) δ 159.19, 156.65, 152.07, 143.57, 133.27, 132.58, 129.85, 128.46, 127.36, 127.12, 125.01, 122.93, 116.60, 112.58, 107.27, 105.77, 37.48, 28.73; HRMS (ESI, m/z): calcd for $C_{19}H_{13}ClN_2O_5$ (M+H$^+$) 384.0513, found: 384.0515.

4.2.6. *4-(4-fluorophenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one* (**4f**). Yield 89%; yellow solid; Mp: 265-267 ^{o}C; IR (ν_{max}) cm^{-1}: 3208 (N-H$_{str}$), 2950 & 2816 (C-H$_{str}$), 1707 (C=O$_{str}$), 1240 & 1118 (C-O$_{str}$), 1652 & 1458 (C=C$_{str}$), 1042 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.39 (d, J = 5.0 Hz, 1H), 8.00 (d, J = 7.9 Hz, 1H), 7.74 – 7.71 (m, 1H), 7.52 – 7.46 (m, 2H), 7.38 (dd, J = 8.4, 5.5 Hz, 2H), 7.07 (t, J = 8.8 Hz, 2H), 5.07 (s, 1H), 3.32 (d, J = 4.9 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.97, 160.35, 159.17, 156.68, 152.02, 151.87, 137.38, 133.19, 130.46, 125.01, 122.85, 116.59, 114.84, 114.74, 112.59, 107.66, 106.36, 36.85, 28.69; HRMS (ESI, m/z): calcd for $C_{19}H_{13}FN_2O_5$ (M+H$^+$) 368.0808, found: 368.0808.

4.2.7. 2-(methylamino)-3-nitro-4-(4-nitrophenyl)-4H,5H-pyrano[3,2-c]chromen-5-one (**4g**). Yield 85%; yellow solid; Mp: 267-269 ^{o}C; IR (ν_{max}) cm^{-1}: 3211 (N-H$_{str}$), 2994 & 2835 (C-H$_{str}$), 1745 (C=O$_{str}$), 1285 & 1130 (C-O$_{str}$), 1643 & 1428 (C=C$_{str}$), 1009 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.45 (d, J = 5.0 Hz, 1H), 8.13 – 8.11 (m, 2H), 8.03 (dd, J = 7.9, 1.3 Hz, 1H), 7.77 – 7.74 (m, 1H), 7.68 – 7.66 (m, 2H), 7.54 – 7.49 (m, 2H), 5.20 (s, 1H), 3.33 (d, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.18, 156.59, 152.30, 152.14, 148.71, 146.51, 133.43, 130.11, 125.09, 123.04, 116.66, 112.52, 107.02, 105.28, 37.77, 28.78; HRMS (ESI, m/z): calcd for $C_{19}H_{13}N_3O_7$ (M+H$^+$) 395.0753, found: 395.0753.

4.2.8. 4-(4-bromophenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4h**). Yield 86%; yellow solid; Mp: 265-267 ^{o}C; IR (ν_{max}) cm^{-1}: 3184 (N-H$_{str}$), 2932 & 2858 (C-H$_{str}$), 1735 (C=O$_{str}$), 1254 & 1121 (C-O$_{str}$), 1617 & 1410 (C=C$_{str}$), 1021 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.40 (d, J = 5.1 Hz, 1H), 8.01 (dd, J = 7.9, 1.4 Hz, 1H), 7.76 – 7.73 (m, 1H), 7.53 – 7.48 (m, 2H), 7.46 – 7.44 (m, 2H), 7.33 – 7.31 (m, 2H), 5.05 (s, 1H), 3.32 (d, J = 4.9 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.18, 156.66, 152.01, 140.64, 133.25, 130.85, 125.03, 122.90, 120.16, 116.62, 112.58, 107.40, 106.01, 37.18, 28.71; HRMS (ESI, m/z): calcd for $C_{19}H_{13}BrN_2O_5$ (M+H$^+$) 428.0008, found: 428.0010.

