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One-Pot Synthesis of B-Ring *ortho*-Hydroxylated Sappanin-type Homoisoflavonoids

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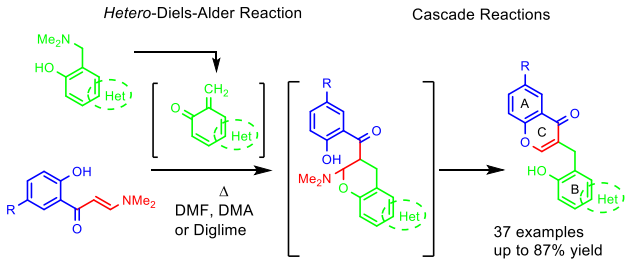
Supporting Information Placeholder

ABSTRACT: A reliable method for the synthesis of B-ring hydroxylated homoisoflavonoids and 3-hetarylmethyl chromones has been developed. The method involves an initial *oxa*-Diels–Alder reaction of *ortho*-quinone methides generated from aryl/hetaryl-substituted *ortho*-(*N,N*-dimethylaminomethyl)phenols with (2*E*)-3-(*N,N*-dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-ones and the subsequent cascade of reactions. This synthetic strategy avoids conventional multistep protocols and does not require the protection of hydroxyl groups, thus allowing the facile synthesis of a library of various aromatic and heterocyclic analogs of naturally occurring homoisoflavonoids.



INTRODUCTION

The homoisoflavonoids are a small but diverse family of natural compounds that derive biosynthetically from 2'-methoxychalcones and usually classified into five main structural subtypes including sappanin-, scillascillin-, brazilin-, caesalpin-, and protosappanin-types.[1] Among them, the sappanin-type homoisoflavonoids (Fig. 1), that contain chromanone or chromone ring with 3-benzyl substituents, are the most diverse and well-studied ones. They are often used in biosynthetic pathways as precursors for the synthesis of other types.[2] Like other flavonoid counterparts, naturally occurring homoisoflavonoids typically bear hydroxylic, methoxy, and methylenedioxy groups in rings A and B [3] and possess a broad spectrum of biological activities, ranging from anti-oxidant, anti-microbial, anti-diabetic and immunomodulatory effects, to specific effects as protein kinase inhibitors. Therefore, the development of innovative and efficient approaches to the natural/semisynthetic homoisoflavonoids continues to be an active synthetic direction for the discovery of novel analogs with unique bioactivities.

Methodology in the literature for the synthesis of homoisoflavonoids follows patterns seen in the synthesis of the corresponding isoflavones from 2-hydroxydeoxybenzoines by the ring-closure reactions and typically involves an application of the corresponding 1-(2-hydroxyphenyl)-3-phenylpropan-1-ones in Vilsmayer–Haak reaction,[4] Claisen condensation,[5] *ortho*-ether condensation[6] reactions, and in cyclization with anhydrides[7]. Alternatively, 9-hydroxyderivatives have been synthesized by Baylis–Hillman reaction of chromones with aromatic aldehydes.[8] These approaches include multiple steps and require the introduction of B-ring fragment at the initial stage of the synthesis 1-(2-hydroxyphenyl)-3-(aryl/hetaryl)propan-1-ones, and therefore, they are often inconvenient for the synthesis of B-ring hydroxylated homoisoflavonoids and their hydroxylated heteroaryl analogs.

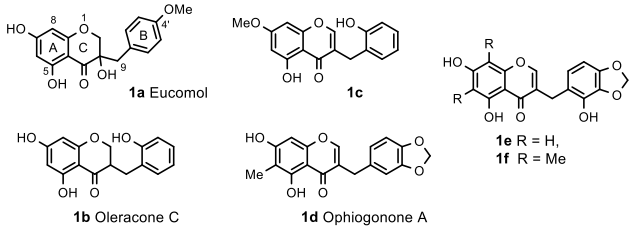
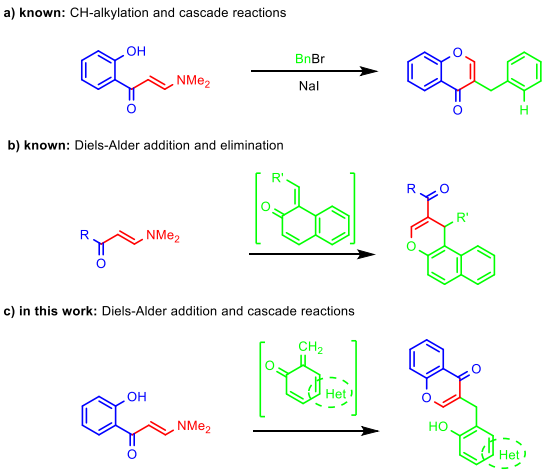


Figure 1. Chemical structures of some sappanin-type natural homoisoflavonoids

On the other hand, 2'-hydroxy derivatives of (*E*)-1-phenyl-3-(*N,N*-dimethylamino)prop-2-en-1-ones **2** (commonly

named as enaminones) have proven to be efficient substrates for constructing chromone frameworks. Thus, treatment of enaminones with acids is a common pathway to the formation of 2,3-unsubstituted naphtopyrones and chromones.[9] Oxidative reactions of enaminones with halogens or *tert*-butyl hypochlorite[10] are simple methods for the synthesis of 3-halogenochromones[11] which in turn are useful compounds for the synthesis of isoflavones by Suzuki coupling reactions. A related oxidative reaction for the synthesis of 3-thiocyanatochromones from enaminones with KSCN in the presence of $K_2S_2O_8$ was also reported.[12] At last, alkylation/acylation of the enamine fragment and subsequent cyclization reactions are effective methods for the preparation of alkylchromones[13] and 3-acylchromones.[14] As example, the alkylation of 2-hydroxylated enaminones with benzyl bromides led to the formation of homoisoflavones[13a,15] (Scheme 1a) and recently reported interaction of β-naphthol Mannich bases with enaminoketones provided access to the synthesis of 3-acyl-4*H*-chromenes (Scheme 1b).[16] The latter transformation was achieved by inverse-electron-demand *hetero*-Diels–Alder reaction of enaminones with *ortho*-quinone methides (*o*-QMs), which have found to be useful in the syntheses of oxygen-containing heterocycles.[17,18]

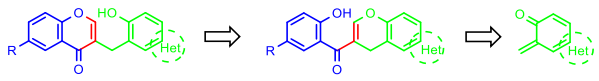
Scheme 1. Application of enaminones in the synthesis of chromones



Taking into account this information and our previous report,[19] we anticipated that utilizing of *ortho*-hydroxyphenyl enaminones in Diels–Alder addition with thermally generated *o*-QMs from Mannich bases would provide adducts similar to the ones shown in Scheme 1b. However, these adducts due to the presence of *ortho*-hydroxyl could undergo the subsequent intramolecular rearrangement involving nucleophilic attack of the hydroxylic group at position 2 of 4*H*-chromene ring that resulted in the formation of the 3-(2-hydroxybenzyl)-4*H*-chromen-4-one skeleton (Scheme 1c). The retrosynthetic pathway of such homoisoflavonoids synthesis is presented in Scheme 2.

Herein, in continuation of our research program aimed at the development of novel flavonoids for the search of pharmaceutical agents, we report a one-pot approach for the synthesis of hydroxylated homoisoflavonoids. This approach involves initial inverse-electron-demand Diels-Alder reaction of thermally generated from phenolic Mannich bases *ortho*-quinone methides with (2*E*)-3-(*N*,*N*-dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-ones and the subsequent cascading reactions.

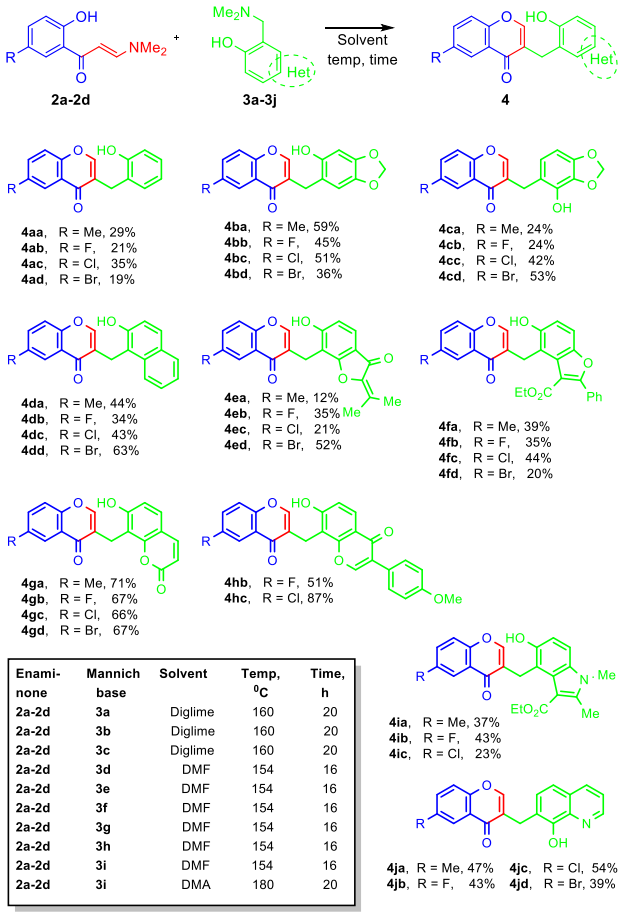
Scheme 2. Retrosynthetic Pathway



RESULTS AND DISCUSSION

To optimize the reaction conditions, we investigated the reaction between (*E*)-3-(dimethylamino)-1-(2-hydroxy-5-methylphenyl)prop-2-en-1-one (**2a**) and 1-((dimethylamino)methyl)naphthalen-2-ol (**3d**). A screen of various solvents revealed that DMF was the best choice for this transformation to afford the desired product **4da** in 44% yield. The reaction could also proceed in other solvents, such as diglyme and dimethylacetamide (DMA), but the yields of **4da** were lower (data not shown). All attempts to improve the yield by extending the reaction time were unsuccessful.

