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# Efficient Heck cross-coupling of 3-iodo-benzopyrones with olefins under microwave irradiation without phosphine

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ABSTRACT

An efficient and effective microwave-assisted Heck cross-coupling of different terminal olefins with various 3-iodo-benzopyrones including sterically hindered, electron-rich, electron-neutral, and electron-deficient is developed. It proceeded faster and generally gave good to excellent yields under microwave irradiation, phosphine-free, and air condition. The reaction could render this method particularly attractive for the efficient preparation of biologically and medicinally interesting molecules.

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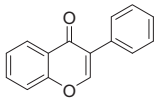
## 1. Introduction

In modern synthetic organic chemistry laboratories, metal-catalyzed cross-coupling reactions are a group of organic synthetic method primarily utilized for the formation of the carbon–carbon bond and the carbon–heteroatom bond. Reactions such as the Heck, Sonogashira, Suzuki, Buchwald–Hartwig, Stille, and Negishi reactions have been found with wide application in organic synthesis.[1–6] The palladium-catalyzed Heck coupling of aryl and vinyl halides with olefins in the presence of a base allows a one-step mild way for $C_{sp^2}$–$C_{sp^2}$ bond formation, which is utilized extensively as bioactive compounds, natural products, pharmaceuticals, and precursors of conjugated polymers.[7,8] Therefore, the Heck reaction has recently been the focus of attention in both the academic and industrial communities.[9–11] Despite many advantages associated with this reaction including its applicability to unactivated alkenes, tolerance of water and other functional groups in the substrate, interest in the reaction has been sporadic, largely due to the problems of long reaction time, air- and moisture-sensitive phosphine ligand, low product yields of α-halo-α,β-unsaturated ketones, and an incomplete understanding of the reaction mechanism.[12,13]

Various palladium species and several ligands such as phosphines, phosphites, carbenes, and thioethers employed for this reaction are necessary in traditional Heck conditions.[14–18] However, the usage of phosphines in the Heck reactions was undesirable as they are toxic as well as air- and moisture-sensitive.[19] In addition, it could be converted to phosphine oxide species, which would poison the catalysts leading to loss of the catalytic ability. Furthermore, phosphorus compounds could also cause environmental pollution and the simplest and cheapest Pd-catalysts are assuredly phosphine-free systems. Consequently, various ligandless catalytic systems have been developed. However, most of them showed poor efficiency in palladium-catalyzed Heck reactions.[20–31]

Isoflavones (Fig. 1), found at high levels in soy plants, are the most active and common in phytoestrogen and play the various biological activities via complex mechanisms, such as anti-viral, anti-cancer, anti-oxidative, anti-hyperglycemic, anti-inflammatory, insecticidal, anti-fungal, anti-microbial, and protect skin from sun damage.[32–36] Furthermore, some isoflavone derivatives with unsaturated bond between ring B and ring C also presented excellent bioactivities. 3-Iodo-benzopyrone offered chemists a convenient way of synthesizing isoflavones.[37] However, the 3-iodo-benzopyrone coupling with olefins via Heck reaction had low product yield maybe because of the α-iodo-α,β-unsaturated ketone part.[38,39]



Isoflavone

**Fig. 1.** Chemical structures of isoflavone.

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To the best of our knowledge there is no literature precedent to optimizing the condition of palladium-mediated cross-coupling reaction of 3-iodo-benzopyrones with olefins. Thus, we recently established the novel approach, which allowed a wide range of 3-iodo-benzopyrones were easily prepared in excellent yields under very mild conditions. We report herein (1) a small-scale microwave heating Heck protocol under air, (2) phosphine-free for Heck reaction, (3) applying α-iodo-α,β-unsaturated ketone as coupling components in the Heck reaction with olefins, and (4) high yield, short reaction time, and environmentally friend reaction condition.

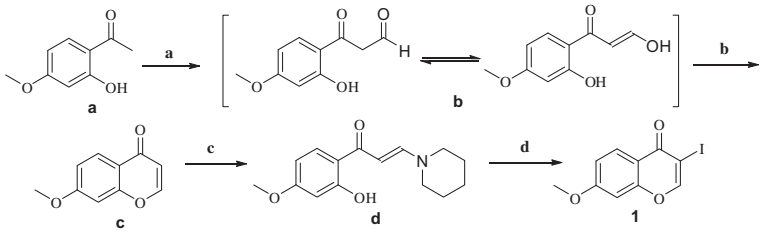
## 2. Results and discussion

Compound **1** was first synthesized by a reported procedure[37] (Scheme 1). In initial investigations, we examined the Heck coupling reaction of the model substrate 3-iodo-7-methoxy-4*H*-chromen-4-one (**1**) with methyl acrylate (**2**), using $Pd(OAc)_2$ (5 mol %) as the catalyst, $Cu(OAc)_2$ as base and DMF/DMSO (9:1) as solvent at 120 °C for 6 h (Table 1, entry 1). A series of different solvents, temperatures, catalysts, bases, and reaction time were screened under nitrogen protection. As can be seen from Table 1, of the solvents screened, $H_2O$/DMF (1:9) showed the best result and the corresponding coupling product **3** and byproduct **4** were obtained in 75.3% and 3% yield, respectively (Table 1, entry 6). There were indications that the choice of solvent had distinct impact both on the main product yield and de-iodine byproduct yield. It was found that if the reaction temperature was elevated to 100 °C, the corresponding reaction could be finished with 78% yield and the byproduct was decreased to 0.5% yield (Table 1, entry 10), which presented that higher temperature would lead to more side product. When catalyst was replaced by other palladium complex such as $PdCl_2(Ph_3P)_2$, $Pd_2(dba)_3$, and $Pd(Ph_3P)_4$ (Table 1, entries 12–14), results showed that the reaction did not work with $Pd_2(dba)_3$ and $Pd(Ph_3P)_4$. However, $PdCl_2(Ph_3P)_2$ was found slightly better than $Pd(OAc)_2$. Furthermore, other bases like $Na_2CO_3$, NaOH, $K_2CO_3$, pyridine, and triethylamine were used and $K_2CO_3$ showed the best result (Table 1, entry 17). Finally, reaction time was adjusted to 4, 8, 10 and 12 h, respectively. The results showed that 6 h was exactly the best reaction time for the main product yield (Table 1, entries 20–23).

The results above indicate that high temperature (≥100 °C) and long time (≥6 h) would cause de-iodine byproduct. The main product yield was also influenced by solvent, catalyst, and base. Thus, the optimal reaction condition was using $PdCl_2(Ph_3P)_2$ (5 mol %) as the catalyst, $K_2CO_3$ (2.0 equiv) as the base, and $H_2O$/DMF (1:9) (2.0 mL) as the solvent at the temperature of 100 °C for 6 h.

Table 1 showed that high temperature was helpful to the main product (**3**) yield and low temperature could avoid generating de-iodine compound (**4**), which made it difficult to conclude the best temperature for this reaction. Enlightened by the different heating principle between oil heating and microwave heating,[40] the introduction of microwave heating method could solve the problem well. The current investigation has been focused on a study of the effect of microwave irradiation on the Heck reaction of α-iodo-α,β-unsaturated ketone with olefins.

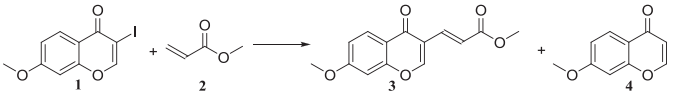
In initial investigations, we examined the microwave-promoted Heck coupling reaction of the model 3-iodo-7-methoxy-4*H*-chromen-4-one (**1**) and methyl acrylate (**2**), using $PdCl_2(Ph_3P)_2$ (5 mol %) as the catalyst, $K_2CO_3$ (2.0 equiv) as the base, and $H_2O$/DMF (1:9) (2.0 mL) as the solvent at the temperature of 100 °C for 10 min (Table 2, entry 1). The experiment revealed that the microwave-assisted Heck reaction under optimal oil heating condition mentioned above did not proceed satisfactorily. When the temperature was decreased to 90, 80 and 70 °C, respectively, the side product (**4**) disappeared and 80 °C was the best temperature for the main product (**3**) yield (70.0%) (Table 2, entries 2–4). According to the analysis above, reaction time was another important factor for the yield of compound **3** and a series of time screening experiments




Reagents and conditions: (a) Na, Ethyl Formate, Ethyl Ether, 0°C-r.t., 18h; (b) HOAc/HCl, reflux, 30min; (c) Piperidine, $CH_3OH$, reflux, 3h; (d) $I_2$, Pyridine, $CH_2Cl_2$, r.t., 20h

**Scheme 1.** Synthesis of the key intermediate **1**.

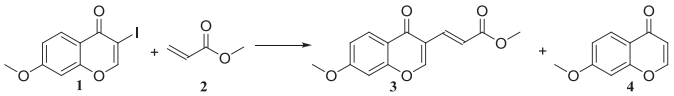
**Table 1**
Synthesis of compound **3** under oil heating[a]




| Entry | Solvent | Catalyst | Base | Temp (°C) | Time (h) | Yield[b] **3**/**4** (%) |
|---|---|---|---|---|---|---|
| 1 | DMF/DMSO=9:1 | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 120 | 6 | 70.5:5 |
| 2 | DMF | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 120 | 6 | 54.0:1 |
| 3 | DMSO | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 120 | 6 | 69.5:1.6 |
| 4 | $CH_3CN$ | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 120 | 6 | 12.0:0 |
| 5 | THF | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 120 | 6 | 67.0:3.6 |
| 6 | $H_2O$/DMF=1:9 | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 120 | 6 | 75.3:3 |
| 7 | $H_2O$/DMF=5:5 | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 120 | 6 | 66.5:1.2 |
| 8 | $H_2O$/DMF=1:9 | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 130 | 6 | 69.0:10 |
| 9 | $H_2O$/DMF=1:9 | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 110 | 6 | 71.0:2 |
| 10 | $H_2O$/DMF=1:9 | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 100 | 6 | 78.0:0.5 |
| 11 | $H_2O$/DMF=1:9 | $Pd(OAc)_2$ | $Cu(OAc)_2$ | 90 | 6 | 50.0:0 |
| 12 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $Cu(OAc)_2$ | 100 | 6 | 80.1:0 |
| 13 | $H_2O$/DMF=1:9 | $Pd_2(dba)_3$ | $Cu(OAc)_2$ | 100 | 6 | 0:0 |
| 14 | $H_2O$/DMF=1:9 | $Pd(Ph_3P)_4$ | $Cu(OAc)_2$ | 100 | 6 | 0:0 |
| 15 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $Na_2CO_3$ | 100 | 6 | 72.3:0 |
| 16 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | NaOH | 100 | 6 | 11.0:0 |
| 17 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 100 | 6 | 84.7:0.1 |
| 18 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | Pyridine | 100 | 6 | 65.3:0 |
| 19 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | TEA | 100 | 6 | 62.1:0 |
| 20 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 100 | 4 | 60.8:0 |
| 21 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 100 | 8 | 85:0.5 |
| 22 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 100 | 10 | 84:0.1 |
| 23 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 100 | 12 | 85:0.1 |

[a] Unless otherwise specified, all reactions were performed with compound **1** (4 mmol), methyl acrylate (4.8 mmol), catalyst (5 mmol %), and base (8 mmol) in solvent (50 mL) via oil heating.
[b] Isolated yield.