4.2.9. 4-(3-methoxyphenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4i**). Yield 90%; yellow solid; Mp: 267-269 ^{o}C; IR (ν_{max}) cm^{-1}: 3201 (N-H$_{str}$), 2957 & 2833 (C-H$_{str}$), 1702 (C=O$_{str}$), 1265 & 1145 (C-O$_{str}$), 1606 & 1430 (C=C$_{str}$), 1039 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.38 (d, J = 4.9 Hz, 1H), 8.01 (d, J = 7.9 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.51 (dd, J = 15.9, 8.1 Hz, 2H), 7.20 – 7.17 (m, 1H), 6.87 (dd, J = 4.5, 1.8 Hz, 2H), 6.80 – 6.78 (m, 1H), 5.08 (s, 1H), 3.71 (s, 3H), 3.32 (d, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.22, 158.93, 156.82, 151.98, 142.70, 133.17, 129.21, 125.01, 122.85, 120.40, 116.60, 115.12, 112.64, 111.78, 107.63, 106.57, 54.98, 037.32, 28.69; HRMS (ESI, m/z): calcd for $C_{20}H_{16}N_2O_6$ (M+H$^+$) 380.1008, found: 380.1010.

4.2.10. 2-(methylamino)-3-nitro-4-(2-nitrophenyl)-4H,5H-pyrano[3,2-c]chromen-5-one (**4j**). Yield 87%; yellow solid; Mp: 269-271 ^{o}C; IR (ν_{max}) cm^{-1}: 3213 (N-H$_{str}$), 2938 & 2862 (C-H$_{str}$), 1690 (C=O$_{str}$), 1290 & 1106 (C-O$_{str}$), 1634 & 1426 (C=C$_{str}$), 1012 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.49 (d, J = 4.9 Hz, 1H), 8.03 (d, J = 7.9 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.58 (d, J = 6.2 Hz, 2H), 7.54 – 7.49 (m, 2H), 7.47 – 7.44 (m, 1H), 6.07 (s, 1H), 3.32 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 157.11, 153.03, 152.65, 150.12, 133.96, 133.75, 128.81, 125.58, 124.75, 123.56, 117.15, 112.98, 107.78, 105.69, 79.71, 40.07, 33.27, 29.29; HRMS (ESI, m/z): calcd for $C_{20}H_{16}N_2O_6$ (M+H$^+$) 395.0753, found: 395.0755.

4.2.11. 2-(methylamino)-3-nitro-4-phenyl-4H,5H-pyrano[3,2-c]chromen-5-one (**4k**). Yield 94%; yellow solid; Mp: 270-272 ^{o}C; IR (ν_{max}) cm^{-1}: 3203 (N-H$_{str}$), 2968 & 2818 (C-H$_{str}$), 1715 (C=O$_{str}$), 1281 & 1142 (C-O$_{str}$), 1646 & 1420 (C=C$_{str}$), 1037 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.39 (d, J = 5.1 Hz, 1H), 8.01 (dd, J = 7.9, 1.5 Hz, 1H), 7.75 – 7.72 (m, 1H), 7.53 – 7.48 (m, 2H), 7.34 (dd, J = 5.2, 3.4 Hz, 2H), 7.27 (dd, J = 10.3, 4.9 Hz, 2H), 7.21 – 7.18 (m, 1H), 5.09 (s, 1H), 3.32 (d, J = 5.0 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.19, 156.80, 151.94, 141.25, 133.16, 128.45, 128.06, 127.05, 125.01, 122.84, 116.60, 112.63, 107.81, 106.69, 37.43, 28.68; HRMS (ESI, m/z): calcd for $C_{19}H_{14}N_2O_5$ (M+H$^+$) 350.0903, found: 350.0905.

4.2.12. 4-(2,5-dimethoxyphenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4l**). Yield 92%; yellow solid; Mp: 265-267 ^{o}C; IR (ν_{max}) cm^{-1}: 3197 (N-H$_{str}$), 2947 & 2834 (C-H$_{str}$), 1730 (C=O$_{str}$), 1275 & 1095 (C-O$_{str}$), 1648 & 1408 (C=C$_{str}$), 1019 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.43 (d, J = 5.1 Hz, 1H), 8.03 (dd, J = 7.9, 1.5 Hz, 1H), 7.74 – 7.71 (m, 1H), 7.50 (ddd, J = 17.1, 8.6, 0.8 Hz, 2H), 6.95 (d, J = 3.1 Hz, 1H), 6.82 (d, J = 8.9 Hz, 1H), 6.78 (dd, J = 8.9, 3.1 Hz, 1H), 5.00 (s, 1H), 3.71 (s, 3H), 3.53 (s, 3H), 3.34 (d, J = 5.1 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.17, 157.61, 152.48, 152.13, 151.92, 132.98, 128.02, 125.01, 122.56, 119.40, 116.59, 112.78, 112.52, 106.45, 104.34, 56.03, 55.36, 36.04, 28.48; HRMS (ESI, m/z): calcd for $C_{21}H_{18}N_2O_7$ (M+H$^+$) 410.1114, found: 410.1115.