Table 1. Substrate Scope of Enaminoketones 2 and Mannich Bases 3 [a]



Enaminone	Mannich base	Solvent	Temp, °C	Time, h
2a-2d	3a	Diglime	160	20
2a-2d	3b	Diglime	160	20
2a-2d	3c	Diglime	160	20
2a-2d	3d	DMF	154	16
2a-2d	3e	DMF	154	16
2a-2d	3f	DMF	154	16
2a-2d	3g	DMF	154	16
2a-2d	3h	DMF	154	16
2a-2d	3i	DMF	154	16
2a-2d	3i	DMA	180	20

[a] Isolated yield

To define the scope of this approach to homoisoflavonoids **4**, we studied the reactions of methyl- and halogen-substituted (*E*)-1-(2-hydroxyphenyl)-3-(*N*,*N*-dimethylamino)prop-2-en-1-ones **2a-2d** with *ortho*-*N*,*N*-dimethylaminomethyl derivatives of various carbocyclic/heterocyclic phenols **3a-3j** (Table 1).

In all cases, the *oxa*-Diels-Alder addition of the ortho-quinone methides, generated from **3a-j**, with the enaminones **2a-d** in diglyme, DMF or DMA at temperatures more than 150°C led to the formation of the homoisoflavonoids **4** in yields ranging from moderate to high (Table 1). Thus, the reaction of enaminones **2a-2d** with phenolic Mannich bases **3a-3c** provided better yields of the corresponding products **4** by refluxing in diglyme, whereas the reaction of the same enaminones **2a-2d** with bases **3d-3i** gave higher yields of **4** by refluxing in DMF or DMA (in case of the reaction with compound **3j**).

The substituents on the aryl ring of the enaminoketones **2** had little influence on the reaction outcome. The reaction mainly depended on nature of Mannich bases. For example, the reaction of **2a-2d** with the Mannich bases that contained condensed aromatic rings such as **3d**, **3g**, **3h**, and **3j** furnished higher yields of corresponding **4** compared to their reaction with Mannich base **3a** (Table 1). Such results could be rationalized by their propensity to the charges delocalization effects that contributed to the stabilization of *o*-QM intermediates.

The molecular structure of products **4** was unambiguously confirmed by 2D NMR techniques. Thus, the presence of HMBC correlations between H-2, H-5, H-7 and C-8a in compound **4ga** confirmed the formation of chromone ring (Fig. 2, see Supporting Information for spectra and detailed information).

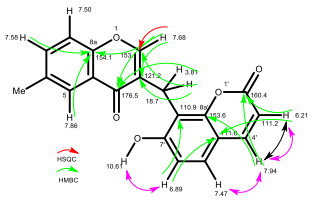


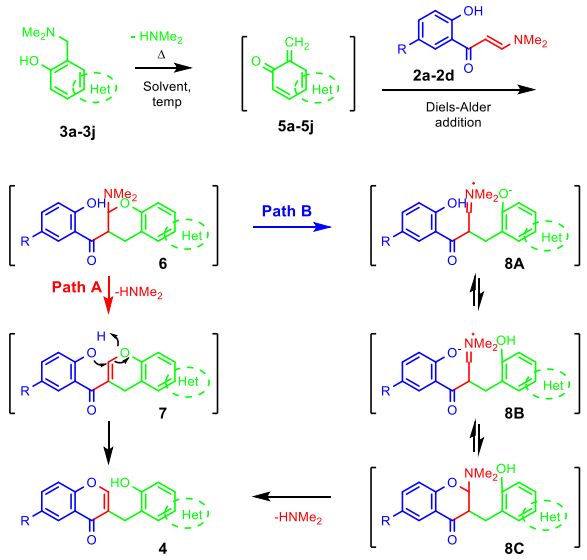
Figure 2. Principal 2D NMR correlations for 4ga

In our opinion, the initial steps of such transformation proceeded in the same manner as it was described for the aforementioned reaction of non-hydroxylated enaminoketones with phenol or naphtol Mannich bases.[16] Obviously, that initial thermal generation of o-QMs **5** from carbocyclic or heterocyclic phenolic Mannich bases **3** and their following inverse electron-demand *oxa*-Diels-Alder addition to the hydroxylated enaminoketones **2** furnished hemi-aminal adducts **6** (Scheme 3).

Such unstable Diels–Alder adducts **6** underwent further deamination and afforded 4*H*-benzopyrane derivatives **7**, which underwent a base-catalyzed intramolecular nucleophilic attack of the hydroxylic group at position 2 of *4*H-chromene ring and provided the desired products **4**. (Scheme 3, Path A) We also can consider an alternate rearrangement of adducts **6** to intermediates **8A-8C** and their further deamination to derivatives **4** (Scheme 3, Path B). The preferable formation of compounds **4** from intermediates **7** can be explained by the thermodynamic control. The formation of 10π electron aromatic system for **4** is more energetically favorable than the 6π+2π electron non-conjugated system for compounds **7**. It should be also noted, that in all cases we only isolated compounds **4** as the final products and did not detect the formation of compounds **6-8**.

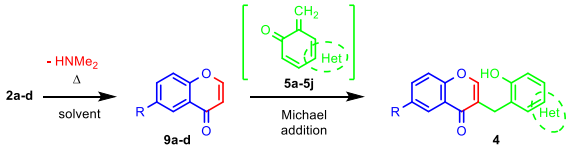
Taking into account Michael addition of *o*-QMs to 2-aminochromones reported earlier,[20] we could not ignore the possible Michael addition reaction of *o*-QMs **5** with chromones **9** as a plausible pathway in the formation of homoisoflavonoids **4** (Scheme 4).

Scheme 3. Proposed Reaction Mechanism



It is important to notice that during the conditions optimizing studies of the reaction of *ortho*-hydroxyphenyl enaminones **2** with Mannich bases we indeed isolated traces of chromones **9a-d** in those cases when the reaction was not completed at low temperatures. In order to determine a contribution of such mechanism to the synthesis of **4**, we performed additional studies and carried out the reactions of enaminone **2a** with **3a** or **3d** (Table 2) and Michael addition reactions of chromone **9a** with **3a** or **3d** (Table 3) at different conditions during 4 h. According to our observations, this time was usually insufficient for full conversion of enaminones **2** or chromones **9** to homoisoflavonoids **4**, therefore, we expected to isolate intermediates of the reaction of enaminone **2a** with Mannich bases **3a** or **3d**.

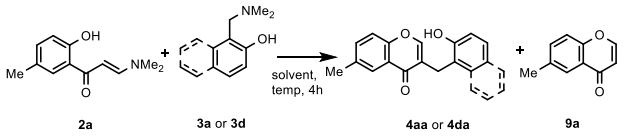
Scheme 4. Alternate Reaction Mechanism *via* Michael Addition of *o*-QMs 5 to Chromones 9



Thus, the reaction of enaminone **2a** with 2-(*N*,*N*-dimethylaminomethyl)phenol (**3a**) at temperatures less than 120°C, led to the increased amounts of **9a** relative to the target homoisoflavonoids **4aa** (Table 2, entries 1–3). However, the direct addition of **5a** generated from **3a** to chromone **9a** at the same conditions did not occur (Table 3, entries 1–3). Moreover, the reaction of enaminone **2a** with **3a** at temperatures 154-160 ºC gave much higher yields of **4aa** (Table 2, entries 4,5) compared to the reaction of chromone **9a** with **3a** that resulted in very low yield of **4aa** (Table 3, entries 4,5). The similar results were observed for the reactions of enaminone **2a** or chromone **9a** with 1-(*N*,*N*-dimethylaminomethyl)-2-naphthol (**3d**) that forms more

stable *o*-QM intermediate **5d**. In all cases, the direct addition of *o*-QM **5d** generated from **3d** to chromone **9a** provided much lower yields of the desired homoisoflavonoid **4da** (Table 3, entries 6–10) than the corresponding reactions of enaminone **2a** with **3d** (Table 2, entries 6–10).

