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Domino Reactions of Alkenyl *p*-Benzoquinones: Access to Aryl Sulfide Derivatives of Coumarins

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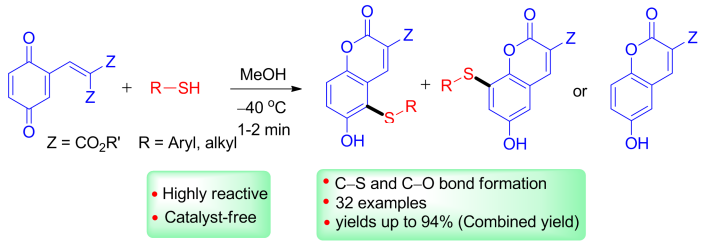

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Domino Reactions of Alkenyl *p*-Benzoquinones: Access to Aryl Sulfide Derivatives of Coumarins

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ABSTRACT

An efficient domino approach has been developed for the synthesis of coumarin aryl sulfides utilizing alkenyl arenes derived electrophilic alkenyl *p*-benzoquinones through Michael addition of thiols followed by cyclization. The reaction proceeds regioselectively under mild conditions within short reaction time to afford the title products in good to excellent yields. This catalyst-free reaction has good substrate scope.

1. Introduction

In the enormously progressing field of synthetic chemistry, the edifice of carbon–heteroatom bond formation is an important strategy for the construction of complex organic molecules.[1] Domino approach is one of the major tool to construct biologically important complex molecules from simple substrates in one-pot fashion which is ecologically and economically benign.[2] *p*-Quinone[3,4] is one of the potent starting materials for the synthesis of compounds having biological profiles.[5,6] *p*-Quinones react with thiols to generate hydroquinones bearing arylthio moiety.[7] In recent years, *p*-quinones have been derivatized in more useful forms like nitrovinyl *p*-quinones[8] and alkenyl *p*-benzoquinones.[9] The alkenyl *p*-benzoquinones are fascinating precursors for the cascade protocol due to their inherent multiple functionalities. The alkenyl *p*-benzoquinones have potential to react with alkyl and aryl thiols to generate alkyl or aryl sulfide derivatives of coumarins which seem to be promising bioactive compounds since coumarins[10] and biaryl sulfides[11] have enriched literature of bioactivity such as anti-inflammatory, anti-malarial, anti-cancer and anti-HIV activities (Figure 1).[12–14] In addition, coumarin derivatives derived from alkenyl *p*-benzoquinone have also found application in fluorescence probe.[15] However, the reports on the synthesis of coumarin-coupled aryl sulfides are scarce.[16] Keeping the above in mind, we hypothesized that alkenyl *p*-benzoquinones, having multiple sites for nucleophilic attack, can undergo Michael addition with thiols followed by cyclization in domino fashion, resulting in the formation of novel aryl sulfide derivatives of coumarin of types I, II and III (Scheme 1). These compounds are interesting due to the presence of both coumarin and aryl sulfide moiety. In continuation of our work on harnessing the reactivity

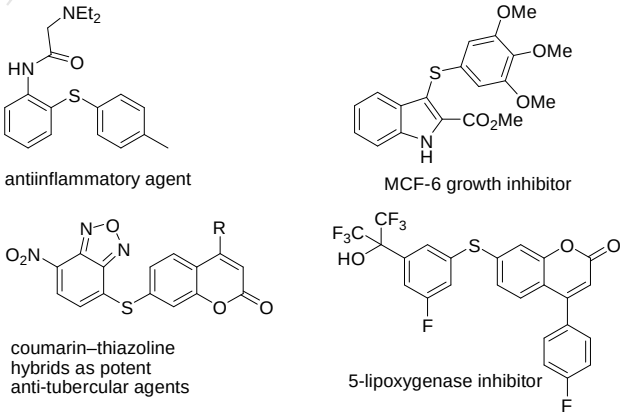
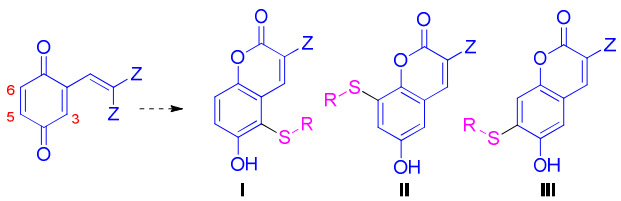


Figure 1. Some of the diaryl sulfide containing biologically active compounds.

of benzoquinone derivatives[17] and synthesis of diaryl sulphides,[18] herein, we report a rapid, novel and efficient method for the



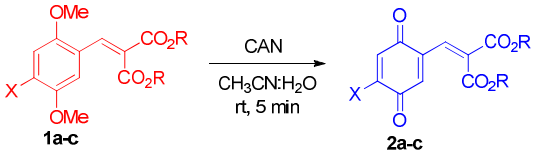
Scheme 1. Working hypothesis.

synthesis of aryl sulfide derivatives of coumarin through sequential construction of C–S and C–O bonds in a domino sequence. The current strategy involves one-pot domino Michael

addition cyclization protocol to produce coumarin-based aryl sulfides.

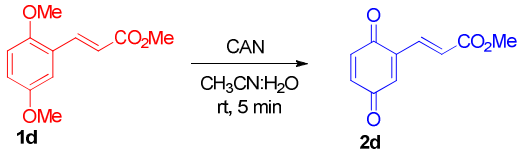
2. Results and Discussion

Accordingly, the alkenyl *p*-benzoquinones **2a-d**, were synthesized[19] by the oxidative demethylation of the corresponding alkenylarenes **1a-d** (Scheme 2). Since the oxidized products **2a-d** are pure, as checked by ^{1}H NMR, they are used as such after work-up without purification.



a: X = H, R = Me
b: X = H, R = Et
c: X = Br, R = Me

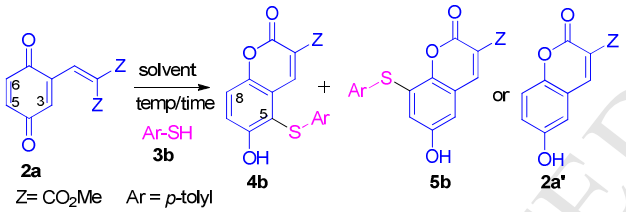
Used after work-up
without further purification



Used after work-up
without further purification

Scheme 2. Oxidation of 1,4-dimethoxy-alkenyl arenes to *p*-quinones **2a-d**.

Table 1. Optimization of reaction conditions.[a]



Entry	solvent	temp/ time (min)	yield (%)[b] 4b	5b/2a′
1	CH_3CN	rt/5	55	18[c]
2	THF	rt/5	47	35[c]
3	Ethyl lactate	rt/5	50	22[c]
4	Toluene	rt/5	57	20[c]
5	CH_2Cl_2	rt/5	60	23[c]
6	$CHCl_3$	rt/5	55	22[c]
7	H_2O	rt/10	41	**2a′** (22)
8	Ethanol	rt/5	55	**5b** (19)
9	MeOH	rt/1	63	**5b** (21)
10[d]	MeOH+H_2O	rt/10	42	**2a′** (27)
11	MeOH	0 °C /1	65	**5b** (18)
12	MeOH	–20 °C /1	68	**5b** (17)
13	MeOH	–40 °C /1	70	**5b** (18)
14[e]	MeOH	–40 °C /1	73	**5b** (18)

[a] All reactions were performed with **2a** (0.5 mmol), **3b** (0.5 mmol) in 1 mL of solvent. [b] Yield of isolated products after column chromatography, unless otherwise noted. [c] Combined yield of **5b** and **2a′** as determined by ^{1}H NMR analysis. [d] MeOH and H_2O (1:1). [e] **2a** (1.0 mmol) and **3b** (0.6 mmol) were used.