4.2.13. 4-(2-methoxyphenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4m**). Yield 89%; yellow solid; Mp: 271-273 ^{o}C; IR (ν_{max}) cm^{-1}: 3215 (N-H$_{str}$), 2964 & 2844 (C-

H_{str}), 1699 (C=O_{str}), 1250 & 1113 (C-O_{str}), 1634 & 1417 (C=C_{str}), 1026 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.43 (d, J = 5.1 Hz, 1H), 8.04 (dd, J = 7.9, 1.5 Hz, 1H), 7.74 – 7.71 (m, 1H), 7.53 – 7.47 (m, 2H), 7.40 (dd, J = 7.9, 1.7 Hz, 1H), 7.21 – 7.18 (m, 1H), 6.91 (dd, J = 10.7, 4.4 Hz, 2H), 5.08 (s, 1H), 3.60 (s, 3H), 3.35 (d, J = 5.1 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.19, 157.65, 152.17, 151.94, 132.94, 128.60, 126.82, 125.00, 122.56, 119.79, 116.59, 112.60, 111.85, 106.55, 104.53, 79.15, 55.46, 35.88, 28.49; HRMS (ESI, m/z): calcd for $C_{20}H_{16}N_2O_6$ (M+H$^+$) 380.1008, found: 380.1008.

4.2.14. 2-(methylamino)-4-(naphthalen-1-yl)-3-nitro-4a,10b-dihydro-4H,5H-pyrano[3,2-c]chromen-5-one (**4n**). Yield 88%; yellow solid; Mp: 272-274 ^{o}C; IR (ν_{max}) cm^{-1}: 3206 (N-H_{str}), 2924 & 2830 (C-H_{str}), 1720 (C=O_{str}), 1260 & 1130 (C-O_{str}), 1620 & 1439 (C=C_{str}), 1009 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.41 (s, 1H), 8.70 (d, J = 8.6 Hz, 1H), 8.07 (dd, J = 8.0, 1.5 Hz, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.79 – 7.72 (m, 2H), 7.62 (ddd, J = 8.4, 6.9, 1.2 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.47 (d, J = 8.2 Hz, 1H), 7.39 – 7.36 (m, 2H), 6.02 (s, 1H), 3.37 (d, J = 5.0 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.28, 156.74, 152.93, 151.76, 150.94, 143.51, 133.19, 132.90, 132.78, 131.80, 129.71, 127.93, 127.59, 125.65, 125.46, 124.98, 122.86, 116.58, 112.68, 109.21, 83.82, 37.24, 28.72; HRMS (ESI, m/z): calcd for $C_{23}H_{18}N_2O_5$ (M+H$^+$) 402.1216, found: 402.1214.

4.2.15. 4-(3-fluorophenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4o**). Yield 86%; yellow solid; Mp: 263-265 ^{o}C; IR (ν_{max}) cm^{-1}: 3186 (N-H_{str}), 2916 & 2822 (C-H_{str}), 1724 (C=O_{str}), 1269 & 1124 (C-O_{str}), 1616 & 1416 (C=C_{str}), 1041 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.40 (s, 1H), 8.00 (d, J = 1.0 Hz, 1H), 7.75 (d, J = 15.4 Hz, 1H), 7.51 (dd, J = 8.6, 2.5 Hz, 2H), 7.31 (dd, J = 13.3, 6.0 Hz, 1H), 7.19 (d, J = 8.7 Hz, 2H), 7.03 (d, J = 8.0 Hz, 1H), 5.10 (s, 1H), 3.32 (s, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.07, 159.20, 156.69, 152.06, 143.95, 133.25, 129.78, 125.01, 124.65, 122.93, 116.61, 115.51, 115.37, 114.18, 114.02, 113.92, 112.61, 107.34, 105.93, 37.39, 28.71; HRMS (ESI, m/z): calcd for $C_{23}H_{18}N_2O_5$ (M+H$^+$) 368.0808, found: 368.0808.