Table 2. Screening Conditions for the Reaction of Enaminone 2a with Mannich Bases 3a, 3d [a]

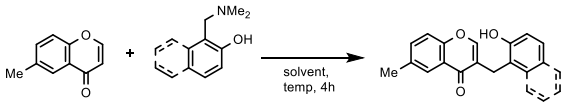


2a **3a** or **3d** **4aa** or **4da** **9a**

entry	solvent	temp (^{0}C)	Mannich base	**4aa** or **4da** yield (%)[b]	**9a** yield (%)[b]
1	$MeOCH_2CH_2OMe$	80	**3a**	-	32
2	1,4-Dioxane	100	**3a**	5.6	78.6
3	$EtOCH_2CH_2OEt$	121	**3a**	10.1	86.1
4	DMF	154	**3a**	75.9	24.1
5	Diglyme	160	**3a**	43.6	56.4
6	$MeOCH_2CH_2OMe$	80	**3d**	81.5	-
7	1,4-Dioxane	100	**3d**	87.5	1.9
8	$EtOCH_2CH_2OEt$	121	**3d**	72.5	-
9	DMF	154	**3d**	90.8	-
10	Diglyme	160	**3d**	95	-

[a] All reactions were carried out using **2a** (1 mmol), **3a** or **3d** (1 mmol), and corresponding solvent (5mL) for 4 h at the indicated temperatures. [b] Yields were determined by the LC-MS

Table 3. Screening Conditions for Michael Addition of 9a with Mannich Bases 3a, 3d[a]



9a **3a** or **3d** **4aa** or **4da**

entry	solvent	temp (^{0}C)	Mannich base	product	yield (%)[b]
1	$MeOCH_2CH_2OMe$	80	**3a**	**4aa**	-
2	1,4-Dioxane	100	**3a**	**4aa**	-
3	$EtOCH_2CH_2OEt$	121	**3a**	**4aa**	-
4	DMF	154	**3a**	**4aa**	7.6
5	Diglime	160	**3a**	**4aa**	2.8
6	$MeOCH_2CH_2OMe$	80	**3d**	**4da**	6.4
7	1,4-Dioxane	100	**3d**	**4da**	14.2
8	$EtOCH_2CH_2OEt$	121	**3d**	**4da**	39.7
9	DMF	154	**3d**	**4da**	70.0
10	Diglime	160	**3d**	**4da**	30.9

[a] All reactions were carried out using **9a** (1 mmol), either **3a** or **3d** (1 mmol), and corresponding solvent (5 mL) for 4 h at the indicated temperatures.[b] Yields were determined by the LC-MS.

Such observations suggested that 6-methyl-*4*H-chromen-4-one (**9a**) was not a dominant player in the reactions of enaminones **2** with *o*-QMs **5a** and **5d** generated from the corresponding Mannich bases **3a** and **3d**. Otherwise, the yields of **4aa** or **4ad** obtained in the reactions of enaminone **2a** or chromone **9a** with **3a** and **3d** under the same reaction conditions would be comparable. These results indicate that, although possible, the alternative conversion of enaminone **2a** to chromone **9a** and its further Michael addition to *o*-QMs (path **2a→9a→4aa**, Scheme 4) cannot be the primary synthetic route to homoisoflavonoid **4aa**. With respect to the aforementioned studies, we conclude that the most appropriate pathway is based on *oxa*-Diels-Alder addition of thermally generated o-QMs **5** to enaminones **2** with formation of hemiaminals **6**, followed by their deamination to 4*H*-chromene derivatives **7**, and their subsequent intramolecular base-catalyzed rearrangement to the target compounds **4.** Despite the moderate yields of the synthesized homoflavonoids, the simplicity, accessibility, and available variety of starting reagents make this method an attractive choice for the synthesis of various aromatic and heterocyclic analogs of naturally occurring homoisoflavonoids that would be difficult or impossible to synthesize by other methods.

In conclusion, we have developed an efficient one-pot method for the synthesis of B-ring hydroxylated homoisoflavonoids that does not require the protection of the phenolic groups. The reaction provides a novel preparative route for the synthesis of sappanin-type flavonoids and their heteroaryl analogs in moderate yields. Further practical scope and potential application of these promising homoisoflavonoids are currently under investigation in our laboratory.

EXPERIMENTAL SECTION

Chemicals were purchased from Sigma Aldrich or Fisher Scientific or were synthesized according to literature procedures. Solvents were used from commercial vendors without further purification unless otherwise noted. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded on a Bruker 500 (500 MHz / 125 MHz) or Bruker 400 (400 MHz / 100 MHz) spectrometers in $CDCl_3$ or DMSO-d_6. ^{19}F NMR spectra were recorded on a Bruker 400 (376 MHz) relative to $CFCl_3$. Melting points were determined in open capillarity tubes using a Buchi B-535 apparatus and were uncorrected. Mass spectra were obtained with an Agilent 1100 spectrometer under chemical ionization conditions. Elemental analysis was performed on a varioMICROcube automated CHNS-analyzer. Column chromatography was performed using Macherey-Nagel Silica 60, 0.04-0.063 mm silica gel.

The enaminones **2a-2d**[21] and Mannich adducts **3a**,[22] **3d**,[23] **3f**,[24] **3h**,[25] **3i**,[26] and **3j**[27] were prepared as previously described.

6-[(Dimethylamino)methyl]-1,3-benzodioxol-5-ol (3b). A solution of sesamol (966 mg, 7 mmol), paraformaldehyde (210 mg, 7 mmol), and dimethylamine (0.840 mL, 40% aqueous solution, 7.4 mmol) in ethanol (10 mL) was stirred at room temperature for 24 h. The solvent was evaporated *in vacuo* and residue was purified by recrystallization from isopropanol-hexanes mixture (1:5). Yield 1.110 g (82%). Beige solid, mp 87 - 89 ^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.26 (s, 6H), 3.47 (s, 2H), 5.81 (s, 2H), 6.37 (s, 1H), 6.40 (s, 1H), 10.81 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 44.2, 62.6, 98.4, 100.7, 107.8, 113.0, 139.9, 147.5, 153.1 ppm. MS (APCI) *m/z*: 196.0 $[M+H]^+$. Anal. Calcd (%) for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.18. Found (%): C, 61.38; H, 6.89; N, 6.92.

5-[(Dimethylamino)methyl]-1,3-benzodioxol-4-ol (3c) was synthesized by the similar procedure described for **3b** from 4-hydroxy-1,3-benzodioxol. Yield 675 mg (49%). Beige solid, ^{1}H mp 125 - 127 ^{0}C. NMR (400 MHz, $CDCl_3$) δ: 2.31 (s, 6H), 3.61 (s, 2H), 5.93 (s, 2H), 6.30 (d, *J* = 7.8 Hz, 1H), 6.43 (d, *J* = 7.8 Hz, 1H), 10.55 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 44.4, 62.8, 99.5, 101.3, 117.6, 120.7, 134.2, 142.5, 148.5 ppm. MS (APCI) *m/z*: 196.0 $[M+H]^+$. Anal. Calcd (%) for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.18. Found (%): C, 61.77; H, 6.99; N, 7.24.

7-[(Dimethylamino)methyl]-6-hydroxy-2-(1-methylethylidene)-1-benzofuran-3(2*H*)-one (3e). To a stirred suspension of 6-hydroxy-2-(1-methylethylidene)-1-benzofuran-3(2*H*)-one (950 mg, 5 mmol) in 10 mL of isopropanol were added 0.816 mL (6 mmol, 1.2 eq) of bis(N,N-dimethylamino)methane at 70ºC. After stirring at 80ºC for 2 h the mixture was cooled, triturated with hexane and formed precipitate collected by filtration to afford **3e** that was re-crystalized from isopropanol-hexane. Yield 888 mg (72%). Yellow solid, mp 153 - 155 ^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.05 (s, 3H), 2.32 (s, 3H), 2.41 (s, 6H), 3.81 (s, 2H), 6.56 (d, *J* = 8.5 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 10.65 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 17.2, 20.0, 44.6, 54.8, 104.0, 112.7, 115.5, 124.6, 129.2, 145.7, 163.9, 166.9, 182.5 ppm. MS (APCI) *m/z*: 248.0 $[M+H]^+$. Anal. Calcd (%) for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found (%): C, 68.21; H, 6.78; N, 5.49.

