Palladium-Catalyzed Coupling of 3-Halocoumarins, –Chromenes and –Quinolones with Various Nitrogen-Containing Nucleophiles

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An efficient and general palladium-catalyzed coupling of 3-bromocoumarins, 3-bromoquinolin-2(1*H*)-ones and 3-iodo-2*H*-chromenes with a variety of nitrogen-containing nucleophiles (azole, amide, lactame, sulfonamide, amine, and urea) is described. The reaction proceeds rapidly and cleanly in dioxane providing the coupling products in good to excellent yields. The chemoselectivity in the amina-

tion of polybromocoumarins with anilines and *n*BuNH₂ was studied. Under the conditions of Pd (OAc)₂/ Xantphos/ Cs₂CO₃, polyhalocoumarins underwent selective amination on the C3-Br bond. Further Pd-coupling reactions furnished disubstituted coumarins in good yields.

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Introduction

Heterocyclic compounds are indispensable structural units finding use in medicinal chemistry and as valuable organic synthetic building blocks. Among the various classes of heterocyclic compounds, the coumarin ring is present in a very broad range of natural and non natural products of biological interest.^[1] Over the past decades, synthesis and screening of coumarin compounds for drug discovery has been a subject of constant interest in medicinal chemistry. 3-*N*-Substituted coumarins represent a promising class of synthetic compounds because of their noticeable biological activities, including antimicrobial,^[2] antiviral,^[3] antiallergic,^[4] and anticancer^[5] properties. Recent works demonstrated that novobiocin^[Erreur ! Signet non défini. a,b] and its denoviose analogue 4TCNA,^[6] two 3-amidocoumarin derivatives, have been shown to bind to the C-terminal domain of heat shock protein 90 (hsp90), an exciting new target in cancer drug discovery,^[7] leading to a decrease in hsp90 client proteins in various cancer cell lines.^[8]

In contrast to the numerous applications of 3-aminocoumarin derivatives, there are very few synthetic approaches to these compounds. To introduce a variety of amine substitutions at the 3-position, the most common route is undoubtedly the *N*-functionalization of 3-NH₂-coumarins,^[9] readily obtained from the reduction of 3-NO₂-coumarins,^[10] or by reaction of 3-bromocoumarins with sodium azide under copper-catalysis.^[11] Alternative route consists on the condensation of salicylaldehydes with glycine derivatives^[12,9a] Although these multi-step procedures are useful to prepare 3-*N*-substituted coumarins, however, most of them require an extra step for the *N*-functionalization, and thus find somewhat limited applications in library synthesis. Therefore, the search for simple and selective procedures as well as diversity oriented reactions, such as metal-catalyzed couplings, presents an interesting challenge.

In 2007, Wu reported the preparation of 3-aminocoumarins via the coupling of 3-bromocoumarins with anilines^[13] using Pd₂(dba)₃/Xantphos couple in the presence of K₂CO₃ in toluene. In

the same year, we reported a general access to a wide range of 3-*N*-substituted aminocoumarins by the palladium-catalyzed coupling of 3-bromocoumarins with a wider variety of nitrogen-containing nucleophiles,^[14] including amides, sulfonamides, carbamates, ureas, and functionalized amines. We demonstrated that the use of Pd(OAc)₂/Xantphos as the catalytic system in the presence of Cs₂CO₃ in dioxane proved to be a versatile protocol for the preparation of various 3-*N*-substituted coumarins^[Erreur ! Signet non défini. 15] as well as related heterocyclic structures, 3-*N*-substituted quinolin-2(1*H*)-ones.^[15] From a synthetic viewpoint, these C–N bond couplings represent the shortest and most efficient route to 3-*N*-substituted coumarins and quinolin-2(1*H*)-ones for the purpose of our medicinal chemistry screening programs.^[16]

As part of our continuing effort at the functionalization of heterocycles via transition metal-catalyzed reactions,^[17] combined with our interest in discovering new hsp90 inhibitors,^[6,8,16a] we decided to expand the scope of this reaction, to study the palladium-catalyzed coupling of a series of heterocyclic substrates, such as 3-halocoumarin, -quinolin-2(1*H*)-one and 2*H*-chromene derivatives with a wider variety of nitrogen-containing nucleophiles, including amides, sulfonamides, lactams, urea, anilines, benzylamines and azoles derivatives. In this paper we wish to detail our progress in this reaction, which allows for the high yielding synthesis of a wide range of 3-*N*-substituted aminocoumarins and related heterocyclic structures of biological interest.

Results and Discussion

The starting material functionalized 3-bromocoumarins **1** were prepared from substituted salicylaldehydes by a one-pot bromination/Wittig/cyclization reaction according to our previous protocol.^[18] Initially, we studied the reaction of a 3-bromocoumarin (1 equiv) with phenylacetamide (1.2 equiv). The optimum conditions for the palladium-catalyzed coupling were found through a series of experiments in which sequential changes were made to the catalyst, the ligand, the base and the solvent used for the reaction. The best conditions required, in a sealed tube, the use of Pd(OAc)₂ (4 mol%), Xantphos (4 mol%) as the ligand, Cs₂CO₃ (1.5 equiv.) as the base, in dioxane at 100 °C. Accordingly, the expected 3-amidocoumarin **2a** was obtained in a satisfactory 76% yield after only 0.5 h. It is worthy to note that the reaction does not seem to be sensitive to steric hindrance, since the presence

of a methyl (entry 1) or a phenyl (entry 3) substituent on the C-4 position of 3-bromocoumarins, does not alter the course of the coupling. The reaction also worked well in the presence of a variety of nucleophiles, including aromatic, heteroaromatic and aliphatic amides (entries 2-5). The selectivity of this reaction must be underlined with respect to both coupling partners. For coumarin containing two C-Br bonds, the reaction gave selectively the monocoupling product **2b** (51%, entry 2), clearly indicating that the oxidative addition of palladium into the C-Br bond was facilitate on C3 rather than on C8. With 2-hydroxypropanamide, the amidation reaction of 3-bromocoumarin occurred rather than the etherification process, giving exclusively the amide **2e** (60%, entry 5). Next, the conditions employed for entries 1-5 were applied for the preparation of compounds **2f-h**. At 100 °C, 3-bromocoumarin did not react with lactams even if other ligands and palladium sources were used (data not shown). Nevertheless, performing the reaction at a higher temperature (130° C), we were pleased to observe the formation of lactams-containing coumarin, whatever the size of the lactame ring used. Thus, **2f**, **2g** and **2h** were obtained in satisfactory to good yields (86%, 65% and 41% respectively, entries 6-8). Next, arylsulfonamides which are poor nucleophilic partners were examined (entries 9 and 10). In these examples, although the desired products **2i** and **2j** were obtained, the yields were moderate (53% and 42%, respectively), possibly due to the low reactivity of the sulfonamide function. Anilines and benzylamines also react efficiently to produce the corresponding coupling products **2k-m** in good yields (entries 10-12). Next, we were pleased to observe that the ethoxycarbonyl function of a glycine ester was well tolerated under the coupling-conditions as **2o** was obtained in a satisfactory 57% yield, although a longer reaction time was needed (12 h, entry 15).

Since the molecules containing heteroaryl-azole linkages are prevalent in biological and pharmaceutical sciences, azoles nucleus (e.g., indole, 1*H*-indazole, 1*H*-benzimidazole, 1*H*-[2,3-*b*]pyrrolopyridine, 1*H*-pyrrole and 1*H*-pyrazole) were next evaluated as coupling partners with 3-bromocoumarins. As it was previously observed for lactams, reactions of azoles with 3-bromocoumarins occurred at 130 °C, and the coupling products **2p-v** were isolated in yields ranging from 36 to 95%, (entries 16-22). The efficiency of this protocol was also demonstrated in the coupling of indoles with 3-bromoquinolin-2(1*H*)-ones, as electrophilic partners. As shown in entries 23 and 24, reaction of indole and 5-methoxyindole with 3-bromo-1-methylquinolin-2-(1*H*)-one under optimal conditions gave the desired coupling products **3a** and **3b** in excellent yields (84% and 98%, respectively).

To expand the scope of this protocol in the case of other heterocyclic substrates, we next focused our attention to the coupling of these nitrogen-containing-nucleophiles with 4-substituted-3-iodo-2*H*-chromenes.^[19] A variety of nucleophiles,

including amides, amines, sulfonamides, lactams and urea derivatives were examined to establish the scope and the generality of the present transformation; the results are summarized in Table 2. Several functionalized aromatic amides were firstly evaluated and the expected chromenes **5a-d** were isolated in excellent yields within one hour at 100 °C (entries 1-4). One can note that the presence of a substituent on the C-4 position of the chromene nucleus, does not interfere with the general scope of this reaction. Interestingly, products **5c** and **5d** revealed excellent chemical selectivities preserving the C-OTs and C-Cl bonds, which could undergo further metal-catalyzed functionalization processes.^[20] Aliphatic amides also were coupled successfully with 3-iodo-4-phenylchromene and provided the desired chromenes **5e-f** in acceptable yields (entries 5-6). As shown in entries 7-9 the coupling protocol was also quite effective with arylsulfonamide, urea and aniline derivatives to prepare the corresponding 3-*N*-substituted chromenes **5g-i**. Finally, as it was previously observed with 3-bromocoumarins (Table 1, entries 6-8), by achieving the coupling reaction with lactams at 130° C, we were pleased to observe the total conversion of the starting materials and chromenes **5j, k** were isolated in excellent yields (entries 10-11).