As a prelude to our objective, we performed the reaction of alkenyl *p*-benzoquinone **2a** and 4-methylthiophenol (**3b**) in acetonitrile at room temperature. To our delight, aryl sulfide derivative of coumarin **4b** was obtained in 55% yield along with a mixture of **5b** and **2a′** in a combined yield of 18% (Table 1, entry 1) where the regioisomers **4b** and **5b** resulted from the addition of **3b** on alkenyl *p*-benzoquinone **2a** at position 3 and position 6, respectively.

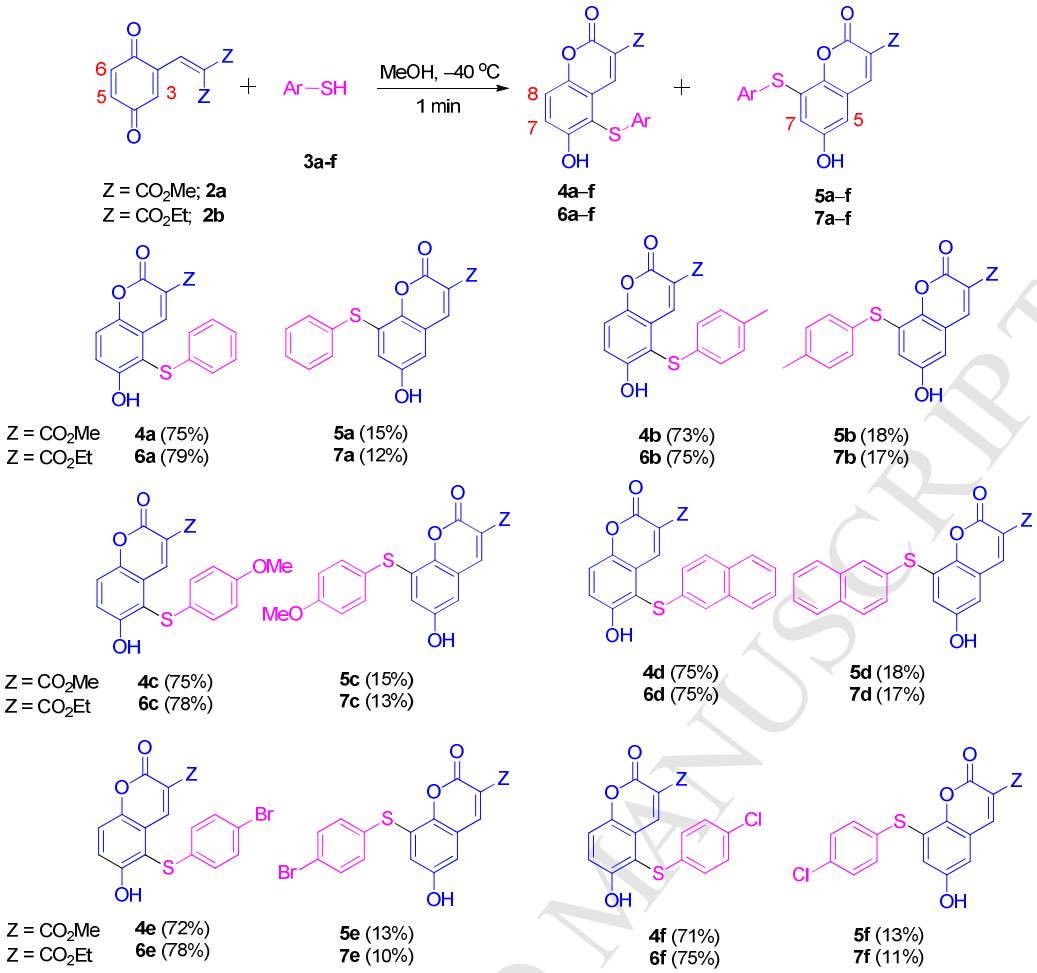
Encouraged by this result, we sought to optimize the reaction conditions in various solvents such as THF, ethyl lactate, toluene, CH_2Cl_2, $CHCl_3$, EtOH, MeOH, H_2O and found that the nature of solvent has great impact on the reaction outcome. In polar/non-polar aprotic solvents, **4b** was obtained in comparatively lower yield along with varying amounts of **5b** and **2a′** (entries 2–6). On switching towards the polar protic solvents, as in case of water, **4b** was obtained selectively in 41% yield along with **2a′** (22%) (entry 7). In the reaction performed in EtOH and MeOH, both regioisomers **4b** and **5b** were formed in good yield (entries 8 and 9). Further, the reaction in a 1:1 mixture of MeOH and H_2O proved to be less reactive (entry 10). Though the reaction proceeds in all solvents, it worked more efficiently in MeOH where **4b** was obtained as major isomer and **5b** in minor quantity.

After identifying the suitable solvent, we performed the reaction at lower temperature and found that the reaction temperature had a great influence on the reaction outcome. The decrease in temperature led to an increase in the yield of the products (entries 11–13). When the amount of **2a** was increased from 1 equiv to 1.3 equiv, the reaction worked efficiently to afford a separable mixture of two regioisomers **4b** and **5b** in 73 and 18% yield, respectively (Table 1, entry 14). Thus, the screening of various parameters identified the above condition as the optimal for this transformation.

In view of the success of the above reaction, the scope of the reaction of **2a** was exemplified with various substituted thiophenols under the optimized reaction conditions. The nature of substituent on aryl ring of thiophenols **3a–f** affected the reaction yield of diaryl sulfides **4a–f** and **5a–f** slightly. Electron–donating groups on aryl ring of thiophenol showed more reactivity than those with electron-withdrawing groups (Table 2). For example, 4-methoxythiophenol (**3c**) produced the products **4c** and **5c** in 75 and 15% yield, respectively. Use of 2-naphthalenethiol (**3d**), delivered **4d** and **5d** in 75 and 18% yield, respectively. Notably, the reactions of **3e** and **3f** bearing electron-withdrawing halo groups furnished the sulfides **4e** and **5e** in 72 and 13%, and **4f** and **5f** in 71 and 13% yield, respectively. The slight reduction in the yield may be attributed to the moderate electron-withdrawing nature of the halo substituents. The structures of the both regioisomers were unambiguously confirmed by ^{1}H NMR analysis by the inspection of coupling constants. In case of **4c**, *ortho* coupling (J = 9.5 Hz) is observed between H-7 and H-8 protons which indicates that thiophenol is attached at 3rd position of alkenyl *p*-benzoquinone **2a**. In case of **5c**, H-5 and H-7 protons showed *meta* coupling (J = 2.5 Hz) confirming the addition of thiophenol at 6th position of **2a**. Moreover, the structures of **4e** and **5e** were confirmed by their single crystal X-ray analysis (Figure 2).[20]

Inspired by the above results, we further extended the scope of the reaction of alkenyl *p*-benzoquinone **2b** bearing ethyl ester with various thiophenols and here again the reaction proceeded smoothly under the optimized conditions. Moreover, electron-donating and withdrawing groups on the aryl ring of thiophenol were well tolerated, leading to the desired major products **6a–f** and minor **7a-f** in good yields (Table 2).

Table 2. Scope of thiols and alkenyl *p*-benzoquinones.[a,b]



[a]The reaction was carried out using **2a**/**2b** (1.0 mmol) and **3a**–**f** (0.6 mmol) in MeOH (1 mL) at –40 °C. [b]Isolated yield after column chromatography.