8-Dimethylaminomethyl-7-hydroxy-chromen-2-one (3g) was synthesized similar to compound **3e**. Yield 613 mg (56%). Beige solid, mp 117 - 119 ^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.40 (s, 6H), 4.01 (s, 2H), 6.17 (d, *J*=9.4 Hz, 1H), 6.75 (d, *J*=8.5 Hz, 1H), 7.27 (d, *J*=8.5 Hz, 1H), 7.61 (d, *J*=9.4 Hz, 1H), 12.37 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 44.5, 55.0, 108.2, 111.1, 111.3, 113.8, 128.0, 144.3, 153.0, 161.3, 163.3 ppm. MS (APCI) *m/z*: 220.0 $[M+H]^+$. Anal. Calcd (%) for $C_{14}H_{17}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found (%): C, 65.93; H, 7.06; N, 5.24.

General Procedure for the synthesis of Homoisoflavonoids 4. A mixture of enaminone **2a-d** (2 mmol) and corresponding Mannich base **3a-j** (2.4 mmol) in appropriate solvent (10 mL) was stirred at reflux for the indicated period of time (Tab.1). The reaction mixture was cooled, solvent was evaporated, and formed residue was washed with water and purified by recrystallization from EtOH or column chromatography.

3-(2-Hydroxybenzyl)-6-methyl-4*H*-chromen-4-one (4aa). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 154 mg (29%). Off-white solid, mp 175 - 177 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.38 (s, 3H), 3.64 (s, 2H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 7.02 (t, *J* = 7.7 Hz, 1H), 7.05 – 7.14 (m, 1H), 7.44 (d, *J* = 8.6 Hz, 1H), 7.53 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.82 (d, *J* = 2.2 Hz, 1H), 8.04 (s, 1H), 9.48 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 20.4, 25.4, 115.1, 118.1, 118.9, 122.4, 122.8, 124.2, 125.1, 127.4, 130.0, 134.7, 135.0, 153.9, 154.2, 155.1, 176.5 ppm. MS (APCI) *m/z*: 267.2 $[M+H]^+$. Anal. Calcd (%) for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found (%): C, 76.84; H, 5.11.

6-Fluoro-3-(2-hydroxybenzyl)-4*H*-chromen-4-one (4ab). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 114 mg (21%). Off-white solid, mp 194 - 196 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.63 (s, 2H), 6.69 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 7.9 Hz, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.51 – 7.73 (m, 3H), 8.09 (s, 1H), 9.51 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 25.3, 109.4 (d, J_{C-F} = 23.5 Hz), 115.1, 118.9, 121.1 (d, J_{C-F} = 8.3 Hz), 122.0, 122.0 (d, J_{C-F} = 25.5 Hz), 124.2 (d, J_{C-F} = 7.1 Hz), 124.8, 127.4, 130.1, 152.3, 154.4, 155.2, 158.8 (d, J_{C-F} = 244.1 Hz), 175.8 ppm (d, *J* = 2.2 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ: -116.1 ppm. MS (APCI) *m/z*: 271.0 $[M+H]^+$. Anal. Calcd (%) for $C_{16}H_{11}FO_3$: C, 71.11; H, 4.10. Found (%): C, 70.93; H, 4.35.

6-Chloro-3-(2-hydroxybenzyl)-4*H*-chromen-4-one (4ac). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 201 mg (35%). Off-white solid, mp 197 - 199 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.64 (s, 2H), 6.69 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 7.02 (t, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 9.0 Hz, 1H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.93 (s, 1H), 8.08 (s, 1H), 9.48 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 25.3, 115.1, 118.9, 120.8, 122.7, 124.0, 124.1, 124.6, 127.4, 129.7, 130.0, 133.8, 154.4, 154.4, 155.2, 175.3 ppm. MS (APCI) *m/z*: 287.0 $[M+H]^+$. Anal. Calcd (%) for $C_{16}H_{11}ClO_3$: C, 67.03; H, 3.87. Found (%): C, 67.31; H, 4.12.

6-Bromo-3-(2-hydroxybenzyl)-4*H*-chromen-4-one (4ad). Purified by column chromatography using 1:100 methanol-dichloromethane. 126 mg (19%). Off-white solid, mp 171 - 173 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.63 (s, 2H), 6.69 (t, *J* = 7.4 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 7.02 (t, *J* = 7.7 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.85 – 7.94 (m, 1H), 8.04 – 8.16 (m, 2H), 9.48 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 25.3, 115.0, 117.6, 118.9, 121.1, 122.8, 124.6, 124.6, 127.1, 127.4, 130.0, 136.5, 154.4, 154.8, 155.1, 175.2 ppm. MS (APCI) *m/z*: 331.0 $[M+H]^+$. Anal. Calcd (%) for $C_{16}H_{11}BrO_3$: C, 58.03; H, 3.35. Found (%): C, 57.88; H, 3.42.

3-[(6-Hydroxy-1,3-benzodioxol-5-yl)methyl]-6-methyl-4*H*-chromen-4-one (4ba). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 366 mg (59%). Pale yellow solid, mp 239 - 241 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.38 (s, 3H), 3.54 (s, 2H), 5.85 (s, 2H), 6.45 (s, 1H), 6.71 (s, 1H), 7.45 (d, *J* = 8.6 Hz, 1H), 7.54 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.82 (d, *J* = 2.2 Hz, 1H), 8.04 (s, 1H), 9.23 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 20.4, 25.4, 97.8, 100.5, 109.6, 116.5, 118.1, 122.8, 124.2, 134.7, 135.0, 139.6, 145.9, 149.5, 153.9, 154.2, 176.7 ppm. MS (APCI) *m/z*: 311.0 $[M+H]^+$. Anal. Calcd (%) for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55. Found (%): C, 69.49; H, 4.69.

6-Fluoro-3-[(6-hydroxy-1,3-benzodioxol-5-yl)methyl]-4*H*-chromen-4-one (4bb). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 283 mg (45%). Pale yellow solid, mp 229 - 231 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.54 (s, 2H), 5.84 (s, 2H), 6.44 (d, *J* = 1.9 Hz, 1H), 6.70 (d, *J* = 1.9 Hz, 1H), 7.46 – 7.76 (m, 3H), 8.07 (s, 1H), 9.22 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 25.4, 97.7, 100.5, 109.4 (d, J_{C-F} = 23.5 Hz), 109.7, 116.2, 121.1 (d, J_{C-F} = 8.3 Hz), 122.1 (d, J_{C-F} = 25.5 Hz), 122.3, 124.2 (d, J_{C-F} = 7.1 Hz), 139.6, 146.0, 149.6, 152.4, 154.3, 158.8 (d, J_{C-F} = 244.1 Hz), 176.0 ppm (d, *J* = 2.3 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ: -116.1 ppm. MS (APCI) *m/z*: 315.0 $[M+H]^+$. Anal. Calcd (%) for $C_{17}H_{11}FO_5$: C, 64.97; H, 3.53. Found (%): C, 65.11; H, 3.27.

6-Chloro-3-[(6-hydroxy-1,3-benzodioxol-5-yl)methyl]-4*H*-chromen-4-one (4bc). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 337 mg (51%). Pale yellow solid, mp 208 - 210 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.55 (s, 2H), 5.84 (s, 2H), 6.44 (s, 1H), 6.70 (s, 1H), 7.67 (d, J = 9.0 Hz, 1H), 7.81 (d, J = 9.0 Hz, 1H), 7.98 (s, 1H), 8.09 (s, 1H), 9.15 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 25.3, 97.7, 100.5, 109.7, 116.1, 120.7, 123.0, 123.9, 124.1, 129.7, 133.7, 139.6, 146.0, 149.6, 154.2, 154.4, 175.5 ppm. MS (APCI) *m/z*: 331.0 [M+H]$^+$. Anal. Calcd (%) for $C_{17}H_{11}ClO_5$: C, 61.74; H, 3.35. Found (%): C, 61.97; H, 3.48.

6-Bromo-3-[(6-hydroxy-1,3-benzodioxol-5-yl)methyl]-4*H*-chromen-4-one (4bd). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 270 mg (36%). Pale yellow solid, mp 224 - 226 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.55 (s, 2H), 5.84 (s, 2H), 6.44 (s, 1H), 6.70 (s, 1H), 7.58 (d, J = 8.9 Hz, 1H), 77.84 – 7.94 (m, 1H), 8.03 – 8.17 (m, 2H), 9.14 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 25.3, 97.7, 100.5, 109.7, 116.1, 117.6, 121.1, 123.0, 124.6, 127.1, 136.5, 139.5, 145.9, 149.6, 154.3, 154.8, 175.4 ppm. MS (APCI) *m/z*: 375.0 [M+H]$^+$. Anal. Calcd (%) for $C_{17}H_{11}BrO_5$: C, 54.42; H, 2.96. Found (%): C, 54.18; H, 3.17.

