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$FeCl_3$ or $MeSO_3H$-Promoted Multicomponent Reactions for Facile Synthesis of Structurally Diverse Furan Analogues

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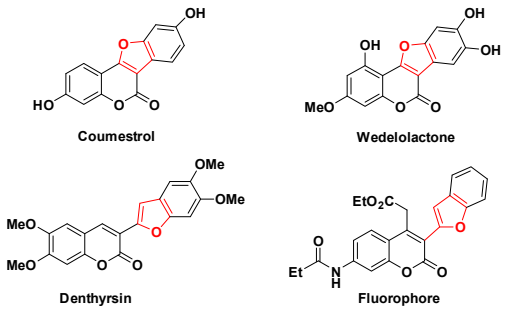
An intriguing conversion of arylglyoxal, cyclic dicarbonyl compounds and phenols to diverse furan analogues under $FeCl_3$ or $MeSO_3H$ catalysis is reported. Utilizing this synthetic protocol, a variety of furan analogues could be easily obtained in moderate to good yields with different substituted patterns by varying reaction medium. Atom-economical characteristics and mild conditions of this method are in accord with the concept of modern green chemistry.

Introduction

Highly functionalized furan rings are very important fundamental heterocyclic motifs widely found in biologically active natural products, pharmaceuticals, and materials.[1] They have also frequently been used as basic building blocks in synthetic chemistry.[2] Coumarin derivatives, particularly coumarin furan derivatives are an important class of fused coumarins produced by a variety of plants.[3] Coumarins and their derivatives are well-recognized naturally occurring compounds with diverse biological activities[4] including *antivirals*, *anti-tumor*, *antimicrobials*, *anti-oxidants*, *anti-asthmatics*, *anti-coagulants* and *antiinflammatories*.[5] Some naturally occurring biologically active coumestans have been developed such as coumestrol, wedelolactone, denthyrsin (from dendrobium thyrsiflorum) and fluorophore (Scheme **1**). Furthermore, coumarin derivatives have been widely used as functional materials such as fluorescentlabeling probes and laser dyes.

Arylglyoxal monohydrates have been used for the construction of a wide variety of heterocyclic compounds.[6] Numerous efficient approaches that employ arylglyoxal monohydrates have been developed for the construction of heterocyclic compounds. Recently, Wu and co-workers[7] have reported an acid-promoted multicomponent reaction for the synthesis of fully substituted oxazole derivatives from arylglyoxal monohydrates, nitriles, and various carbon nucleophiles (Scheme **2a**). Besides, Bhuyan and co-workers[8] described a novel synthesis of indoles and 2,3′-Biindoles derived from anilines, arylglyoxal monohydrates, and cyclic diketones/indoles under the catalysis of PTSA/$FeCl_3$ (Scheme **2b**). Recently, our group[9] have succeeded on developing a straightforward synthesis of chromeno[3,4-b]pyrrol-4(3H)-ones through the domino cyclization of 3-aminocoumarins with arylglyoxal monohydrates (Scheme **2c**). Herein, we reported a novel $FeCl_3$ or $MeSO_3H$ promoted multicomponent tandem cyclization reaction to synthesize diversified furan analogues from readily available starting materials in one pot condition (Scheme **2d**).



Scheme 1 Examples of some naturally occurring coumestans

Results and discussion

To start the investigation, 4-hydroxycoumarin **1a**, arylglyoxal **2a** and chlorophenol **3a** were chosen as model substrates to explore the reaction conditions (Table **1**). The reaction was first carried out in the presence of different lewis acids, such as $AlCl_3$, $ZnCl_2$, $CuCl_2$, $Cu(OAc)_2$ and $FeCl_3$ (Table 1, entries 1–5). $FeCl_3$ was found to be the best choice for the generation of **4a**, with trace amount of **5a** formed (86% yield; Table 1, entry 5). No desired product was observed in the absence of iron catalyst (Table 1, entry 6). Moreover, varying the reaction temperature didn't improve the yield (Table 1, entries 7 and 8). Notably, other solvents, such as CH_3NO_2, DCM, toluene, THF, and EtOH, were inferior compared with DCE (Table 1, entries 9–13). Unexpectedly, the target product **4a** was significantly reduced when employing Brønsted acids as catalyst, however, the yield of compound **5a** was increased to 23% (Table 1, entries 14 and 15). Delightfully, an increment on yield of

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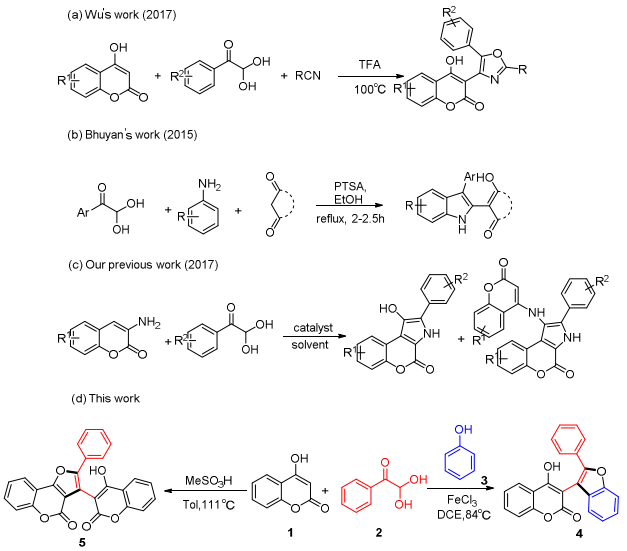
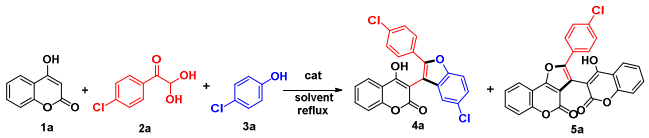


Scheme 2 Selected examples of synthetic a wide variety of heterocyclic compounds via arylglyoxal and other building block.

5a was observed by using stoichiometric $MeSO_3H$, which making the compound **5a** becoming the major product (Table 1, entries 15-18). Furthermore, switching DCE to other solvents (toluene, xylene, EtOH) indicated that toluene was the best solvent to achieve the highest yield up to 91% (Table 1, entries 19–21). Contrarily, TFA and CH_3COOH were failed to give the target product **5a**, may owing to their less acidic nature. (Table 1, entries 22 and 23).

With the optimal conditions for the synthesis of **4** in hand (Table 1, entry 5), we firstly set out to investigate the substrate scope and limitations of the multiple reaction of coumarin **1**, arylglyoxal **2** and phenol **3**. Upon experimentation, it was found that this methodology offered a broad scope with respect to the selected substrates and it was quite tolerant to a variety of functional groups (Scheme **3**). The scope of this reaction was initially explored with 4-hydroxycoumarin **1a** ,chlorophenol **3a** and a range of arylglyoxal **2**. The substitution pattern of the aryl moieties had a great effect on the efficiency of the reaction. It was found that *meta*-substituted arylglyoxal produced the corresponding products (**4b** and **4c**) in relatively higher yields than the *para*- and *ortho*-substituted products (**4a**, **4e** and **4f**). In addition, when the benzene ring contained an electron-donating group (**4d**), the reaction gave the desired product in better yield than those with electron-withdrawing counterparts (**4a**, **4g**, **4h** and **4i**). Besides, other arylglyoxals, such as no substituents arylglyoxal and 1-naphthylglyoxal were also tolerated in this reaction, affording the desired products in moderate yields (**4j** and **4k**). Next, the scope of this reaction with respect to the phenol **3** was studied, and the electron-withdrawing groups gave a higher yield than electron-donating groups. Furthermore, substituents at different positions also affected the efficiency of the reaction, and the desired products were achieved in 47–68% yield (**4l–q**). Notably, sterically hindered (2-naphthyl) substituent was also suitable for this transformation, affording the corresponding products **4r** in 69% yield. Finally, the scope of this reaction with substituted coumarins and their analogues were examined. The results indicated that 6-chloro-4-hydroxycoumarin, 4-hydroxy-6-methylcoumarin and 4-hydroxy-1-methylquinolin-2-one underwent this reaction smoothly to afford the desired products **4s**, **4t** and **4u** in good yields. However, the reaction of 4-hydroxy-6-methylpyran-2-one failed to afford the desired product **4x**. Interestingly, 5,5-dimethyl-1,3-cyclohexadione and 2,4-furandione were also readily took part in this reaction, leading to the formation of the **4v** and **4w** in 61% and 64% yields, respectively.