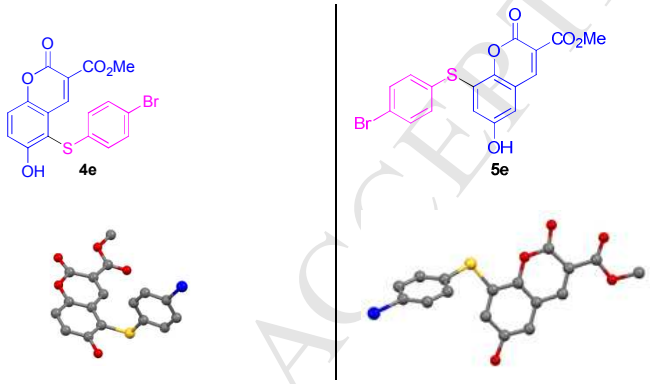
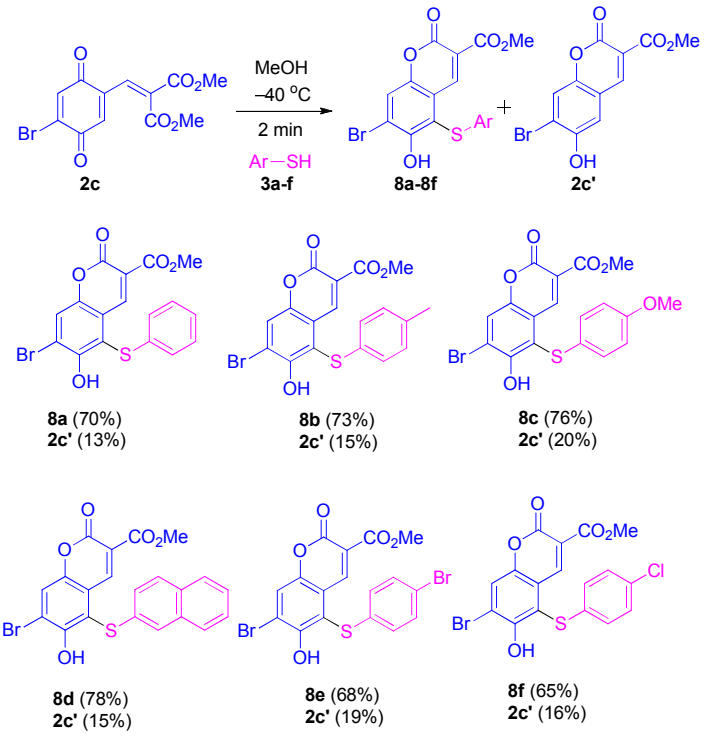


Figure 2. Single crystal X-ray structure of compound **4e** and **5e.**

To further extend the scope of the current domino protocol, bromo derivative **2c** of alkenyl *p*-benzoquinone was treated with various thiophenols under the same conditions. Astonishingly, regioselective addition of the nucleophile at position 3 of **2c** was observed resulting in the formation of the diaryl sulfides **8**. This may be attributed due to the stereoelectronic effect of bromo group situated at 5[th] position of **2c**. Thus a series of thiophenols bearing methyl, methoxy, chloro, bromo substituted at *para* position of phenyl ring and 2-naphthylthiol were well tolerated under the optimized conditions and afforded the anticipated products **8a**–**f** in good yields of 65–78% (Table 3). In addition, **2c′** was obtained as minor product in each case.

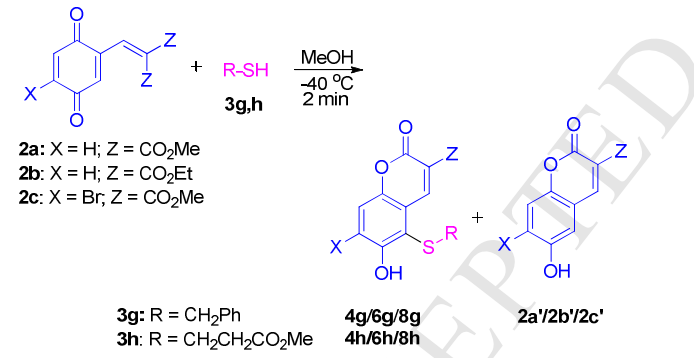
The feasibility and scope of the above reaction was also evaluated with aliphatic thiols **3g** and **3h**. To our delight, it was found that when aliphatic thiols reacted with alkenyl *p*-benzoquinones **2a-c**, a single regioisomer was produced exclusively in each case in very good yield along with **2a′-c′** in 2 min (Table 4). This observation reflected the fact that the reactions of arylthiols are relatively faster than those of alkylthiols as recorded in the literature.[21]

Table 3 Scope of domino reaction of alkenyl *p*-benzoquinones **2c** with thiols.[a,b]



[a]The reaction was carried out using **2c** (1.0 mmol) and **3a–f** (0.6 mmol) in MeOH (1 mL) at –40 °C. [b]Isolated yield after column chromatography.

Table 4 Scope of aliphatic thiols.[a,b]

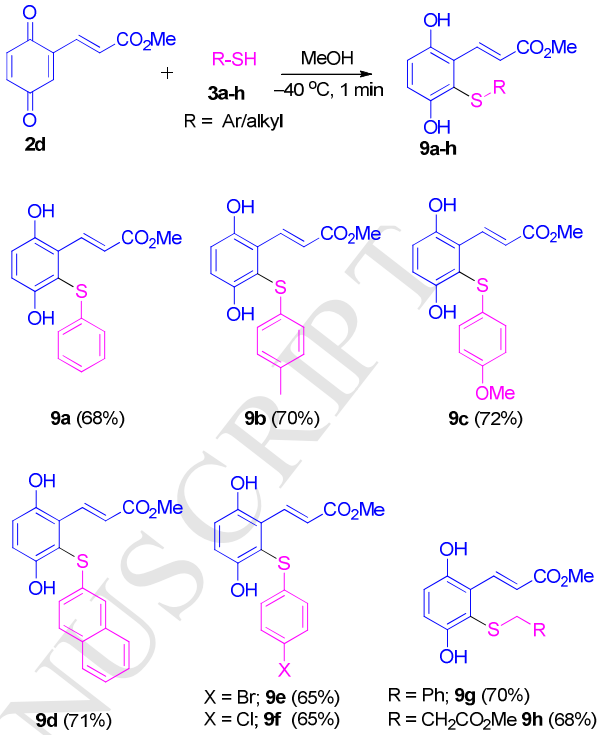


2a	R = CH_2Ph	**4g** (70%)	**2a′** (12%)
2a	R = $CH_2CH_2CO_2Me$	**4h** (69%)	**2a′** (11%)
2b	R = CH_2Ph	**6g** (73%)	**2b′** (13%)
2b	R = $CH_2CH_2CO_2Me$	**6h** (70%)	**2b′** (12%)
2c	R = CH_2Ph	**8g** (70%)	**2c′** (13%)
2c	R = $CH_2CH_2CO_2Me$	**8h** (68%)	**2c′** (17%)

[a]The reaction was carried out using **2a–c** (1.0 mmol) and **3g,h** (0.6 mmol) in MeOH (1 mL) at –40 °C. [b]Isolated yield after column chromatography.

Encouraged by these results, we further employed this protocol to the addition of various thiophenols bearing either electron-donating groups **3b**, **3c** and **3d** or electron-withdrawing groups **3e** and **3f** with alkenyl *p*-benzoquinone **2d**. The reaction underwent smoothly and afforded the sole Michael addition products **9a–f** in 1 min in good yield as shown in Scheme 5. This may be due to the less electrophilicity of **2d** as comparision to **2a**-**2b**. The reaction of **2d** with aliphatic thiols **3g** and **3h** worked well to afford the products **9g** and **9h** regioselectively in 70 and 68% yield, respectively (Table 5).

Table 5. Thiolation of alkenyl *p*-benzoquinone **2d**[a,b]



[a]The reaction was carried out using **2d** (1.0 mmol) and **3a–h** (0.6 mmol) in MeOH (1 mL) at –40 °C. [b]Isolated yield after column chromatography.