**Table 2**
Synthesis of compound **3** under microwave heating[a]



| Entry | Solvent | Catalyst | Base | Temp (°C) | Time (min) | Yield[b] **3**/**4** (%) |
|---|---|---|---|---|---|---|
| 1 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 100 | 10 | 67.3:2 |
| 2 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 90 | 10 | 70.6:0 |
| 3 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 80 | 10 | 70.0:0 |
| 4 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 70 | 10 | 54.0:0 |
| 5 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 80 | 11 | 70.1:0 |
| 6 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 80 | 8 | 70.6:0 |
| 7 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 80 | 6 | 69.9:0 |
| 8 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 80 | 5 | 70.5:0 |
| 9 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $K_2CO_3$ | 80 | 4 | 36.9:0 |
| 10 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | $Na_2CO_3$ | 80 | 5 | 59.1:0 |
| 11 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | NaOH | 80 | 5 | 23.4:0 |
| 12 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | TEA | 80 | 5 | 81.3:0 |
| 13 | $H_2O$/DMF=1:9 | $PdCl_2(Ph_3P)_2$ | Pyridine | 80 | 5 | 79.6:0 |
| 14 | DMF | $PdCl_2(Ph_3P)_2$ | TEA | 80 | 5 | 90.9:0 |
| 15 | DMSO | $PdCl_2(Ph_3P)_2$ | TEA | 80 | 5 | 81.8:0 |
| 16 | $CH_3CN$ | $PdCl_2(Ph_3P)_2$ | TEA | 80 | 5 | 10.2:0 |
| 17 | EtOH | $PdCl_2(Ph_3P)_2$ | TEA | 80 | 5 | 0:0 |
| 18 | $H_2O$ | $PdCl_2(Ph_3P)_2$ | TEA | 80 | 5 | 0:0 |
| 19 | DMF | $Pd(OAc)_2$ | TEA | 80 | 5 | 93.5:0 |
| 20 | DMF | $PdCl_2(dppf)_2$ | TEA | 80 | 5 | 85.6:0 |
| 21 | DMF | $Pd(Ph_3P)_4$ | TEA | 80 | 5 | 0:0 |
| 22 | DMF | $Pd_2(dba)_3$ | TEA | 80 | 5 | 0:0 |
| 23 | DMF | $Pd(OAc)_2$ | TEA | 80 | 4 | 80.6:0 |
| 24 | DMF | $Pd(OAc)_2$ | TEA | 80 | 6 | 93.1:0 |

[a] Unless otherwise specified, all reactions were performed with compound **1** (4 mmol), methyl acrylate (4.8 mmol), catalyst (5 mmol %), and base (8 mmol) in solvent (50 mL) via microwave heating.
[b] Isolated yield.

showed that 5 min was the best one for the reaction (Table 2, entries 5–9). Moreover, base selection experiment proved that when the inorganic bases were substituted by organic bases, the yield of main product was augmented and the triethylamine (TEA) was the best choice (Table 2, entries 10–13). Considering the alteration of base from inorganic to organic one, the solvent also needs to be changed correspondingly. Thereby, solvents such as DMF, DMSO, $CH_3CN$, EtOH, and $H_2O$ were used, respectively, and the results showed that DMF could drastically boost the desired compound yield (90.9%) (Table 2, entries 14–18) and on the contrary, pure water was certificated to be negative for this reaction (Table 2, entry 18). Furthermore, $Pd(OAc)_2$ displayed superiority over the other palladium catalysts (Table 2, entries 19–22). Finally, due to the reaction conditions regulation, we considered that the reaction time adjustment might be helpful to increase product yield. Nevertheless, the results showed that neither adding nor decreasing the time was necessary (Table 2, entries 23 and 24).

Thereby, the optimal reaction conditions under microwave irradiation were using $Pd(OAc)_2$ (5 mol %) as the catalyst, TEA (2.0 equiv) as the base, and DMF (2.0 mL) as the solvent at the temperature of 80 °C for 5 min.

Under the optimized reaction conditions, the generality of the reaction was investigated by using 3-iodo-7-methoxy-4*H*-chromen-4-one/7-hydroxy-3-iodo-4*H*-chromen-4-one and a variety of olefins to produce benzopyrone derivatives. The results are summarized in Table 3. The findings showed that these reactions led to production of the corresponding chromone derivatives in moderate to excellent yields (Table 3). Reaction of compound **1** with allyl alcohol (Table 3, entry 2) gave complicated products, and (*E*)-3-(7-methoxy-4-oxo-4*H*-chromen-3-yl) acrylaldehyde was found to be the major product in 59.6% yield, which appeared to be reasonable according to the report.[41] Moreover, it is clear that olefins with acidic group were unfavorable to this type reaction. (Table 3, entries 5, 6, and 8). Notably, although electron-withdrawing group or electron-donating groups with olefins were applied and the reaction could be smoothly performed, an electron-donating group was more favored than an electron-withdrawing group. Furthermore, the presence of hydroxy group on the benzopyrone led to slightly decreased yields (Table 3, entries 18–23) as a consequence of weak acidic of the phenol. It is noted that the existence of strong electron-withdrawing group such as nitro-group on the benzene ring of the benzopyrone would hinder the reaction procedure and no product could be observed (Table 3, entry 24).

Reactions of various 3-iodine flavonoid derivatives with different olefins under the modified optimal conditions were explored to further probe the scope of the process (Table 4). Although, the steric hindrance effect of the benzene ring at β-position of the α-iodo-α,β-unsaturated ketone might be the key reason for the difficulty of the Heck reaction, both reaction temperature and time regulation (110 °C and 90 min) could result in generation of desired functionalized flavonoid in moderate to good yields (Table 4). Likewise, the electronic effects of substituents on the olefins affected the reactions and it is clear that an electron-donating group will increase the reactivity of the double bond. Notably, heterocyclic compounds appeared to have lower yield than benzene ring and alkyl groups (Table 4, entries 22–24). Clearly, the phenolic hydroxyl group on the flavonoid also strongly contributed to the yield decrease of the Heck coupling reaction (Table 4, entries 14–24).

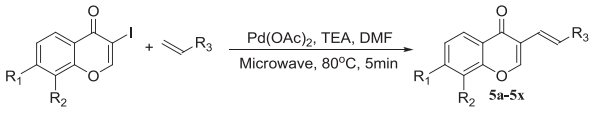
Despite the merits of palladium-catalyzed coupling reactions with phosphine-free condition have been known to all, researches to disclose the mechanism of reactions under 'phosphineless' conditions are more challenging than those of systems reacting through phosphine and carbene ligands. Based on the reports published concerning investigations of the mechanistic pathway,[42,43] a tentative mechanism for the Heck reaction is proposed in Scheme 2. First, palladium(II) acetate with triethylamine resulted in the conversion of the palladium complex to $[Pd_2I_6][NEt_3H]_2$ (A) in step 1. $[Pd_2I_6]^{2-}$ is a well known counter-ion,[35] which inserted itself to carbon iodine bond (B) according to an oxidative addition reaction (step 2). Intermediate C was then transformed into a solvated structure (D) in step 3. The π-complex formation of palladium with methyl acrylate in step 4 enabled the alkene inserted itself between the Pd–C bond in a *syn*-insertion step (step 5). Subsequently, an internal rotation happened due to the torsional strain in step 6 and step 7 was a β-hydride elimination step (generation of trans-double bond) with the formation of desired product H. At the same time, the palladium complex (A) was regenerated via reductive elimination of the palladium–iodine complex (I) by triethylamine in the final step 8.

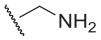
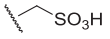
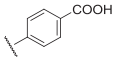
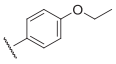
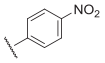
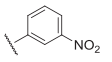
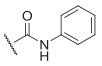
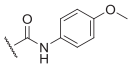
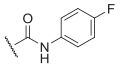
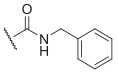
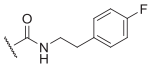
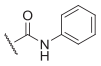
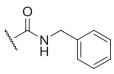
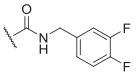
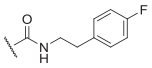
The analysis of $^1H$ NMR spectrum of all of the final products showed the doublet of olefins observed with coupling constant (*J*) from 14.7 to 16.4 Hz of two olefinic protons confirmed the trans-double bond, which could be one of the proof of our hypothetic mechanism.

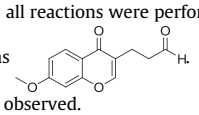
## 3. Conclusion

In summary, we have developed an efficient, mild, and phosphine-free Heck reaction of α-iodo-α,β-unsaturated ketone with different olefins under microwave irradiation to provide the desired products in minutes. Our reaction condition was as follows: 5 mol % of $Pd(OAc)_2$ as catalyst, DMF as solution, and triethylamine as base. The short reaction times and simple reaction conditions coupled with a broad spectrum of olefins render this method particularly attractive for the efficient preparation of biologically and medicinally interesting molecules. The developed Heck method was worth to drawing attention due to the convenient, non-expensive, and environmentally friendly experimental procedure

**Table 3**
Synthesis of compounds **5a**–**5x**[a]




| Entry | $R_1$ | $R_2$ | $R_3$ | Product | Yield[b] (%) | Entry | $R_1$ | $R_2$ | $R_3$ | Product | Yield[b] (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $OCH_3$ | H |  | **5a** | 94.2 | 13 | $OCH_3$ | H |  | **5m** | 77.8 |
| 2 | $OCH_3$ | H |  | **5b**[c] | 59.6 | 14 | $OCH_3$ | H |  | **5n** | 74.6 |
| 3 | $OCH_3$ | H |  | **5c** | 21.8 | 15 | $OCH_3$ | H |  | **5o** | 73.4 |
| 4 | $OCH_3$ | H |  | **5d** | 47.6 | 16 | $OCH_3$ | H |  | **5p** | 81.8 |
| 5 | $OCH_3$ | H |  | **5e** | —[d] | 17 | $OCH_3$ | H |  | **5q** | 83.1 |
| 6 | $OCH_3$ | H |  | **5f** | —[d] | 18 | OH | H |  | **5r** | 88.9 |
| 7 | $OCH_3$ | H |  | **5g** | 85.7 | 19 | OH | H |  | **5s** | 86.3 |
| 8 | $OCH_3$ | H |  | **5h** | —[d] | 20 | OH | H |  | **5t** | 71.6 |
| 9 | $OCH_3$ | H |  | **5i** | 90.3 | 21 | OH | H |  | **5u** | 76.8 |
| 10 | $OCH_3$ | H |  | **5j** | 78.0 | 22 | OH | H |  | **5v** | 72.6 |
| 11 | $OCH_3$ | H |  | **5k** | 10.5 | 23 | OH | H |  | **5w** | 77.2 |
| 12 | $OCH_3$ | H |  | **5l** | 8.1 | 24 | $OCH_3$ | $NO_2$ |  | **5x** | —[d] |

[a] Unless otherwise specified, all reactions were performed with 3-iodine chromone (4 mmol), olefin (4.8 mmol), $Pd(OAc)_2$ (5 mmol %) and $Et_3N$ (8 mmol) in DMF (50 mL).
[b] Isolated yield.
[c] The main product of **5b** was 
[d] '—' means no product was observed.

under air and could be readily adopted to prepare large libraries, and the versatility of this methodology is suitable for library synthesis in drug discovery efforts.