3-[(4-Hydroxy-1,3-benzodioxol-5-yl)methyl]-6-methyl-4*H*-chromen-4-one (4ca). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 149 mg (24%). Pale yellow solid, mp 198 - 200 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.39 (s, 3H), 3.54 (s, 2H), 5.84 (s, 2H), 6.45 (s, 1H), 6.71 (s, 1H), 7.46 (d, J = 8.6 Hz, 1H), 7.55 (dd, J = 8.6, J = 2.2 Hz, 1H), 7.82 (d, J = 2.2 Hz, 1H), 8.04 (s, 1H), 9.22 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 20.5, 25.1, 100.1, 100.6, 118.1, 121.5, 122.3, 122.7, 122.9, 124.2, 134.8, 134.9, 135.2, 138.8, 146.9, 154.1, 154.2, 176.7 ppm. MS (APCI) *m/z*: 311.0 [M+H]$^+$. Anal. Calcd (%) for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55. Found (%): C, 69.88; H, 4.78.

6-Fluoro-3-[(4-hydroxy-1,3-benzodioxol-5-yl)methyl]-4*H*-chromen-4-one (4cb). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 151 mg (24%). Pale yellow solid, mp 236 - 237 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.61 (s, 2H), 5.93 (s, 2H), 6.36 (d, J=8.0, 1H), 6.62 (d, J=8.0, 1H), 7.57 – 7.78 (m, 3H), 8.12 (s, 1H), 9.53 (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ = 25.0, 100.0, 100.6, 109.5 (d, $J_{C\text{-}F}$ = 23.5 Hz), 121.2, 121.2 (d, $J_{C\text{-}F}$ = 8.5 Hz), 122.3 (d, $J_{C\text{-}F}$ = 25.6 Hz), 122.4, 124.1 (d, $J_{C\text{-}F}$ = 7.1 Hz), 134.7, 138.8, 146.9, 152.4, 154.5, 158.9(d, $J_{C\text{-}F}$ = 244.0 Hz), 176.0 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ: -116.0 ppm. MS (APCI) *m/z*: 315.0 [M+H]$^+$. Anal. Calcd (%) for $C_{17}H_{11}FO_5$: C, 64.97; H, 3.53. Found (%): C, 64.86; H, 3.78.

6-Chloro-3-[(4-hydroxy-1,3-benzodioxol-5-yl)methyl]-4*H*-chromen-4-one (4cc). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 278 mg (42%). Pale yellow solid, mp 230 - 232 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.60 (s, 2H), 5.94 (s, 2H), 6.36 (d, J = 8.0 Hz, 1H), 6.62 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.9 Hz, 1H), 7.81 (d, J = 8.9 Hz, 1H), 7.97 (s, 1H), 8.11 (s, 1H), 9.53 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 25.0, 100.0, 100.6, 120.9, 121.1, 122.4, 123.1, 124.0, 124.1, 129.7, 133.9, 134.7, 138.8, 146.9, 154.4, 175.5 ppm. MS (APCI) *m/z*: 331.0 [M+H]$^+$. Anal. Calcd (%) for $C_{17}H_{11}ClO_5$: C, 61.74; H, 3.35. Found (%): C, 61.52; H, 3.09.

6-Bromo-3-[(4-hydroxy-1,3-benzodioxol-5-yl)methyl]-4*H*-chromen-4-one (4cd). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 398 mg (53%). Pale yellow solid, mp 208 - 210 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.59 (s, 2H), 5.94 (s, 2H), 6.35 (d, J = 8.0 Hz, 1H), 6.62 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 8.9 Hz, 1H), 7.87 (dd, J = 8.9, 2.6 Hz, 1H), 8.02 – 8.13 (m, 2H), 9.55 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 25.1, 100.0, 100.6, 117.7, 121.0, 121.1, 122.4, 123.2, 124.5, 127.1, 134.7, 136.6, 138.8, 146.9, 154.4, 154.8, 175.4 ppm. MS (APCI) *m/z*: 375.0 [M+H]$^+$. Anal. Calcd (%) for $C_{17}H_{11}BrO_5$: C, 54.42; H, 2.96. Found (%): C, 54.70; H, 3.22.

3-[(2-Hydroxy-1-naphthyl)methyl]-6-methyl-4*H*-chromen-4-one (4da). Yield 278 mg (44%). Pale yellow solid, mp 193 - 195 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.38 (s, 3H), 4.12 (s, 2H), 7.16 – 7.30 (m, 2H), 7.31 – 7.43 (m, 2H), 7.45 – 7.56 (m, 2H), 7.72 (d, J = 8.8 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.84 (d, J = 8.5 Hz, 1H), 7.90 (s, 1H), 9.93 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 20.1, 20.4, 115.5, 118.0, 118.3, 122.4, 122.5, 122.7, 124.3, 126.4, 128.3, 128.3, 128.4, 133.1, 134.8, 135.0, 153.0, 153.4, 154.0, 176.7 ppm. MS (APCI) *m/z*: 317.3 [M+H]$^+$. Anal. Calcd (%) for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found (%): C, 79.45; H, 5.23.

6-Fluoro-3-[(2-hydroxy-1-naphthyl)methyl]-4*H*-chromen-4-one (4db). Yield 218 mg (34%). Pale yellow solid, mp 202 - 204 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 4.12 (s, 2H), 7.20 – 7.29 (m, 2H,), 7.34 – 7.43 (m, 1H), 7.55 (s, 1H), 7.56 – 7.68 (m, 2H), 7.72 (d, J = 8.9 Hz, 1H), 7.75 – 7.81 (m, 1H), 7.83 (d, J = 8.6 Hz, 1H), 9.91 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 20.0, 109.5 (d, $J_{C\text{-}F}$ = 23.5 Hz), 115.2, 118.3, 121.1 (d, $J_{C\text{-}F}$ = 8.4 Hz), 122.1, 122.3, 122.5, 122.7, 123.9 (d, $J_{C\text{-}F}$ = 7.2 Hz), 126.5, 128.3, 128.3, 128.4, 133.1, 152.2, 153.1, 153.8, 158.8 (d, $J_{C\text{-}F}$ = 244.1 Hz), 176.1 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ: -115.9 ppm. MS (APCI) *m/z*: 321.0 [M+H]$^+$. Anal. Calcd (%) for $C_{20}H_{13}FO_3$: C, 74.99; H, 4.09. Found (%): C, 75.26; H, 4.30.

6-Chloro-3-[(2-hydroxy-1-naphthyl)methyl]-4*H*-chromen-4-one (4dc). Yield 290 mg (43%). Pale yellow solid, mp 211 - 213 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 4.11 (s, 2H), 7.17 – 7.29 (m, 2H), 7.38 (t, J = 7.7 Hz, 1H), 7.44 – 7.59 (m, 2H), 7.66 – 7.85 (m, 4H), 8.02 (s, 1H), 9.90 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 20.0, 115.0, 118.2, 120.7, 122.4, 122.7, 123.0, 123.9, 124.0, 126.5, 128.2, 128.4, 129.7, 133.1, 133.8, 153.1, 153.8, 154.3, 175.6 ppm. MS (APCI) *m/z*: 337.0 [M+H]$^+$. Anal. Calcd (%) for $C_{20}H_{13}ClO_3$: C, 71.33; H, 3.89. Found (%): C, 71.09; H, 4.07.

6-Bromo-3-[(2-hydroxy-1-naphthyl)methyl]-4*H*-chromen-4-one (4dd). Yield 480 mg (63%). Pale yellow solid, mp 210 - 212 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 4.12 (s, 2H), 7.16 – 7.31 (m, 2H), 7.38 (t, J = 7.8 Hz, 1H), 7.44 (d, J = 8.9 Hz, 1H), 7.52 (s, 1H), 7.64 – 7.90 (m, 4H), 8.15 (s, 1H), 9.89 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 20.1, 115.1, 117.6, 118.3, 120.7, 122.4, 122.7, 123.1, 124.2, 126.4, 127.1, 128.2, 128.3, 133.1, 136.4, 153.1, 153.7, 154.5, 175.4 ppm. MS (APCI) *m/z*: 381.0 [M+H]$^+$. Anal. Calcd (%) for $C_{20}H_{13}BrO_3$: C, 63.01; H, 3.44. Found (%): C, 79.48; H, 4.82.