4.2.16. 4-(4-chlorophenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4p**). Yield 89%; yellow solid; Mp: 252-254 ^{o}C; IR (ν_{max}) cm^{-1}: 3220 (N-H_{str}), 2923 & 2840 (C-H_{str}), 1688 (C=O_{str}), 1245 & 1140 (C-O_{str}), 1642 & 1429 (C=C_{str}), 1056 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.40 (d, J = 5.1 Hz, 1H), 8.01 (dd, J = 7.9, 1.4 Hz, 1H), 7.76 – 7.73 (m, 1H), 7.51 (dd, J = 8.7, 1.3 Hz, 2H), 7.39 – 7.37 (m, 2H), 7.32 – 7.30 (m, 2H), 5.07 (s, 1H), 3.32 (d, J = 5.0 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.18, 156.67, 152.05, 140.21, 133.23, 131.63, 130.45, 127.94, 125.03, 122.89, 116.62, 106.14, 100.80, 32.47, 28.71; HRMS (ESI, m/z): calcd for $C_{19}H_{13}ClN_2O_5$ (M+H$^+$) 384.0513, found: 384.0515.

4.2.17. 2-(methylamino)-3-nitro-4-(3-nitrophenyl)-4H,5H-pyrano[3,2-c]chromen-5-one (**4q**). Yield 85%; yellow solid; Mp: 265-267 ^{o}C; IR (ν_{max}) cm^{-1}: 3194 (N-H_{str}), 2988 & 2856 (C-H_{str}), 1701 (C=O_{str}), 1285 & 1115 (C-O_{str}), 1641 & 1440 (C=C_{str}), 1022 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.46 (s, 1H), 8.17 (t, J = 2.0 Hz, 1H), 8.08 (ddd, J = 8.2, 2.2, 0.8 Hz, 1H), 8.04 (dd, J = 7.9, 1.4 Hz, 1H), 7.86 (dd, J = 7.9, 1.1 Hz, 1H), 7.77 – 7.74 (m, 1H), 7.58 – 7.49 (m, 3H), 5.21 (s, 1H), 3.34 (d, J = 5.0 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.25, 156.64, 152.31, 152.16, 147.45, 143.29, 135.42, 133.38, 129.49, 125.06, 123.30, 123.03, 122.17, 116.65, 112.56, 107.07, 105.30, 37.73, 28.78; HRMS (ESI, m/z): calcd for $C_{19}H_{13}N_3O_7$ (M+H$^+$) 395.0753, found: 395.0755.

4.2.18. 4-(2-bromophenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4r**) Yield 88%; yellow solid; Mp: 284-286 ^{o}C; IR (ν_{max}) cm^{-1}: 3202 (N-H_{str}), 2923 & 2862 (C-H_{str}), 1728 (C=O_{str}), 1252 & 1120 (C-O_{str}), 1625 & 1450 (C=C_{str}), 1029 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.46 (d, J = 5.0 Hz, 1H), 8.03 (d, J = 7.9 Hz, 1H), 7.75 (t, J = 7.8 Hz, 1H), 7.54 – 7.48 (m, 4H), 7.29 (t, J = 7.5 Hz, 1H), 7.15 – 7.12 (m, 1H), 5.40 (s, 1H), 3.34 (d, J = 5.0 Hz, 3H), ^{13}C NMR (151 MHz, DMSO- d_6) δ 158.84, 156.79, 152.08, 133.34, 132.87, 128.86, 127.23, 125.02, 122.97, 116.59, 115.78, 112.35, 28.67; HRMS (ESI, m/z): calcd for $C_{19}H_{13}BrN_2O_5$ (M+H$^+$) 428.0008, found: 428.0008.

4.2.19. 4-(2-bromo-6-chlorophenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4s**). Yield 90%; yellow solid; Mp: 282-284 ^{o}C; IR (ν_{max}) cm^{-1}: 3208 (N-H_{str}), 2947 & 2820 (C-H_{str}), 1740 (C=O_{str}), 1242 & 1140 (C-O_{str}), 1624 & 1412 (C=C_{str}), 1010 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.46 (d, J = 5.1 Hz, 1H), 8.31 (s, 1H), 8.02 (dd, J = 7.9, 1.5 Hz, 1H), 7.77 – 7.74 (m, 1H), 7.60 (dd, J = 6.7, 2.5 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.09 (dd, J = 10.2, 8.8 Hz, 1H), 5.23 (s, 1H), 3.33 (s, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 160.93, 159.17, 158.99, 158.93, 156.69, 152.32, 152.11, 133.37, 131.85, 125.05, 122.92, 117.61, 117.45, 116.66, 115.69, 112.43, 106.30, 104.28, 79.15, 32.56, 28.70; HRMS (ESI, m/z): calcd for $C_{19}H_{12}BrClN_2O_5$ (M+H$^+$) 461.9618, found: 461.9620.