Table 1. Optimization of the Reaction Conditions



Entry	Catalyst/mol%	Solvent	Yield[b](%) **4a**	Yield[b](%) **5a**
1	$AlCl_3$/20	DCE	trace	trace
2	$ZnCl_2$/20	DCE	<5	trace
3	$CuCl_2$/20	DCE	28	trace
4	$Cu(OAc)_2$/20	DCE	<5	trace
5	***$FeCl_3$/20***	***DCE***	***86***	***trace***
6	-	DCE	0	0
7[c]	$FeCl_3$/20	DCE	87	trace
8[d]	$FeCl_3$/20	DCE	85	trace
9	$FeCl_3$/20	CH_3NO_2	80	trace
10	$FeCl_3$/20	DCM	58	trace
11	$FeCl_3$/20	Toluene	32	trace
12	$FeCl_3$/20	THF	trace	trace
13	$FeCl_3$/20	EtOH	<5	trace
14	PTSA/20	DCE	30	23
15	$MeSO_3H$/20	DCE	36	30
16	$MeSO_3H$/40	DCE	0	49
17	$MeSO_3H$/100	DCE	0	80
18	$MeSO_3H$/120	DCE	0	79
19	***$MeSO_3H$/100***	***Toluene***	***0***	***91***
20	$MeSO_3H$/100	Xylene	0	88
21	$MeSO_3H$/100	EtOH	0	trace
22	TFA/100	Toluene	0	trace
23	CH_3COOH/100	Toluene	0	trace

[a]Reaction conditions: Synthesis of **4a**: **1a** (1 mmol), **2a** (1 mmol), **3a** (1 mmol), and 20 mol% of $FeCl_3$ were heated in 5 mL of DCE under air for 1 h. Synthesis of **5a**: **1a** (1 mmol), **2a** (0.5 mmol), catalyst (100 mmol%), were heated in 5 mL of toluene under air for 1 h. [b]Isolated yield. [c]Reaction temperature: 100 °C. [d]Reaction temperature: 60 °C. PTSA = *para*-toluenesulfonic acid. TFA = trifluoroacetic acid. DCE = 1,2-dichloroethane.

Having identified the optimized conditions for the synthesis of **5** (Table 1, entry 19), the generality and scope of this reaction was subsequently investigated as shown in Scheme **4**. Arylglyoxals bearing electron-neutral (4-H), electron-rich (4-OMe, 3-Me, 2-Me), electron-deficient (4-NO_2, 4-OH) substituents were smoothly converted to the corresponding products in good to excellent yields (70–96%; **5b**–**5g**). Pleasingly, *halo*-substituted (4-Cl, 4-F, 4-Br, 3-Cl, 2-Cl) arylglyoxals were also found to furnish the desired products in excellent yields (80–92%; **5a** and **5h**–**5k**). 2-thienyl and 1-naphthyl

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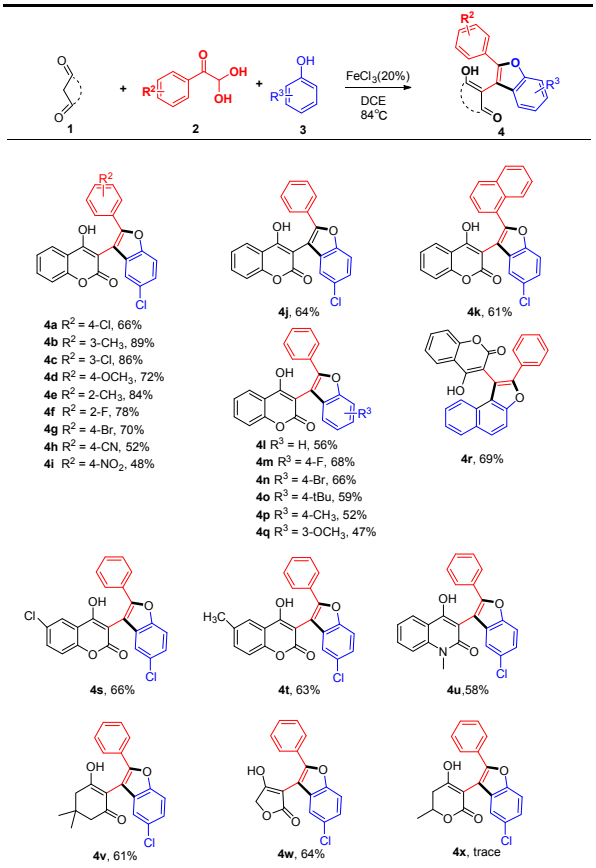
substituents were also suitable for this transformation, affording the corresponding products **5l** and **5m** in 82% and 70% yield, respectively. 6-substitued-4-hydroxycoumarin were also examined, and it was observed that electronic nature of the substituents on the phenyl ring of 4-hydroxycoumarin had a slight influence on the reaction, which generated the corresponding products in moderate yields (52–67%; **5n**–**5q**).

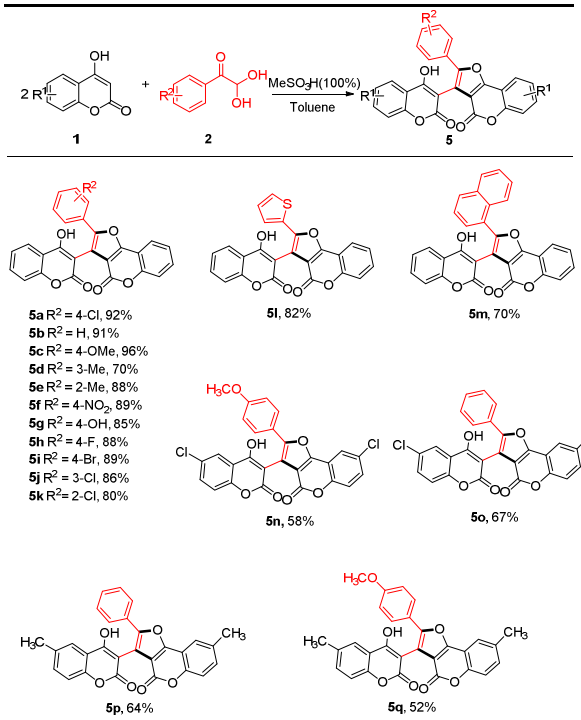
Scheme 3. Scope of Substrates to Form 4[a]



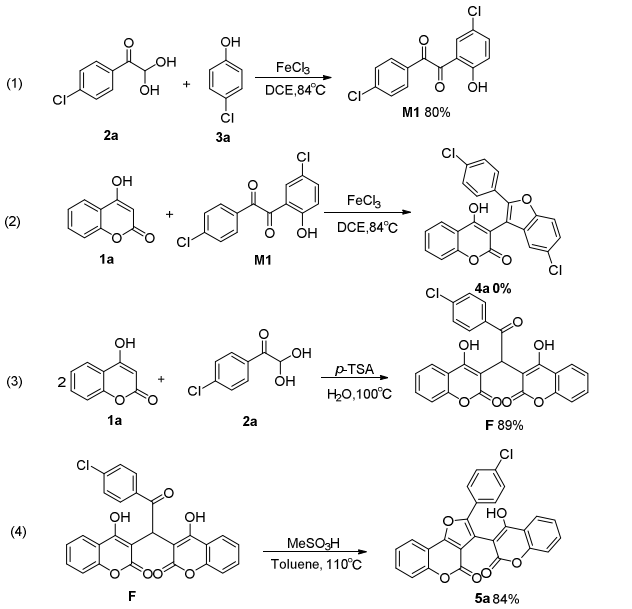
[a]Reaction conditions: cyclic dicarbonyl compounds (1mmol), arylglyoxal (1mmol), phenol (1mmol), and 20 mol% of $FeCl_3$ were heated in 5 mL of DCE under air for 1 h.