3-{[6-Hydroxy-2-(1-methylethylidene)-3-oxo-2,3-dihydro-1-benzofuran-7-yl]methyl}-6-methyl-4*H*-

chromen-4-one (4ea). Yield 167 mg (23%). Off-white solid, mp 204 - 206 ^{0}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.87 (s, 3H), 2.19 (s, 3H), 2.37 (s, 3H), 3.76 (s, 2H), 6.73 (d, J = 8.5 Hz, 1H), 7.33 – 7.46 (m, 2H), 7.46 – 7.56 (m, 1H), 7.81 (s, 1H), 7.94 (s, 1H), 10.87 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 16.37, 18.66, 19.36, 20.41, 107.89, 111.79, 115.08, 117.96, 121.28, 122.57, 123.19, 124.18, 128.74, 134.73, 134.98, 144.74, 153.48, 154.13, 163.20, 164.38, 176.36, 181.47 ppm. MS (APCI) *m/z*: 363.1 [M+H]$^+$. Anal. Calcd (%) for $C_{22}H_{18}O_5$: C, 72.92; H, 5.01. Found (%): C, 73.20; H, 5.30.

6-Fluoro-3-{[5-hydroxy-2-(1-methylethylidene)-3-oxo-2,3-dihydro-1-benzofuran-4-yl]methyl}-4*H*-chromen-4-one (4eb). Yield 256 mg (35%). Off-white solid, mp 239 - 241 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.87 (s, 3H), 2.19 (s, 3H), 3.76 (s, 2H), 6.72 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.54 – 7.80 (m, 3H), 8.04 (s, 1H), 10.92 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 16.4, 18.6, 19.3, 107.6, 109.4 (d, $J_{C\text{-}F}$ = 23.6 Hz), 111.7, 115.1, 120.9, 121.0 (d, $J_{C\text{-}F}$ = 8.7 Hz), 122.0 (d, $J_{C\text{-}F}$ = 25.5 Hz), 123.2, 124.0 (d, $J_{C\text{-}F}$ = 7.1 Hz), 128.6, 144.8, 152.3, 153.9, 158.8 (d, $J_{C\text{-}F}$ = 244.2 Hz), 163.2, 164.4, 175.7 (d, $J_{C\text{-}F}$ = 2.2 Hz), 181.4 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ: -116.0 ppm. MS (APCI) *m/z*: 367.2 [M+H]$^+$. Anal. Calcd (%) for $C_{21}H_{15}FO_5$: C, 68.85; H, 4.13. Found (%): C, 71.36; H, 4.27.

6-Chloro-3-{[6-hydroxy-2-(1-methylethylidene)-3-oxo-2,3-dihydro-1-benzofuran-7-yl]methyl}-4*H*-chromen-4-one (4ec). Yield 161 mg (21%). Off-white solid, mp 232 - 234 ^{0}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ: δ 1.87 (s, 3H), 2.19 (s, 3H), 3.75 (s, 2H), 6.72 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 9.0 Hz, 1H), 7.76 (dd, J = 9.0, 2.9 Hz, 1H), 7.94 (s, 1H), 8.03 (s, 1H), 10.92 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 16.4, 18.6, 19.4, 107.5, 111.7, 115.0, 120.8, 121.6, 123.3, 123.9, 128.8, 129.7, 133.8, 144.7, 154.0, 154.4, 163.2, 164.3, 175.2, 181.4 ppm. MS (APCI) *m/z*: 383.1 [M+H]$^+$. Anal. Calcd (%) for $C_{21}H_{15}ClO_5$: C, 65.89; H, 3.95. Found (%): C, 66.04; H, 4.20.

6-Bromo-3-{[5-hydroxy-2-(1-methylethylidene)-3-oxo-2,3-dihydro-1-benzofuran-4-yl]methyl}-4*H*-chromen-4-one (4ed). Yield 444 mg (52%). Off-white solid, mp 278 - 280 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.90 (s, 3H), 2.22 (s, 3H), 3.80 (s, 2H), 6.73 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 8.8 Hz, 1H), 7.88 (dd, J = 8.8, J = 2.5 Hz, 1H), 8.03 (s, 1H), 8.13 (s, 1H), 10.66 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 16.4, 18.7, 19.4, 107.5, 111.7, 115.0, 117.7, 121.0, 121.7, 123.3, 124.4, 127.1, 128.8, 136.6, 144.7, 154.0, 154.8, 163.2, 164.4, 175.1, 181.5 ppm. MS (APCI) *m/z*: 427.0 [M+H]$^+$. Anal. Calcd (%) for $C_{21}H_{15}BrO_5$: C, 59.04; H, 3.54. Found (%): C, 58.86; H, 3.69.

Ethyl 5-Hydroxy-4-[(6-methyl-4-oxo-4*H*-chromen-3-yl)methyl]-2-phenyl-1-benzofuran-3-carboxylate (4fa). Yield 355 mg (39%). Off-white solid, mp 150 - 152 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 0.92 (t, J = 7.1 Hz, 3H), 2.40 (s, 3H), 3.80 – 4.10 (m, 4H), 7.03 (d, J = 8.9 Hz, 1H), 7.32 (s, 1H), 7.37 – 7.58 (m, 6H), 7.56 – 7.72 (m, 2H), 7.89 (s, 1H), 9.56 (s, 1H) ppm. ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 13.3, 20.4, 21.9, 61.3, 110.4, 110.7, 114.4, 114.5, 118.0, 122.3, 122.5, 124.2, 126.1, 126.9, 128.8, 129.0, 129.8, 134.7, 135.0, 147.6, 152.2, 152.5, 154.1, 154.8, 165.2, 176.4 ppm. MS (APCI) *m/z*: 455.2 [M+H]$^+$. Anal. Calcd (%) for $C_{28}H_{22}O_6$: C, 74.00; H, 4.88. Found (%): C, 74.27; H, 5.12.

Ethyl 4-[(6-Fluoro-4-oxo-4*H*-chromen-3-yl)methyl]-5-hydroxy-2-phenyl-1-benzofuran-3-carboxylate (4fb). Yield 321 mg (35%). Off-white solid, mp 177 - 178 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 0.93 (t, J = 7.1 Hz, 3H), 3.93 – 4.07 (m, 4H), 7.04 (d, J = 8.8 Hz, 1H), 7.38 – 7.54 (m, 5H), 7.60 – 7.68 (m, 4H), 7.76 (d, J = 8.3 Hz, 1H), 9.58 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 13.3, 21.8, 61.4, 109.4 (d, $J_{C\text{-}F}$ = 23.4 Hz), 110.5, 110.7, 114.2, 114.5, 121.0 (d, $J_{C\text{-}F}$ = 8.3 Hz), 121.9, 122.2 (d, $J_{C\text{-}F}$ = 25.4 Hz), 123.8 (d, $J_{C\text{-}F}$ = 7.2 Hz), 126.1, 127.0, 128.8, 129.0, 129.8, 147.7, 152.3, 152.3, 153.2, 155.0, 158.8 (d, $J_{C\text{-}F}$ = 244.2 Hz), 165.2, 175.8 ppm (d, $J_{C\text{-}F}$ = 2.2 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ: -116.0 ppm. MS (APCI) *m/z*: 459.0 [M+H]$^+$. Anal. Calcd (%) for $C_{27}H_{19}FO_6$: C, 70.74; H, 4.18. Found (%): C, 70.97; H, 4.32.

Ethyl 4-[(6-chloro-4-oxo-4*H*-chromen-3-yl)methyl]-5-hydroxy-2-phenyl-1-benzofuran-3-carboxylate (4fc). Yield 418 mg (44%). Off-white solid, mp 179 - 181 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 0.94 (t, J = 7.1 Hz, 3H), 3.80 – 4.23 (m, 4H), 7.03 (d, J = 8.9 Hz, 1H), 7.40 – 7.53 (m, 5H), 7.61 (d, J = 9.0 Hz, 1H), 7.64 – 7.69 (m, 2H), 7.78 (dd, J = 8.9, J = 2.7 Hz, 1H), 7.93 – 8.06 (m, 1H), 9.57 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 13.3, 21.8, 61.3, 110.5, 110.7, 114.1, 114.4, 120.8, 122.6, 123.8, 123.9, 126.1, 127.0, 128.8, 129.0, 129.7, 129.8, 133.9, 147.7, 152.2, 153.2, 154.3, 155.0, 165.2, 175.4 ppm. MS (APCI) *m/z*: 475.0 [M+H]$^+$. Anal. Calcd (%) for $C_{27}H_{19}ClO_6$: C, 68.29; H, 4.03. Found (%): C, 68.37; H, 4.29.

Ethyl 4-[(6-bromo-4-oxo-4*H*-chromen-3-yl)methyl]-5-hydroxy-2-phenyl-1-benzofuran-3-carboxylate (4fd). Yield 208 mg (20%). Off-white solid, mp 182 - 184 ^{0}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.95 (t, J = 7.1 Hz, 3H), 3.95 – 4.05 (m, 4H), 7.02 (d, J = 8.9 Hz, 1H), 7.44 (s, 1H), 7.46 – 7.54 (m, 4H), 7.58 (d, J = 9.0 Hz, 1H), 7.63 – 7.73 (m, 2H), 7.93 (dd, J = 9.0, 2.5 Hz, 1H), 8.17 (d, J = 2.5 Hz, 1H), 9.53 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 13.3, 21.8, 61.3, 110.5, 110.7, 114.0, 114.4, 117.7, 121.0, 122.7, 124.2, 126.1, 127.0, 127.1, 128.8, 129.0, 129.8, 136.6, 147.6, 152.2, 153.2, 154.7, 155.0, 165.2, 175.2 ppm. MS (APCI) *m/z*: 519.0 [M+H]$^+$. Anal. Calcd (%) for $C_{27}H_{19}BrO_6$: C, 62.44; H, 3.69. Found (%): C, 73.74; H, 4.97.