## 4. Experimental section

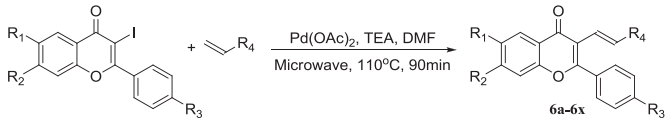
### 4.1. General

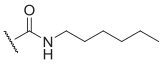
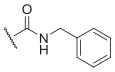
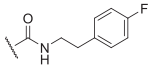
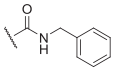
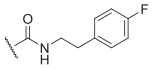
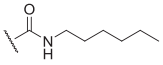
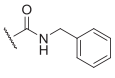
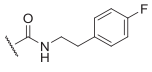
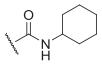
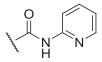
All reactions were carried out in an oven-dried glassware. Progress of reactions was monitored by thin layer chromatography (TLC) while purification of crude compounds was done by column chromatography using silica gel (200–300 mesh). Microwave irradiation was performed with Sineo MAS-II microwave synthesis workstation. Melting points were recorded on a YUHUA X-5 melting point apparatus and are uncorrected. Elemental analysis was performed with a Carlo Erba 1106 elemental analyzer. NMR experiments were performed on Bruke Avance 300 and Bruke Avance 600 instruments and samples were obtained in $CDCl_3$ (referenced to residual $CHCl_3$ at 7.26 ppm for $^1H$ and 77.0 ppm for $^{13}C$) or DMSO-$d_6$ (referenced to residual DMSO at 2.50 ppm for $^1H$ and 39.5 ppm for $^{13}C$). Coupling constants ($J$) are in hertz. The multiplicities of the signals are described using the following abbreviations: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad. Mass spectra were recorded using Finigan LCQ Deca XP MAX mass spectrometer. Yields refer to quantities obtained after chromatography. Elemental analyses were performed with a MOD-1106 instrument and were consistent with theoretical values within 0.4%.

### 4.2. General experimental procedure for Heck reaction under oil heating condition

To a solution of 3-iodo-7-methoxy-4*H*-chromen-4-one (**1**) (4 mmol) and methyl acrylate (**2**) (4.8 mmol) in solvent was added

**Table 4**
Synthesis of compounds **6a**–**6x**[a]




| Entry | $R_1$ | $R_2$ | $R_3$ | $R_4$ | Product | Yield[b] (%) |
|---|---|---|---|---|---|---|
| 1 | H | $OCH_3$ | $OCH_3$ |  | **6a** | 79.6 |
| 2 | H | $OCH_3$ | $OCH_3$ |  | **6b** | 82.7 |
| 3 | H | $OCH_3$ | $OCH_3$ |  | **6c** | 85.0 |
| 4 | H | $OCH_3$ | $OCH_3$ |  | **6d** | 80.9 |
| 5 | H | H | H |  | **6e** | 75.3 |
| 6 | H | $OCH_3$ | $OCH_3$ |  | **6f** | 60.4 |
| 7 | H | $OCH_3$ | $OCH_3$ |  | **6g** | 68.0 |
| 8 | H | $OCH_3$ | $OCH_3$ |  | **6h** | 66.7 |
| 9 | $OCH_3$ | $OCH_3$ | H |  | **6i** | 81.2 |
| 10 | $OCH_3$ | $OCH_3$ | H |  | **6j** | 83.5 |
| 11 | $OCH_3$ | $OCH_3$ | H |  | **6k** | 55.8 |
| 12 | $OCH_3$ | $OCH_3$ | H |  | **6l** | 64.4 |
| 13 | $OCH_3$ | $OCH_3$ | H |  | **6m** | 68.0 |
| 14 | H | OH | OH |  | **6n** | 73.5 |
| 15 | H | OH | OH |  | **6o** | 77.6 |
| 16 | H | OH | OH |  | **6p** | 77.5 |
| 17 | H | OH | OH |  | **6q** | 72.8 |
| 18 | H | OH | OH |  | **6r** | 48.1 |
| 19 | H | OH | OH |  | **6s** | 53.3 |
| 20 | H | OH | OH |  | **6t** | 55.9 |
| 21 | H | OH | OH |  | **6u** | 60.3 |
| 22 | H | OH | OH |  | **6v** | 41.5 |
| 23 | H | OH | OH |  | **6w** | 58.8 |
| 24 | H | OH | OH |  | **6x** | 40.7 |

[a] Unless otherwise specified, all reactions were performed with 3-iodine flavonoid (4 mmol), olefin (4.8 mmol), $Pd(OAc)_2$ (5 mmol %) and $Et_3N$ (8 mmol) in DMF (50 mL).
[b] Isolated yield.

catalyst (5 mmol %) and base (8 mmol). The reaction mixture was stirred via oil heating under nitrogen protection. Then the mixture was poured into 10% HCl ice-water (300 mL) slowly with stirring. The suspension was filtered through a filter and filter cake was collected and dried. The crude product was purified by chromatography over silica gel to give compound **3** or **4**.

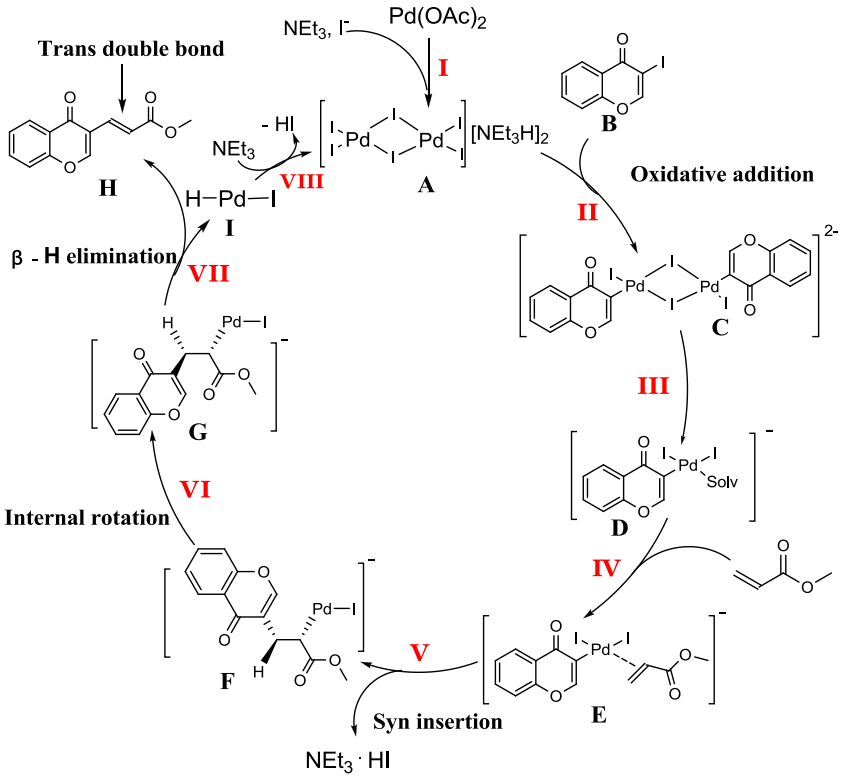
*4.2.1. (E)-Methyl 3-(5-hydroxy-7-methoxy-4-oxo-4H-chromen-3-yl) acrylate (**3**).* Color: yellow; mp: 176.5–177.6 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.78 (s, 3H, $CH_3$), 3.86 (s, 3H, $CH_3$–O), 6.84 (d, 1H, $J$=3 Hz, Ar–H), 7.02–7.05 (dd, 1H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 7.24 (d, 1H, $J$=15.9 Hz, O=C–CH=C), 7.37 (d, 1H, $J$=15.9 Hz, O=C–C=CH), 8.04 (s, 1H, O–CH=C), 8.16 ppm (d, 1H, $J$=9 Hz, Ar–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 51.40, 55.85, 101.31, 115.85, 116.64, 117.65, 119.45, 127.82, 136.07, 156.91, 159.78, 162.94, 167.01, 174.49 ppm; ESI-MS ($m/z$): 261.11 $(M+1)^+$. Anal. ($C_{14}H_{12}O_5$): C 64.61, H 4.65. Found: C 64.65, H 4.67%.

*4.2.2. 7-Methoxy-4H-chromen-4-one (**4**).* Color: white; mp: 105.4–106.0 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.90 (s, 3H, $CH_3$–O), 6.28 (d, $J$=6.3 Hz, 1H, O=C–CH=C), 6.84 (d, 1H, $J$=4 Hz, Ar–H), 7.02–7.05 (dd, 1H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 7.78 (d, 1H, Ar–H, $J$=6.3 Hz, O=C–CH=C), 8.12 ppm (d, 1H, $J$=9 Hz, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 55.2, 102.6, 107.5, 110.6, 116.2, 128.7, 142.1, 157.6, 163.2, 179.6 ppm; ESI-MS ($m/z$): 177.06 $(M+1)^+$. Anal. ($C_{10}H_8O_3$): C 68.18, H 4.58. Found: C 68.22, H 4.57%.

## 4.3. General experimental procedure for Heck reaction under microwave heating condition

To a solution of 3-iodo-chromone (4 mmol) and olefin (4.8 mmol) in solvent was added catalyst (5 mmol %) and base (8 mmol). The reaction mixture was stirred via microwave heating under air. Then the mixture was poured into 10% HCl ice-water (300 mL) slowly with stirring. The suspension was filtered through a filter and filter cake was collected and dried. The crude product was purified by chromatography over silica gel to give resulting product.