To support the observed regioselectivity of the reaction, we calculated Fukui functions[22] for alkenyl *p*-benzoquinones. These calculations were performed with GAUSSIAN 09 program at B3LYP/6-31** level of theory. The Fukui function for nucleophilic attack was associated with the lowest unoccupied

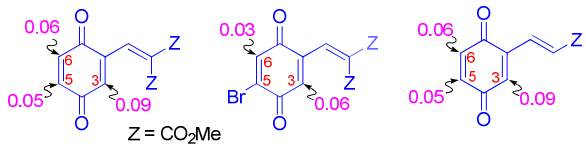
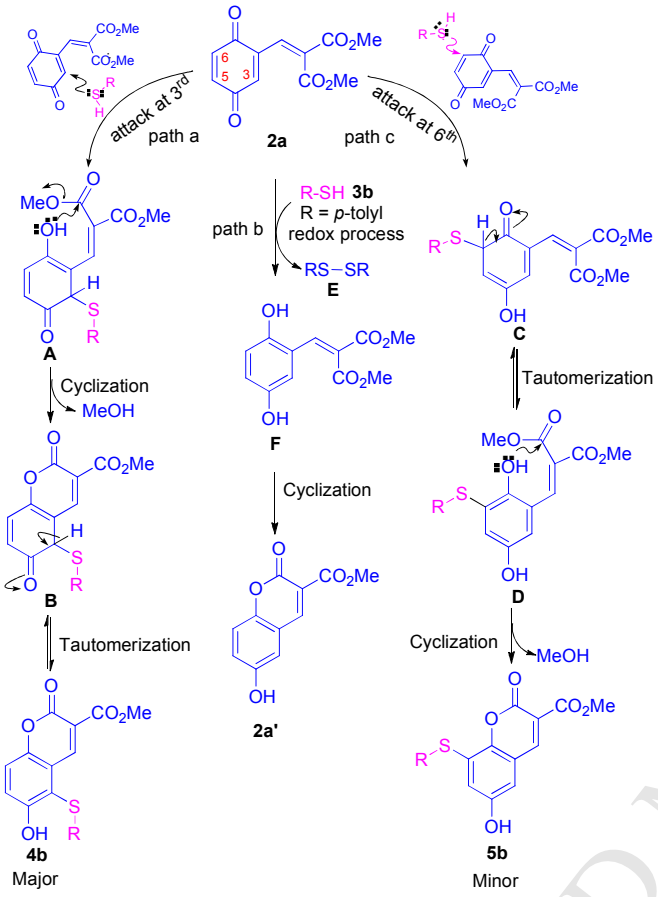


Figure 3. Fukui functions (f_k^+) of alkenyl *p*-benzoquinones for attack of thiol.

molecular orbital (LUMO) density. Higher the electrophilic activation (f_k^+) value, greater the probability for nucleophilic attack of thiols. There are three electrophilic sites (C-3, C-5, C-6) available in alkenyl *p*-benzoquinones **2a-d** for the attack of thiols. The calculated f_k^+ indicate that the C-3 is more electrophilic (f_k^+ = 0.09) site than C-6 (f_k^+ = 0.06), and C-5 (f_k^+ = 0.05) (**2a**, Figure 3). Similar electrophilic trend is observed in quinones **2c** and **2d**. These calculated values supported our experimental results where thiols are attached at 3rd (major) and 6th (minor) positions of alkenyl *p*-benzoquinones.

Based on the above experimental results, a reasonable mechanism for the formation of coumarin aryl sulfide derivatives **4b**, **5b** and cyclised product **2a′** is depicted in Scheme 3. Since the C_2-C_3 double bond is in conjugation with C-1 carbonyl and two ester groups of vinylic moiety at 2nd position and as supported by theoretical observations (Figure 3), 3rd position of **2a** is more electrophilic than 6th position. More electrophilicity of 3rd position facilitates the quick Michael attack of 4-

methylthiophenol (**3b**) to form species **A** (*path a*). Then the nucleophilic oxygen of hydroxy function of **A** attacks on the electrophilic carbon of ester moiety to give the cyclised species **B** spontaneously with the concomitant release of methanol. Tautomerization of **B** produces **4b** as major product. In addition



Scheme 3. Proposed mechanism for the formation of coumarin derivatives **4b**, **5b** and cyclized product **2a′**

to affording **4b** and **5b**, the alkenyl *p*-benzoquinone **2a** may also undergo self-cyclisaton to produce **2a′** (*path b*). This cyclization is triggered by the oxidation of thiophenol **3b** by quinone **2a** to disulfide **E** with simultaneous reduction of **2a** to hydroquinone **F**, which undergoes cyclisation to form coumarin **2a′** (*path b*). Michael attack of **3b** on the less electrophilic 6th position of **2a** leads to the formation of minor product **5b** from *path c*. Initial attack of thiol results in generation of intermediate **C** which immediately tautomerizes to hydroquinone **D**. Cyclization of **D** gives the minor product **5b** with the release of MeOH.

3. Conclusion

In summary, we have demonstrated a concise simple, efficient and novel approach for the generation of coumarin aryl sulfide derivatives *via* regioselective Michael addition of thiols on alkenyl *p*-benzoquinones in domino fashion. Thus this protocol constitutes a straight forward route to aryl sulfide derivatives of coumarin in good to excellent yields. As the products contain coumarin as well as coumarin aryl sulfide moieties, these are potential structural motifs in medicinal chemistry. The calculation of Fukui indices on the benzoquinone derivatives supported the obtained regioselectivity of the reaction. Further investigations are underway in our laboratory to expand the scope of the reactivity of these quinone synthons.

4. Experimental section

4.1 General information:

Unless otherwise noted, chemicals were purchased from the highest purity grade available and were used without further purification. Thin layer chromatography was performed on Merck pre-coated 0.25 mm silica gel plates (60F-254) using UV light as visualizing agent. Silica gel (100–200 mesh) was used for column chromatography. IR spectra of the compounds were recorded on FT-IR and are expressed as wave number (cm^{-1}). NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 using TMS as an internal standard on 500 MHz and 400 MHz instruments. Chemical shifts (δ) were reported as parts per million (ppm) in δ scale downfield from TMS. ^{1}H NMR spectra were referenced to $CDCl_3$ (7.26 ppm) or DMSO-d_6 (2.50 ppm), and ^{13}C NMR spectra were referenced to $CDCl_3$ (77.0 ppm, the middle peak) or DMSO-d_6 (39.5 ppm, the middle peak). Coupling constants were expressed in Hz. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectra (HRMS) were obtained on a Brüker micrOTOF™-Q II mass spectrometer (ESI-MS).

4.2 General procedure for the synthesis of aryl sulfide derivatives of coumarins 4/5 and 6/7:

A solution of ceric ammonium nitrate (2.5 mmol) in H_2O (3 mL) was added to a solution of dimethoxy arene **1** (1 mmol) in CH_3CN (1 mL) with rapid stirring. The color changed rapidly from orange to red. After 5 min, dichloromethane (10 mL) and brine solution were added and the organic layer was separated. The aqueous layer was extracted with DCM. The combined organic layer was dried over anhyd. Na_2SO_4, concentrated under reduced pressure and the residue was used further without purification. Thus obtained benzoquinone **2** was dissolved in MeOH (0.5 mL) at –40 ^{o}C was added thiol derivative **3** (0.6 mmol) in MeOH (0.5 mL) and stirred the reaction mixture for 1 min. After completion of the reaction, as checked by TLC, the solvent was removed under *vacuo* and the residue was purified by silica gel column chromatography using 30% ethyl acetate in hexanes to furnish the pure aryl sulfide derivative of coumarin.