Next, we have studied the reactivity of various nitrogen-containing nucleophiles (e.g.) towards a variety of polyhalogenated coumarins^[18]. The results of this study are summarized in Table 3. Under the above experimental conditions, amination of coumarins **6a-e** with 4-methoxyaniline as well as *n*-BuNH₂ furnished 3-aminocoumarins **7a-e** and **8a-e** with a total chemoselectivity and in good isolated yields. In each case, amination occurs at the more reactive C3-Br bond, and the other bromo and chloro substituents remains unchanged. In the case of 3,5-dibromo-2*H*-chromen-2-one **6a**, a small amount of 3-5-diaminocoumarin and 5-amino-3-bromocoumarin byproducts were also observed when using 4-MeO-aniline and *n*BuNH₂ as nucleophiles parthners. A similar selectivity was observed when morpholine was used as nucleophile to provide compound **9** in a good 79% yield (entry 11).

The 3-amino-bromocoumarins **7-9** thus obtained are useful synthetic intermediates for the introduction of various substituents on the surviving C-Br bond. Examples reported in Table 4 illustrate some coupling reactions of these substrates with boronic acids, anilines and *N*-tosylhydrazones. As observed in entries 1-3, Suzuki couplings using Pd(PPh₃)₄, K₂CO₃ (2 equiv) in toluene/EtOH (2:1) at 100 °C^[21] furnished the required Suzuki-coupling products in good to excellent yields. Amination of **7a** was achieved with Pd(OAc)₂ as catalyst, Xantphos as ligand and Cs₂CO₃ as base in hot dioxane to give **10d** in an acceptable yield of 60% (entry 4). Finally the Pd-coupling of **7b** with a *N*-tosylhydrazone furnished the 1,1-diarylethylene derivative **10e** which will be evaluated in our group as a *iso*CA-4 analogue of biological interest.^{Erreur ! Signet non défini.}

Table 1. Synthesis of functionalized 3-*N* substituted aminocoumarins **2** and aminoquinolin-2(1*H*)-ones **3**.

Entry	Compound	Entry	Compound	Entry	Compound
1		9		17	
2		10		18	
3		11		19	
4		12		20	
5		13		21	
6		14		22	
7		15		23	
8		16		24	

[a] The reaction was performed at 130 °C.

[b] Reaction conducted with 4-amino aniline (1 equiv) and 3-bromocoumarin derivative (2 equiv). Under these conditions, a 15% of monocoupling product was obtained.

[c] Reaction time: 12 h.

Table 2. Synthesis of functionalized 3-*N*-substituted aminochromenes **5**.

Entry	Compound	Entry	Compound	Entry	Compound
1	<p>5a 82%</p>	5	<p>5e 60%</p>	9	<p>5i^[a] 68%</p>
2	<p>5b 95%</p>	6	<p>5f 57%</p>	10	<p>5j^[b] 90%</p>
3	<p>5c 86%</p>	7	<p>5g 61%</p>	11	<p>5k^[b] 92%</p>
4	<p>5d 97%</p>	8	<p>5h^[a] 50%</p>		

^[a] Reaction conducted with nitrogen nucleophile (1 equiv) and 3-iodochromene derivative (2 equiv).

^[b] Reaction was performed at 130 °C.

Table 3. Synthesis of bromo-substituted-3-*N*-substituted aminocoumarins **7**, **8**.

Entry	Polyhalogenated coumarin	Nucleophile	Product
1			 7a ^[a] 74%
2		„	 7b 88%
3		„	 7c 99%
4		„	 7d 61%
5		„	 7e 73%
6		$n\text{Bu-NH}_2$	 8a ^[b] 74%
7		„	 8b 66%
8		„	 8c 66%
9		„	 8d 76%
10		„	 8e 82%
11			 9 79%

^[a] 20 % of the *bis*-coupled product **7aa** on the 3- and 5-position was also isolated.

^[b] 21 % of the mono-coupled product **8aa** on the 5-position was also isolated.

Table 4. Synthesis of polysubstituted chromenes **10**.

Entry	bromo-coumarin	Nucleophile	Product
1	7a		 10a^[a] (90%)
2	7c	“	 10b^[a] (58%)
3	9	“	 10c^[a] (99%)
4	7a		 10d^[b] (60%)
5	7b		 10e^[c] (55%)

^[a] The reactions were performed with 1 equiv. of **7a**, **7c** or **9**, 1.2 equiv of 4-OMeC₆H₄B(OH)₂, 5 mol% of Pd(PPh₃)₄, K₂CO₃ (2 equiv), in toluene/EtOH (2:1) at 100 °C for 2-3 h.

^[b] The reaction was performed with 1 equiv. of **7a**, 2 equiv of 3,4,5-trimethoxyaniline, 10 mol% of Pd(OAc)₂, Xantphos (10 mol%), Cs₂CO₃ (1.5 equiv), in dioxane at 100 °C for 24 h.

^[c] The reaction was performed with 1 equiv. of **7b**, 1.2 equiv of *N*-tosylhydrazine, 10 mol% of Pd₂(dba)₃, Xphos (20 mol%), *t*BuOLi (2.5 equiv), in dioxane at 80 °C for 3 h.

Conclusions

In summary of this study, we demonstrated that the use of Pd(OAc)₂/Xantphos couple is a versatile and efficient catalytic system for the coupling of a wide range of nitrogen-containing nucleophiles with 3-halocoumarins, -quinolinones and -chromenes. Various amide, lactame, amine, sulfonamide, urea and azole derivatives were successfully used to give the coupling products in high yields. We also showed that amination of various polyhalogenated coumarins selectively provides 3-amino-coumarin **7**, **8** in good yields. A subsequent coupling on the remaining C-Br bond furnished various disubstituted coumarins in excellent yields. The exploitation of this procedure will allow us to quickly

synthesize a library of polysubstituted coumarins as potent inhibitors of hsp90.

Experimental Section

General comments

All glasswares were oven-dried at 140 °C and all reactions were conducted under an argon atmosphere. Solvents: Et₂O, cyclohexane, ethyl acetate (EtOAc), for chromatography were technical grade. All new compounds were characterized by ¹H-NMR, ¹³C-NMR, and IR spectroscopy. ¹H and ¹³C NMR spectra were measured in CDCl₃ with a Bruker Avance 300. ¹H chemical shifts are reported in ppm from an internal standard TMS or of residual chloroform (7.27 ppm). The following abbreviation are used: m (multiplet), s (singlet), br s (broad singlet), d (doublet), t (triplet), dd (doublet of doublet), dt (doublet of triplet). ¹³C chemical shifts are reported in ppm from the central peak of deuteriochloroform (77.14). IR spectra were measured on a Bruker Vector 22 spectrophotometer (neat, cm⁻¹). Analytical TLC was performed on Merck precoated silica gel 60 F-254 plates. Merck silica gel 60 (230-400 mesh) was used for column chromatography. The plates were visualized by either UV light (254 nm), or by a solution of phosphomolybdic acid in ethanol. Melting points (m.p.) were recorded on a Büchi B-450 apparatus and were uncorrected.

General procedure for the synthesis of coumarins **2a-v**, quinolones **3a, b** and chromenes **5a-l**.

A flame-dried resealable Schlenk tube was charged with Pd(OAc)₂ (0.04 mmol, 4 mol%), Xantphos (0.04 mmol, 4 mol%), heterocyclic halide (1.0 mmol), nitrogen nucleophile (1.2 mmol) and Cs₂CO₃ (1.5 mmol). The Schlenk tube was capped with a rubber septum, evacuated and backfilled with argon; this evacuation/ backfill sequence was repeated one additional time. The liquid reactant(s) and 1,4-dioxane (2 mL per mmol) were added through the septum. The septum was replaced with a teflon screwcap. The Schlenk tube was sealed, and the mixture was stirred at 100 °C or 130 °C (for temperature and reaction time: see, Tables 1 and 2). The resulting suspension was cooled to room temperature and filtered through a pad of Celite eluting with ethyl acetate, and the inorganic salts were removed. The filtrate was concentrated and purification of the residue by silica gel column chromatography gave the desired product.

4-Methoxy-N-(7-methoxy-4,8-dimethyl-2-oxo-2H-chromen-3-yl)-benzamide (2a). Yield 76%. White solid, m.p.: 239-241 °C. R_f: 0.20 (Et₂O). NMR ¹H (300 MHz): 7.92 (s, 1H), 7.82 (d, 2H, *J* = 9.0 Hz), 7.44 (d, 1H, *J* = 8.1 Hz), 6.88 (d, 2H, *J* = 9.0 Hz), 6.82 (d, 1H, *J* = 8.1 Hz), 3.86 (s, 3H), 3.80 (s, 3H), 2.31 (s, 3H), 2.24 (s, 3H). NMR ¹³C (75 MHz): 165.6, 162.8, 160.5, 159.7, 150.2, 143.7, 129.6 (2), 126.0, 123.0, 118.1, 114.4, 114.0, 113.9 (2), 107.3, 56.0, 55.5, 16.0, 8.2. MS (ESI⁺) *m/z*: 376.0 [M+Na]⁺. IR (cm⁻¹): 3322, 2922, 1672, 1595, 1488, 1373, 1352, 1318, 1290, 1252, 1171, 1154, 1115, 1026, 967, 898, 835, 807, 772, 759, 702, 637, 610, 592, 561.