4.2.20. 4-(3-bromo-6-chloro-2-hydroxyphenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4t**). Yield 87%; yellow solid; Mp: 245-247 ^{o}C; IR (ν_{max}) cm^{-1}: 3228 (N-H_{str}), 2962 & 2826 (C-H_{str}), 1698 (C=O_{str}), 1292 & 1122 (C-O_{str}), 1651 & 1420 (C=C_{str}), 1014 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.31 (s, 1H), 10.45 (d, J = 5.1 Hz, 1H), 8.03 (dd, J = 8.0, 0.8 Hz, 1H), 7.86 (d, J = 2.3 Hz, 1H), 7.63 – 7.60 (m, 1H), 7.37 (dd, J = 11.4, 4.0 Hz, 1H), 7.34 – 7.31 (m, 2H), 5.94 (s, 1H), 3.21 (d, J = 5.0 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 160.98, 158.87, 152.08, 146.30, 135.79, 133.57, 132.32, 129.98, 124.05, 116.70, 116.25, 116.08, 110.42, 31.92, 28.44; HRMS (ESI, m/z): calcd for $C_{17}H_{12}BrClN_2O_6$ (M+H$^+$) 477.9567, found: 477.9567.

4.2.21. 4-(2,3-dihydroxyphenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4u**). Yield 86%; yellow solid; Mp: 258-260 ^{o}C; IR (ν_{max}) cm^{-1}: 3203 (N-H_{str}), 2986 & 2843 (C-H_{str}), 1714 (C=O_{str}), 1265 & 1108 (C-O_{str}), 1618 & 1421 (C=C_{str}), 1023 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.05 (s, 1H), 10.55 (d, J = 5.1 Hz, 1H), 9.87 (s, 1H), 8.01 (d, J = 7.5 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.32 (d, J = 8.2 Hz, 1H), 6.90 (t, J = 7.9 Hz, 1H), 6.80 (dd, J = 8.0, 1.3 Hz, 1H), 6.61 (d, J = 7.6 Hz, 1H), 5.87 (s, 1H), 3.19 (d, J = 5.1 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 160.18, 159.54, 151.95, 144.71, 137.09, 132.04, 125.01, 123.98, 117.89, 116.13, 115.15, 56.02, 31.75, 28.03; HRMS (ESI, m/z): calcd for $C_{19}H_{14}N_2O_7$ (M+H$^+$) 382.0801, found: 382.0803.

4.2.22. 4-(3,5-dichloro-2-hydroxyphenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4v**). Yield 90%; yellow solid; Mp: 247-249 ^{o}C; IR (ν_{max}) cm^{-1}: 3186 (N-H_{str}), 2957 & 2815 (C-H_{str}), 1703 (C=O_{str}), 1236 & 1106 (C-O_{str}), 1645 & 1409 (C=C_{str}), 1025 (C-O-C_{str}); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.31 (s, 1H), 10.47 (d, J = 5.1 Hz, 1H), 8.03 (d, J = 7.9 Hz, 1H), 7.66 (d, J = 2.4 Hz, 1H), 7.63 – 7.60 (m, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.33 (d, J = 8.2 Hz, 1H), 7.17 (d, J = 2.4 Hz, 1H), 5.93 (s, 1H), 3.20 (d, J = 5.1 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 160.99, 158.70, 152.08, 143.20, 132.32, 128.68, 128.22, 126.53, 126.51, 124.05, 121.14, 116.24, 116.06, 31.93, 28.26; HRMS (ESI, m/z): calcd for $C_{19}H_{12}Cl_2N_2O_6$ (M+H$^+$) 434.0072, found: 434.0072.

4.2.23. 4-(4-(dimethylamino)phenyl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4w**). Yield 89%; yellow solid; Mp: 253-255 ^{o}C; IR (ν_{max}) cm^{-1}: 3223 (N-H$_{str}$), 2925 & 2837 (C-H$_{str}$), 1718 (C=O$_{str}$), 1258 & 1121 (C-O$_{str}$), 1640 & 1435 (C=C$_{str}$), 1006 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.34 (d, J = 5.1 Hz, 1H), 8.00 (dd, J = 7.9, 1.5 Hz, 1H), 7.74 – 7.71 (m, 1H), 7.52 – 7.48 (m, 2H), 7.10 (d, J = 8.8 Hz, 2H), 6.60 (d, J = 8.8 Hz, 2H), 4.98 (s, 1H), 3.31 (d, J = 5.1 Hz, 3H), 2.82 (s, 6H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.21, 156.81, 151.88, 151.41, 149.53, 132.95, 128.82, 124.96, 122.71, 116.56, 112.71, 112.04, 108.19, 107.27, 79.15, 36.25, 28.62; HRMS (ESI, m/z): calcd for $C_{21}H_{12}N_3O_5$ (M+H$^+$) 393.1325, found: 395.1326.