7-Hydroxy-8-[(6-methyl-4-oxo-4*H*-chromen-3-yl)methyl]-2*H*-chromen-2-one (4ga). Yield 475 mg (71%). Off-white solid, mp 252 - 254 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.42 (s, 3H, CH_3), 3.81 (s, 2H, CH_2), 6.21 (d, J = 9.4 Hz, 1H, H-3′), 6.89 (d, J = 8.5 Hz, 1H, H-6′), 7.45 – 7.50 (m, 2H, H-8, 5′), 7.58 (dd, J = 8.5, J = 2.2 Hz, 1H, H-7), 7.68 (s, 1H, H-2), 7.86 (d, J = 2.2 Hz, 1H, H-5), 7.94 (d, J = 9.4 Hz, 1H, H-4′), 10.63 ppm (s, 1H, OH-7′). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 18.7 (CH_2), 20.5 (CH_3), 110.9 (C-8′), 111.2 (CH-3′), 111.6 (C-4a′), 112.6 (CH-6′), 118.1 (CH-8), 121.2 (C-3), 122.5 (C-4a), 124.2 (CH-5), 127.8 (CH-5′), 134.9 (C-6), 135.2 (CH-7), 144.9 (CH-4′), 153.1 (CH-2), 153.6 (C-8a′), 154.1 (C-8a), 159.2 (C-7′), 160.4 (C-2′), 176.5 ppm (CO-4). MS (APCI) *m/z*: 335.1 [M+H]$^+$. Anal. Calcd (%) for $C_{20}H_{14}O_5$: C, 71.85; H, 4.22. Found (%): C, 71.97; H, 4.03.

8-[(6-Fluoro-4-oxo-4*H*-chromen-3-yl)methyl]-7-hydroxy-2*H*-chromen-2-one (4gb). Yield 453 mg (67%).

Off-white solid, mp 254 - 256 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.82 (s, 2H), 6.20 (d, J = 9.4 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.60 – 7.75 (m, 3H), 7.77 (s, 1H), 7.93 (d, J = 9.4 Hz, 1H), 10.62 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 18.5, 109.2 (d, J_{C-F} = 23.4 Hz), 110.5, 111.0, 111.4, 112.3, 120.6, 120.9 (d, J_{C-F} = 8.2 Hz), 122.0 (d, J_{C-F} = 25.7 Hz), 123.7 (d, J_{C-F} = 7.3 Hz), 127.6, 144.6, 152.1, 153.4, 153.5, 158.6 (d, J_{C-F} = 244.1 Hz), 159.1, 160.2, 175.7 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ = -116.0 ppm. MS (APCI) *m/z*: 339.0 [M+H]$^+$. Anal. Calcd (%) for $C_{19}H_{11}FO_5$: C, 67.46; H, 3.28. Found (%): C, 67.73; H, 3.53.

8-[(6-Chloro-4-oxo-4*H*-chromen-3-yl)methyl]-7-hydroxy-2*H*-chromen-2-one (4gc). Yield 468 mg (66%). Off-white solid, mp 268 - 270 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.84 (s, 2H), 6.19 (d, J = 9.4 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.75 – 7.86 (m, 2H), 7.93 (d, J = 9.4 Hz, 1H), 8.01 (d, J = 2.7 Hz, 1H), 10.52 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 18.7, 110.6, 111.2, 111.6, 112.5, 120.9, 121.6, 123.9, 124.0, 127.9, 129.8, 133.9, 144.9, 153.6, 153.7, 154.4, 159.3, 160.4, 175.4 ppm. MS (APCI) *m/z*: 354.9 [M+H]$^+$. Anal. Calcd (%) for $C_{19}H_{11}ClO_5$: C, 64.33; H, 3.13. Found (%): C, 64.08; H, 3.02.

8-[(6-Bromo-4-oxo-4*H*-chromen-3-yl)methyl]-7-hydroxy-2*H*-chromen-2-one (4gd). Yield 615 mg (77%). Off-white solid, mp 314 - 315 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.82 (s, 2H), 6.20 (d, J = 9.4 Hz, 1H), 6.89 (d, J = 8.5 Hz, 1H), 7.47 (d, J = 8.5 Hz, 1H), 7.58 (d, J = 8.9 Hz, 1H), 7.77 (s, 1H), 7.88 – 8.00 (m, 2H), 8.14 (d, J = 2.5 Hz, 1H), 10.60 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 18.7, 110.6, 111.2, 111.6, 112.5, 117.7, 121.0, 121.6, 124.2, 127.1, 127.9, 136.6, 144.8, 153.6, 153.6, 154.7, 159.3, 160.4, 175.35 ppm. MS (APCI) *m/z*: 310.2 [M+H]$^+$. Anal. Calcd (%) for $C_{19}H_{11}BrO_5$: C, 57.17; H, 2.78. Found (%): C, 57.43; H, 3.03.

8-[(6-Fluoro-4-oxo-4*H*-chromen-3-yl)methyl]-7-hydroxy-3-(4-methoxyphenyl)-4*H*-chromen-4-one (4hb). Yield 453 mg (51%). Off-white solid, mp 118 - 120 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.76 (s, 3H), 3.90 (s, 2H), 6.95 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 8.7 Hz, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.59 – 7.77 (m, 3H), 7.83 (s, 1H), 7.93 (d, J = 8.7 Hz, 1H), 8.35 (s, 1H), 10.84 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 18.8, 55.1, 109.5 (d, J_{C-F} = 23.5 Hz), 110.9, 113.6, 114.5, 117.0, 120.9, 121.1 (d, J_{C-F} = 8.2 Hz), 122.3 (d, J_{C-F} = 25.2 Hz), 122.8, 123.9 (d, J_{C-F} = 7.1 Hz), 124.3, 125.3, 130.0, 152.3, 153.2, 153.8, 155.6, 158.9 (d, J_{C-F} = 244.2 Hz), 158.9, 160.4, 175.0, 175.9 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ: -116.0 ppm. MS (APCI) *m/z*: 445.0 [M+H]$^+$. Anal. Calcd (%) for $C_{26}H_{17}FO_6$: C, 70.27; H, 3.86. Found (%): C, 70.54; H, 4.11.

8-[(6-Chloro-4-oxo-4*H*-chromen-3-yl)methyl]-7-hydroxy-3-(4-methoxyphenyl)-4*H*-chromen-4-one (4hc). Yield 802 mg (87%). Off-white solid, mp 250 - 252 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.77 (s, 3H), 3.91 (s, 2H), 6.97 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 8.7 Hz, 1H), 7.50 (d, J = 8.7 Hz, 2H), 7.66 (d, J = 9.0 Hz, 1H), 7.81 (dd, J = 9.0, J = 2.7 Hz, 1H), 7.84 (s, 1H), 7.94 (d, J = 8.7 Hz, 1H), 8.01 (d, J = 2.7 Hz, 1H), 8.37 (s, 1H), 10.84 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 18.8, 55.1, 110.8, 113.5, 114.4, 116.9, 120.8, 121.6, 122.8, 123.8, 123.9, 124.2, 125.3, 129.7, 129.9, 133.9, 153.1, 153.7, 154.4, 155.6, 158.9, 160.3, 175.0, 175.4 ppm. MS (APCI) *m/z*: 461.0 [M+H]$^+$. Anal. Calcd (%) for $C_{26}H_{17}ClO_6$: C, 67.76; H, 3.72. Found (%): C, 67.53; H, 3.99.

Ethyl 5-hydroxy-1,2-dimethyl-4-[(6-methyl-4-oxo-4*H*-chromen-3-yl)methyl]-1*H*-indole-3-carboxylate (4ia). Yield 300 mg (37%). Off-white solid, mp 157 - 159 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.01 (t, J = 7.1 Hz, 3H), 2.40 (s, 3H), 2.50 (s, 3H), 3.64 (s, 3H), 3.95 (q, J = 7.1 Hz, 2H), 4.15 (s, 2H), 6.87 (d, J = 8.7 Hz, 1H), 7.06 (s, 1H), 7.26 (d, J = 8.7 Hz, 1H), 7.38 (d, J = 8.6 Hz, 1H), 7.52 (d, J = 8.6 Hz, 1H), 7.89 (s, 1H), 8.96 ppm (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ: 11.9, 14.0, 20.5, 22.7, 29.7, 59.2, 104.8, 109.0, 111.6, 113.1, 117.9, 122.6, 123.4, 124.2, 125.2, 131.3, 134.5, 134.8, 143.0, 150.4, 152.1, 154.0, 165.6, 176.8 ppm. MS (APCI) *m/z*: 406.2 [M+H]$^+$. Anal. Calcd (%) for $C_{24}H_{23}NO_5$: C, 71.10; H, 5.72; N, 3.45. Found (%): C, 71.34; H, 5.99; N, 3.73.