N-(8-Bromo-7-methoxy-2-oxo-2H-chromen-3-yl)-4-methoxybenzamide (2b). (stirring for 0.5 h at 100 °C). Yield 51%. Yellow solid, m.p.: 282-284 °C. R_f: 0.29 (CH₂Cl₂/ *c*-hexane: 8/2). NMR ¹H (300 MHz, DMSO-*d*₆): 9.55 (s, 1H), 8.57 (s, 1H), 7.98 (d, 2H, *J* = 9.1 Hz), 7.82 (d, 1H, *J* = 9.1 Hz), 7.24 (d, 1H, *J* = 9.1 Hz), 7.10 (d, 2H, *J* = 9.1 Hz), 3.99 (s, 3H), 3.87 (s, 3H). MS (ESI⁺) *m/z*: 426 ([M+Na]⁺, ⁷⁹Br), 428 ([M+Na]⁺, ⁸¹Br). IR (cm⁻¹): 3412, 2924, 1705, 1665, 1600, 1531, 1504, 1448, 1428, 1365, 1323, 1294, 1242, 1191, 1173, 1152, 1116, 1084, 1018, 974, 907, 893, 846, 806, 756, 684, 647, 636, 619, 575. **Pas de C13**

N-(7-Benzoyloxy-8-methyl-2-oxo-4-phenyl-2H-chromen-3-yl)-4-methoxybenzamide (2c). (stirring for 1 h at 130 °C). Yield 84%. White solid, m.p.: 200 °C. R_f: 0.27 (EtOAc/*c*-hexane: 3/7). NMR ¹H (300 MHz): 7.62-7.60 (m, 2H), 7.46-7.33 (m, 11H), 7.06 (d, 1H, *J* = 8.9 Hz), 6.85-6.78 (m, 3H), 5.15 (s, 2H), 3.80 (s, 3H), 2.42 (s, 3H). NMR ¹³C (75 MHz): 165.8, 162.6, 160.5, 159.2, 151.5, 148.9, 136.5, 133.7, 129.4 (2), 128.9,

128.8 (2), 128.5 (4), 128.2, 127.2 (2), 126.1, 125.6, 117.9, 114.7, 114.2, 113.8 (2), 108.7, 70.6, 55.5, 8.6. (one C missing). MS (APCI⁺) *m/z*: 492.2 [M+H]⁺ IR (cm⁻¹): 2925, 1988, 1731, 1604, 1479, 1260, 1177, 1111, 1029, 845, 699.

N-(6-Methoxy-2-oxo-2H-chromen-3-yl)thiophene-2-carbox-amide (**2d**). (stirring for 2 h at 130 °C). Yield 93%. Yellow solid, m.p.: 195 °C. R_f: 0.72 (CH₂Cl₂). NMR ¹H (300 MHz): 8.73 (1H, s), 8.69 (bs, 1H), 7.71 (d, 1H, *J* = 3.7 Hz), 7.64 (d, 1H, *J* = 5.0 Hz), 7.30 (d, 1H, *J* = 8.8 Hz), 7.26-7.18 (m, 1H), 7.06 (dd, 1H, *J* = 8.8 Hz, *J* = 2.8 Hz), 7.00 (d, 1H, *J* = 2.8 Hz), 3.87 (s, 3H). NMR ¹³C (75 MHz): 160.5, 158.9, 156.8, 144.4, 138.3, 132.1, 129.2, 128.2, 124.3, 123.2, 120.4, 118.0 (2), 109.9, 55.9. MS (APCI⁺) *m/z*: 299.7 [M-H]⁺. IR (cm⁻¹): 1711, 1695, 1650, 1581, 1529, 1513, 1493, 1417, 1261, 1033.

2-Hydroxy-*N*-(2-oxo-2H-chromen-3-yl)propanamide (**2e**). (stirring for 0.5 h at 100 °C). Yield 60%. White solid, m.p.: 131-133 °C. R_f: 0.51 (CH₂Cl₂/EtOAc: 7/3). NMR ¹H (300 MHz): 9.18 (br s, 1H), 8.62 (s, 1H), 7.50-7.30 (m, 2H), 7.26-7.19 (m, 2H), 4.38 (q, 1H, *J* = 7.1 Hz), 2.85 (br s, 1H), 1.50 (d, 3H, *J* = 7.1 Hz). NMR ¹³C (75 MHz): 173.8, 158.6, 150.1, 129.8, 127.8, 125.1, 123.7, 123.5, 119.7, 116.3, 69.0, 21.0. MS (ESI⁺) *m/z*: 256.0 [M+Na]⁺. IR (cm⁻¹): 3350, 1721, 1661, 1628, 1606, 1517, 1485, 1450, 1366, 1315, 1294, 1180, 1141, 1111, 1069, 1030, 949, 912, 868, 757, 650, 599, 579.

1-(2-Oxo-2H-chromen-3-yl)-azetidin-2-one (**2f**). (stirring for 1 h at 130 °C). Yield 86%. Yellow solid, m.p.: 169 °C. R_f: 0.50 (EtOAc/c-hexane: 4/6). NMR ¹H (300 MHz): 8.22 (s, 1H), 7.40-7.35 (m, 2H), 7.29-7.20 (m, 2H), 4.12 (t, 2H, *J* = 4.7 Hz), 3.14 (t, 2H, *J* = 7.7 Hz). NMR ¹³C (75 MHz): 166.9, 156.7, 150.7, 129.9, 127.4, 125.4, 125.0, 123.8, 119.4, 116.3, 42.9, 38.3. MS (ESI⁺) *m/z*: 238.0 [M+Na]⁺. IR (cm⁻¹): 2964, 2163, 1719, 1616, 1460, 1360, 1166, 757.

1-(2-Oxo-2H-chromen-3-yl)-pyrrolidin-2-one (**2g**). (stirring for 1 h at 130 °C). Yield 65%. White solid, m.p.: 137 °C. R_f: 0.52 (EtOAc). NMR ¹H (300 MHz): 7.96 (s, 1H), 7.50-7.47 (m, 2H), 7.32-7.25 (m, 2H), 3.98 (t, 2H, *J* = 8.2 Hz), 2.56 (t, 2H, *J* = 8.2 Hz), 2.24-2.09 (m, 2H). NMR ¹³C (75 MHz): 175.8, 158.0, 152.4, 137.4, 131.3, 128.1, 124.8, 124.5, 118.9, 116.4, 48.7, 31.4, 18.8. MS (APCI⁺) *m/z*: 230.0 [M+H]⁺. IR (cm⁻¹): 2989, 1721, 1692, 1608, 1492, 1389, 1123, 923, 755, 629.

1-(2-Oxo-2H-chromen-3-yl)-piperidin-2-one (**2h**). (stirring for 1 h at 130 °C). Yield 41 %. White solid, m.p.: 164 °C. R_f: 0.30 (EtOAc). NMR ¹H (300 MHz): 7.70 (s, 1H), 7.55-7.45 (m, 2H), 7.35-7.25 (m, 2H), 3.61 (t, 2H, *J* = 6 Hz), 2.56 (t, 2H, *J* = 6.0 Hz), 1.94-1.98 (m, 4H). ¹³C (75 MHz): 170.8, 158.1, 153.1, 140.5, 131.8, 129.1, 128.2, 124.7, 118.9, 116.7, 50.1, 32.6, 23.2, 21.3. MS (APCI⁺) *m/z*: 244.0 [M+H]⁺. IR (cm⁻¹): 2947, 2034, 1722, 1651, 1630, 1607, 1458, 1412, 982, 756.

N-(7-Methoxy-4,8-dimethyl-2-oxo-2H-chromen-3-yl)-4-methylbenzene sulfonamide (**2i**). (stirring for 0.5 h at 100 °C). Yield 53%. Orange solid, m.p.: 185-187 °C. R_f: 0.42 (CH₂Cl₂). NMR ¹H (300 MHz): 8.97 (s, 1H), 8.06 (d, 2H, *J* = 8.3 Hz), 7.37-7.34 (m, 3H), 6.93 (d, 1H, *J* = 8.6 Hz), 3.91 (s, 3H), 2.50 (s, 3H), 2.44 (s, 3H), 2.35 (s, 3H). NMR ¹³C (75 MHz): 158.5, 156.5, 153.9, 145.1, 139.6, 135.9, 129.7 (2), 128.6 (2), 128.3, 122.7, 118.4, 110.0, 108.5, 56.5, 21.7, 9.3, 8.6. MS (ESI⁺) *m/z*: 396.0 [M+Na]⁺. IR (cm⁻¹): 3265, 2920, 2852, 1695, 1602, 1503, 1385, 1342, 1285, 1254, 1189, 1163, 1127, 1109, 1094, 1036, 880, 850, 816, 795, 778, 748, 708, 664, 616.

N-(2-Oxo-2H-chromen-3-yl)-benzenesulfonamide (**2j**). (stirring for 0.5 h at 100 °C). Yield 42%. White solid, m.p.: 141-143 °C. R_f: 0.50 (CH₂Cl₂). NMR ¹H (300 MHz): 7.85-7.81 (m, 2H), 7.72 (s, 1H), 7.56-7.46 (m, 1H), 7.46-7.30 (m, 5H), 7.27-7.18 (m, 2H). NMR ¹³C (75 MHz): 158.3, 150.3, 138.7, 133.8, 130.2, 129.4 (2), 127.6, 127.2 (2), 125.3, 123.2, 123.0, 119.0, 116.5. MS (ESI⁺) *m/z*: 324.0 [M+Na]⁺. IR (cm⁻¹): 3328, 3056, 1703, 1627, 1589, 1531, 1493, 1444, 1362, 1321, 1280, 1243, 1189, 1139, 1109, 1027, 925, 872, 751, 707, 687, 635, 590, 573.

3,3'-(1,4-Phenylenebis(azanediyl))bis(7-(benzyloxy)-4,8-dimethyl-2H-chromen-2-one) (**2k**).