To gain insight into the reaction mechanism, several control experiments were performed (Scheme **5**). In DCE, compounds **2a** and **3a** were stirred under the standard conditions without addition of **1a**. The α-diketone **M1** was formed (Scheme 5, entry 1). Moreover, **4a** could not be obtained when **M1** was reacted with **1a**, which suggested that **M1** might not be the key intermediate (Scheme 5, entry 2). In the process of forming **5a**. Initially, the condensation between **1a** and **2a** in the presence of catalytic amounts of *p*-toluenesulfonic acid (*p*-TSA) in water under reflux produces dicoumarols **F** (Scheme 5, entry 3). Additionally, when **F** was used as a substrate in the reaction, the desired product **5a** was formed in 84% yield under the standard conditions, which indicated that **F** was a possible intermediate for the reaction (Scheme 5, entry 4).

Scheme 4. Scope of Substrates to Form 5[a]



[a]Reaction conditions: 4-Hydroxycoumarin (1mmol), arylglyoxal (0.5mmol), and $MeSO_3H$ (0.5mmol) were heated in 5 mL of Tol under air for 1 h.



Scheme 5 Control Experiments

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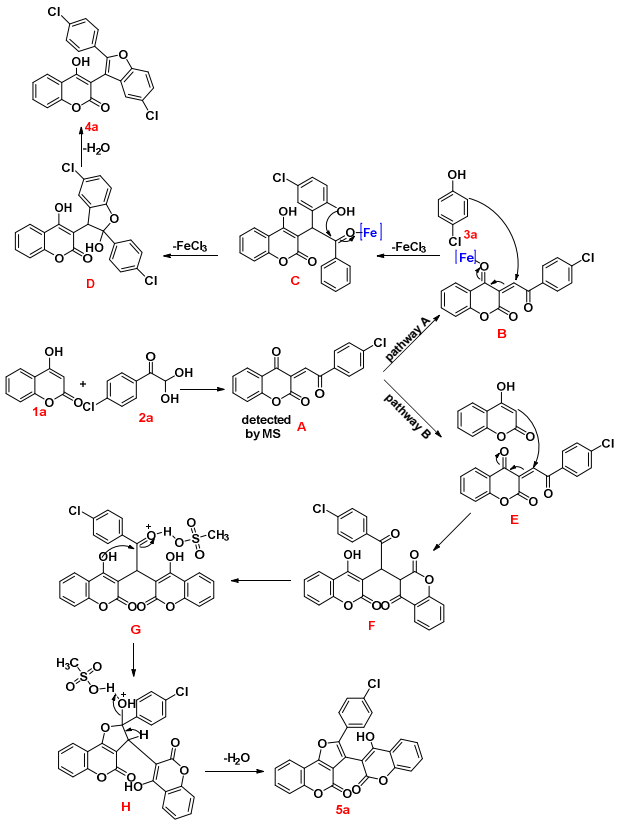
Based on the above results and previous reports,[8] a plausible mechanism for this multicomponent tandem cyclization is proposed using **1a**, **2a**, and **3a** as an example (Scheme **6**). Initially, phenylglyoxal **2a** and 4-hydroxycoumarin **1a** underwent dehydrative condensation to form intermediate **A**. The selectivity with regard to the conversion of **A** into **C** versus **A** into **F** depends on the reaction solvent and catalyst. In DCE, intermediate **A** underwent a 1,4-addition by the attack of the α-C of phenol leading to intermediate **C**. Subsequently, intermediate **C** directly went through an intramolecular cyclization to form intermediate **D**, followed by dehydration to afford the desired product **4a**. (Scheme 6, Pathway A) In toluene, 1,4-addition was proposed to generate intermediate **E** to give intermediate **F**. In the next step, intramolecular cyclization of intermediate **F** gave intermediate **H** followed by final dehydration to form **5a**. (Scheme 6, Pathway B).



Scheme 6 Proposed reaction mechanism.

Conclusions

In conclusion, we have developed a simple and efficient method which is applicable for the synthesis of highly functionalized furan analogues. The reaction proceeds via arylglyoxal, 4-hydroxycoumarin and phenols in the presence of $FeCl_3$ or $MeSO_3H$ as catalyst. In the reaction, three components were used in DCE, conditions were moderate, the workup procedure was simple. And most of the products **5** were obtained in solid form during the reaction of two components. Hence, a large number of heterocycles of biological significances could be synthesized in a short period of time. Further biological activity investigation of these new compounds is underway and published in due course.

Experimental section

General: All reagents were obtained from commercial sources (purity > 99%) and used without further purification, unless otherwise indicated. Melting points were determined with a Büchi B-540 capillary melting point apparatus. The ^1H and ^{13}C NMR spectroscopic data were recorded with a Varian instrument at 600 and 150 MHz, respectively, and TMS was used as the internal standard. Mass spectrometry was performed with a Thermo Finnigan LCQ-Advantage instrument. High resolution mass spectral (HRMS) analyze was measured on an Agilent 1290-6540 UHPLC Q-Tof HR-MS System ESI spectrometer. Silica gel for column chromatography was purchased from Qingdao Haiyang Chemical Co., Ltd. Reactions were stirred using Teflon-coated magnetic stir bars.

Experimental Procedure for the Synthesis of 4: A mixture of the cyclic dicarbonyl compounds **1** (1 mmol), arylglyoxal monohydrate **2** (1mmol), phenol **3** (1mmol) and $FeCl_3$ (0.2mmol) in DCE (5 mL) was stirred at reflux for 0.5 – 1.0 h. Upon completion of the reaction (progress was monitored by TLC), the mixture was cooled to room temperature and aqueous NH_4Cl (30 mL) was added. The aqueous phase was extracted with ethyl acetate (3 x 25 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding products **4**.

3-(5-Chloro-2-(4-chlorophenyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4a**). Pale yellow solid, 66% yield, mp: 208-210 °C; FTIR (neat) *v*: 3424, 1608, 1142 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.89 (s, 1H), 7.99 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.79 – 7.75 (m, 2H), 7.73 (m, 2H), 7.56 – 7.48 (m, 4H), 7.46 – 7.38 (m, 2H). ^{13}C NMR (150 MHz, DMSO) δ 163.6, 161.5, 153.9, 153.3, 152.5, 134.3, 133.4, 132.2, 131.6, 129.6 (2C), 129.3, 128.1 (2C), 125.4, 124.6, 124.5, 120.6, 116.9, 116.6, 113.2, 108.3, 95.9. HRMS (ESI): m/z calcd for $C_{23}H_{13}Cl_2O_4$ $[M + H]^+$ 423.0185, found 423.0184.