*4.3.1. (E)-Ethyl 3-(7-methoxy-4-oxo-4H-chromen-3-yl)acrylate (**5a**).* Color: pink; mp: 139.3–139.7 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 1.30–1.35 (t, 3H, $CH_3$), 3.92 (s, 3H, $CH_3$–O), 4.22–4.29 (q, 2H, $CH_2$), 6.85 (d, 1H, $J$=2.4 Hz, Ar–H), 6.99–7.03 (dd, 1H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 7.27 (d, 1H, $J$=15.9 Hz, O=C–CH=C), 7.40 (d, 1H, $J$=15.9 Hz, O=C–C=CH), 8.04 (s, 1H, O–CH=C), 8.18 ppm (d, 1H, $J$=9 Hz, Ar–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$:




**Scheme 2.** Putative reaction mechanism.

14.22, 55.85, 101.33, 56.31, 115.83, 116.45, 117.60, 119.25, 127.82, 135.76, 156.90, 159.78, 162.94, 167.01, 174.28 ppm; ESI-MS (*m*/*z*): 275.09 $(M+1)^+$. Anal. ($C_{15}H_{14}O_5$): C 65.69, H 5.15. Found: C 65.72, H 5.47%.

*4.3.2. 3-(7-Methoxy-4-oxo-4H-chromen-3-yl)propanal (**5b**).* Color: yellow; mp: 125.5–126.1 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 2.57–2.62 (t, 2H, $CH_2$–$CH_2$), 2.68–2.73 (t, 2H, $CH_2$–C=O), 3.67 (s, 3H, $CH_3$–O), 7.00–7.05 (m, 2H, Ar–H), 7.90–7.9 4 (dd, 1H, $J_1$=1.5 Hz, $J_2$=1.8 Hz, Ar–H), 8.17 (s, 1H, O–CH=C), 9.70 ppm (s, 1H, CHO); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 20.34, 40.64, 55.83, 100.20, 114.22, 116.01, 124.04, 127.64, 154.61, 158.2, 164.13, 176.53, 202.11 ppm; ESI-MS (*m*/*z*): 233.08 $(M+1)^+$. Anal. ($C_{13}H_{12}O_4$): C 67.23, H 5.21. Found: C 67.62, H 5.82%.

*4.3.3. (E)-3-(7-Methoxy-4-oxo-4H-chromen-3-yl)acrylonitrile (**5c**).* Color: yellow; mp: 223.6–224.3 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.90 (s, 3H, $CH_3$–O), 6.98 (d, 1H, $J$=2.4 Hz, Ar–H), 6.08–7.14 (dd, 1H, $J_1$=1.8 Hz, $J_2$=1.8 Hz, Ar–H), 7.23 (d, 1H, $J$=15.9 Hz, C=CH–C–N), 7.35 (d, 1H, $J$=15.9 Hz, CH=C–C–N), 8.01 (s, 1H, O–CH=C), 8.70 ppm (d, 1H, $J$=9 Hz, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 55.84, 92.53, 100.11, 114.22, 115.84, 116.24, 123.64, 127.81, 149.35, 150.43, 158.24, 1675.12, 121.55 ppm; ESI-MS (*m*/*z*): 228.06 $(M+1)^+$. Anal. ($C_{13}H_9NO_3$): C 68.72, H 3.99, N 6.16. Found: C 68.41, H 3.55, N 6.23%.

*4.3.4. (E)-3-(3-Aminoprop-1-enyl)-7-methoxy-4H-chromen-4-one (**5d**).* Color: yellow; mp: 136.6–137.4 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 1.23 (s, 2H, $NH_2$), 3.36 (s, 2H, $CH_2$–N), 3.85 (s, 3H, $CH_3$–O), 5.86–5.97 (m, 1H, C=CH–C–N), 6.74–6.77 (dd, 1H, $J_1$=2.1 Hz, $J_2$=2.1 Hz, Ar–H), 6.81 (s, 1H, O–CH=C), 6.90 (d, 1H, $J$=15.6 Hz, CH=C–C–N), 7.52 (d, 1H, ArH), 7.80 ppm (d, 1H, ArH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 43.87, 55.84, 100.13, 114.43, 116.53, 120.23, 125.32, 127.84, 133.45, 149.34, 163.26, 167.41, 120.34 ppm; ESI-MS (*m*/*z*): 232.08 $(M+1)^+$. Anal. ($C_{13}H_{13}NO_3$): C 67.52, H 5.67, N 6.06. Found: C 67.95, H 5.29, N 6.06%.

*4.3.5. (E)-7-Methoxy-3-styryl-4H-chromen-4-one (**5g**).* Color: yellow; mp: 134.1–135.0 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.91 (s, 3H, $CH_3$–O), 6.84 (d, 1H, $J$=2.2 Hz, Ar–H), 6.98 (d, 1H, $J$=16.2 Hz, Ar–CH=C), 6.93–7.03 (dd, 1H, $J_1$=9.2 Hz, $J_2$=2.2 Hz, Ar–H), 7.26–7.37 (m, 3H, Ar–H), 7.50–7.53 (m, 2H, Ar–H), 7.63 (d, 1H, $J$=16.2 Hz, Ar–C=CH), 8.04 (s, 1H, O–CH=C), 8.21 (d, 1H, $J$=9.2 Hz, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 55.8, 100.1, 114.7, 118.3, 119.2, 121.7, 126.6, 127.6, 127.8, 128.6, 131.5, 137.4, 152.5, 157.6, 164.0, 176.0 ppm; ESI-MS (*m*/*z*): 278.30 $(M+1)^+$. Anal. ($C_{18}H_{14}O_3$): C 77.68, H 5.07. Found: C 77.19, H 5.17%.

*4.3.6. (E)-3-(4-Ethoxystyryl)-7-methoxy-4H-chromen-4-one (**5i**).* Color: yellow; mp: 147.6–148.4 °C; $^1$H NMR: (500 MHz, $CDCl_3$) $\delta$: 1.43 (t, 3H, $CH_3$–C–O), 3.91 (s, 3H, $CH_3$–O), 4.06 (q, 2H, $CH_2$–O), 6.84 (d, 1H, $J$=2.4 Hz, Ar–H), 6.85 (d, 1H, $J$=16.4 Hz, Ar–CH=C), 6.88 (d, 2H, $J$=8.7 Hz, Ar–H), 6.93–7.03 (dd, 1H, $J_1$=8.9 Hz, $J_2$=2.4 Hz, Ar–H), 7.43–7.45 (m, 2H, Ar–H), 7.51 (d, 1H, $J$=16.4 Hz, Ar–C=CH), 8.03 (s, 1H, O–CH=C), 8.20 (d, 1H, $J$=8.9 Hz, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 14.8, 55.8, 63.4, 100.0, 114.6, 116.7, 117.6, 118.3, 119.3, 121.9, 127.8, 130.0, 131.0, 152.0, 157.2, 158.8, 163.9, 176.1 ppm; ESI-MS (*m*/*z*): 322.11 $(M+1)^+$. Anal. ($C_{18}H_{14}O_3$): C 74.52, H 5.63. Found: C74.58, H 5.79%.

*4.3.7. (E)-3-(3-Fluorostyryl)-7-methoxy-4H-chromen-4-one (**5j**).* Color: Yellow; mp: 193.5–194.3 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.91 (s, 3H, $CH_3$–O), 6.85–7.02 (m, 4H, Ar–H, Ar–CH=C), 7.25–7.27 (m, 1H, Ar–H), 7.67 (d, 1H, $J$=16.2 Hz, Ar–C=CH), 8.04 (s, 1H, O–CH=C), 8.10–8.13 (m, 1H, Ar–H), 8.21 (d, 1H, $J$=9.2 Hz, Ar–H), 8.35–8.40 ppm (t, 1H, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 55.94, 100.16, 113.23, 115.71, 116.33, 120.64, 122.78, 123.43, 127.64, 129.46, 131.98, 132.61, 139.46, 146.21, 155.02, 157.57, 165.32,

175.13 ppm; ESI-MS ($m/z$): 297.09 $(M+1)^+$. Anal. ($C_{18}H_{13}FO_3$): C 72.97, H 4.42. Found: C 73.02, H 4.20%.

*4.3.8. (E)-7-Methoxy-3-(4-nitrostyryl)-4H-chromen-4-one (**5k**).* Color: yellow; mp: 173.1–174.6 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.95 (s, 3H, $CH_3$–O), 6.89 (d, 1H, $J$=2.4 Hz, Ar–H), 7.04–7.06 (dd, 1H, $J_1$=8.8 Hz, $J_2$=2.4 Hz, Ar–H), 7.08 (d, 1H, $J$=16.2 Hz, Ar–CH=C), 7.66 (d, 2H, $J$=8.8 Hz, Ar–H), 7.80–7.85 (m, 1H, Ar–H), 7.87 (d, 1H, $J$=16.2 Hz, Ar–C=CH), 8.10 (s, 1H, O–CH=C), 8.23 (d, 1H, $J$=8.9 Hz, Ar–H) ,8.35–8.39 ppm (t, 1H, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 55.9, 100.2, 115.0, 118.0, 120.7, 124.0, 126.9, 127.6, 129.4, 144.1, 146.8, 154.2, 157.5, 164.2, 175.8 ppm; ESI-MS ($m/z$): 324.08 $(M+1)^+$. Anal. ($C_{18}H_{13}NO_5$): C, 66.87; H 4.05, N 4.33. Found: C 66.85, H 4.09, N 4.30%.

*4.3.9. (E)-7-Methoxy-3-(3-nitrostyryl)-4H-chromen-4-one (**5l**).* Color: yellow; mp: 173.1–174.6 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.93 (s, 3H, $CH_3$–O), 6.87 (d, 1H, $J$=2.4 Hz, Ar–H), 7.00–7.02 (dd, 1H, $J_1$=8.9 Hz, $J_2$=2.4 Hz, Ar–H), 7.03 (d, 1H, $J$=16.3 Hz, Ar–CH=C), 7.50–7.52 (t, 1H, Ar–H), 7.78–7.82 (m, 1H, Ar–H), 7.85 (d, 1H, $J$=16.3 Hz, Ar–C=CH), 8.08 (s, 1H, O–CH=C), 8.10–8.12 (m, 1H, Ar–H), 8.21 (d, 1H, $J$=8.9 Hz, Ar–H), 8.35–8.39 ppm (t, 1H, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 55.9, 100.2, 114.9, 115.5, 118.34, 120.6, 122.2, 122.5, 127.6, 129.4, 129.6, 132.6, 139.4, 146.2, 153.9, 157.5, 166.3, 175.1 ppm; ESI-MS ($m/z$): 324.08 $(M+1)^+$. Anal. ($C_{18}H_{13}NO_5$): C, 66.87; H 4.05, N 4.33. Found: C 66.85, H 4.07, N 4.31%.