(stirring for 0.5 h at 100 °C). Yield 60%. Yellow solid, m.p.: 238-240 °C. R_f: 0.44 (CH₂Cl₂/c-hexane: 9/1). NMR ¹H (300 MHz, DMSO-*d*₆): 7.54-7.31 (m, 12H), 7.14 (d, 2H, *J* = 9.1 Hz), 7.07 (s, 2H), 6.54 (s, 4H), 5.27 (s, 4H), 2.27 (s, 6H), 2.18 (s, 6H). MS (APCI⁺) *m/z*: 665.0 [M+H]⁺. IR (cm⁻¹): 3360, 2922, 1698, 1599, 1515, 1454, 1373, 1347, 1326, 1278, 1159, 1120, 843, 805, 766, 739, 698.

7-Benzyloxy-8-methyl-4-phenyl-3-(3,4,5-trimethoxyphenylamino)-chromen-2-one (**2l**). (stirring for 1 h at 100 °C). Yield 71%. Yellow solid, m.p.: 162 °C. R_f: 0.61 (EtOAc/c-hexane: 4/6). NMR ¹H (300 MHz): 7.45-7.20 (m, 10H), 7.01 (d, 1H, *J* = 9.0 Hz), 6.78 (d, 1H, *J* = 9.0 Hz), 5.89 (s, 2H), 5.81 (s, 1H), 5.15 (s, 2H), 3.70 (s, 9H), 2.46 (s, 3H). NMR ¹³C (75 MHz): 160.8, 157.5, 153.0 (2), 149.5, 138.8, 136.8, 134.6, 133.7, 133.4, 129.4 (2), 128.8 (2), 128.7 (3), 128.2, 127.2 (2), 123.9, 123.6, 115.0, 114.7, 108.7, 97.9 (2), 70.7, 61.0 (2), 56.1, 8.7. MS (APCI⁺) *m/z*: 546.3 [M+Na]⁺. IR (cm⁻¹): 3331, 1695, 1596, 1503, 1266, 1232, 1124, 731.

3-(indolin-1-yl)-2H-chromen-2-one (**2m**). (stirring for 1 h at 130 °C). Yield 99%. Yellow solid, m.p.: 130 °C. R_f: 0.68 (EtOAc/c-hexane: 3/7). NMR ¹H (300 MHz): 7.53 (s, 1H), 7.42-7.32 (m, 3H), 7.28-7.19 (m, 2H), 7.12 (t, 1H, *J* = 8.0 Hz), 6.86-6.81 (m, 2H), 4.09 (t, 2H, *J* = 8.6 Hz), 3.17 (t, 2H, *J* = 8.6 Hz). NMR ¹³C (75 MHz): 158.8, 151.0, 146.5, 131.8, 131.5, 128.9, 126.9, 126.4, 125.3, 124.7, 123.9, 120.4, 120.0, 116.3, 111.3, 53.1, 28.8. MS (APCI⁺) *m/z*: 264.0 [M+H]⁺ IR (cm⁻¹): 2930, 1726, 1603, 1567, 1483, 1457, 1387, 1249, 1126, 747.

3-(Benzylamino)-2H-chromen-2-one (**2n**). (stirring for 0.5 h at 100 °C). Yield 65%. White solid, m.p.: 95-97 °C. R_f: 0.21 (CH₂Cl₂). NMR ¹H (300 MHz): 7.59 (d, 1H, *J* = 7.5 Hz), 7.43 (s, 1H), 7.40-7.17 (m, 8H), 6.89 (br s, 1H), 4.61 (m, 2H). ¹³C (75 MHz): 158.8, 154.7, 148.6, 137.8, 128.8 (2), 128.0 (2), 127.8, 127.6, 126.9, 123.7, 122.8, 111.7, 110.7, 43.4. MS (ESI⁺) *m/z*: 274.0 [M+Na]⁺, 525.0 [2M+Na]⁺. IR (cm⁻¹): 3309, 2928, 1647, 1598, 1524, 1495, 1447, 1425, 1350, 1317, 1298, 1258, 1231, 1175, 1078, 1028, 927, 884, 835, 800, 743, 694, 614.

Ethyl-2-(7-(benzyloxy)-4,8-dimethyl-2-oxo-2H-chromen-3-ylamino)acetate (**2o**). (stirring for 12 h at 100 °C). Yield 57%. Yellow solid, m.p.: 105-107 °C. R_f: 0.44 (CH₂Cl₂). NMR ¹H (300 MHz): 7.38-7.26 (m, 6H), 6.79 (d, 1H, *J* = 9.0 Hz), 5.06 (s, 2H), 4.45 (bs, 1H), 4.10 (q, 2H, *J* = 14.1 Hz), 3.88 (s, 2H), 2.28 (s, 3H), 2.25 (s, 3H), 1.17 (t, 3H, *J* = 7.0 Hz). ¹³C (75 MHz): 170.4, 159.1, 158.4, 155.9, 150.5, 147.8, 135.5, 128.2, 127.6 (2C), 127.0, 126.0 (2), 120.0, 113.2, 107.5, 69.5, 60.2, 48.3, 15.3, 12.4, 7.4. MS (ESI⁺) *m/z*: 404.0 [M+Na]⁺. IR (cm⁻¹): 3402, 2923, 1730, 1698, 1610, 1500, 1453, 1372, 1334, 1275, 1209, 1167, 1122, 1018, 860, 801, 767, 732, 696, 591.

3-(1H-Indol-1-yl)-2H-chromen-2-one (**2p**). (stirring for 1 h at 130 °C). Yield 95%. Yellow solid, m.p.: 160 °C. R_f: 0.34 (CH₂Cl₂/c-hexane: 3/7). NMR ¹H (300 MHz): 7.87 (s, 1H), 7.68 (d, 1H, *J* = 8.1 Hz), 7.59-7.01 (m, 8H), 6.72 (d, 1H, *J* = 3.1 Hz). NMR ¹³C (75 MHz): 158.5, 152.7, 136.4, 134.7, 131.8, 129.7, 128.6, 128.1, 126.0, 125.3, 123.1, 121.7, 121.4, 119.1, 117.0, 110.8, 105.0. MS (ESI⁺) *m/z*: 284.0 [M+Na]⁺ IR (cm⁻¹): 2918, 1722, 1632, 1604, 1463, 1335, 1157, 923, 910, 753, 720.

3-(3-Methyl-1H-indol-1-yl)-2H-chromen-2-one (**2q**). (stirring for 2 h at 130 °C). Yield 71%. Yellow solid, m.p.: 130 °C. R_f: 0.59 (Et₂O/c-hexane: 3/7). NMR ¹H (300 MHz): 7.82 (s, 1H), 7.65-7.50 (m, 3H), 7.47-7.40 (m, 2H), 7.38-7.18 (m, 4H), 2.38 (s, 3H). NMR ¹³C (75 MHz): 158.4, 152.2, 136.4, 133.4, 131.3, 130.2, 127.8, 125.9, 125.7, 125.1, 122.8, 120.8, 119.5, 119.0, 116.7, 114.0, 110.6, 9.7. MS (APCI⁺) *m/z*: 276.0 [M+H]⁺ IR (cm⁻¹): 2920, 1718, 1608, 1449, 1373, 1142, 1054, 928, 757, 733, 642, 623.

3-(1H-Indazol-1-yl)-2H-chromen-2-one (**2r**). (stirring for 2 h at 130 °C). Yield 36%. White solid, m.p.: 166 °C. R_f: 0.34 (Et₂O/c-hexane: 3/7). NMR ¹H (300 MHz): 8.37 (s, 1H), 8.12 (dd, 1H, *J* = 8.1 Hz, *J* = 1.1 Hz), 7.87 (d, 1H, *J* = 8.1 Hz), 7.70 (dd, 1H, *J* = 8.1 Hz, *J* = 1.1 Hz), 7.67 (td, 1H,

$J = 8.5$ Hz, $J = 1.5$ Hz), 7.54 (td, 1H, $J = 8.5$ Hz, $J = 1.5$ Hz), 7.46 (dd, $J = 8.1$ Hz, $J = 8.1$ Hz, 1H), 7.38-7.29 (m, 2H), 6.63 (s, 1H). NMR ^{13}C (75 MHz): 161.2, 154.8, 149.5, 140.1, 138.5, 132.9, 128.5, 127.1, 125.9, 124.5, 123.4, 121.9, 117.5, 116.0, 111.4, 107.9. MS (APCI $^{+}$) m/z : 263.1 [M+H] $^{+}$. IR (cm $^{-1}$): 2927, 1724, 1607, 1427, 1256, 1104, 938, 736.

3-(1H-benzo[d]imidazol-1-yl)-6-methyl-2H-chromen-2-one (2s), (stirring for 3.5 h at 130 °C). Yield 56%. Yellow solid, m.p.: 157 °C. R_f: 0.26 (EtOAc/c-hexane: 4/6). NMR ^1H (300 MHz): 8.26 (bs, 1H), 7.94 (d, 1H, $J = 6.0$ Hz), 7.49-7.41 (m, 5H), 6.56 (s, 1H), 2.33 (s, 3H). NMR ^{13}C (75 MHz): 160.3, 152.6, 147.2, 143.5, 141.7, 135.1, 134.8, 133.5, 125.0, 124.2, 124.1, 121.0, 117.7, 115.5, 111.9, 111.2, 21.0. MS (APCI $^{+}$) m/z : 277.1 [M+H] $^{+}$. IR (cm $^{-1}$): 2920, 2204, 1979, 1721, 1626, 1573, 1387, 1288, 939, 763, 606.