3-(5-Chloro-2-(m-tolyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4b**). Pale yellow solid, 89% yield, mp: 221-223 °C; FTIR (neat) *v*: 3406, 1607, 1551, 1147 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.84 (s, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.75 – 7.70 (m, 2H), 7.63 (s, 1H), 7.52 (d, *J* = 1.8 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.45 – 7.40 (m, 1H), 7.38 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 163.5, 161.6, 154.6, 153.5, 152.5, 138.6, 133.3, 132.4, 130.4, 129.4, 128.0, 126.8, 125.0, 124.6, 124.4, 123.6, 120.4, 116.9, 116.6, 113.1, 107.5, 96.2, 21.6. HRMS (ESI): m/z calcd for $C_{24}H_{16}ClO_4$ $[M + H]^+$ 403.0732, found 403.0733.

3-(5-Chloro-2-(3-chlorophenyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4c**). Pale yellow solid, 86% yield, mp: 178-180 °C; FTIR (neat) *v*: 3446, 1616, 1576, 1172 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.98 (s, 1H), 8.03 – 7.98 (m, 1H), 7.79 – 7.72 (m, 3H), 7.71 – 7.66 (m, 1H), 7.58 (d, *J* = 1.8 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.43 (dd, *J* = 16.2, 7.8 Hz, 2H). ^{13}C NMR (150 MHz, DMSO) δ 163.7, 161.5, 153.6, 152.7, 152.6, 134.1, 133.4, 132.3, 132.0, 131.5, 129.4, 128.2, 125.8, 125.6, 125.0, 124.6, 124.5, 120.8,

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117.0, 116.6, 113.3, 109.0, 95.8. HRMS (ESI): m/z calcd for $C_{23}H_{13}Cl_2O_4$ $[M + H]^+$ 423.0185, found 423.0187.

3-(5-Chloro-2-(4-methoxyphenyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4d**). Pale yellow solid, 72% yield, mp: 212-215 ^oC; FTIR (neat) *v*: 3424, 2974, 1610, 1508, 1254, 1149 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.80 (s, 1H), 7.99 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.74 – 7.71 (m, 1H), 7.71 – 7.68 (m, 3H), 7.50 (dd, *J* = 8.4, 0.6 Hz, 1H), 7.47 (d, *J* = 2.4 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.35 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.05 – 7.01 (dt, *J* = 9.6, 2.4 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (150 MHz, DMSO) ^{13}C NMR (151 MHz, DMSO) δ 163.5, 161.6, 160.4, 154.7, 153.5, 152.3, 133.3, 132.6, 128.0 (2C), 127.9, 124.6, 124.5, 124.4, 122.9, 120.0, 116.9, 116.6, 115.0 (2C), 112.9, 105.8, 96.3, 55.7. HRMS (ESI): m/z calcd for $C_{24}H_{16}ClO_5$ $[M + H]^+$ 419.0681, found 419.0688.

3-(5-Chloro-2-(o-tolyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4e**). Pale yellow solid, 84% yield, mp: 172-174 ^oC; FTIR (neat) *v*: 3418, 1608, 1557, 1149 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.72 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.60 – 7.56 (m, 1H), 7.43 (d, *J* = 7.8 Hz, 2H), 7.40 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.38 – 7.34 (m, 1H), 7.34 – 7.28 (m, 2H), 7.23 – 7.19 (m, 1H), 2.36 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 163.2, 161.7, 156.7, 153.3, 153.0, 137.7, 133.18, 131.7, 131.2, 130.1, 130.0, 129.8, 127.8, 126.2, 124.7, 124.5, 124.3, 120.5, 116.8, 116.4, 113.2, 109.3, 96.1, 20.3. HRMS (ESI): m/z calcd for $C_{24}H_{16}ClO_4$ $[M + H]^+$ 403.0732, found 403.0735.

3-(5-Chloro-2-(2-fluorophenyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4f**). Pale yellow solid, 78% yield, mp: 228-230 ^oC; FTIR (neat) *v*: 3418, 1608, 1557, 1149 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.76 (s, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.74 (t, *J* = 7.8 Hz, 1H), 7.72 – 7.68 (m, 1H), 7.59 (d, *J* = 0.6 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.43 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.31 (m, 2H). ^{13}C NMR (150 MHz, DMSO) δ 162.7, 161.5, 160.2, 158.6, 153.3, 153.1, 150.88, 150.86, 133.2, 132.2 (d, *J* = 9.06 Hz), 131.6, 130.4 (d, J = 3.0), 128.0, 125.3, 124.5, 124.3, 120.9, 118.5 (d, *J* = 13.5 Hz), 117.0, 116.9, 116.6, 113.3, 110.6, 96.4. HRMS (ESI): m/z calcd for $C_{23}H_{13}ClFO_4$ $[M + H]^+$ 407.0481, found 407.0488.

3-(2-(4-Bromophenyl)-5-chlorobenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4g**). Pale yellow solid, 70% yield, mp: 173-175 ^oC; FTIR (neat) *v*: 3424, 1608, 1550, 1149 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.88 (s, 1H), 7.99 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.73 (m, 2H), 7.71 – 7.64 (m, 4H), 7.54 (d, *J* = 2.4 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.45 – 7.38 (m, 2H). ^{13}C NMR (150 MHz, DMSO) δ 163.6, 161.4, 153.6, 153.4, 152.5, 133.4, 132.5 (2C), 132.2, 129.6, 128.3 (2C), 128.1, 125.4, 124.6, 124.5, 123.0, 120.6, 117.0, 116.6, 113.2, 108.4, 95.9. HRMS (ESI): m/z calcd for $C_{23}H_{13}BrClO_4$ $[M + H]^+$ 466.9680, found 466.9681.

4-(5-Chloro-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)benzofuran-2-yl)benzonitrile (**4h**). Pale yellow solid, 52% yield, mp: 219-221 ^oC; FTIR (neat) *v*: 3431, 2219, 1609, 1551, 1147 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.93 (s, 1H), 7.92 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.88 – 7.81 (m, 4H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.53 (d, *J* = 1.8 Hz, 1H), 7.43 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.39 – 7.32 (m, 2H). ^{13}C NMR (150 MHz, DMSO) δ 170.8, 163.8, 161.4, 153.6, 152.8, 152.3, 134.5, 133.4 (2C), 131.9, 128.3, 126.9 (2C), 126.1, 124.6, 124.5, 121.0, 119.0, 117.0, 116.7, 113.4, 111.6, 110.7, 95.6. HRMS (ESI): m/z calcd for $C_{24}H_{13}ClNO_4$ $[M + H]^+$ 414.0528, found 414.0531.

3-(5-Chloro-2-(4-nitrophenyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4i**). Yellow solid, 48% yield, mp: 245-247 ^oC; FTIR (neat) *v*: 3423, 1608, 1558, 1520, 1169 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.90 (s, 1H), 8.30 (d, *J* = 9.0 Hz, 2H), 8.05 – 8.01 (m, 2H), 8.00 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.77 – 7.71 (m, 1H), 7.62 (d, *J* = 2.4 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.47 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.9, 161.4, 153.7, 152.9, 152.1, 147.5, 136.3, 133.4, 131.9, 131.2, 128.4, 127.3 (2C), 126.4, 124.8 (2C), 124.5, 121.2, 117.0, 116.8, 113.5, 111.3, 95.6. HRMS (ESI): m/z calcd for $C_{23}H_{13}ClNO_6$ $[M + H]^+$ 434.0426, found 434.0422.