4.2.24. 2-(methylamino)-3-nitro-4-(pyridin-4-yl)-4H,5H-pyrano[3,2-c]chromen-5-one (**4x**). Yield 87%; yellow solid; Mp: 226-228 ^{o}C; IR (ν_{max}) cm^{-1}: 3214 (N-H$_{str}$), 2994 & 2854 (C-H$_{str}$), 1697 (C=O$_{str}$), 1290 & 1145 (C-O$_{str}$), 1644 & 1427 (C=C$_{str}$), 1038 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.45 (d, J = 4.0 Hz, 1H), 8.58 (d, J = 5.2 Hz, 1H), 8.50 (s, 1H), 8.02 (d, J = 7.9 Hz, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.76 (dd, J = 11.6, 4.1 Hz, 1H), 7.63 (d, J = 5.4 Hz, 1H), 7.51 (s, 1H), 7.25 (td, J = 7.9, 1.3 Hz, 1H), 5.11 (s, 1H), 3.33 (d, J = 2.1 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.19, 156.68, 155.68, 152.65, 152.47, 152.13, 148.49, 133.44, 131.47, 125.08, 124.21, 123.05, 119.44, 116.66, 115.68, 112.51, 79.15, 37.45, 28.77; HRMS (ESI, m/z): calcd for $C_{18}H_{13}N_3O_5$ (M+H$^+$) 351.0855, found: 351.0855.

4.2.25. 4-(furan-2-yl)-2-(methylamino)-3-nitro-4H,5H-pyrano[3,2-c]chromen-5-one (**4y**). Yield 90%; yellow solid; Mp: 265-267 ^{o}C; IR (ν_{max}) cm^{-1}: 3210 (N-H$_{str}$), 2918 & 2845 (C-H$_{str}$), 1710 (C=O$_{str}$), 1252 & 1104 (C-O$_{str}$), 1635 & 1408 (C=C$_{str}$), 1032 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.35 (d, J = 4.9 Hz, 1H), 8.00 (d, J = 7.1 Hz, 1H), 7.78 – 7.75 (m, 1H), 7.54 – 7.51 (m, 2H), 7.46 (s, 1H), 6.36 – 6.32 (m, 2H), 5.34 (s, 1H), 3.30 (d, J = 5.0 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.07, 156.99, 152.03, 151.88, 144.57, 142.09, 133.38, 125.10, 122.75, 116.70, 110.63, 109.04, 107.45, 104.07, 31.13, 28.69; HRMS (ESI, m/z): calcd for $C_{17}H_{12}N_2O_6$ (M+H$^+$) 340.0695, found: 340.0697.

4.2.26. 2-(methylamino)-3-nitro-4-(thiophen-2-yl)-4H,5H-pyrano[3,2-c]chromen-5-one (**4z**). Yield 88%; yellow solid; Mp: 266-268 ^{o}C; IR (ν_{max}) cm^{-1}: 3184 (N-H$_{str}$), 2988 & 2832 (C-H$_{str}$), 1708 (C=O$_{str}$), 1254 & 1130 (C-O$_{str}$), 1629 & 1412 (C=C$_{str}$), 1016 (C-O-C$_{str}$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.35 (s, 1H), 8.02 – 8.00 (m, 1H), 7.78 – 7.75 (m, 1H), 7.55 – 7.50 (m, 2H), 7.34 (t, J = 4.1 Hz, 1H), 6.97 (t, J = 3.2 Hz, 1H), 6.90 (dd, J = 8.4, 4.3 Hz, 1H), 5.48 (s, 1H), 3.30 (d, J = 4.3 Hz, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.26, 156.74, 152.37, 152.06, 144.28, 133.38, 126.73, 125.43, 125.12, 124.82, 122.87, 116.72, 112.57, 107.52, 106.21, 32.04, 28.71; HRMS (ESI, m/z): calcd for $C_{17}H_{12}N_2O_5S$ (M+H$^+$) 356.0467, found: 356.0467.

Supporting Information

All Compounds NMR spectra were provided as Supplementary material.

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