3-(1H-Pyrrolo[2,3-b]pyridin-1-yl)-2H-chromen-2-one (2t), (stirring for 2.5 h at 130 °C). Yield 60%. White solid, m.p.: 169 °C. R_f: 0.19 (Et₂O/c-hexane: 3/7). NMR ^1H (300 MHz): 8.53 (s, 1H), 8.35 (dd, 1H, $J = 4.7$ Hz, $J = 1.4$ Hz), 7.80 (dd, 1H, $J = 7.8$ Hz, $J = 1.5$ Hz), 7.88 (d, $J = 3.8$ Hz, 1H), 7.62 (dd, 1H, $J = 7.8$ Hz, $J = 1.5$ Hz), 7.58-7.49 (m, 1H), 7.42-7.37 (m, 1H), 7.33 (td, 1H, $J = 7.8$ Hz, $J = 1.1$ Hz), 7.16 (dd, 1H, $J = 8.2$ Hz, $J = 5.0$ Hz), 6.63 (d, $J = 4$ Hz, 1H). NMR ^{13}C (75 MHz): 158.4, 152.2, 148.2, 143.3, 135.3, 131.3, 129.3, 128.9, 128.4, 125.0, 123.4, 121.7, 119.1, 117.5, 116.5, 102.0. MS (ESI $^{+}$) m/z : 285.2 [M+Na] $^{+}$. IR (cm $^{-1}$): 2925, 1724, 1631, 1608, 1520, 1421, 1271, 1070, 908, 747, 718.

3-(1H-Pyrrol-1-yl)-2H-chromen-2-one (2u), (stirring for 1 h at 130 °C). Yield 56%. Brown solid, m.p.: 137 °C. R_f: 0.52 (CH₂Cl₂/c-hexane: 3/7). NMR ^1H (300 MHz): 7.61 (s, 1H), 7.55-7.50 (m, 2H), 7.40-7.30 (m, 2H), 7.25 (m, 2H), 6.36 (m, 2H). NMR ^{13}C (75 MHz): 157.6, 151.9, 131.1, 129.8, 128.9, 127.7, 126.9, 125.1, 121.1, 119.0, 116.5, 110.9 (2). MS (APCI $^{+}$) m/z : 212.0 [M+H] $^{+}$. IR (cm $^{-1}$): 2915, 2194, 1709, 1626, 1607, 1480, 1342, 1260, 1100, 910, 756, 733, 637.

3-(1H-Pyrazol-1-yl)-2H-chromen-2-one (2v), (stirring for 2 h at 130 °C). Yield 58%. White solid, m.p.: 127 °C. R_f: 0.56 (EtOAc/c-hexane: 4/6). NMR ^1H (300 MHz): 8.25 (d, 1H, $J = 8.1$ Hz), 7.93-7.91 (m, 2H), 7.61 (t, 1H, $J = 8.1$ Hz), 7.42 (d, 1H, $J = 8.1$ Hz), 7.33 (t, 1H, $J = 8.1$ Hz), 6.60 (m, 1H), 6.44 (m, 1H). NMR ^{13}C (75 MHz): 160.8, 154.6, 149.6, 143.6, 132.9, 130.8, 126.8, 124.6, 117.5, 115.1, 109.1, 107.2. MS (APCI $^{+}$) m/z : 213.0 [M+H] $^{+}$. IR (cm $^{-1}$): 3113, 2926, 2172, 1727, 1621, 1438, 1248, 1189, 1038, 753, 615.

3-(1H-Indol-1-yl)-1-methylquinolin-2(1H)-one (3a), (stirring for 1 h at 130 °C). Yield 84%. Orange solid, m.p.: 170 °C. R_f: 0.34 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.90 (s, 1H), 7.71-7.55 (m, 4H), 7.40-7.37 (m, 2H), 7.32 (td, 1H, $J = 7.5$ Hz, $J = 1.0$ Hz), 7.28-7.15 (m, 2H), 6.71 (m, 1H), 3.85 (s, 3H). NMR ^{13}C (75 MHz): 159.2, 138.7, 136.4, 132.1, 130.6, 129.5, 129.3, 129.0, 128.8, 122.9, 122.3, 121.2, 120.6, 119.7, 114.3, 110.7, 103.7, 30.4. MS (APCI $^{+}$) m/z : 275.1 [M+H] $^{+}$. IR (cm $^{-1}$): 3838, 2030, 1641, 1625, 1594, 1449, 1013, 778, 649.

3-(5-Methoxy-1H-indol-1-yl)-1-methylquinolin-2(1H)-one (3b), (stirring for 1 h at 130 °C). Yield 98%. Brown solid, m.p.: 104 °C. R_f: 0.23 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.86 (s, 1H), 7.66-7.57 (m, 2H), 7.55 (d, 1H, $J = 3.1$ Hz), 7.42 (d, 1H, $J = 9.0$ Hz), 7.38-7.23 (m, 2H), 7.13 (s, 1H), 6.88 (m, 1H), 6.62 (d, 1H, $J = 3.2$ Hz), 3.87 (s, 3H), 3.84 (s, 3H). NMR ^{13}C (75 MHz): 159.2, 154.7, 138.5, 131.6, 131.4, 130.4, 129.9, 129.6, 128.7, 122.9, 119.8, 114.3, 112.2, 111.6, 103.4, 103.0, 55.9, 30.4 (one C missing). MS (APCI $^{+}$) m/z : 305.1 [M+H] $^{+}$. IR (cm $^{-1}$): 1654, 1601, 1474, 1265, 1244, 1160, 731.

4-Methoxy-N-(4-methyl-2H-chromen-3-yl)benzamide (5a), (stirring for 1 h at 100 °C). Yield 82%. Brown solid, m.p.: 166 °C. R_f: 0.40 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.81 (d, 2H, $J = 9.0$ Hz), 7.52 (s, 1H), 7.23-7.07 (m, 2H), 7.02-6.92 (m, 3H), 6.89 (dd, 1H, $J = 8.0$ Hz, $J = 1.0$ Hz), 5.02 (s, 2H), 3.86 (s, 3H), 2.01 (s, 3H). NMR ^{13}C (75 MHz): 165.7, 162.9, 153.1, 129.2 (2), 128.2, 126.0, 125.7, 125.7, 123.6, 121.7, 116.9,

115.9, 114.2 (2), 66.1, 55.6, 12.0. MS (APCI $^{+}$) m/z : 296.1 [M+H] $^{+}$. IR (cm $^{-1}$): 1732, 1265, 1045, 733.

4-Methoxy-N-(4-phenyl-2H-chromen-3-yl)benzamide (5b), (stirring for 1 h at 100 °C). Yield 95%. Yellow solid, m.p.: 160 °C. R_f: 0.55 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.53-7.40 (m, 6H), 7.35-7.32 (m, 2 H), 7.14-7.08 (m, 1H), 6.94 (m, 1H), 6.88-6.80 (m, 3H), 6.71 (m, 1H), 5.39 (s, 2H), 3.88 (s, 3H). NMR ^{13}C (75 MHz): 165.0, 162.8, 153.0, 134.2, 130.42 (2), 129.5, (2), 129.1 (2), 128.6, 128.0, 127.3, 125.7, 125.5, 124.6, 121.7, 119.6, 115.9, 114.1 (2), 65.5, 55.6. MS (APCI $^{+}$) m/z : 358.2 [M+H] $^{+}$. IR (cm $^{-1}$): 1605, 1575, 1476, 1247, 1174, 1115, 1209, 757.

4-Chloro-N-(4-phenyl-2H-chromen-3-yl)benzamide (5c), (stirring for 2 h at 100 °C). Yield 86%. Yellow solid, m.p.: 132 °C. R_f: 0.75 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.54-7.44 (m, 6H), 7.38-7.31 (m, 4H), 7.17-7.07 (m, 1H), 6.94 (dd, 1H, $J = 8.1$ Hz, $J = 1.1$ Hz), 6.84 (td, 1H, $J = 7.5$ Hz, $J = 1.1$ Hz), 6.71 (dd, 1H, $J = 7.7$ Hz, $J = 1.1$ Hz), 5.38 (s, 2H). NMR ^{13}C (75 MHz): 164.4, 153.1, 138.7, 134.0, 131.8, 130.3 (2), 129.6 (2), 129.2 (2), 128.8, 128.5 (2); 128.4, 126.7, 125.6, 124.4, 121.8, 120.6, 115.9, 65.4. MS (APCI $^{+}$) m/z : 384.1 [M+Na] $^{+}$. IR (cm $^{-1}$): 2925, 2197, 1675, 1478, 1243, 1042, 751, 702, 616.

4-((4-Phenyl-2H-chromen-3-yl)carbamoyl)phenyl 4-methyl -benzene sulfonate (5d), (stirring for 2 h at 100 °C). Yield 97%. Yellow solid, m.p.: 121 °C. R_f: 0.50 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.68 (d, 2H, $J = 8.5$ Hz), 7.54-7.44 (m, 6H), 7.31 (d, 4H, $J = 7.0$ Hz), 7.15-7.09 (m, 1H), 7.01 (d, 2H, $J = 8.5$ Hz), 6.93 (d, 1H, $J = 8.1$ Hz), 6.87-6.80 (m, 1H), 6.70 (dd, 1H, $J = 8.1$ Hz, $J = 1.5$ Hz), 5.34 (s, 2H), 2.49 (s, 3H). NMR ^{13}C (75 MHz): 164.2, 153.0, 152.3, 145.9, 133.9, 132.2, 130.3 (2), 130.0 (2), 129.6 (2); 128.8 (3), 128.5 (2), 128.3, 126.5, 125.6, 124.3, 122.8 (2), 121.8, 120.8, 115.9, 65.3, 21.8 (one C missing). MS (APCI $^{+}$) m/z : 498.1 [M+H] $^{+}$. IR (cm $^{-1}$): 2919, 1669, 1600, 1478, 1376, 1244, 1178, 1154, 1092, 1017, 863, 738, 665.