3-(5-Chloro-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4j**). Pale yellow solid, 64% yield, mp: 223-225 ^oC; FTIR (neat) *v*: 3448, 1603, 1550, 1151 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.89 (s, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 7.78 (d, *J* = 7.2 Hz, 2H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.60 – 7.49 (m, 2H), 7.49 – 7.33 (m, 5H). ^{13}C NMR (150 MHz, DMSO) δ 163.6, 161.6, 154.4, 153.6, 152.5, 133.3, 132.4, 130.4, 129.7, 129.5 (2C), 128.0, 126.4 (2C), 125.1, 124.6, 124.4, 120.4, 117.0, 116.6, 113.1, 107.6, 96.2. HRMS (ESI): m/z calcd for $C_{23}H_{14}ClO_4$ $[M + H]^+$ 389.0575, found 389.0576.

3-(5-Chloro-2-(naphthalen-1-yl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4k**). Pale yellow solid, 61% yield, mp: 229-231 ^oC; FTIR (neat) *v*: 3423, 1611, 1548, 1144 cm^{-1};^1H NMR (600 MHz, DMSO) δ 11.76 (s, 1H), 8.14 – 8.10 (m, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 8.00 – 7.96 (m, 1H), 7.83 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 7.2 Hz, 1H), 7.66 (d, *J* = 1.8 Hz, 1H), 7.65 – 7.61 (m, 1H), 7.59 – 7.55 (m, 1H), 7.55 – 7.50 (m, 2H), 7.45 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.3, 161.8, 155.9, 153.3, 153.2, 133.7, 133.2, 131.8, 131.1, 130.7, 128.81, 128.75, 128.0, 127.6, 127.2, 126.8, 126.1, 125.8, 124.9, 124.5, 124.2, 120.7, 116.8, 116.4, 113.4, 110.4, 96.2. HRMS (ESI): m/z calcd for $C_{27}H_{16}ClO_4$ $[M + H]^+$ 439.0732, found 439.0734.

4-Hydroxy-3-(2-phenylbenzofuran-3-yl)-2H-chromen-2-one (**4l**). Pale yellow solid, 56% yield, mp: 174-176 ^oC; FTIR (neat) *v*: 3367, 1696, 1515, 1151 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.84 (s, 1H), 7.98 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.77 – 7.74 (m, 2H), 7.74 – 7.69 (m, 2H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.46 – 7.41 (m, 3H), 7.41 – 7.35 (m, 3H), 7.25 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.4, 161.6, 154.0, 153.4, 152.8, 133.3, 130.9, 130.4, 129.4, 129.3, 129.1, 126.2, 125.2, 124.6, 124.4, 123.4, 120.8, 117.0, 116.6, 115.9, 111.6, 107.8, 96.6. HRMS (ESI): m/z calcd for $C_{23}H_{15}O_4$ $[M + H]^+$ 355.0965, found 355.0974.

3-(5-Fluoro-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4m**). Pale yellow solid, 68% yield, mp: 231-233 ^oC; FTIR (neat) *v*: 3423, 1607, 1512, 1148 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.85 (s, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.80 – 7.69 (m, 4H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.48 – 7.41 (m, 3H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.21 (m, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.5, 161.5, 160.1, 158.5, 154.7, 153.5, 150.3, 133.3, 131.9 (d, *J* = 10.5 Hz), 130.6, 129.6, 129.4, 126.3, 124.6, 124.4, 117.0, 116.6, 112.8, 112.7 (d, *J* = 9.0 Hz), 108.2, 106.6, 106.4, 96.3. HRMS (ESI): m/z calcd for $C_{23}H_{14}FO_4$ $[M + H]^+$ 373.0871, found 373.0873.

3-(5-Bromo-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4n**). Pale yellow solid, 66% yield, mp: 218-220 ^oC; FTIR (neat) *v*: 3409, 1602, 1521, 1153 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.88 (s, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.75 – 7.71 (m, 1H), 7.71 – 7.66 (m, 2H), 7.55 – 7.49 (m, 2H), 7.49 – 7.37 (m, 4H). ^{13}C NMR (150 MHz, DMSO) δ 163.6, 161.6, 154.2, 153.5, 152.8, 133.3, 132.9, 130.3, 129.7, 129.4 (2C), 127.8, 126.4 (2C), 124.6, 124.4, 123.4, 116.9, 116.6, 115.9, 113.6, 107.5, 96.1. HRMS (ESI): m/z calcd for $C_{23}H_{14}BrO_4$ $[M + H]^+$ 433.0070, found 433.0075.

3-(5-(Tert-butyl)-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4o**). Pale yellow solid, 59% yield, mp: 211-213 ^oC; FTIR (neat) *v*: 3423, 2958, 1609, 1555, 1362, 1146 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.77 (s, 1H), 8.00 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.77 – 7.70 (m, 3H), 7.62 (d, *J* = 9.0 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.47 – 7.40 (m, 4H), 7.38 – 7.33 (m, 2H), 1.31 (s, 9H). ^{13}C NMR (150 MHz,

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DMSO) δ 163.3, 161.6, 153.5, 153.0, 152.3, 146.1, 133.2, 131.0, 130.3, 129.3 (2C), 129.1, 126.1 (2C), 124.6, 124.4, 123.1, 117.0, 116.6, 116.5, 110.9, 107.9, 96.8, 35.0, 32.1 (3C). HRMS (ESI): m/z calcd for $C_{27}H_{23}O_4$ $[M + H]^+$ 411.1591, found 411.1592.

4-Hydroxy-3-(5-methyl-2-phenylbenzofuran-3-yl)-2H-chromen-2-one (**4p**). Pale yellow solid, 52% yield, mp: 207-209 °C; FTIR (neat) *v*: 3426, 1608, 1551, 1145 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.81 (s, 1H), 8.00 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.78 – 7.72 (m, 3H), 7.58 (d, *J* = 9.0 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.44 (m, 3H), 7.36 (m, 1H), 7.19 (d, *J* = 5.4 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 163.3, 161.5, 153.4, 153.0, 152.4, 133.3, 132.5, 131.0, 130.7, 129.3 (2C), 129.1, 126.4, 126.1 (2C), 124.6, 124.4, 120.4, 116.9, 116.5, 111.1, 107.5, 96.8, 21.3. HRMS (ESI): m/z calcd for $C_{24}H_{17}O_4$ $[M + H]^+$ 369.1121, found 369.1131.

4-Hydroxy-3-(6-methoxy-2-phenylbenzofuran-3-yl)-2H-chromen-2-one (**4q**). Pale yellow solid, 47% yield, mp: 217-219 °C; FTIR (neat) *v*: 3428, 2971, 1607, 1509, 1248, 1143 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.78 (s, 1H), 7.99 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.72 (m, 3H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 3H), 7.36 – 7.30 (m, 2H), 7.27 (d, *J* = 8.4 Hz, 1H), 6.89 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 163.2, 161.5, 158.7, 155.0, 153.4, 151.9, 133.3, 131.1, 129.3 (2C), 128.7, 125.7 (2C), 124.6, 124.4, 123.8, 121.0, 116.9, 116.6, 112.3, 107.7, 96.8, 96.4, 56.2. HRMS (ESI): m/z calcd for $C_{24}H_{17}O_5$ $[M + H]^+$ 385.1071, found 385.1073.

4-Hydroxy-3-(2-phenylnaphtho[2,1-b]furan-1-yl)-2H-chromen-2-one (**4r**). Pale yellow solid, 69% yield, mp: 171-173 °C; FTIR (neat) *v*: 3423, 1607, 1551, 1143 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.09 (s, 1H), 8.10 – 8.05 (m, 1H), 8.02 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.97 – 7.91 (m, 3H), 7.82 – 7.74 (m, 3H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.51 – 7.43 (m, 5H), 7.37 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.7, 161.9, 153.6, 152.5, 152.0, 133.6, 130.9, 130.8, 129.52, 129.49 (2C), 129.1, 128.4, 127.2, 126.4, 126.1 (2C), 125.1, 124.9, 124.6, 123.8, 122.3, 117.2, 116.4, 112.9, 108.8, 98.1. HRMS (ESI): m/z calcd for $C_{27}H_{17}O_4$ $[M + H]^+$ 405.1121, found 405.1122.