*4.3.10. (E)-3-(7-Methoxy-4-oxo-4H-chromen-3-yl)-N-phenylacrylamide (**5m**).* Color: yellow; mp: 222.5–223.9 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.93 (s, 3H, $CH_3$–O), 6.87 (d, 1H, $J$=3 Hz, Ar–H), 7.02–7.05 (dd, 2H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 7.30–7.43 (m, 5H, Ar–H, O=C–CH=C), 7.72 (d, 1H, $J$=12 Hz, O=C–C=CH), 8.09 (s, 1H, O–CH=C), 8.19 ppm (d, 1H, $J$=9 Hz, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 55.83, 100.16, 114.95, 116.48, 119.56, 120.36, 121.01, 127.55, 128.32, 128.64, 133.86, 137.20, 140.63, 149.64, 157.26, 157.77, 164.74 ppm; ESI-MS ($m/z$): 322.11 $(M+1)^+$. Anal. ($C_{19}H_{15}NO_4$): C 71.02, H 4.71, N 4.36. Found: C 71.00, H 4.79, N 4.44%.

*4.3.11. (E)-3-(7-Methoxy-4-oxo-4H-chromen-3-yl)-N-(4-methoxyphenyl)acrylamide (**5n**).* Color: yellow; mp: 236.3–236.8 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.81 (s, 3H, $CH_3$–O), 3.93 (s, 3H, $CH_3$–O), 6.87–6.90 (m, 2H, Ar–H), 7.02 (dd, 2H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 7.36 (s, 1H, Ar–H), 7.36 (d, 1H, $J$=14.7 Hz, O=C–CH=C), 7.54 (d, 1H, $J$=9 Hz, Ar–H), 7.70 (d, 1H, $J$=15 Hz, O=C–C=CH), 8.06 (d, 1H, $J$=3 Hz, O–CH=C), 8.19 ppm (d, 1H, $J$=9 Hz, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 56.74, 101.50, 114.97, 115.45, 116.40, 119.34, 120.32, 122.75, 126.51, 128.90, 134.16, 150.23, 158.50, 159.04, 165.59, 166.43, 166.99, 175.16 ppm; ESI-MS ($m/z$): 352.11 $(M+1)^+$. Anal. ($C_{20}H_{17}NO_5$): C 68.37, H 4.88, N 3.99. Found: C 68.41, H 4.74, N 3.95%.

*4.3.12. (E)-N-(4-Fluorophenyl)-3-(7-methoxy-4-oxo-4H-chromen-3-yl)acrylamide (**5o**).* Color: yellow; mp: 240.1–240.8 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.93 (s, 3H, $CH_3$–O), 6.88 (d, 2H, $J$=2.4 Hz, Ar–H), 7.03 (dd, 2H, $J_1$=1.2 Hz, $J_2$=2.1 Hz, Ar–H), 7.37 (d, 1H, $J$=15 Hz, O=C–CH=C), 7.58 (dd, 2H, $J_1$=5.1 Hz, $J_2$=5.4 Hz, Ar–H), 7.70 (d, 1H, $J$=15 Hz, O=C–C=CH), 8.08 (s, 1H, O–CH=C), 8.19 ppm (d, 1H, $J$=9 Hz, Ar–H); $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$: 55.65, 100.03, 115.18, 117.23, 118.12, 121.30, 122.51, 125.65, 125.95, 126.32, 128.66, 133.81, 134.76, 156.89, 157.81, 166.24 ppm, 175.55; ESI-MS ($m/z$): 340.08 $(M+1)^+$. Anal. ($C_{19}H_{14}FNO_4$): C 67.25, H 4.16, N 4.13. Found: C 67.33, H 4.17, N 4.13%.

*4.3.13. (E)-N-Benzyl-3-(7-methoxy-4-oxo-4H-chromen-3-yl)acrylamide (**5p**).* Color: yellow; mp: 257.1–257.5 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.93 (s, 3H, $CH_3$–O), 4.53 (d, 2H, $J$=6 Hz, $CH_2$–Ar), 5.96 (s, 1H, NH), 6.85–6.90 (dd, 1H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 6.98–7.03 (m, 1H, Ar–H), 7.28–7.37 (m, 6H, Ar–H, O=C–CH=C), 7.74 (d, 1H, $J$=15 Hz, O=C–C=CH), 8.03 (s, 1H, O–CH=C), 8.16 ppm (d, 1H, $J$=9 Hz, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 43.01, 55.87, 100.20, 115.20, 116.45, 119.11, 125.74, 126.01, 127.82, 129.33, 129.44, 130.05, 135.54, 150.65, 157.85, 164.54, 166.25, 175.79 ppm; ESI-MS ($m/z$): 336.12 $(M+1)^+$. Anal. ($C_{20}H_{17}NO_4$): C 71.63, H 5.11, N 4.18. Found: C 71.56, H 5.20, N 4.15%.

*4.3.14. (E)-N-(4-Fluorophenethyl)-3-(7-methoxy-4-oxo-4H-chromen-3-yl)acrylamide (**5q**).* Color: yellow; mp: 177.5–178.5 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 2.83–2.87 (m, 2H, $CH_2$–Ar) 3.60–3.66 (m, 2H, $CH_2$–N), 3.92(s, 3H, $CH_3$–O), 5.70 (s, 1H, NH), 6.86 (d, 1H, $J$=2.1 Hz, Ar–H), 6.99–7.03 (m, 3H, Ar–H), 7.15–7.20 (m, 2H, Ar–H), 7.27 (d, 1H, $J$=15 Hz, O=C–CH=C), 7.45 (d, 1H, $J$=15 Hz, O=C–C=CH), 8.03 (s, 1H, O–CH=C), 8.15 ppm (d, 1H, $J$=8.7 Hz, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 35.30, 40.75, 55.40, 100.11, 114.99, 115.13, 116.45, 119.03, 123.35, 127.54, 131.00, 135.53, 141, 156.32, 158.44, 161.78, 166.32, 167.11, 177.83 ppm; ESI-MS ($m/z$): 368.13 $(M+1)^+$. Anal. ($C_{21}H_{18}FNO_4$): C 68.66, H 4.94, N 3.81. Found: C 68.70, H 5.00, N 3.85%.

*4.3.15. (E)-Methyl 3-(7-hydroxy-4-oxo-4H-chromen-3-yl)acrylate (**5r**).* Color: yellow; mp: 221.7–222.0 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 3.70 (s, 3H, $CH_3$), 6.89 (d, 1H, $J$=2.1 Hz, Ar–H), 6.97 (dd, 1H, $J_1$=2.1 Hz, $J_2$=2.1 Hz, Ar–H), 7.18 (d, 1H, $J$=15.9 Hz, O=C–CH=C), 7.45 (d, 1H, $J$=15.9 Hz, O=C–C=CH), 7.96 (d, 1H, $J$=8.7 Hz, Ar–H), 8.76 (s, 1H, O–CH=C), 10.93 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 51.41, 102.43, 115.69, 116.21, 117.57, 119.44, 127.25, 136.85, 156.89, 159.62, 163.01, 166.94, 174.48 ppm; ESI-MS ($m/z$): 247.06 $(M+1)^+$. Anal. ($C_{13}H_{10}O_5$): C 63.42, H 4.09. Found: C 63.41, H 4.14%.

*4.3.16. (E)-Ethyl 3-(7-hydroxy-4-oxo-4H-chromen-3-yl)acrylate (**5s**).* Color: brown; mp: 264.5–264.9 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 1.23 (m, 3H, $CH_3$–$CH_2$), 4.16 (m, 2H, $CH_3$–$CH_2$), 6.88 (d, 1H, $J$=2.1 Hz, Ar–H), 6.94 (m, 1H, Ar–H), 7.15 (d, 1H, $J$=15.9 Hz, O=C–CH=C), 7.43 (d, 1H, $J$=15 Hz, O=C–C=CH), 7.95 (d, 1H, $J$=8.7 Hz, Ar–H), 8.74 (s, 1H, O–CH=C), 10.93 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 14.16, 59.80, 102.75, 116.31, 116.52, 117.93, 119.05, 128.22, 136.20, 156.78, 158.80, 162.86, 166.74, 174.20 ppm; ESI-MS ($m/z$): 261.07 $(M+1)^+$. Anal. ($C_{14}H_{12}O_5$): C 64.61, H 4.65. Found: C 64.61, H 4.62%.

*4.3.17. (E)-3-(7-Hydroxy-4-oxo-4H-chromen-3-yl)-N-phenylacrylamide (**5t**).* Color: yellow; mp: 282.8–229.1 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 6.86 (d, 1H, $J$=2.1 Hz, Ar–H), 6.93 (dd, 1H, $J_1$=2.1 Hz, $J_2$=2.1 Hz, Ar–H), 7.01 (dd, 1H, $J_1$=2.1 Hz, $J_2$=2.1 Hz, Ar–H), 7.04–7.28 (m, 2H, Ar–H), 7.30 (d, 1H, $J$=15 Hz, O=C–CH=C), 7.33 (s, 1H, Ar–H), 7.65 (d, 1H, $J$=7.5 Hz, Ar–H), 7.77 (d, 1H, $J$=15 Hz, O=C–C=CH), 8.03 (d, 1H, $J$=8.7 Hz, Ar–H), 8.81 (s, 1H, O–CH=C), 10.30 (s, 1H, NH), 10.97 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 102.38, 115.59, 116.37, 118.22, 119.27, 123.20, 124.65, 127.25, 128.70, 132.67, 139.47, 156.87, 159.18, 162.90, 164.18, 174.76 ppm; ESI-MS ($m/z$): 308.10 $(M+1)^+$. Anal. ($C_{18}H_{13}NO_4$): C, 70.35; H, 4.26; N, 4.56. Found: C 70.38, H 4.33, N 4.56%.

*4.3.18. (E)-N-Benzyl-3-(7-hydroxy-4-oxo-4H-chromen-3-yl)acrylamide (**5u**).* Color: yellow; mp: 352.6–253.5 °C; yield: 46%; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 4.38 (d, 2H, $J$=6 Hz, $CH_2$–Ar), 6.88 (d, 1H, $J$=2.1 Hz, Ar–H), 6.95 (dd, 1H, $J_1$=2.1 Hz, $J_2$=2.1 Hz, Ar–H), 7.21 (s, 1H, Ar–H), 7.23 (d, 1H, $J$=2.4 Hz, Ar–H), 7.23–7.35 (m, 4H, Ar–H, O=C–CH=C), 7.40 (d, 1H, $J$=15.3 Hz, O=C–C=CH), 7.96 (d, 1H, $J$=8.7 Hz, Ar–H), 8.63 (s, 1H, O–CH=C), 8.73 (s, 1H, NH), 10.89 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 42.22, 102.31, 115.50, 116.32, 118.29, 124.36, 126.71, 127.22, 128.25, 131.31, 139.54, 156.87,

158.41, 162.80, 165.44, 174.68 ppm; ESI-MS ($m/z$): 322.09 $(M+1)^+$. Anal. ($C_{19}H_{15}NO_4$): C 71.02, H 4.71, N 4.36. Found: C 71.05, H 4.75, N 4.38%.