Methyl 6-hydroxy-2-oxo-5-(phenylthio)-2H-chromene-3-carboxylate (**4a**): Reaction time: 1 min; Yield: 0.147 g (75%) as yellow solid; mp: 167–168 ^{o}C; IR (KBr): ν_{max} 3467, 2945, 2728, 1743, 1701, 1566, 1363, 1263, 1226, 1039, 691 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.94 (s, 1H), 7.39 (AB quartet, *J* = 9.0, 13.5 Hz, 2H), 7.25–7.20 (m, 2H), 7.19–7.14 (m, 1H), 7.03 (d, *J* = 7.5 Hz, 2H), 6.89 (s, 1H), 3.88 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (*C*O), 156.2 (*C*O), 155.2 (C), 150.2 (C), 146.6 (*C*H), 133.7 (C), 129.6 (*C*H), 126.9 (*C*H), 122.3 (*C*H), 120.6 (*C*H), 120.3 (*C*H), 118.9 (C), 113.9 (C), 52.9 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{12}O_5SNa$ [M + Na]$^+$: 351.0298, found: 351.0302.

Methyl 6-hydroxy-2-oxo-8-(phenylthio)-2H-chromene-3 carboxylate (**5a**): Reaction time: 1 min; Yield: 0.029 g (15%) as yellow solid; mp: 219–220 ^{o}C; IR (KBr): ν_{max} 3433, 2949, 1750, 1566, 1385, 1260, 1039, 688 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.96 (s, 1H), 8.71 (s, 1H), 7.49–7.46 (m, 5H), 7.11 (d, *J* = 2.5 Hz, 1H), 6.68 (d, *J* = 2.5 Hz, 1H), 3.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.1 (*C*O), 155.5 (*C*O), 153.9 (C), 148.9 (*C*H), 144.8 (*C*), 133.1 (*C*H), 130.8 (*C*), 130.0 (*C*H), 128.8 (*C*H), 124.9 (C), 121.5 (*C*H), 118.7 (C), 117.8 (C), 112.8 (*C*H), 52.4 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{12}O_5SNa$ [M + Na]$^+$: 351.0298, found: 351.0299.

Methyl 6-hydroxy-2-oxo-5-(4-methylphenylthio)-2H-chromene-3-carboxylate (**4b**): Reaction time: 1 min; Yield: 0.150 g (73%) as yellow solid; mp: 151–152 °C; IR (KBr): ν_{max} 3383, 2954, 2907, 1753, 1707, 1567, 1261, 1228, 1026, 800, 673 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.97 (s, 1H), 7.37 (AB quartet, *J* = 9.5, 13.0 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.88 (s, 1H), 3.90 (s, 3H), 2.26 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (*C*O), 156.3 (*C*O), 155.0 (C), 150.2 (C), 146.8 (*C*H), 137.3 (C), 130.4 (*C*H), 130.0 (C), 127.5 (*C*H), 122.2 (*C*H), 120.5 (C), 120.1 (*C*H), 118.8 (C), 114.7 (C), 52.9 (O*C*H_3), 20.9 (*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found: 365.0447.

Methyl 6-hydroxy-2-oxo-8-(4-methylphenylthio)-2H-chromene-3-carboxylate (**5b**): Reaction time: 1 min; Yield: 0.036 g (18%) as yellow solid; mp: 196–197 °C; IR (KBr): ν_{max} 3430, 2916, 2849, 2366, 1747, 1566, 1403, 1268, 1026, 803, 641 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 9.90 (s, 1H), 8.69 (s, 1H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.05 (s, 1H), 6.58 (s, 1H), 3.83 (s, 3H), 2.36 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.6 (*C*O), 156.1 (*C*O), 154.4 (C), 149.5 (*C*H), 144.8 (C), 139.7 (C), 134.6 (*C*H), 131.3 (*C*H), 126.9 (C), 126.8 (C), 120.8 (*C*H), 119.0 (C), 118.3 (C), 112.6 (*C*H), 53.0 (O*C*H_3), 21.3 (*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found: 365.0446.

Methyl 6-hydroxy-5-(4-methoxyphenylthio)-2-oxo-2H-chromene-3-carboxylate (**4c**): Reaction time: 1 min; Yield: 0.161 g (75%) as yellow solid; mp: 105–106 °C; IR (KBr): ν_{max} 3415, 2928, 2848, 1749, 1624, 1562, 1436, 1241, 1032, 815, 623 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 10.40 (s, 1H), 9.00 (s, 1H), 7.40 (d, *J* = 9.5 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 9.0 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 3.68 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (*C*O), 156.3 (*C*O), 154.9 (C), 150.0 (C), 146.9 (*C*H), 130.0 (*C*H), 124.3 (C), 122.3 (*C*H), 120.3 (C), 119.7 (C), 119.6 (*C*H), 118.6 (C), 116.0 (C), 115.2 (*C*H), 55.3 (O*C*H_3), 52.8 (O*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_6SNa$ $[M + Na]^+$: 381.0403, found: 381.0399.

Methyl 6-hydroxy-8-(4-methoxyphenylthio)-2-oxo-2H-chromene-3-carboxylate (**5c**): Reaction time: 1 min; Yield: 0.032 g (15%) as yellow solid; mp: 199–200 °C; IR (KBr): ν_{max} 3420, 2937, 2848, 1750, 1629, 1570, 1433, 1260, 1032, 820, 620 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 9.85 (s, 1H), 8.69 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 9.0 Hz, 2H), 6.99 (d, *J* = 2.5 Hz, 1H), 6.43 (d, *J* = 2.5 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2 (*C*O), 158.2 (*C*O), 156.1 (C), 155.7 (C), 148.9 (C), 146.5 (*C*H), 129.9 (*C*H), 126.4 (C), 123.0 (*C*H), 120.6 (C), 118.8 (C), 118.0 (*C*H), 116.2 (C), 114.9 (*C*H), 55.2 (O*C*H_3), 52.6 (O*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_6SNa$ $[M + Na]^+$: 381.0403, found: 381.0391.

Methyl 6-hydroxy-5-(napthalen-2-ylthio)-2-oxo-2H-chromene-3-carboxylate (**4d**): Reaction time: 1 min; Yield: 0.170 g (75%) as yellow solid; mp: 123–124 °C; IR (KBr): ν_{max} 3346, 2919, 2852, 2375, 1757, 1566, 1373, 1262, 1030, 829, 606 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.99 (s, 1H), 7.78–7.72 (m, 2H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.48–7.38 (m, 5H), 7.16 (d, *J* = 8.5 Hz, 1H), 6.85 (s, 1H), 3.88 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (*C*O), 156.2 (*C*O), 155.3 (C), 150.2 (C), 146.6 (*C*H), 133.6 (C), 131.9 (C), 131.1 (C), 129.5 (*C*H), 127.7 (*C*H), 127.1 (*C*H), 126.4 (*C*H), 125.4 (*C*H), 124.6 (*C*H), 122.4 (*C*H), 120.6 (*C*), 120.4 (*C*H), 119.0 (C), 113.8 (C), 52.9 (O*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{21}H_{14}O_5SNa$ $[M + Na]^+$: 401.0454, found: 401.0451.

Methyl 6-hydroxy-8-(napthalen-2-ylthio)-2-oxo-2H-chromene-3-carboxylate (**5d**): Reaction time: 1 min; Yield: 0.041 g (18%) as yellow solid; mp: 238–239 °C; IR (KBr): ν_{max} 3429, 2928, 2852, 2360, 1754, 1575, 1397, 1265, 1038, 806, 591 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 9.89 (s, 1H), 8.72 (s, 1H), 8.15 (s, 1H), 8.02–7.96 (m, 3H), 7.60–7.59 (m, 2H), 7.51– 7.50 (m, 1H), 7.11 (d, *J* = 2.5 Hz, 1H), 6.70 (d, *J* = 2.5 Hz, 1H), 3.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.0 (*C*O), 155.6 (*C*O), 154.0 (C), 149.0 (*C*H), 144.7 (C), 133.5 (C), 132.8 (*C*H), 132.6 (C), 130.0 (*C*H), 129.7 (*C*H), 128.0 (*C*H), 127.8 (*C*H), 127.7 (C), 127.2 (*C*H), 127.0 (*C*H), 125.2 (C), 121.2 (*C*H), 118.7 (C), 117.8 (C), 112.7 (*C*H), 52.5 (O*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: $C_{21}H_{14}O_5SNa$ $[M + Na]^+$: 401.0454, found: 401.0454.