6-Chloro-3-(5-chloro-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4s**). Pale yellow solid, 66% yield, mp: 235-237 °C; FTIR (neat) *v*: 3431, 1608, 1555, 1146 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.15 (s, 1H), 7.97 (s, 1H), 7.77 (d, *J* = 8.4 Hz, 3H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 9.0 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.43 – 7.37 (m, 2H). ^{13}C NMR (150 MHz, DMSO) δ 162.5, 161.2, 154.4, 152.4, 152.2, 132.8, 132.2, 130.3, 129.7, 129.5 (2), 128.6, 128.0, 126.4 (2), 125.1, 123.6, 120.4, 119.1, 118.3, 113.1, 107.4, 97.0. HRMS (ESI): m/z calcd for $C_{23}H_{13}Cl_2O_4$ $[M + H]^+$ 423.0185, found 423.0188.

3-(5-Chloro-2-phenylbenzofuran-3-yl)-4-hydroxy-6-methyl-2H-chromen-2-one (**4t**). Pale yellow solid, 63% yield, mp: 242-244 °C; FTIR (neat) *v*: 3423, 1620, 1577, 1145 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.77 (s, 1H), 7.78 (s, 1H), 7.77 – 7.72 (m, 3H), 7.54 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.50 (d, *J* = 2.4 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.42 – 7.37 (m, 3H), 2.42 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 163.5, 161.7, 154.4, 152.5, 151.7, 134.1, 133.9, 132.4, 130.4, 129.7, 129.4 (2C), 128.0, 126.3 (2C), 125.1, 124.0, 120.3, 116.7, 116.2, 113.1, 107.7, 96.0, 20.9. HRMS (ESI): m/z calcd for $C_{24}H_{16}ClO_4$ $[M + H]^+$ 403.0732, found 403.0735.

3-(5-Chloro-2-phenylbenzofuran-3-yl)-4-hydroxy-1-methylquinolin-2(1H)-one (**4u**). Pale yellow solid, 58% yield, mp: 256-258 °C; FTIR (neat) *v*: 3424, 2428, 1604, 1504, 1158 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 10.56 (s, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.72 (m, 4H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 6.6 Hz, 2H), 7.39 – 7.24 (m, 4H), 3.67 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 161.8, 159.2, 154.0, 152.6, 140.2, 132.8, 132.1, 130.7, 129.4, 129.3 (2C), 127.7, 126.2 (2C), 124.8, 124.3, 122.0, 120.2, 116.3, 115.2, 113.0, 109.3, 101.9, 29.8. HRMS (ESI): m/z calcd for $C_{24}H_{17}ClNO_3$ $[M + H]^+$ 402.0891, found 402.0892.

2-(5-Chloro-2-phenylbenzofuran-3-yl)-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one (**4v**). Pale yellow solid, 61% yield, mp: 225-227 °C; FTIR (neat) *v*: 3423, 2958, 1596, 1153 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 10.96 (s, 1H), 7.72 (d, *J* = 7.8 Hz, 2H), 7.64 (d, *J* = 9.0 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.32 (dd, *J* = 9.0, 1.8 Hz, 1H), 7.20 (d, *J* = 1.8 Hz, 1H), 2.61 (s, 2H), 2.35 (s, 2H), 1.16 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (150 MHz, DMSO) δ 153.1, 152.2, 132.8, 131.0, 129.1, 127.5, 126.3, 124.6, 120.1, 113.0, 109.7, 105.7, 32.2, 28.8, 28.4. HRMS (ESI): m/z calcd for $C_{22}H_{20}ClO_3$ $[M + H]^+$ 367.1095, found 367.1098.

3-(5-Chloro-2-phenylbenzofuran-3-yl)-4-hydroxyfuran-2(5H)-one (**4w**). Pale yellow, 64% yield, mp: 240-242 °C; FTIR (neat) *v*: 3432, 2925, 1630, 1560, 1142 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.85 (s, 1H), 7.83 – 7.79 (m, 2H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.54 (d, *J* = 2.4 Hz, 1H), 7.50 (t, *J* = 7.2 Hz, 2H), 7.45 – 7.41 (m, 1H), 7.39 (dd, *J* = 9.0, 2.4 Hz, 1H), 4.96 (s, 2H). ^{13}C NMR (150 MHz, DMSO) δ 177.8, 172.8, 153.5, 152.1, 131.6, 130.3, 129.6, 129.3 (2C), 128.0, 126.6 (2C), 125.3, 120.6, 113.2, 105.4, 91.8, 68.0. HRMS (ESI): m/z calcd for $C_{18}H_{12}ClO_4$ $[M + H]^+$ 327.0419, found 327.0425.

Experimental Procedure for the Synthesis of 5: A mixture of the 4-Hydroxycoumarin **1** (1 mmol), arylglyoxal monohydrate **2** (0.5mmol), and $MeSO_3H$ (0.5mmol) in toluene (5 mL) was stirred at reflux for 0.5 – 1.0 h. Upon completion of the reaction (progress was monitored by TLC), the mixture was cooled to room temperature.The solid was removed by filtration, washed with water and a little cold toluene, and then dried to give the pure product **5**.

2-(4-Chlorophenyl)-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-4H-furo[3,2-c]chromen-4-one (5a). White solid, 92% yield, mp: >300 °C; FTIR (neat) *v*: 3432, 1728, 1673, 1633, 1609, 1499, 1153 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.04 (s, 1H), 8.17 (d, *J* = 7.2 Hz, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.76 (t, *J* = 7.2 Hz, 1H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.60 – 7.49 (m, 5H), 7.45 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.4, 161.2, 156.9, 156.4, 153.4, 152.6, 152.3, 134.3, 133.6, 132.0, 129.7 (2C), 128.3, 127.5 (2C), 125.6, 124.8, 124.5, 121.5, 117.5, 117.0, 116.4, 112.9, 112.4, 111.0, 95.3. HRMS (ESI): m/z calcd for $C_{26}H_{14}ClO_6$ $[M + H]^+$ 457.0473, found 457.0478.

3-(4-Hydroxy-2-oxo-2H-chromen-3-yl)-2-phenyl-4H-furo[3,2-c]chromen-4-one (**5b**). White solid, 91% yield, mp: >300 °C; FTIR (neat) *v*: 3219, 1724, 1675,1631, 1497, 1156 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.99 (s, 1H), 8.18 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.00 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.81 (dd, *J* = 3.0, 1.2 Hz, 2H), 7.75 (m, 1H), 7.69 (m, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.56 – 7.47 (m, 4H), 7.46 – 7.39 (m, 2H). ^{13}C NMR (150 MHz, DMSO) δ 163.2, 161.3, 157.0, 156.3, 153.4, 152.5, 133.6, 131.9, 129.8, 129.6 (2C), 129.4, 128.7, 125.8 (2C), 125.6, 124.8, 124.5, 121.4, 117.5, 117.0, 116.3, 113.0, 112.5, 110.3, 95.6. HRMS (ESI): m/z calcd for $C_{26}H_{15}O_6$ $[M + H]^+$ 423.0863, found 423.0864.