*4.3.19. (E)-N-(3,4-Difluorobenzyl)-3-(7-hydroxy-4-oxo-4H-chromen-3-yl)acrylamide (**5v**).* Color: white; mp: 253.2–253.7 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 4.35 (d, 2H, $J$=6 Hz, $CH_2$–Ar), 6.87 (d, 1H, $J$=2.1 Hz, Ar–H), 6.94 (dd, 1H, $J_1$=2.1 Hz, $J_2$=2.1 Hz, Ar–H), 7.12 (m, 1H, Ar–H), 7.21 (s, 1H, Ar–H), 7.27 (d, 1H, $J$=3.3 Hz, Ar–H), 7.24–7.35 (m, 2H, Ar–H, O=C–CH=C), 7.40 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.96 (d, 1H, $J$=8.7 Hz, Ar–H), 8.63 (s, 1H, O–CH=C), 10.89 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 42.21, 102.29, 115.50, 116.31, 118.29, 124.38, 126.70, 127.22, 128.11, 131.33, 139.54, 156.87, 158.34, 162.42, 165.44, 174.68 ppm; ESI-MS ($m/z$): 358.08 $(M+1)^+$. Anal. ($C_{19}H_{13}F_2NO_4$): C 63.87, H 3.67, N 3.92. Found: C 63.81, H 3.62, N 3.90%.

*4.3.20. (E)-N-(4-Fluorophenethyl)-3-(7-hydroxy-4-oxo-4H-chromen-3-yl)acrylamide (**5w**).* Color: brown; mp: 217.9–218.3 °C; yield: 77%; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 2.72–2.85 (m, 2H, $CH_2$–Ar), 3.35–3.47 (m, 2H, $CH_2$–N), 6.87 (d, 1H, $J$=2.1 Hz, Ar–H), 7.07–7.14 (m, 3H, Ar–H), 7.19–7.25 (m, 2H, Ar–H), 7.29 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.45 (d, 1H, $J$=15.3 Hz, O=C–C=CH), 7.96 (s, 1H, O–CH=C), 8.46 (d, 1H, $J$=1.5 Hz, Ar–H), 8.65 (s, 1H, NH), 10.88 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 34.23, 40.90, 102.40, 115.17, 115.65, 116.38, 118.35, 124.53, 127.16, 127.29, 128.36, 130.53, 135.72, 156.99, 158.41, 162.97, 165.57, 174.84 ppm; ESI-MS ($m/z$): 354.11 $(M+1)^+$. Anal. ($C_{20}H_{16}FNO_4$): C 67.98, H 4.56, N 3.96. Found: C 68.00, H 4.55, N 4.02%.

*4.3.21. (E)-Methyl 3-(7-methoxy-2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)acrylate (**6a**).* Color: yellow; mp: 156.2–156.6 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 3.30 (s, 3H, $CH_3$), 3.88 (s, 3H, $CH_3$–O), 3.89 (s, 3H, $CH_3$–O), 7.08–7.10 (dd, 2H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 7.16–7.19 (m, 2H, Ar–H), 7.19 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.33 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.65–7.67 (m, 2H, Ar–H), 8.01 ppm (d, 1H, $J$=9 Hz, Ar–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 51.47, 55.63, 56.25, 100.72, 113.67, 114.26, 115.24, 116.49, 120.89, 123.77, 126.91, 131.85, 137.09, 156.64, 161.84, 164.15, 167.11, 167.35, 175.39 ppm; ESI-MS ($m/z$): 367.11 $(M+1)^+$. Anal. ($C_{21}H_{18}O_6$): C 68.85, H 4.95. Found: C 68.88, H 4.99%.

*4.3.22. (E)-Ethyl 3-(7-methoxy-2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)acrylate (**6b**).* Color: white; mp: 157.9–158.3 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 1.17–1.22 (t, 3H, $CH_3$–C–O), 3.87 (s, 3H, $CH_3$–O), 3.88 (s, 3H, $CH_3$–O), 4.07–4.14 (q, 2H, $CH_2$–O), 7.07 (d, 1H, $J$=9 Hz, Ar–H) 7.15–7.18 (m, 3H, Ar–H), 7.26 (d, 1H, $J$=15.9 Hz, O=C–CH=C), 7.33 (d, 1H, $J$=15.9 Hz, O=C–C=CH), 7.64–7.66 (m, 2H, Ar–H), 7.99 ppm (d, 1H, $J$=6 Hz, Ar–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 14.20, 51.47, 55.31, 56.25, 100.71, 113.70, 114.26, 115.24, 116.29, 129.89, 123.18, 126.91, 131.90, 136.79, 156.64, 161.84, 164.15, 167.11, 167.35, 175.51 ppm; ESI-MS ($m/z$): 381.12 $(M+1)^+$. Anal. ($C_{22}H_{20}O_6$): C 69.46, H 5.30. Found: C 69.32, H 3.55%.

*4.3.23. (E)-N-Hexyl-3-(7-methoxy-2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)acrylamide (**6c**).* Color: white; mp: 185.1–185.3 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 0.83–0.86 (t, 3H, $CH_3$), 1.22–1.27 (m, 6H, $CH_2$), 1.38–1.41 (q, 2H, $CH_2$), 3.07–3.11 (q, 2H, $CH_2$), 3.87 (s, 3H, $CH_3$–O), 3.88 (s, 3H, $CH_3$–O), 7.06–7.08 (dd, 2H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 7.11 (d, 1H, $J$=15 Hz, O=C–CH=C), 7.14–7.16 (q, 2H, Ar–H), 7.17 (d, 1H, $J$=1.8 Hz, Ar–H), 7.48 (d, 1H, $J$=15 Hz, O=C–C=CH), 7.62–7.64 (q, 2H, Ar–H), 8.01 (d, 1H, $J$=8.4 Hz, Ar–H), 8.16–8.17 ppm (t, 1H, NH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 13.91, 22.06, 26.16, 29.06, 30.99, 42.59, 55.51, 56.16, 100.51, 114.09, 114.39, 115.02, 116.52, 124.14, 126.06, 126.80, 130.68, 131.60, 156.59, 161.45, 163.91, 165.13, 165.46, 175.47 ppm; ESI-MS ($m/z$): 426.20 $(M+1)^+$. Anal. ($C_{26}H_{29}NO_5$): C 71.70, H 6.71, N 3.22. Found: C 71.64, H 6.70, N 3.23%.

*4.3.24. (E)-N-tert-Butyl-3-(7-methoxy-2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)acrylamide (**6d**).* Color: white; mp: 131.1–131.5 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 1.27 (s, 9H, $CH_3$), 3.86 (s, 3H, $CH_3$–O), 3.87 (s, 3H, $CH_3$–O), 7.03 (d, 2H, $J$=9 Hz, Ar–H), 7.08 (d, 1H, $J$=15 Hz, O=C–CH=C), 7.11–7.14 (m, 2H, Ar–H), 7.51 (d, 1H, $J$=15 Hz, O=C–C=CH), 7.60–7.69 (dd, 2H, $J_1$=7.2 Hz, $J_2$=7.8 Hz, Ar–H), 7.80 (s, 1H, NH), 7.91 ppm (d, 1H, $J$=8.4 Hz, Ar–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 28.62, 50.13, 55.51, 56.14, 100.42, 114.10, 114.53, 114.97, 116.53, 125.20, 126.78, 127.33, 130.02, 131.55, 156.55, 161.40, 163.88, 165.17, 165.41, 175.47 ppm; ESI-MS ($m/z$): 408.18 $(M+1)^+$. Anal. ($C_{24}H_{25}NO_5$): C 70.74, H 6.18, N 3.44. Found: C 70.71, H 6.20, N 3.45%.

*4.3.25. (E)-2-Phenyl-3-styryl-4H-chromen-4-one (**6e**).* Color: yellow; mp: 168.0–168.5 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 6.83 (d, 1H, $J$=16.3 Hz, O=C–CH=C), 7.19–7.57 (m, 10H, Ar–H), 7.68 (m, 1H, Ar–H), 7.73–7.75 (m, 2H, Ar–H), 8.03 (d, 1H, $J$=16.3 Hz, O=C–C=CH), 8.32 ppm (d, 1H, $J$=8 Hz, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 105.3, 117.9, 118.1, 120.4, 123.8, 125.4, 126.5, 126.8, 127.8, 128.8, 130.1, 131.0, 133.5, 133.7, 134.7, 138.5, 155.7, 163.3, 177.7 ppm; ESI-MS ($m/z$): 325.11 $(M+1)^+$. Anal. ($C_{23}H_{16}O_2$): C 85.16, H 4.97. Found: C 85.20, H 4.95%.

*4.3.26. (E)-3-(7-Methoxy-2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)-N-phenylacrylamide (**6f**).* Color: yellow; mp: 127.4–127.9 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 3.88 (s, 3H, $CH_3$–O), 3.90 (s, 3H, $CH_3$–O), 7.01–7.04 (t, 1H, Ar–H), 7.08 (d, 1H, $J$=15 Hz, O=C–CH=C), 7.17–7.19 (m, 2H, Ar–H), 7.21 (d, 1H, $J$=9 Hz, Ar–H), 7.27–7.30 (t, 3H, Ar–H), 7.67–7.70 (m, 4H, Ar–H), 7.77 (d, 1H, $J$=15 Hz, O=C–C=CH), 8.05 (d, 1H, $J$=9 Hz, Ar–H), 10.27 ppm (s, 1H, NH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 55.53, 56.18, 100.57, 114.14, 114.26, 115.10, 116.52, 119.13, 123.15, 124.02, 125.65, 126.82, 128.66, 131.72, 132.57, 139.48, 156.61, 161.58, 163.99, 164.36, 166.20, 175.49 ppm; ESI-MS ($m/z$): 428.15 $(M+1)^+$. Anal. ($C_{26}H_{21}NO_5$): C 73.06, H 4.95, N 3.28. Found: C 73.08, H 4.90, N 3.31%.

*4.3.27. (E)-N-Benzyl-3-(7-methoxy-2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)acrylamide (**6g**).* Color: yellow; mp: 220.3–221.0 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 3.87 (s, 3H, $CH_3$–O), 3.89 (s, 3H, $CH_3$–O), 4.34 (d, 2H, $J$=6 Hz, $CH_2$–N), 7.07–7.09 (dd, 1H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 7.17 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.15–7.19 (m, 3H, Ar–H), 7.21–7.26 (m, 3H, Ar–H), 7.30–7.32 (m, 2H, Ar–H), 7.56 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.55–7.65 (m, 2H, Ar–H), 8.02 (d, 1H, $J$=9 Hz, Ar–H), 8.70 ppm (s, 1H, NH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 42.25, 55.52, 56.17, 100.54, 108.92, 114.11, 115.04, 116.53, 124.11, 125.64, 126.73, 126.82, 127.30, 128.26, 131.36, 131.62, 139.56, 156.60, 161.48, 163.94, 165.63, 175.46 ppm; ESI-MS ($m/z$): 442.16 $(M+1)^+$. Anal. ($C_{27}H_{23}NO_5$): C 73.46, H 5.25, N 3.17. Found: C 73.41, H 5.21, N 3.18%.