Methyl 5-(4-bromophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**4e**): Reaction time: 1 min; Yield: 0.175 g (72%) as yellow solid; mp: 182–183 °C; IR (KBr): ν_{max} 3421, 2946, 2849, 1757, 1566, 1315, 1247, 125, 1079, 803, 670 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.90 (s, 1H), 7.43 (s, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.76 (s, 1H), 3.92 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (*C*O), 156.1 (*C*O), 155.2 (C), 150.3 (C), 146.3 (*C*H), 132.9 (*C*H), 132.7 (C), 128.4 (*C*H), 122.5 (*C*H), 121.0 (C), 120.8 (*C*H), 120.5 (C), 119.3 (C), 113.2 (C), 53.0 (O*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}BrO_5SNa$ $[M + Na]^+$: 428.9403, found: 428.9404.

Methyl 8-(4-bromophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**5e**): Reaction time: 1 min; Yield: 0.032 g (13%) as yellow solid; mp: 221–222 °C; IR (KBr): ν_{max} 3422, 2854, 2372, 1751, 1569, 1391, 1264, 1032, 841, 659 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 10.00 (s, 1H), 8.71 (s, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 2.8 Hz, 1H), 6.81 (d, *J* = 2.8 Hz, 1H), 3.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.0 (*C*O), 155.5 (*C*O), 153.9 (C), 148.8 (*C*H), 145.2 (C), 134.1 (*C*H), 132.8 (*C*H), 131.1 (C), 123.4 (C), 122.4 (*C*H), 121. 8 (C), 118.9 (C), 117.9 (C), 113.6 (*C*H), 52.4 (O*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}BrO_5SNa$ $[M + Na]^+$: 428.9403, found: 428.9402.

Methyl 5-(4-chlorophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**4f**): Reaction time: 1 min; Yield: 0.154 g (71%) as yellow solid; mp: 177–178 °C; IR (KBr): ν_{max} 3355, 2937, 2840, 1748, 1558, 1364, 1036, 800, 610 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.90 (s, 1H), 7.41 (s, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.85 (s, 1H), 3.90 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (*C*O), 156.2 (*C*O), 155.2 (C), 150.4 (C), 146.4 (*C*H), 133.2 (C), 132.4 (C), 129.8 (*C*H), 128.3 (*C*H), 122.6 (*C*H), 120.7 (*C*H), 120.6 (C), 119.3 (C), 113.5 (C), 53.1 (O*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}ClO_5SNa$ $[M + Na]^+$: 384.9908, found: 384.9907.

Methyl 8-(4-chlorophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**5f**): Reaction time: 1 min; Yield: 0.028 g (13%) as yellow solid; mp: 210–211 °C; IR (KBr): ν_{max} 3418, 2923, 2852, 2345, 1747, 1632, 1574, 1390, 1270, 1032, 832, 606 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 10.00 (s, 1H), 8.71 (s, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 2.0 Hz, 1H), 6.77 (d, *J* = 1.5 Hz, 1H), 3.82 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.1 (*C*O), 155.5 (*C*O), 153.9 (C), 148.9 (*C*H), 145.2 (*C*), 134.1 (*C*H), 133.5 (C), 130.5 (C), 129.9 (*C*H), 123.8 (*C*H), 122.2 (*C*), 118.9 (C), 118.0 (C), 113.4 (*C*H), 52.5 (O*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}ClO_5SNa$ $[M + Na]^+$: 384.9908, found: 384.9906.

Methyl 5-(benzylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**4g**): Reaction time: 2 min; Yield: 0.144 g (70 %) as yellow solid; mp: 121–122 °C; IR (KBr): ν_{max} 3403, 2919, 1748,

1633, 1559, 1312, 1224, 1044, 709, 600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.42 (s, 1H), 7.29 (AB quartet, *J* = 9.0, 11.6 Hz, 2H), 7.18–7.13 (m, 3H), 6.90 (d, *J* = 7.0 Hz, 2H), 6.84 (s, 1H), 3.92 (s, 3H), 3.82 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (*C*O), 156.3 (*C*O), 155.0 (C), 150.0 (C), 146.6 (*C*H), 136.0 (C), 128.8 (*C*H), 128.7 (*C*H), 127.8 (*C*H), 121.2 (*C*H), 119.5 (*C*H), 117.8 (C), 115.4 (C), 52.7 (O*C*H_3), 40.9 (*C*H_2) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found : 365.0453.

Methyl 6-hydroxy-5-(3-methoxy-3-oxopropylthio)-2-oxo-2H-chromene-3-carboxylate (**4h**): Reaction time: 2 min; Yield: 0.139 g (69%) as yellow solid; mp: 108–109 °C; IR (KBr): ν_{max} 3469, 2922, 1742, 1698, 1565, 1465, 1377, 1256, 1224, 1035, 676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.00 (s, 1H), 7.40 (s, 1H), 7.27 (AB quartet, *J* = 9.2, 15.6 Hz , 2H), 3.90 (s, 3H), 3.66 (s, 3H), 2.92 (t, *J* = 6.8 Hz, 2H), 2.51 (t, *J* = 6.8 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8 (*C*O), 163.4 (*C*O), 156.4 (*C*O), 155.6 (C), 149.3 (C), 147.1 (*C*H), 122.3 (*C*H), 120.5 (C), 118.4 (*C*H), 117.6 (C), 116.2 (C), 52.6 (O*C*H_3), 51.7 (O*C*H_3), 33.5 (*C*H_2), 30.1 (*C*H_2) ppm; HRMS (ESI+): *m/z* calcd for $C_{15}H_{14}O_7SNa$ $[M + Na]^+$: 361.0352, found: 361.0355.

Methyl 6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**2a′**): mp: 195–196 °C; IR (KBr): ν_{max} 3437, 2928, 2369, 1731, 1569, 1486, 1378, 1026, 800 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 9.95 (s, 1H), 8.69 (s, 1H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.21 (d, *J* = 3.0 Hz, 1H), 7.16 (dd, *J* = 3.0, 9.0 Hz, 1H), 3.82 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO- d_6): δ 163.2 (*C*O), 156.8 (*C*O), 153.8 (C), 148.8 (C), 148.8 (*C*H), 148.2 (*C*), 122.9 (*C*H), 117.7 (C), 116.9 (*C*H), 113.0 (*C*H), 52.2 (O*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{11}H_8O_5Na$ $[M + Na]^+$: 243.0263, found : 243.0133.

Ethyl 6-hydroxy-2-oxo-5-(phenylthio)-2H-chromene-3-carboxylate (**6a**): Reaction time: 1 min; Yield: 0.162 g (79%) as yellow solid; mp: 132–133 °C; IR (KBr): ν_{max} 3165, 1740, 1676, 1561, 1453, 1306, 1229, 1135, 1045, 797, 726 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.92 (s, 1H), 7.42 (s, 2H), 7.28–7.24 (m, 2H), 7.22–7.20 (m, 1H), 7.06 (d, *J* = 7.5 Hz, 2H), 7.05 (s, 1H), 4.37 (q, *J* = 7.0 Hz, 2H), 1.37 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0 (*C*O), 156.3 (*C*O), 155.1 (C), 150.2 (C), 146.1 (*C*H), 133.8 (C), 129.6 (*C*H), 127.1 (*C*H), 127.0 (*C*H), 122.1 (*C*H), 120.6 (*C*), 120.3 (*C*H), 119.4 (C), 113.9 (C), 62.0 (*C*H_2), 14.1 (*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found: 365.0460.