N-(4-Phenyl-2H-chromen-3-yl)-acetamide (5e), (stirring for 5 h at 100 °C). Yield 60%. Brown solid, m.p.: 123 °C. R_f: 0.30 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.52-7.40 (m, 3H), 7.28 (d, 1H, $J = 2.1$ Hz), 7.09 (td, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 6.90 (d, 1H, $J = 7.5$ Hz), 6.85-6.73 (m, 2H), 6.63 (dd, 1H, $J = 8.1$ Hz, $J = 1.5$ Hz), 5.22 (s, 2H), 1.94 (s, 3H) (NH not seen). NMR ^{13}C (75 MHz): 168.8, 152.9, 134.2, 130.3 (2), 129.48 (2), 128.5, 128.1, 126.8, 125.5, 124.5, 121.7, 119.6, 115.8, 65.4, 23.8. MS (APCI $^{+}$) m/z : 266.0 [M+H] $^{+}$. IR (cm $^{-1}$): 3279, 2924, 1664, 1576, 1482, 1329, 1042, 757, 702, 631.

2-Hydroxy-N-(4-phenyl-2H-chromen-3-yl)propanamide (5f), (stirring for 3 h at 100 °C). Yield 57%. Brown solid, m.p.: 151 °C. R_f: 0.20 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 8.02 (bs, 1H), 7.51-7.38 (m, 3H), 7.28-7.23 (m, 2H), 7.10 (td, 1H, $J = 7.7$ Hz, $J = 1.6$ Hz), 6.90 (dd, 1H, $J = 7.7$ Hz, $J = 1.1$ Hz), 6.81 (td, 1H, $J = 8.0$ Hz, $J = 1.1$ Hz), 6.67 (dd, 1H, $J = 8.0$ Hz, $J = 2.0$ Hz), 5.31 (s, 2H), 4.20-4.13 (m, 1H), 1.61 (br s, 1H), 1.37 (d, 3H, $J = 7.8$ Hz). NMR ^{13}C (75 MHz): 172.6, 152.9, 133.9, 130.2 (2), 129.4 (2), 128.5, 128.2, 126.1, 125.5, 125.2, 124.5, 121.7, 115.8, 68.6, 65.1, 21.2. MS (APCI $^{+}$) m/z : 296.1 [M+H] $^{+}$. IR (cm $^{-1}$): 2922, 2022, 1659, 1504, 1483, 1227, 1122, 1042, 756.

4-Methyl-N-(4-phenyl-2H-chromen-3-yl)benzenesulfonamide (5g) (stirring for 2 h at 100 °C). Yield 61%. Yellow solid, m.p.: 110 °C. R_f: 0.58 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.59 (d, 2H, $J = 8.0$ Hz), 7.37-7.24 (m, 5 H), 7.09 (td, 1H, $J = 8.0$ Hz, $J = 2.0$ Hz), 6.90 (dd, 1H, $J = 8.0$ Hz, $J = 1.0$ Hz), 6.75 (td, 1H, $J = 8.0$ Hz, $J = 1.0$ Hz), 6.57 (m, 2H), 6.45 (dd, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 6.10 (s, 1H), 5.12 (s, 2H), 2.48 (s, 3H). NMR ^{13}C (75 MHz): 152.5, 144.5, 135.7, 132.7, 130.1 (2), 129.7 (2), 129.4 (2), 128.7 (2), 127.5 (2), 125.8, 124.2 (3), 121.7, 115.9, 65.5, 21.8. MS (APCI $^{+}$) m/z : 376.1 [M+H] $^{+}$. IR (cm $^{-1}$): 3636, 3253, 1597, 1574, 1482, 1456, 1339, 1164, 963, 758, 671.

1,3-bis(4-Phenyl-2H-chromen-3-yl)urea (5h), (stirring for 12 h at 100 °C). (Not stable) Yield 50%. White solid, m.p.: 94 °C. R_f: 0.36 (EtOAc/c-hexane: 1/9). NMR ^1H (300 MHz): 7.52 (bs, 2H), 7.45-7.30 (m, 6H), 7.21-

7.18 (m, 4H), 7.12-7.00 (m, 2H), 6.87 (dd, 2H, $J = 8.0$ Hz, $J = 1.0$ Hz), 6.79 (td, 2H, $J = 8.0$ Hz, $J = 1.0$ Hz), 6.54 (dd, 2H, $J = 8.0$ Hz, $J = 1.0$ Hz), 5.14 (s, 4H). NMR ^{13}C (75 MHz): 186.9, 152.2, 134.6, 130.4 (2), 129.0 (2), 127.9, 127.5, 127.2, 125.2, 124.8, 121.4, 117.3, 115.3, 65.4. MS (APCI $^{+}$) m/z : 471 [M-H] $^{+}$. IR (cm $^{-1}$): 2989, 1713, 1373, 1324, 1044, 737.

N-(4-phenyl-2H-chromen-3-yl)-2-(4-phenyl-2H-chromen-3-ylamino)benzamide (**5i**). (stirring for 12 h at 100 °C). Yield 68%. Yellow solid, m.p.: 117 °C. R $_f$: 0.40 (EtOAc/c-hexane: 1/9). NMR ^1H (300 MHz): 8.63 (s, 1H), 7.55 (s, 1H), 7.50-7.35 (m, 6H), 7.31-7.26 (m, 5H), 7.13-7.06 (m, 2H), 7.02 (dd, 1H, $J = 8.0$ Hz, $J = 1.4$ Hz), 6.96-6.89 (m, 2H), 6.87-6.79 (m, 3H), 6.72-6.65 (m, 3H), 5.21 (s, 2H); 4.80 (s, 2H). NMR ^{13}C (75 MHz): 166.8, 153.0, 144.6, 135.0, 134.1, 133.1, 130.3 (2), 130.2 (2), 129.5 (2), 129.0 (2), 128.7, 128.2, 128.1, 127.9 (2); 127.2, 126.9, 125.8, 125.6, 125.5, 124.7, 122.0, 121.8, 121.7, 120.4, 119.0, 118.5, 118.1, 115.8, 115.7, 65.7, 65.4. (one C missing) m/z : 549.2 [M+H] $^{+}$. IR (cm $^{-1}$): 3340, 2253, 1642, 1622, 1501, 1245, 1039, 755.

1-(4-Phenyl-2H-chromen-3-yl)-azetidin-2-one (**5j**). (stirring for 1 h at 100 °C). Yield 90%. White solid, m.p.: 90 °C. R $_f$: 0.51 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.46-7.39 (m, 3 H), 7.29-7.26 (m, 2 H), 7.14-6.99 (m, 1 H), 6.88 (dd, 1H, $J = 8$ Hz, $J = 1.5$ Hz), 6.78 (td, 1H, $J = 7.5$ Hz, $J = 1.5$ Hz), 6.58 (dd, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 5.32 (s, 2H), 2.81-2.72 (m, 4H). NMR ^{13}C (75 MHz): 165.8, 152.2, 134.7, 131.2 (2), 128.5 (2), 128.2, 127.9, 127.0, 125.6, 125.0, 121.7, 116.9, 115.6, 64.4, 41.7, 36.7. MS (APCI $^{+}$) m/z : 278.2 [M+H] $^{+}$. IR (cm $^{-1}$): 1745, 1485, 1352, 1265, 1145, 1072, 732, 702.

1-(4-Phenyl-2H-chromen-3-yl)-pyrrolidin-2-one (**5k**). (stirring for 2 h at 100 °C). Yield 92%. Yellow solid, R $_f$: 0.31 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.44-7.35 (m, 3H), 7.30-7.22 (m, 2H), 7.19-7.10 (m, 1H), 6.92 (dd, 1H, $J = 8.0$ Hz, $J = 1.1$ Hz), 6.83 (td, 1H, $J = 7.5$ Hz, $J = 1.1$ Hz), 6.75 (dd, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 4.94 (s, 2H), 2.97 (t, 2H, $J = 7.1$ Hz), 2.30 (t, 2H, $J = 8.1$ Hz), 1.98-1.70 (m, 2H). NMR ^{13}C (75 MHz): 176.4, 153.5, 135.4 (2), 129.9 (2), 129.1, 128.7 (2), 128.3, 126.8, 126.3, 124.3, 121.6, 115.9, 66.8, 48.8, 30.8, 20.0. MS (APCI $^{+}$) m/z : 292.2 (one C missing) MS (APCI $^{+}$) m/z : 292.2 [M+H] $^{+}$. IR (cm $^{-1}$): 2921, 2851, 1680, 1480, 1452, 1401, 1216, 1034, 760, 706, 622.

5-Bromo-3-((4-methoxyphenyl)amino)-2H-chromen-2-one (**7a**) (stirring for 2 h at 100 °C). Yield 74%. Yellow solid, m.p.: 154 °C. R $_f$: 0.54 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.45 (d, 1H, $J = 8.0$ Hz), 7.27-7.20 (m, 4H), 7.10 (t, 1H, $J = 8.0$ Hz), 6.97 (d, 2H, $J = 8.8$ Hz), 6.72 (s, 1H), 3.84 (s, 3H). NMR ^{13}C (75 MHz): 159.3, 156.8, 148.5, 132.0, 131.5, 128.8, 126.5, 123.6 (2), 121.5, 119.3, 115.6, 115.1 (2), 105.4, 55.6. MS (APCI $^{+}$) m/z : 346.1 ([M+H] $^{+}$, ^{79}Br), 348.0 ([M+H] $^{+}$, ^{81}Br), [M+H] $^{+}$. IR (cm $^{-1}$): 2336, 1699, 1651, 1540.