Ethyl 4-[(6-fluoro-4-oxo-4*H*-chromen-3-yl)methyl]-5-hydroxy-1,2-dimethyl-1*H*-indole-3-carboxylate (4ib). Yield 352 mg (43%). Off-white solid, mp 179 - 180 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.01 (t, J = 7.1 Hz, 3H), 2.52 (s, 3H), 3.65 (s, 3H), 3.95 (q, J = 7.1 Hz, 2H), 4.14 (s, 2H), 6.86 (d, J = 8.7 Hz, 1H), 7.13 (s, 1H), 7.28 (d, J = 8.7 Hz, 1H), 7.61 – 7.69 (m, 2H), 7.80 – 7.72 (m, 1H), 8.96 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 11.9, 13.9, 22.6, 29.7, 59.2, 104.7, 109.0, 109.4 (d, J_{C-F} = 23.6 Hz), 111.5, 112.8, 121.0 (d, J_{C-F} = 7.6 Hz), 122.0 (d, J_{C-F} = 25.6 Hz), 123.1, 123.9 (d, J_{C-F} = 6.8 Hz), 125.2, 131.3, 143.0, 150.4, 152.2, 152.5, 158.7 (d, J_{C-F} = 243.4 Hz), 165.5, 176.1 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ: -116.3 ppm. MS (APCI) *m/z*: 410.0 [M+H]$^+$. Anal. Calcd (%) for $C_{23}H_{20}FNO_5$: C, 67.48; H, 4.92; N, 3.42. Found (%): C, 67.71; H, 4.66; N, 3.20.

Ethyl 4-[(6-chloro-4-oxo-4*H*-chromen-3-yl)methyl]-5-hydroxy-1,2-dimethyl-1*H*-indole-3-carboxylate (4ic). Yield 196 mg (23%). Off-white solid, mp 185 - 187 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.01 (t, J = 7.1 Hz, 3H), 2.50 (s, 3H), 3.63 (s, 3H), 3.94 (q, J = 7.1 Hz, 2H), 4.13 (s, 2H), 6.85 (d, J = 8.7 Hz, 1H), 7.11 (s, 1H), 7.26 (d, J = 8.7 Hz, 1H), 7.57 (d, J = 8.9 Hz, 1H), 7.76 (dd, J = 8.9, J = 2.7 Hz, 1H), 8.02 (d, J = 2.7 Hz, 1H), 8.95 ppm (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 11.9, 13.9, 22.6, 29.7, 59.2, 104.7, 109.0, 111.5, 112.7, 120.7, 123.8, 123.9, 125.2, 129.5, 131.3, 133.7, 143.1, 150.4, 152.5, 154.3, 165.5, 175.6 ppm. MS (APCI) *m/z*: 426.1 [M+H]$^+$. Anal. Calcd (%) for $C_{23}H_{20}ClNO_5$: C, 64.87; H, 4.73; N, 3.29. Found (%): C, 65.03; H, 4.68; N, 3.40.

3-[(8-Hydroxyquinolin-7-yl)methyl]-6-methyl-4*H*-chromen-4-one (4ja). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 298 mg (47%). Pale yellow solid, mp 156 - 158 ^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.37 (s, 3H), 4.01 (s, 2H), 7.19 – 7.27 (m, 2H), 7.28 – 7.40 (m, 2H), 7.56 (d, J = 8.4 Hz, 1H), 7.86 (s, 1H), 7.97 (d, J = 2.1 Hz, 1H), 8.04 (dd, J = 8.4, 1.6 Hz, 1H), 8.70 ppm (dd, J = 4.2, 1.6 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 21.0, 26.0, 117.5, 117.8, 120.9, 121.3, 123.1, 123.6, 125.2, 127.4, 130.4, 134.6, 134.8, 136.1, 138.3, 148.0, 149.8, 153.7, 154.8, 177.8 ppm. MS (APCI) *m/z*: 318.2 [M+H]$^+$. Anal. Calcd (%) for $C_{20}H_{15}NO_3$: C, 75.70; H, 4.76; N, 4.41. Found (%): C, 75.90; H, 4.97; N, 4.64.

6-Fluoro-3-[(8-hydroxyquinolin-7-yl)methyl]-4*H*-chromen-4-one (4jb). Purified by column chromatography

using 1:100 methanol-dichloromethane. Yield 276 mg (43%). Pale yellow solid, mp 161 - 163 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.89 (s, 2H), 7.33 (d, J = 8.4 Hz, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.50 (dd, J = 8.3, 4.2 Hz, 1H), 7.62 – 7.81 (m, 3H), 8.20 (s, 1H), 8.28 (d, J = 8.3 Hz, 1H), 8.83 (d, J = 4.2 Hz, 1H), 9.87 ppm (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 26.03, 110.66 (d, J_{C-F} = 23.6 Hz), 117.62, 120.22 (d, J_{C-F} = 8.1 Hz), 120.47, 121.42, 121.67 (d, J_{C-F} = 25.6 Hz), 122.75, 125.10 (d, J_{C-F} = 7.3 Hz), 127.50, 130.45, 136.12, 138.23, 148.03, 149.85, 152.76, 153.98, 159.41 (d, J_{C-F} = 246.4 Hz), 177.03 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -116.1 ppm. MS (APCI) *m/z*: 322.0 $[M+H]^+$. Anal. Calcd (%) for $C_{19}H_{12}FNO_3$: C, 71.03; H, 3.76; N, 4.36. Found (%): C, 71.31; H, 3.94; N, 4.46.

6-Chloro-3-[(8-hydroxyquinolin-7-yl)methyl]-4H-chromen-4-one (4jc). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 365 mg (54%). Pale yellow solid, mp 180 - 182 ^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.01 (s, 2H), 7.28 (d, J = 8.5 Hz, 1H), 7.32 (d, J = 8.5 Hz, 1H), 7.37 (dd, J = 8.3, 4.3 Hz, 1H), 7.52 (dd, J = 8.5, 2.6 Hz, 1H), 7.57 (d, J = 8.5 Hz, 1H), 7.90 (s, 1H), 8.09 (d, J = 8.3 Hz, 1H), 8.16 (d, J = 2.6 Hz, 1H), 8.73 ppm (d, J = 4.3 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 26.0, 117.7, 119.9, 120.3, 121.5, 123.5, 125.0, 125.4, 127.5, 130.5, 130.9, 133.7, 136.1, 138.3, 148.1, 149.9, 153.9, 154.9, 176.6 ppm. MS (APCI) *m/z*: 338.0 $[M+H]^+$. Anal. Calcd (%) for $C_{19}H_{12}ClNO_3$: C, 67.57; H, 3.58; N, 4.15. Found (%): C, 67.39; H, 3.72; N, 4.23.

6-Bromo-3-[(8-hydroxyquinolin-7-yl)methyl]-4H-chromen-4-one (4jd). Purified by column chromatography using 1:100 methanol-dichloromethane. Yield 298 mg (39%). Pale yellow solid, mp 198 - 200 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.89 (s, 2H), 7.33 (d, J = 8.4 Hz, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.51 (dd, J = 8.3, 4.2 Hz, 1H), 7.63 (d, J = 8.9 Hz, 1H), 7.93 (dd, J = 9.0, 2.6 Hz, 1H), 8.11 (d, J = 2.5 Hz, 1H), 8.21 (s, 1H), 8.29 (dd, J = 8.3, 1.7 Hz, 1H), 8.83 (dd, J = 4.2, 1.7 Hz, 1H), 9.87 ppm (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ: 25.5, 117.0, 117.6, 120.8, 121.1, 121.3, 122.6, 124.6, 127.1, 127.3, 129.3, 136.0, 136.6, 138.0, 148.1, 150.3, 154.6, 154.8, 175.2 ppm. MS (APCI) *m/z*: 382.0 $[M+H]^+$, 384.0 $[M+H]^+$. Anal. Calcd (%) for $C_{19}H_{12}BrNO_3$: C, 59.71; H, 3.16; N, 3.66. Found (%): C, 59.87; H, 3.42; N, 3.78.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.
Copies of ^{1}H, ^{13}C{^{1}H} spectra for all new synthesized compounds and 2D for compound **4ga** (PDF).

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Notes

The authors declare no competing financial interest.

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