Ethyl 6-hydroxy-2-oxo-8-(phenylthio)-2H-chromene-3-carboxylate (**7a**): Reaction time: 1 min; Yield: 0.024 g (12%) as yellow solid; mp: 147–148 °C; IR (KBr): ν_{max} 3400, 3058, 2925, 1748, 1571, 1444, 1385, 1268, 1034, 800, 735 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 9.96 (s, 1H), 8.67 (s, 1H), 7.47–7.46 (m, 5H), 7.10 (s, 1H), 6.69 (s, 1H), 4.29 (q, *J* = 7.0 Hz, 2H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6 (*C*O), 155.7 (*C*O), 154.0 (C), 148.6 (*C*H), 144.8 (C), 133.1 (*C*H), 130.8 (*C*H), 130.1 (C), 128.9 (*C*H), 124.9 (C), 121.5 (*C*H), 118.8 (C), 118.2 (C), 112.8 (*C*H), 61.3 (*C*H_2), 14.1 (*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}O_5SNa$ $[M + Na]^+$: 365.0454, found: 365.0454.

Ethyl 6-hydroxy-2-oxo-5-(4-methylphenylthio)-2H-chromene-3-carboxylate (**6b**): Reaction time: 1 min; Yield: 0.160 g (75%) as yellow solid; mp: 108–109 °C; IR (KBr): ν_{max} 3469, 2922, 1742, 1698, 1565, 1465, 1377, 1256, 1224, 1035, 676 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.93 (s, 1H), 7.37 (AB quartet, *J* = 9.0, 11.0 Hz, 2H), 7.05 (d, *J* = 7.5 Hz, 2H), 6.98 (d, *J* = 7.5 Hz, 2H), 6.86 (s, 1H), 4.36 (q, *J* = 7.0 Hz, 2H), 2.26 (s, 3H), 1.36 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0 (*C*O), 156.3 (*C*O), 154.9 (C), 150.1 (C), 146.2 (*C*H), 137.3 (C), 130.4 (*C*H), 130.2 (C), 127.7 (*C*H), 122.0 (*C*H), 120.5 (C), 120.0 (*C*H), 119.3 (C), 114.8 (C), 62.0 (*C*H_2), 20.9 (O*C*H_3), 14.0 (*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{19}H_{16}O_5SNa$ $[M + Na]^+$: 379.0611, found: 379.0606.

Ethyl 6-hydroxy-2-oxo-8-(4-methylphenylthio)-2H-chromene-3-carboxylate (**7b**): Reaction time: 1 min; Yield: 0.036 g (17%) as yellow solid; mp: 207–208 °C; IR (KBr): ν_{max} 3469, 2920, 1745, 1569, 1460, 1390, 1250, 1229, 1130, 679 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 9.93 (s, 1H), 8.66 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.04 (d, *J* = 2.5 Hz, 1H), 6.56 (d, *J* = 2.5 Hz, 1H), 4.28 (q, *J* = 7.5 Hz, 2H), 2.35 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.9 (*C*O), 156.1 (*C*O), 154.2 (C), 148.9 (*C*H), 144.6 (C), 139.5 (C), 134.2 (*C*H), 131.1 (*C*H), 126.7 (C), 126.4 (C), 120.8 (*C*H), 118.8 (C), 118.4 (C), 112.4 (*C*H), 61.7 (*C*H_2), 21.0 (O*C*H_3), 14.3 (*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{19}H_{16}O_5SNa$ $[M + Na]^+$: 379.0611, found: 379.0606.

Ethyl 6-hydroxy-7-(4-methoxyphenylthio)-2-oxo-2H-chromene-3-carboxylate (**6c**): Reaction time: 1 min; Yield: 0.174 g (78%) as yellow solid; mp: 153–154 °C; IR (KBr): ν_{max} 3419, 2923, 1754, 1683, 1565, 1492, 1380, 1267, 1033, 797, 608 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.98 (s, 1H), 7.33 (AB quartet, *J* = 9.0, 18.5 Hz, 2H), 7.08 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 9.0 Hz, 2H), 4.37 (q, *J* = 7.0 Hz, 2H), 3.72 (s, 3H), 1.37 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0 (*C*O), 159.2 (*C*O), 156.2 (C), 154.7 (C), 150.1 (C), 146.3 (*C*H) 130.2 (*C*H), 124.2 (C), 122.0 (*C*H), 120.3 (C), 119.8 (*C*H), 119.1 (C), 116.0 (C), 115.3 (*C*H), 62.0 (C), 55.3 (*C*H_2), 14.1 (*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{19}H_{16}O_6SNa$ $[M + Na]^+$: 395.0560, found: 395.0565.

Ethyl 6-hydroxy-8-(4-methoxyphenylthio)-2-oxo-2H-chromene-3-carboxylate (**7c**): Reaction time: 1 min; Yield: 0.028 g (13%) as yellow solid; mp: 191–192 °C; IR (KBr): ν_{max} 3424, 2924, 1701, 1573, 1438, 1383, 1266, 1098 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 9.88 (s, 1H), 8.65 (s, 1H), 7.51 (d, *J* = 9.0 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 2.5 Hz, 1H), 6.44 (d, *J* = 3.0 Hz, 1H), 4.28 (q, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): 163.5 (*C*O), 161.2 (*C*O), 156.8 (C), 154.5 (C), 149.6 (*C*H), 144.5 (C), 137.6 (*C*H), 128.5 (C), 120.1 (C), 119.9 (*C*H), 119.0 (C), 118.6 (C), 116.6 (*C*H), 112.0 (*C*H), 62.4 (*C*H_2), 56.1 (O*C*H_3), 14.7 (*C*H_3) ppm. HRMS (ESI+): *m/z* calcd for $C_{19}H_{17}O_6S$ $[M + H]^+$: 373.0740, found: 373.0741.

Ethyl 6-hydroxy-5-(napthalen-2-ylthio)-2-oxo-2H-chromene-3-carboxylate (**6d**): Reaction time: 1 min; Yield: 0.176 g (75%) as yellow solid; mp: 179 °C; IR (KBr): ν_{max} 3414, 2920, 1749, 1570, 1459, 1382, 1252, 1038, 800, 672 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.93 (s, 1H), 7.74–7.69 (m, 2H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.45–7.36 (m, 5H), 7.15 (d, *J* = 8.5 Hz, 1H), 4.32 (q, *J* = 7.0 Hz, 2H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9 (*C*O), 156.3 (*C*O), 155.2 (C), 150.2 (C), 146.1 (*C*H), 133.6 (C), 131.9 (C), 131.2 (C), 129.5 (*C*H), 127.7 (*C*H), 127.1 (*C*H), 126.4 (*C*H), 125.6 (*C*H), 125.6 (*C*H), 124.8 (*C*H), 122.2 (*C*H), 120.6 (C), 120.3 (*C*H), 119.4 (C), 113.9 (C), 62.0 (*C*H_2), 14.0 (*C*H_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{22}H_{16}O_5SNa$ $[M + Na]^+$: 415.0611, found: 415.0612.