3-(4-Hydroxy-2-oxo-2H-chromen-3-yl)-2-(4-methoxyphenyl)-4H-furo[3,2-c]chromen-4-one (**5c**). White solid, 96% yield, mp: >300 °C; FTIR (neat) *v*: 3416, 2958, 1723, 1674, 1631, 1610, 1508, 1258, 1152 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.93 (s, 1H), 8.15 (dd, *J* = 7.8, 1.8 Hz, 1H), 8.00 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.77 – 7.71 (m, 3H), 7.68 – 7.63 (m, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.51 (m, 2H), 7.47 – 7.42 (m, 1H), 7.08 – 7.03 (dt, *J* = 10.2, 3.0 Hz, 2H), 3.78 (s, 3H). ^{13}C NMR (150

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MHz, DMSO) δ 163.2, 161.4, 160.5, 157.1, 155.8, 153.7, 153.3, 152.4, 133.5, 131.6, 127.5, 125.6, 124.8, 124.4, 122.0, 121.3, 117.5, 117.0, 116.3, 115.1, 113.0, 112.6, 108.3, 95.8, 55.7. HRMS (ESI): m/z calcd for $C_{27}H_{17}O_7$ $[M + H]^+$ 453.0969, found 453.0966.

3-(4-Hydroxy-2-oxo-2H-chromen-3-yl)-2-(m-tolyl)-4H-furo[3,2-c]chromen-4-one (**5d**). White solid, 70% yield, mp: >300 °C; FTIR (neat) *v*: 3416, 1728, 1677, 1633, 1611, 1397, 1166 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.97 (s, 1H), 8.19 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.00 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.77 – 7.72 (m, 1H), 7.68 (m, 2H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.53 (m, 3H), 7.47 – 7.41 (m, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 163.2, 161.3, 157.0, 156.2, 153.5, 153.3, 152.5, 138.8, 133.6, 131.8, 130.4, 129.5, 129.4, 126.3, 125.6, 124.8, 124.4, 123.0, 121.4, 117.5, 117.0, 116.3, 113.0, 112.5, 110.2, 95.7, 21.6. HRMS (ESI): m/z calcd for $C_{27}H_{17}O_6$ $[M + H]^+$ 437.1020, found 437.1022.

3-(4-Hydroxy-2-oxo-2H-chromen-3-yl)-2-(o-tolyl)-4H-furo[3,2-c]chromen-4-one (**5e**). White solid, 88% yield, mp: >300 °C; FTIR (neat) *v*: 3415, 1728, 1677, 1633, 1612, 1387, 1130 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.86 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.92 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.69 (m, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.46 – 7.32 (m, 5H), 7.28 – 7.21 (m, 1H), 2.43 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 163.0, 161.4, 157.1, 156.7, 155.4, 153.1, 152.4, 138.0, 133.5, 131.8, 131.4, 130.5, 129.8, 128.5, 126.4, 125.6, 124.8, 124.3, 121.21, 117.6, 116.9, 116.1, 112.7, 112.4, 112.0, 95.5, 20.4. HRMS (ESI): m/z calcd for $C_{27}H_{17}O_6$ $[M + H]^+$ 437.1020, found 437.1025.

3-(4-Hydroxy-2-oxo-2H-chromen-3-yl)-2-(4-nitrophenyl)-4H-furo[3,2-c]chromen-4-one (**5f**). Yellow solid, 89% yield, mp: >300 °C; FTIR (neat) *v*: 3418, 1725, 1671, 1629, 1608, 1536, 1145 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.13 (s, 1H), 8.34 – 8.29 (m, 2H), 8.21 (m, 2H), 8.09 – 8.05 (m, 2H), 8.01 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.80 – 7.75 (m, 2H), 7.74 – 7.70 (m, 1H), 7.47 – 7.43 (m, 1H). ^{13}C NMR (150 MHz, DMSO) δ 168.5, 164.2, 161.0, 157.3, 152.9, 151.1, 149.6, 147.4, 135.2, 133.7, 132.5, 131.9, 128.9, 126.7, 124.9, 124.6, 123.8, 121.8, 119.6, 117.6, 117.1, 116.2, 114.1, 112.2, 100.9, 95.0. HRMS (ESI): m/z calcd for $C_{26}H_{14}NO_8$ $[M + H]^+$ 468.0714, found 468.0720.

3-(4-Hydroxy-2-oxo-2H-chromen-3-yl)-2-(4-hydroxyphenyl)-4H-furo[3,2-c]chromen-4-one (**5g**). White solid, 85% yield, mp: >300 °C; FTIR (neat) *v*: 3358, 1723, 1658, 1611, 1504, 1178 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.87 (s, 1H), 9.99 (s, 1H), 8.13 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.99 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.77 – 7.72 (m, 1H), 7.69 – 7.61 (m, 3H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (150 MHz, DMSO) δ 163.1, 161.4, 159.1, 157.1, 155.6, 154.2, 153.3, 152.3, 133.5, 131.5, 127.6 (2C), 125.6, 124.8, 124.4, 121.2, 120.5, 117.5, 117.0, 116.4 (2C), 116.3, 113.0, 112.7, 107.6, 95.9. HRMS (ESI): m/z calcd for $C_{26}H_{15}O_7$ $[M + H]^+$ 439.0812, found 439.0813.

2-(4-Fluorophenyl)-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-4H-furo[3,2-c]chromen-4-one (**5h**). White solid, 88% yield, mp: >300 °C; FTIR (neat) *v*: 3443, 1726, 1654, 1603, 1497, 1156 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.01 (s, 1H), 8.18 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.00 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.85 (dd, *J* = 9.0, 5.4 Hz, 2H), 7.78 – 7.72 (m, 1H), 7.71 – 7.65 (m, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.52 (m, 2H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 9.0 Hz, 2H). ^{13}C NMR (150 MHz, DMSO) δ 163.7, 163.4, 162.0, 161.3, 157.0, 156.3, 153.4, 152.6, 152.5, 133.6, 131.8, 128.3 (d, *J* = 9.0 Hz), 126.1, 125.6, 124.8, 124.5, 121.4, 117.5, 117.0, 116.8, 116.7, 116.4, 112.9, 112.5, 110.1, 95.4. HRMS (ESI): m/z calcd for $C_{26}H_{14}FO_6$ $[M + H]^+$ 441.0769, found 441.0772.

2-(4-Bromophenyl)-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-4H-furo[3,2-c]chromen-4-one (**5i**). White solid, 89% yield, mp: >300 °C; FTIR (neat) *v*: 3433, 1724, 1643, 1609, 1518, 1163 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.02 (s, 1H), 8.18 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.99 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.77 – 7.72 (m, 3H), 7.71 – 7.66 (m, 3H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.52 (m, 2H), 7.46 – 7.42 (m, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.3, 161.2, 156.9, 156.5, 153.4, 152.6, 152.3, 133.6, 132.7 (2C), 132.0, 128.6, 127.7 (2C), 125.6, 124.8, 124.5, 123.1, 121.5, 117.6, 117.0, 116.4, 112.9, 112.4, 111.1, 95.3. HRMS (ESI): m/z calcd for $C_{26}H_{14}BrO_6$ $[M + H]^+$ 500.9968, found 500.9980.

2-(3-Chlorophenyl)-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-4H-furo[3,2-c]chromen-4-one (**5j**). White solid, 86% yield, mp: >300 °C; FTIR (neat) *v*: 3416, 1736, 1665, 1603, 1497, 1142 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.12 (s, 1H), 8.27 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.90 (s, 1H), 7.76 (t, *J* = 7.2 Hz, 1H), 7.73 – 7.66 (m, 2H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.51 – 7.47 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.4, 161.2, 156.9, 156.7, 153.4, 152.6, 151.6, 134.3, 133.7, 132.1, 131.7, 131.3, 129.5, 125.6, 125.3, 124.9, 124.5, 124.3, 121.8, 117.5, 117.1, 116.2, 112.9, 112.4, 111.6, 95.2. HRMS (ESI): m/z calcd for $C_{26}H_{14}ClO_6$ $[M + H]^+$ 457.0473, found 457.0477.