3,5-bis((4-Methoxyphenyl)amino)-2H-chromen-2-one(**7aa**) Yield 20%. Yellow solid, m.p.: 188 °C. R $_f$: 0.37 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.12 (t, 1H, $J = 8.0$ Hz), 7.03-6.82 (m, 11H), 6.54 (s, 1H), 5.42 (s, 1H), 3.80 (s, 6H). NMR ^{13}C (75 MHz): 159.9, 156.4, 155.4, 149.7, 139.9, 137.0, 132.6, 129.5, 126.8, 123.3, (2), 121.5 (2), 115.0 (2), 114.9 (2), 114.3, 112.9, 109.7, 103.1, 55.7, 55.6. MS (APCI $^{+}$) m/z : 389.2 [M+H] $^{+}$. IR (cm $^{-1}$): 3355, 1677, 1509, 1036.

6-Bromo-3-((4-methoxyphenyl)amino)-2H-chromen-2-one (**7b**) (stirring for 2 h at 100 °C). Yield 88%. Yellow solid, m.p.: 132 °C. R $_f$: 0.61 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.38 (d, 1H, $J = 1.8$ Hz), 7.31 (dd, 1H, $J = 8, 7$ Hz, $J = 1.8$ Hz), 7.17-7.13 (m, 3H), 6.95 (d, 2H, $J = 8.7$ Hz), 6.73 (s, 1H); 6.64 (s, 1H), 3.83 (s, 3H). NMR ^{13}C (75 MHz): 165.4, 157.0, 147.1, 131.9, 131.7, 129.0, 127.6, 124.3 (2), 123.2, 117.8, 117.6, 115.1 (2), 105.2, 55.7. MS (APCI $^{+}$) m/z : 346 ([M+H] $^{+}$, ^{79}Br), 348 ([M+H] $^{+}$, ^{81}Br). IR (cm $^{-1}$): 3340, 1705, 1619, 1509, 1237, 1205, 828.

7-Bromo-3-((4-methoxyphenyl)amino)-2H-chromen-2-one (**7c**) (stirring for 4 h at 100 °C). Yield 99%. Brown solid, m.p.: 138 °C. R $_f$: 0.57 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.43 (d, 1H, $J = 1.7$ Hz), 7.30 (dd, 1H, $J = 8.3$ Hz, $J = 1.8$ Hz), 7.16 (d, 2H, $J = 8.9$ Hz), 7.11 (d, 1H, $J = 8.3$ Hz), 6.94 (d, 2H, $J = 8.9$ Hz), 6.79 (s, 1H), 6.59 (s, 1H), 3.83 (s, 3H). NMR ^{13}C (75 MHz): 159.2, 156.9, 148.4, 132.1, 131.2, 128.1, 126.3, 124.3 (2), 120.4, 119.3, 119.1, 115.0 (2), 106.0, 55.7. MS (APCI $^{+}$) m/z : 345.2

([M] $^{+}$, ^{79}Br), 347.2 ([M] $^{+}$, ^{81}Br). IR (cm $^{-1}$): 3345, 1709, 1620, 1506, 1234, 1037, 871, 738.

8-Bromo-3-((4-methoxyphenyl)amino)-2H-chromen-2-one (**7d**) (stirring for 4 h at 100 °C). Yield 61%. Yellow solid, m.p.: 147 °C. R $_f$: 0.65 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.43 (d, 1H, $J = 2.3$ Hz), 7.18-7.15 (m, 3H), 6.98-6.92 (m, 2H), 6.70 (s, 1H), 6.68 (s, 1H), 3.83 (s, 3H). NMR ^{13}C (75 MHz): 158.6, 157.2, 143.3, 132.2, 131.5, 130.3, 129.1, 124.5 (2), 123.8, 123.7, 115.1 (2), 110.5, 104.6, 55.3. MS (APCI $^{+}$) m/z : 380 ([M] $^{+}$, ^{79}Br), 382 ([M] $^{+}$, ^{81}Br). IR (cm $^{-1}$): 3345, 1709, 1620, 1506, 1234, 1037, 871, 738.

6,8-Dibromo-7-methoxy-3-((4-methoxyphenyl)amino)-2H-chromen-2-one (**7e**) (stirring for 2 h at 100 °C). Yield 73%. Yellow solid, m.p.: 165 °C. R $_f$: 0.45 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.42 (s, 1H), 7.15 (d, 2H, $J = 9.0$ Hz), 6.95 (d, 2H, $J = 9.0$ Hz), 6.70 (s, 1H), 6.61 (s, 1H), 3.92 (s, 3H), 3.84 (s, 3H). NMR ^{13}C (75 MHz): 158.8, 157.0, 152.7, 131.8, 131.0, 127.4, 124.4 (2), 119.8, 115.2 (2), 113.5, 106.5, 104.9, 61.2, 55.3. One C missing. MS (APCI $^{+}$) m/z : 455.9 [M] $^{+}$. IR (cm $^{-1}$): 3361, 1712, 1621, 1345, 980.

5-Bromo-3-(butylamino)-2H-chromen-2-one (**8a**) (stirring for 2 h at 100 °C). Yield 74%. Yellow solid, m.p.: 75 °C. R $_f$: 0.41 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.49 (s, 1H), 7.46 – 7.43 (m, 2H), 7.30 – 7.27 (m, 1H), 6.58 (br s, 1H), 3.49 (q, 2H, $J = 7.0$ Hz), 1.67 – 1.62 (m, 2H), 1.48 – 1.41 (m, 2H), 0.98 (t, 3H, $J = 7.0$ Hz). NMR ^{13}C (75 MHz): 158.4, 154.4, 149.2, 129.5, 127.6, 126.8, 115.8, 110.9, 110.2, 39.3, 31.8, 20.2, 13.9. MS (APCI $^{+}$) m/z : 296.1([M] $^{+}$, ^{79}Br), 298.1 ([M] $^{+}$, ^{81}Br). IR (cm $^{-1}$): 2957, 1648, 1522, 1278, 912.

3-Bromo-5-(butylamino)-2H-chromen-2-one (**8aa**) (stirring for 2 h at 100 °C). Yield 21%. Yellow solid, m.p.: 87.2 °C. R $_f$: 0.80 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.44 (d, 1H, $J = 8.0$ Hz), 7.22 (d, 1H, $J = 8.0$ Hz), 7.05 (t, 1H, $J = 8.0$ Hz), 6.57 (s, 1H), 5.02 (br s, 1H), 3.22-3.15 (m, 2H), 1.75 – 1.66 (m, 2H), 1.52 – 1.43 (m, 2H), 1.0 (t, 3H, $J = 7$ Hz). NMR ^{13}C (75 MHz): 148.0, 134.5, 128.7, 125.6, 122.1, 118.9, 115.6, 102.8, 43.0, 30.6, 20.1, 13.9, one C missing. m/z : 296.1([M] $^{+}$, ^{79}Br), 298.1 ([M] $^{+}$, ^{81}Br). IR (cm $^{-1}$): 3368, 1711, 1611, 1179, 944.

6-Bromo-3-(butylamino)-2H-chromen-2-one (**8b**) (stirring for 1.5 h at 100 °C). Yield 66%. Yellow solid, m.p.: 80 °C. R $_f$: 0.43 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.79 (s, 1H), 7.49 (d, 1H, $J = 8.6$ Hz), 7.38-7.34 (m, 2H), 6.62 (br s, 1H), 3.48 (q, 2H, $J = 6.3$ Hz), 1.67-1.58 (m, 2H), 1.49-1.37 (m, 2H), 0.96-0.94 (t, 3H, $J = 6.8$ Hz). NMR ^{13}C (75 MHz): 158.4, 153.4, 150.1, 129.8, 129.7, 125.3, 116.8, 113.3, 109.5, 39.3, 31.7, 20.2, 13.7. MS (APCI $^{+}$) m/z : 296 ([M+H] $^{+}$, ^{79}Br), 298 ([M+H] $^{+}$, ^{81}Br). IR (cm $^{-1}$): 2958, 1733, 1645, 1563, 1312, 1186, 1049, 961, 797, 699.

7-Bromo-3-(butylamino)-2H-chromen-2-one (**8c**) (stirring for 1.5 h at 100 °C). Yield 66%. Yellow solid, m.p.: 90 °C. R $_f$: 0.40 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.66 (s, 1H), 7.52 (dd, 1H, $J = 8.3$ Hz, $J = 0.9$ Hz), 7.42-7.39 (m, 2H), 6.61 (br s, 1H), 3.48 (q, 2H, $J = 6.1$ Hz), 1.68-1.58 (m, 2H), 1.49-1.37 (m, 2H), 0.96-0.94 (t, 3H, $J = 6.9$ Hz). NMR ^{13}C (75 MHz): 158.5, 154.9, 149.8, 127.4, 126.8, 123.7, 120.2, 115.2, 110.1, 39.3, 31.8, 20.2, 13.9. MS (APCI $^{+}$) m/z : 296 ([M+H] $^{+}$, ^{79}Br), 298 ([M+H] $^{+}$, ^{81}Br). IR (cm $^{-1}$): 2957, 1643, 1599, 1533, 1454, 1288, 1048, 846, 737.