*4.3.28. (E)-N-(4-Fluorophenethyl)-3-(7-methoxy-2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)acrylamide (**6h**).* Color: yellow; mp: 186.2–186.8 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 2.71–2.75 (t, 2H, $CH_2$–Ar), 3.07–3.11 (q, 2H, $CH_2$–N), 3.87 (s, 3H, $CH_3$–O), 3.88 (s, 3H, $CH_3$–O), 7.00–7.03 (m, 2H, Ar–H), 7.06–7.08 (dd, 1H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 7.11 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.14–7.16 (m, 2H, Ar–H), 7.17 (d, 1H, $J$=2.4 Hz, Ar–H), 7.23–7.25 (q, 2H, Ar–H), 7.48 (d, 1H, $J$=15 Hz, O=C–C=CH), 7.62–7.64 (m, 2H, Ar–H), 8.01 (d, 1H, $J$=9 Hz, Ar–H), 8.16–8.18 ppm (t, 1H, NH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 34.17, 40.80, 55.52, 56.17, 100.53, 114.10, 114.34, 114.80, 115.08, 116.52, 124.12, 125.79, 126.80, 130.32, 130.43, 130.92, 131.60, 135.67, 156.60, 161.46,

163.93, 165.60, 175.47 ppm; ESI-MS ($m/z$): 474.16 $(M+1)^+$. Anal. ($C_{28}H_{24}FNO_5$): C 71.03, H 5.11, N 2.96. Found: C 71.00, H 5.11, N 2.95%.

*4.3.29. (E)-Methyl 3-(6,7-dimethoxy-4-oxo-2-phenyl-4H-chromen-3-yl)acrylate (**6i**).* Color: yellow; mp: 291.1–292.6 °C; $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$: 3.75 (s, 3H, $CH_3$), 3.99 (s, 3H, $CH_3$–O), 4.01 (s, 3H, $CH_3$–O), 6.92 (s, 1H, Ar–H), 7.46 (d, 1H, $J$=15.9 Hz, O=C–CH=C), 7.53 (d, 1H, $J$=15.9 Hz, O=C–C=CH), 7.55–7.59 (m, 3H, Ar–H), 7.62 (s, 1H, Ar–H), 7.63–7.67 ppm (m, 2H, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$: 51.45, 55.93, 56.53, 100.61, 113.97, 114.52, 116.034, 116.21, 119.95, 123.77, 126.91, 131.25, 137.09, 153.53, 161.58, 164.05, 167.11, 167.35, 175.05 ppm; ESI-MS ($m/z$): 367.11 $(M+1)^+$. Anal. ($C_{21}H_{18}O_6$): C 69.46, H 5.30. Found: C 69.31, H 3.55%.

*4.3.30. (E)-N-tert-Butyl-3-(6,7-dimethoxy-4-oxo-2-phenyl-4H-chromen-3-yl)acrylamide (**6j**).* Color: white; mp: 243.9–245.3 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 1.26 (s, 9H, $CH_3$), 3.88 (s, 3H, $CH_3$–O), 3.90 (s, 3H, $CH_3$–O), 7.06 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.26 (s, 1H, Ar–H), 7.43 (s, 1H, Ar–H), 7.51 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.60–7.67 (m, 5H, Ar–H), 7.80 ppm (s, 1H, NH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 28.61, 51.31, 55.81, 56.42, 100.32, 114.35, 114.80, 115.21, 116.68, 125.40, 126.78, 127.33, 130.02, 130.95, 156.52, 161.40, 164.15, 165.17, 165.22, 175.04 ppm; ESI-MS ($m/z$): 408.18 $(M+1)^+$. Anal. ($C_{24}H_{25}NO_5$): C 70.74, H 6.18, N 3.44. Found: C 70.72, H 6.20, N 3.44%.

*4.3.31. (E)-3-(6,7-Dimethoxy-4-oxo-2-phenyl-4H-chromen-3-yl)-N-phenylacrylamide (**6k**).* Color: yellow; mp: 264.5–265.5 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 3.90 (s, 3H, $CH_3$–O), 3.91 (s, 3H, $CH_3$–O), 7.00–7.05 (t, 1H, Ar–H), 7.23–7.30 (m, 3H, Ar–H), 7.28 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.46 (s, 1H, Ar–H), 7.46–7.73 (m, 7H, Ar–H), 7.787 (d, 1H, $J$=15.3 Hz, O=C–C=CH), 10.33 ppm (s, 1H, NH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 55.83, 56.46, 100.49, 103.98, 114.41, 115.92, 116.25, 119.19, 123.15, 125.86, 128.66, 129.75, 131.12, 132.04, 132.42, 139.42, 147.71, 151.00, 154.59, 164.26, 165.86, 175.06 ppm; ESI-MS ($m/z$): 428.15 $(M+1)^+$. Anal. ($C_{26}H_{21}NO_5$): C 73.06, H 4.95, N 3.28. Found: C 73.08, H 4.90, N 3.31%.

*4.3.32. (E)-N-Benzyl-3-(6,7-dimethoxy-4-oxo-2-phenyl-4H-chromen-3-yl)acrylamide (**6l**).* Color: yellow; mp: 223.3–223.8 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 3.90 (s, 3H, $CH_3$–O), 391 (s, 3H, $CH_3$–O), 4.33 (d, 2H, $J$=6 Hz, $CH_2$–N), 7.17 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.22–7.26 (m, 3H, Ar–H), 7.28 (s, 1H, Ar–H), 7.30–7.33 (t, 2H, Ar–H), 7.46 (s, 1H, Ar–H), 7.58 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.61–7.65 (m, 3H, Ar–H), 7.68–7.70 (d, 2H, $J$=6 Hz, Ar–H), 8.72–8.74 ppm (t, 1H, NH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 42.27, 55.85, 56.47, 100.48, 104.02, 114.48, 115.95, 125.82, 126.75, 127.33, 128.27, 128.67, 129.70, 131.05, 131.28, 132.14, 139.53, 147.70, 151.01, 154.58, 165.49, 165.58, 175.11 ppm; ESI-MS ($m/z$): 442.16 $(M+1)^+$. Anal. ($C_{27}H_{23}NO_5$): C 73.46, H 5.25, N 3.17. Found: C 73.41, H 5.21, N 3.18%.

*4.3.33. (E)-3-(6,7-Dimethoxy-4-oxo-2-phenyl-4H-chromen-3-yl)-N-(4-fluorophenethyl)acrylamide (**6m**).* Color: yellow; mp: 275.1–276.6 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 2.71–2.74 (t, 2H, $CH_2$–Ar), 3.31–3.34 (q, 2H, $CH_2$–N), 3.87 (s, 3H, $CH_3$–O), 389 (s, 3H, $CH_3$–O), 7.08 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.09 (d, 1H, $J$=3 Hz, Ar–H), 7.12 (s, 1H, Ar–H), 7.21–7.23 (q, 2H, Ar–H), 7.24 (s, 1H, Ar–H), 7.42 (s, 1H, Ar–H), 7.44 (d, 1H, $J$=15 Hz, O=C–C=CH), 7.59–7.62 (m, 5H, Ar–H), 8.26–8.28 ppm (t, 1H, NH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 40.75, 55.85, 56.48, 100.46, 104.03, 114.52, 114.83, 115.10, 115.96, 126.03, 128.67, 129.72, 130.33, 130.44, 130.86, 131.04, 132.19, 135.66, 147.70, 151.02, 154.58, 165.35, 165.57, 175.12 ppm; ESI-MS ($m/z$): 474.16 $(M+1)^+$. Anal. ($C_{28}H_{24}FNO_5$): C 71.03, H 5.11, N 2.96. Found: C 71.02, H 5.11, N 2.93%.

*4.3.34. (E)-Methyl 3-(7-hydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl)acrylate (**6n**).* Color: yellow; mp: 331.2–331.8 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 3.65 (s, 3H, $CH_3$), 6.86 (d, 1H, $J$=9 Hz, Ar–H), 6.93–6.95 (dd, 1H, $J_1$=2.4 Hz, $J_2$=1.8 Hz, Ar–H), 6.95–6.98 (m, 2H, Ar–H), 7.29 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.32 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.52–7.54 (m, 2H, Ar–H), 7.95 (d, 1H, $J$=9 Hz, Ar–H), 10.33 (s, 1H, OH), 10.86 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 51.46, 101.53, 113.75, 114.22, 120.89, 123.60, 126.88, 131.89, 137.16, 156.61, 161.51, 164.24, 167.11, 167.63, 175.35 ppm; ESI-MS ($m/z$): 339.08 $(M+1)^+$. Anal. ($C_{19}H_{14}O_6$): C 67.45, H 4.17. Found: C 67.41, H 4.21%.

*4.3.35. (E)-Ethyl 3-(7-hydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl)acrylate (**6o**).* Color: white; mp: 319.3–319.9 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 1.19–1.21 (t, 3H, $CH_3$–C–O), 4.10–4.13 (q, 2H, $CH_2$–O), 6.87 (d, 1H, $J$=2.4 Hz, Ar–H), 6.94–6.95 (dd, 1H, $J_1$=2.4 Hz, $J_2$=1.8 Hz, Ar–H), 6.96–6.97 (m, 2H, Ar–H), 7.27 (d, 1H, $J$=15.9 Hz, O=C–CH=C), 7.33 (d, 1H, $J$=15.9 Hz, O=C–C=CH), 7.53–7.54 (m, 2H, Ar–H), 7.96 (d, 1H, $J$=9 Hz, Ar–H), 10.33 (s, 1H, OH), 10.86 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 14.15, 59.80, 102.21, 113.02, 115.47, 120.70, 122.16, 127.24, 131.91, 137.28, 156.50, 160.51, 163.94, 166.91, 167.19, 175.32 ppm; ESI-MS ($m/z$): 353.11 $(M+1)^+$. Anal. ($C_{20}H_{16}O_6$): C 68.18, H 4.58. Found: C 68.11, H 4.69%.

*4.3.36. (E)-N-Hexyl-3-(7-hydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl)acrylamide (**6p**).* Color: white; mp: 273.9–274.4 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 0.83–0.85 (t, 3H, $CH_3$), 1.21–1.27 (m, 6H, $CH_2$), 1.37–1.41 (q, 2H, $CH_2$), 3.07–3.10 (q, 2H, $CH_2$), 6.86 (d, 1H, $J$=1.8 Hz, Ar–H), 6.92–6.96 (m, 3H, Ar–H), 7.11 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.45 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.49–7.50 (q, 2H, Ar–H), 7.94 (d, 1H, $J$=9 Hz, Ar–H), 8.10–8.12 ppm (t, 1H, NH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 13.89, 22.04, 26.14, 29.04, 30.95, 40.23, 102.51, 106.26, 113.52, 114.31, 115.32, 116.52, 124.14, 126.46, 126.80, 130.68, 131.55, 156.52, 160.25, 162.80, 165.52, 175.47 ppm; ESI-MS ($m/z$): 408.18 $(M+1)^+$. Anal. ($C_{24}H_{25}NO_5$): C 70.74, H 6.18, N 3.44. Found: C 70.69, H 6.17, N 3.39%.