2-(2-Chlorophenyl)-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-4H-furo[3,2-c]chromen-4-one (**5k**). White solid, 80% yield, mp: >300 °C; FTIR (neat) *v*: 3423, 1736, 1653, 1608, 1498, 1156 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.90 (s, 1H), 8.06 – 8.01 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.93 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.72 – 7.63 (m, 3H), 7.63 – 7.57 (m, 2H), 7.54 – 7.45 (m, 3H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.0, 161.0, 157.1, 156.9, 153.2, 152.5, 152.0, 133.5, 132.8, 132.1, 130.8, 129.4, 128.7, 128.0, 125.8, 125.7, 124.7, 124.3, 121.3, 117.6, 116.9, 116.2, 113.8, 112.5, 112.4, 95.4. HRMS (ESI): m/z calcd for $C_{26}H_{14}ClO_6$ $[M + H]^+$ 457.0473, found 457.0474.

3-(4-Hydroxy-2-oxo-2H-chromen-3-yl)-2-(thiophen-2-yl)-4H-furo[3,2-c]chromen-4-one (**5l**). Gray solid, 82% yield, mp: >300 °C; FTIR (neat) *v*: 3415, 1729, 1676, 1497, 1124 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.11 (s, 1H), 8.12 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.02 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.79 – 7.75 (m, 1H), 7.68 (m, 2H), 7.63 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.48 – 7.44 (m, 1H), 7.20 (dd, *J* = 4.8, 3.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.9, 161.1, 156.9, 156.0, 153.4, 152.5, 150.1, 133.8, 131.9, 130.3, 129.1, 128.5, 126.7, 125.7, 124.9, 124.5, 121.3, 117.6, 117.0, 116.3, 113.0, 112.4, 109.0, 94.7. HRMS (ESI): m/z calcd for $C_{24}H_{13}O_6S$ $[M + H]^+$ 429.0427, found 429.0430.

3-(4-Hydroxy-2-oxo-2H-chromen-3-yl)-2-(naphthalen-1-yl)-4H-furo[3,2-c]chromen-4-one (**5m**). White solid, 70% yield, mp: >300 °C; FTIR (neat) *v*: 3416, 1741, 1637, 1615, 1129 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.90 (s, 1H), 8.18 – 8.11 (m, 1H), 8.09 – 8.03 (m, 2H), 8.01 (m, 1H), 7.88 – 7.82 (m, 1H), 7.75 (d, *J* = 7.2 Hz, 1H), 7.70 (t, *J* = 8.4 Hz, 1H), 7.64 (t, *J* = 9.2 Hz, 2H), 7.62 – 7.55 (m, 3H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 163.1, 161.6, 157.2, 157.1, 154.5, 153.1, 152.5, 133.8, 133.4, 131.9, 131.3, 131.0, 129.4, 128.9, 128.7, 127.5, 127.0, 126.3, 125.9, 125.7, 124.7, 124.3, 121.3, 117.6, 116.8, 116.1, 113.2, 112.7, 112.6, 95.5. HRMS (ESI): m/z calcd for $C_{30}H_{17}O_6$ $[M + H]^+$ 473.1020, found 473.1022.

8-Chloro-3-(6-chloro-4-hydroxy-2-oxo-2H-chromen-3-yl)-2-(4-methoxyphenyl)-4H-furo[3,2-c]chromen-4-one (**5n**). White solid, % yield, mp: >300 °C; FTIR (neat) *v*: 3416, 2951, 1732, 1674, 1625, 1507, 1256, 1153 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.23 (s, 1H), 8.26 (d, *J* = 1.8 Hz, 1H), 7.97 (d, *J* = 1.8 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 3H), 7.67 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.58 (dd, *J* = 23.4, 9.0 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 3.78 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 162.3, 160.9, 160.6, 156.6, 154.5, 154.2, 152.0, 150.9, 133.2, 131.1, 129.6, 128.9, 127.7 (2C), 123.7, 121.8, 120.7, 119.5, 119.2, 118.0, 115.0

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(2C), 113.9, 113.7, 108.1, 96.4. HRMS (ESI): m/z calcd for $C_{27}H_{15}Cl_2O_7$ $[M + H]^+$ 521.0189, found 521.0190.

8-Chloro-3-(6-chloro-4-hydroxy-2-oxo-2H-chromen-3-yl)-2-phenyl-4H-furo[3,2-c]chromen-4-one (**5o**). White solid, 67% yield, mp: >300 ^oC; FTIR (neat) *v*: 3414, 1732, 1668, 1603, 1494, 1149 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 12.23 (s, 1H), 8.31 (d, *J* = 2.4 Hz, 1H), 7.98 (d, *J* = 2.4 Hz, 1H), 7.85 (d, *J* = 7.2 Hz, 2H), 7.79 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.70 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 2H), 7.45 – 7.40 (m, 1H). ^{13}C NMR (150 MHz, DMSO) δ 162.4, 160.9, 156.6, 155.0, 153.9, 152.0, 151.1, 133.2, 131.4, 129.9, 129.7, 129.6 (2C), 129.2, 128.9, 126.0 (2C), 123.7, 120.9, 119.5, 119.2, 117.9, 113.8, 113.6, 110.1, 96.2. HRMS (ESI): m/z calcd for $C_{26}H_{13}Cl_2O_6$ $[M + H]^+$ 491.0084, found 491.0086.

3-(4-Hydroxy-6-methyl-2-oxo-2H-chromen-3-yl)-8-methyl-2-phenyl-4H-furo[3,2-c]chromen-4-one (**5p**). White solid, 64% yield, mp: >300 ^oC; FTIR (neat) *v*: 3419, 1732, 1669, 1582, 1508, 1159 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.89 (s, 1H), 7.99 (s, 1H), 7.79 (d, *J* = 8.4 Hz, 3H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.48 (q, *J* = 7.8 Hz, 4H), 7.41 (t, *J* = 9.6 Hz, 2H), 2.48 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 163.2, 161.4, 157.1, 156.3, 153.2, 151.5, 150.7, 135.1, 134.3, 134.1, 132.7, 129.7, 129.6 (2C), 129.5, 125.7 (2C), 124.0, 120.9, 117.3, 116.8, 116.0, 112.9, 112.2, 110.4, 95.6, 20.9 (2C). HRMS (ESI): m/z calcd for $C_{28}H_{19}O_6$ $[M + H]^+$ 451.1176, found 451.1179.

3-(4-Hydroxy-6-methyl-2-oxo-2H-chromen-3-yl)-2-(4-methoxyphenyl)-8-methyl-4H-furo[3,2-c]chromen-4-one (5q). White solid, 52% yield, mp: >300 ^oC; FTIR (neat) *v*: 3416, 2954, 1735, 1671, 1577, 1510, 1248, 1163 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 11.82 (s, 1H), 7.95 (s, 1H), 7.78 (d, *J* = 1.2 Hz, 1H), 7.74 – 7.69 (m, 2H), 7.55 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.06 – 7.02 (m, 2H), 3.78 (s, 3H), 2.47 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 163.1, 161.5, 160.4, 157.2, 155.8, 153.5, 151.5, 150.6, 135.0, 134.3, 134.1, 132.4, 127.4 (2C), 124.0, 122.0, 120.8, 117.2, 116.7, 116.0, 115.1 (2C), 113.0, 112.3, 108.5, 95.8, 55.7, 20.88, 20.87. HRMS (ESI): m/z calcd for $C_{29}H_{21}O_7$ $[M + H]^+$ 481.1282, found 481.1279.

Conflicts of interest

There are no conflicts to declare

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