8-Bromo-3-(butylamino)-6-chloro-2H-chromen-2-one (**8d**) (stirring for 2 h at 100 °C). Yield 76%. Orange solid, m.p.: 98 °C. R $_f$: 0.50 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.60 (d, 1H, $J = 2.5$ Hz), 7.57 (d, 1H, $J = 2.5$ Hz), 7.45 (s, 1H), 6.68 (br s, 1H), 3.53-3.46 (q, 2H, $J = 6.2$ Hz), 1.70 – 1.60 (m, 2H), 1.50 – 1.38 (m, 2H), 0.98 (t, 3H, $J = 7.3$ Hz). NMR ^{13}C (75 MHz): 158.0, 150.8, 150.6, 129.7, 129.6, 129.4, 121.5, 110.5, 104.8, 39.4, 31.7, 20.3, 13.5. MS (APCI $^{+}$) m/z : 330 ([M+H] $^{+}$, ^{79}Br), 332 ([M+H] $^{+}$, ^{81}Br). IR (cm $^{-1}$): 2927, 1659, 1583, 1178, 732.

6,8-Dibromo-3-(butylamino)-7-methoxy-2H-chromen-2-one (**8e**) (stirring for 2 h at 100 °C). Yield 82%. Brown oil. R $_f$: 0.39 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.80 (s, 1H), 7.42 (s, 1H), 6.65 (br s, 1H), 3.90 (s, 3H), 3.50 (q, 2H, $J = 6.1$ Hz), 1.7 – 1.60 (m, 2H), 1.49 – 1.37 (m, 2H), 0.98 (t, 3H, $J = 7.0$ Hz). NMR ^{13}C (75 MHz): 158.0, 153.2, 152.3, 150.8, 125.6, 125.0, 114.1, 110.1, 100.1, 61.4, 39.4, 31.8, 20.2, 13.9. MS (APCI $^{+}$) m/z : 406.2 [M+H, $^{81}\text{Br}^{79}\text{Br}$] $^{+}$. IR (cm $^{-1}$): 1695, 1590, 1402, 1167, 1051.

8-Bromo-6-chloro-3-morpholino-2H-chromen-2-one (**9**) (stirring for 2 h at 100 °C). (stirring for 2 h at 100 °C). Yield 79%. White solid, m.p.: 124 °C. R $_f$: 0.23 (EtOAc/c-hexane: 3/7). NMR ^1H (300 MHz): 7.60-7.53 (m, 2H), 7.35 (s, 1H), 3.99-3.75 (m, 8H). NMR ^{13}C (75 MHz): 158.5, 150.9, 150.5, 129.9, 129.3, 128.7, 121.0, 112.7, 104.9, 66.9 (4). m/z : 344.0 ([M+H] $^{+}$, ^{79}Br), 346.0 ([M+H] $^{+}$, ^{81}Br). IR (cm $^{-1}$): 3083, 1636, 1613, 1426, 1275, 1171, 1023, 852, 731.

General procedure for Suzuki coupling reactions.

To a mixture of bromocoumarin **7a-c**, **9** (1 mmol) in toluene (4mL) and EtOH (2 mL), were successively added the desired boronic acid (1.2 mmol), K_2CO_3 (2 mmol) and $Pd(PPh_3)_4$ (0.05 mmol). The reaction was heated at 100 °C, under vigorous stirring and monitored by TLC until complete disappearance of starting material. The solvent was evaporated in vacuo and 10 mL of water were added. After extraction with CH_2Cl_2 (3 x 10 mL), the combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude material was purified by column chromatography to afford the expected compounds **10a-c**.

5-(4-Methoxyphenyl)-3-((4-methoxyphenyl)amino)-2H-chromen-2-one (10a). (stirring for 3 h at 100 °C). Yield 90%. Yellow solid, m.p.: 207.7 °C. R_f : 0.56 (EtOAc/c-hexane: 3/7). NMR 1H (300 MHz, DMSO- d_6): 8.10 (s, 1H), 7.38-7.33 (m, 4H), 7.21-7.19 (m, 3H), 7.05 (d, 2H, J = 8.5 Hz), 6.98 (s, 1H), 6.90 (d, 2H, J = 8.5 Hz), 3.79 (s, 3H), 3.71 (s, 3H). NMR ^{13}C (75 MHz, DMSO- d_6): 158.8, 158.2, 155.2, 148.5, 137.2, 132.7, 130.6 (2), 130.0, 126.0, 125.5, 123.0 (2), 118.5, 114.4, 114.3 (2), 114.0 (2), 105.0, 54.90 (2), one C missing. MS (APCI $^+$) m/z : 374 [M+H] $^+$. IR (cm $^{-1}$): 1711, 1617, 1508, 1235.

7-(4-Methoxyphenyl)-3-((4-methoxyphenyl)amino)-2H-chromen-2-one (10b) (stirring for 3 h at 100 °C). Yield 90%. Yellow solid, m.p.: 155.3 °C. R_f : 0.54 (EtOAc/c-hexane: 3/7). NMR 1H (300 MHz): 7.53 (d, 2H, J = 8.5 Hz), 7.46 (s, 1H), 7.40 (d, 1H, J = 8.5 Hz), 7.28 (d, 1H, J = 8.5 Hz), 7.17 (d, 2H, J = 8.5 Hz), 7.00-6.91 (m, 4H), 6.81 (s, 1H), 6.60 (br s, 1H), 3.85 (s, 3H), 3.83 (s, 3H). NMR ^{13}C (75 MHz): 160.1, 159.6, 156.6, 148.8, 139.3, 132.6, 132.3, 130.5, 128.1 (2), 125.7, 123.9 (2), 123.3, 119.8, 115.0 (2), 114.5 (2), 113.8, 107.0, 55.48 (2). MS (APCI $^+$) m/z : 374.1 [M+H] $^+$. IR (cm $^{-1}$): 3328, 1701, 1520, 1267.

6-Chloro-8-(4-methoxyphenyl)-3-morpholino-2H-chromen-2-one (10c) (stirring for 3 h at 100 °C). Yield 99%. White solid, m.p.: 135.3 °C. R_f : 0.20 (EtOAc/c-hexane: 3/7). NMR 1H (300 MHz): 7.73 (d, 2H, J = 8.9 Hz), 7.55 (d, 1H, J = 2.0 Hz), 7.49 (d, 1H, J = 2.0 Hz), 7.35 (s, 1H), 7.02 (d, 2H, J = 8.9 Hz), 3.88 (3H), 3.86-3.71 (m, 8H). NMR ^{13}C (75 MHz): 162.9, 160.1, 159.3, 150.3, 150.2, 129.9, 129.7 (2), 128.7, 127.0, 125.8, 120.1, 114.4 (2), 112.3, 67.1 (4), 55.2. MS (APCI $^+$) m/z : 372.1 [M+H] $^+$. IR (cm $^{-1}$): 1629, 1516, 1426, 1248.

3-((4-Methoxyphenyl)amino)-5-((3,4,5-trimethoxyphenyl) amino)-2H-chromen-2-one (10d) was prepared as for compounds **7** using 2 equiv of 3,4,5-trimethoxyaniline, 10 mol% of $Pd(OAc)_2$, Xantphos (10 mol%), CS_2CO_3 (1.5 equiv) in dioxane at 100 °C for 2 h. Yield 60%. Yellow solid, m.p.: 176.6 °C. R_f : 0.25 (EtOAc/c-hexane: 3/7). NMR 1H (300 MHz): 7.17 (t, 1H, J = 8.1 Hz) 7.03-6.94 (m, 5H), 6.84 (d, 2H, J = 8.8 Hz), 6.55 (s, 1H), 6.14 (s, 2H), 5.33 (br s, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 3.75 (s, 6H). NMR ^{13}C (75 MHz): 159.7, 156.4, 154.0 (2), 149.5, 140.6, 138.5, 132.8, 132.3, 129.6, 126.6, 123.4 (2), 116.5, 114.9, 114.5, 110.8, 102.9, 96.0 (2), 61.2, 56.2, 55.6. MS (APCI $^+$) m/z : 449 [M+H] $^+$. IR (cm $^{-1}$): 3317, 1696, 1502, 1132.

Synthesis of (10e): To a dioxane (6 mL) solution of *N*-tosylhydrazide (1.2 mmol), *t*BuOLi (3 mmol), $Pd_2(dba)_3$ (0.12 mmol), and XPhos (0.24 mmol) was added **7b** (0.5 mmol) in dioxane (2 mL). The reaction vessel was sealed, and then heated at 80 °C for 3 h. The resulting suspension was cooled to room temperature and filtered through a pad of Celite eluting with AcOEt, and the inorganic salts were removed. The filtrate was concentrated and purification of the residue by silica gel column chromatography gave **10e**.

3-((4-Methoxyphenyl)amino)-6-(1-(4-methoxyphenyl)vinyl)-2H-chromen-2-one (10e). Yield 55%. Yellow oil. R_f : 0.58 (EtOAc/c-hexane: 3/7). NMR 1H (300 MHz): 7.30-7.00 (m, 6H), 6.90-6.81 (m, 6H), 6.61 (br s, 1H), 5.32-5.27 (m, 2H), 3.84 (s, 6H). NMR ^{13}C (75 MHz): 159.9, 159.6, 156.7, 148.6, 147.9, 138.7, 133.8, 132.3, 131.1, 129.5 (2), 126.7, 125.1, 124.1 (2), 121.0, 116.0, 115.0 (2), 113.7 (2), 113.4, 107.1, 55.3 (2). MS (APCI $^+$) m/z : 400 [M+H] $^+$. IR (cm $^{-1}$): 3317, 1696, 1502, 1132.

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