*4.3.37. (E)-N-tert-Butyl-3-(7-hydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl)acrylamide (**6q**).* Color: white; mp: 322.4–322.9 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 1.26 (s, 9H, $CH_3$), 6.84 (d, 2H, $J$=2.1 Hz, Ar–H), 6.91–6.97 (m, 3H, Ar–H), 7.06 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.46–7.51 (m, 3H, Ar–H, O=C–C=CH), 7.81 (s, 1H, NH), 7.95 (d, 1H, $J$=8.7 Hz, Ar–H), 10.26 (s, 1H, OH), 10.83 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 28.61, 50.12, 102.20, 114.08, 114.53, 114.27, 115.48, 125.20, 127.38, 127.33, 130.02, 131.68, 156.58, 160.25, 163.88, 165.36, 165.65, 175.48 ppm; ESI-MS ($m/z$): 380.14 $(M+1)^+$. Anal. ($C_{22}H_{21}NO_5$): C, 69.64; H, 5.58; N, 3.69. Found: C 69.49, H 5.55, N 3.66%.

*4.3.38. (E)-3-(7-Hydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl)-N-phenylacrylamide (**6r**).* Color: yellow; mp: 318.9–319.6 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 6.87 (d, 1H, $J$=2.4 Hz, Ar–H), 6.95–6.96 (dd, 1H, $J_1$=2.4 Hz, $J_2$=2.4 Hz, Ar–H), 6.96–6.99 (m, 2H, Ar–H), 7.01–7.03 (t, 1H, Ar–H), 7.28 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.27–7.29 (t, 2H, Ar–H), 7.54–7.56 (m, 2H, Ar–H), 7.69 (d, 2H, $J$=7.8 Hz, Ar–H), 7.75 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.99 (d, 1H, $J$=8.4 Hz, Ar–H), 10.26 (s, 1H, NH), 10.33 (s, 1H, OH), 10.85 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 102.19, 106.43, 113.67, 115.47, 119.15, 122.50, 123.13, 125.19, 127.22, 128.67, 131.85, 133.01, 139.53, 156.54, 160.32, 162.87, 164.52, 166.43, 175.48 ppm; ESI-MS

($m/z$): 400.11 $(M+1)^+$. Anal. ($C_{24}H_{17}NO_5$): C 72.17, H 4.29, N 3.51. Found: C 72.14, H 4.22, N 5.58%.

*4.3.39. (E)-N-Benzyl-3-(7-hydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl)acrylamide (**6s**).* Color: yellow; mp: 279.1–279.5 °C; $^1$H NMR: (600 MHz, DMSO-$d_6$) $\delta$: 4.34 (d, 2H, $J$=6 Hz, $CH_2$–N), 6.86 (d, 1H, $J$=1.8 Hz, Ar–H), 6.93–6.96 (m, 3H, Ar–H), 7.18 (d, 1H, $J$=15 Hz, O=C–CH=C), 7.21–7.26 (m, 3H, Ar–H), 7.30 (d, 1H, $J$=15 Hz, O=C–C=CH), 7.31 (s, 1H, Ar–H), 7.51–7.55 (m, 3H, Ar–H), 7.96 (d, 1H, $J$=8.4 Hz, Ar–H), 3.67–8.69 (t, 1H, NH), 10.26 (s, 1H, OH), 10.81 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 42.23, 102.16, 106.94, 114.02, 115.44, 116.53, 122.46, 125.37, 125.18, 126.73, 126.82, 127.70, 128.28, 131.36, 131.75, 139.61, 156.51, 160.23, 164.44, 165.86, 175.46 ppm; ESI-MS ($m/z$): 414.15 $(M+1)^+$. Anal. ($C_{25}H_{19}NO_5$): C 72.63, H 4.63, N 3.39. Found: C 72.60, H 4.60, N 3.39%.

*4.3.40. (E)-N-(4-Fluorophenethyl)-3-(7-hydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl)acrylamide (**6t**).* Color: yellow; mp: 165.2–165.8 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 2.70–2.75 (t, 2H, $CH_2$–Ar), 3.29–3.32 (q, 2H, $CH_2$–N), 6.86 (s, 1H, Ar–H), 6.92–6.97 (m, 3H, Ar–H), 7.07–7.15 (m, 3H, Ar–H, O=C–CH=C), 7.21–7.26 (q, 2H, Ar–H), 7.46 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.51 (d, 2H, $J$=8.7 Hz, Ar–H), 7.95 (d, 1H, $J$=8.7 Hz, Ar–H), 8.25–8.28 (t, 1H, NH), 10.32 (s, 1H, OH), 10.84 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 34.17, 40.80, 102.16, 106.34, 113.61, 114.55, 114.80, 115.45, 116.52, 123.20, 125.33, 127.40, 130.32, 130.43, 130.92, 131.72, 135.67, 156.53, 160.26, 161.80, 165.60, 175.47 ppm; ESI-MS ($m/z$): 446.15 $(M+1)^+$. Anal. ($C_{26}H_{20}FNO_5$): C 70.11, H 4.53, N 3.14. Found: C 70.19, H 4.56, N 3.25%.

*4.3.41. (E)-N-Cyclohexyl-3-(7-hydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl)acrylamide (**6u**).* Color: yellow; mp: 287.6–288.4 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 1.02–1.31 (m, 4H, cyclohexane), 1.54 (d, 2H, $J$=11.4 Hz, cyclohexane), 1.65–1.75 (t, 4H, cyclohexane), 3.58 (d, 1H, $J$=7.2 Hz, cyclohexane), 6.85 (d, 1H, $J$=2.1 Hz, Ar–H), 6.91–6.96 (m, 3H, Ar–H), 7.11 (d, 1H, $J$=15.6 Hz, O=C–CH=C), 7.47 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.49–7.52 (m, 2H, Ar–H), 7.96 (d, 1H, $J$=9 Hz, Ar–H), 8.07 (d, 1H, $J$=7.8 Hz, NH), 10.30 (s, 1H, OH), 10.81 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 24.85, 25.72, 32.33, 51.15, 102.50, 113.48, 114.32, 115.30, 116.44, 124.14, 126.46, 126.81, 130.68, 131.55, 156.52, 160.26, 162.80, 165.52, 175.49 ppm; ESI-MS ($m/z$): 406.13 $(M+1)^+$. Anal. ($C_{24}H_{23}NO_5$): C 71.10, H 5.72, N 3.45. Found: C 71.11, H 5.85, N 3.45%.

*4.3.42. (E)-3-(7-Hydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl)-N-(pyridin-2-yl)acrylamide (**6v**).* Color: yellow; mp: 311.6–312.2 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 6.88 (s, 1H, Ar–H), 6.93–6.99 (q, 3H, Ar–H, pyridine), 7.05–7.12 (m, 1H, pyridine), 7.33 (d, 1H, $J$=15.3 Hz, O=C–CH=C), 7.54 (d, 2H, $J$=8.4 Hz, Ar–H), 7.72–7.77 (m, 1H, pyridine), 7.78 (d, 1H, $J$=15.6 Hz, O=C–C=CH), 7.98 (d, 1H, $J$=8.7 Hz, Ar–H), 8.17 (d, 1H, $J$=8.4 Hz, Ar–H), 8.31 (d, 1H, $J$=4.5 Hz, pyridine), 10.40 (s, 1H, OH), 10.74 (s, 1H, NH), 10.80 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 102.22, 113.64, 114.26, 115.47, 117.43, 119.27, 123.13, 125.19, 131.85, 133.01, 138.11, 148.66, 150.26, 156.54, 160.32, 162.87, 164.52, 166.43, 175.44 ppm; ESI-MS ($m/z$): 401.11 $(M+1)^+$. Anal. ($C_{23}H_{16}N_2O_5$): C 69.00, H 4.03, N 7.00. Found: C 68.97, H 4.05, N 7.01%.

*4.3.43. (E)-7-Hydroxy-2-(4-hydroxyphenyl)-3-(3-oxo-3-(piperidin-1-yl)prop-1-enyl)-4H-chromen-4-one (**6w**).* Color: white; mp: 300.5–300.9 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 1.46–1.60 (m, 6H, piperidine), 3.50 (s, 4H, piperidine), 6.86 (d, 1H, $J$=2.1 Hz, Ar–H), 6.93–6.97 (m, 3H, Ar–H), 7.19 (d, 1H, $J$=15 Hz, O=C–CH=C), 7.50–7.53 (q, 2H, Ar–H), 7.92–7.97 (t, 2H, Ar–H, O=C–C=CH), 10.30 (s, 1H, OH), 10.84 ppm (s, 1H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 24.33, 25.14, 48.43, 102.21, 106.43, 113.48, 114.96, 115.30, 116.32, 124.11, 126.46, 126.16, 130.68, 131.34, 156.52, 160.23, 162.80, 165.50, 175.50 ppm; ESI-MS ($m/z$): 392.14 $(M+1)^+$. Anal. ($C_{23}H_{21}NO_5$): C 70.58, H 5.41, N 3.58. Found: C 70.42, H 5.38, N 3.52%.

*4.3.44. (E)-7-Hydroxy-2-(4-hydroxyphenyl)-3-(3-oxo-3-(1H-pyrazol-1-yl)prop-1-enyl)-4H-chromen-4-one (**6x**).* Color: yellow; mp: 297.1–297.7 °C; $^1$H NMR: (300 MHz, DMSO-$d_6$) $\delta$: 6.63–6.65 (q, 1H, pyrazole), 6.90 (d, 1H, $J$=2.1 Hz, Ar–H), 6.95–7.00 (m, 3H, Ar–H), 7.58–7.64 (m, 3H, Ar–H, pyrazole, O=C–CH=C), 7.95 (d, 1H, $J$=6 Hz, Ar–H), 7.97 (d, 1H, $J$=15.3 Hz, O=C–C=CH), 8.43–8.44 (t, 1H, Ar–H), 8.75 (d, 1H, $J$=15.6 Hz, pyrazole), 10.56 ppm (s, 2H, OH); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$: 102.22, 106.28, 110.43, 113.64, 115.47, 119.27, 123.13, 125.19, 129.53, 131.85, 133.01, 144.63, 156.54, 160.32, 162.87, 164.52, 166.43, 175.44 ppm; ESI-MS ($m/z$): 375.09 $(M+1)^+$. Anal. ($C_{21}H_{14}NO_5$): C 67.38, H 3.77, N 7.48. Found: C 67.44, H 3.71, N 7.42%.

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## Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2012.09.017. These data include MOL files and InChIKeys of the most important compounds described in this article.

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