Ethyl 6-hydroxy-8-(napthalen-2-ylthio)-2-oxo-2H-chromene-3-carboxylate (**7d**): Reaction time: 1 min; Yield: 0.040 g (17%) as yellow solid; mp: 230–231 °C; IR (KBr): ν_{max} 3414, 2918, 1749, 1570, 1462, 1382, 1250, 1038, 800, 658 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 9.92 (s, 1H), 8.68 (s, 1H), 8.14 (s, 1H), 8.03–7.95 (m, 3H), 7.60–7.57 (m, 2H), 7.50 (dd, *J* = 1.0, 8.5 Hz, 1H), 7.10 (d, *J* = 2.5 Hz, 1H), 6.70 (d, *J* = 2.5 Hz, 1H), 4.29 (q, *J*

= 6.5 Hz, 2H), 1.30 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): 162.6 (*C*O), 156.4 (*C*O), 155.7 (C), 149.1 (C) 146.0 (*C*H) ,134.0 (C), 133.3 (C), 131.2 (C), 128.8 (*C*H), 127.7 (*C*H), 127.0 (*C*H), 126.9 (*C*H), 125.8 (*C*H), 125.2 (*C*H), 124.5 (*C*H), 123.1 (*C*H), 120.9 (C), 119.4 (C), 118.4 (*C*H), 114.1 (C), 61.4 (CH_2), 14.0 (CH_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{22}H_{16}O_5SNa$ $[M + Na]^+$: 415.0611, found: 415.0610.

Ethyl 5-(4-bromophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**6e**): Reaction time: 1 min; Yield: 0.197 g (78%) as yellow solid; mp: 160–161 °C; IR (KBr): ν_{max} 3423, 2921, 1750, 1566, 1381, 1229, 1035, 802, 659 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85 (s, 1H), 7.41 (s, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.73 (s, 1H), 4.38 (q, *J* = 7.0 Hz, 2H), 1.37 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9 (*C*O), 156.1 (*C*O), 155.1 (C), 150.2 (C), 145.8 (*C*H), 133.1 (C), 132.6 (*C*H), 128.5 (*C*H), 122.3 (*C*H), 120.9 (C), 120.6 (*C*H), 120.5 (C), 119.6 (C), 113.3 (C), 62.1 (CH_2), 14.0 (CH_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}BrO_5S$ $[M + H]^+$: 420.9739, found: 420.9753.

Ethyl 8-(4-bromophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**7e**): Reaction time: 1 min; Yield: 0.025 g (10%) as yellow solid; mp: 221–222 °C; IR (KBr): ν_{max} 3421, 2946, 2849, 1757, 1566, 1315, 1247, 1079, 803, 670 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.00 (s, 1H), 8.69 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.16 (s, 1H), 6.80 (s, 1H), 4.29 (q, *J* = 7.0 Hz, 2H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6 (*C*O), 155.6 (*C*O), 154.0 (C), 148.6 (*C*H), 145.3 (C), 134.2 (*C*H), 132.9 (*C*H), 131.2 (C), 123.5 (C), 122.4 (*C*H), 121.9 (C), 119.0 (C), 118.3 (C), 113.6 (*C*H), 61.4 (CH_2), 14.1 (CH_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{14}BrO_5S$ $[M + H]^+$: 420.9739, found: 420.9740.

Ethyl 5-(4-chlorophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**6f**): Reaction time: 1 min; Yield: 0.169 g (75%) as yellow solid; mp: 156–157 °C; IR (KBr): ν_{max} 3432, 2931, 1749, 1632, 1570, 1470, 1370, 1229, 1035, 805 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.87 (s, 1H), 7.41 (s, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 8.5 Hz, 2H), 6.79 (s, 1H), 4.37 (q, *J* = 7.5 Hz, 2H), 1.37 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0 (*C*O), 156.1 (*C*O), 155.1 (C), 150.2 (C), 145.9 (*C*H), 133.1 (C), 132.3 (C), 129.8 (*C*H), 128.3 (*C*H), 122.3 (*C*H), 120.6 (*C*H), 120.4 (C), 119.6 (C), 113.4 (C), 62.2 (CH_2), 14.1 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}ClO_5SNa$ $[M + Na]^+$: 399.0064, found: 399.0060.

Ethyl 8-(4-chlorophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**7f**): Reaction time: 1 min; Yield: 0.025 g (11%) as yellow solid; mp: 233–234 °C; IR (KBr): ν_{max} 3366, 2934, 2857, 1748, 1573, 1477, 1444, 1388, 1270, 1035, 812, 644 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.00 (s, 1H), 8.68 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 2.5 Hz, 1H), 6.77 (d, *J* = 2.5 Hz, 1H), 4.28 (q, *J* = 7.0 Hz, 2H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 162.7 (*C*O), 155.9 (*C*O), 153.9 (C), 148.3 (*C*H), 145.4 (C), 134.8 (*C*H), 134.5 (C), 129.9 (*C*H), 129.7 (C), 129.5 (C), 125.9 (C), 122.3 (*C*H), 118.1 (C), 111.9 (*C*H), 61.6 (CH_2), 13.9 (CH_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}ClO_5SNa$ $[M + Na]^+$: 399.0064, found: 399.0064.

Ethyl 7-(benzylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**6g**): Reaction time: 2 min; Yield: 0.156 g (73 %) as yellow solid; mp: 110–111 °C; IR (KBr): ν_{max} 3369, 2925, 1752, 1563, 1468, 1383, 1248, 1041, 803, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (s, 1H), 7.28 (AB quartet, *J* = 9.0, 12.5 Hz, 2H), 7.17–7.10 (m, 3H), 6.90–6.85 (m, 3H), 4.37 (q, *J* = 7.0 Hz, 2H), 3.82 (s, 2H), 1.41 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.8 (*C*O), 156.3 (*C*O), 154.9 (C), 149.4 (C), 146.1 (*C*H), 136.0 (C), 128.8 (*C*H), 128.6 (*C*H), 127.8 (*C*H), 121.3 (*C*H), 121.1 (C), 119.4 (*C*H), 118.1 (C), 115.4 (C), 61.7 (CH_2), 40.7 (CH_2), 14.2 (CH_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{19}H_{16}O_5SNa$ $[M + Na]^+$: 379.0611, found : 379.0611.

Ethyl-6–hydroxy-5-(3-methoxy-3-oxopropylthio)-2-oxo-2H-chromene-3-carboxylate (**6h**): Reaction time: 2 min; Yield: 0.148 g (70%) as yellow solid; mp: 114–115 °C; IR (KBr): ν_{max} 3246, 2946, 1742, 1697, 1561, 1366, 1251, 1161, 1041, 835, 667 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.02 (s, 1H), 7.42 (s, 1H), 7.32 (AB quartet, *J* = 9.0, 11.0 Hz, 2H), 4.43 (q, *J* = 7.5 Hz, 2H), 3.73 (s, 3H), 2.98 (t, *J* = 6.5 Hz, 2H), 2.57 (t, *J* = 6.5 Hz, 2H), 1.42 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.9 (*C*O), 163.0 (*C*O), 156.4 (*C*O), 155.4 (C), 149.7 (*C*H), 146.3 (C), 122.0 (*C*H), 120.5 (C), 119.3 (*C*H), 118.8 (C), 115.7 (C), 61.9 (CH_2), 52.0 (O*C*H$_3$), 33.2 (CH_2), 31.1 (CH_2), 14.0 (CH_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{16}H_{16}O_7SNa$ $[M + Na]^+$: 375.0509, found : 375.0507.

Ethyl 6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**2b′**): mp: 174–175 °C; IR (KBr): ν_{max} 3333, 2922, 1744, 1572, 1256, 1386, 1184, 1038, 797, 670 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.92 (s, 1H), 8.65 (s, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.20–7.14 (m, 2H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.8 (*C*O), 156.3 (*C*O), 154.0 (C), 148.4 (*C*H), 147.9 (C), 122.7 (*C*H), 118.3 (C), 117.8 (*C*H), 117.1 (C), 113.8 (*C*H), 61.2 (CH_2), 14.1 (CH_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{12}H_{10}O_5Na[M + Na]^+$: 257.0420, found: 257.0430.

4.3 General procedure for the synthesis of aryl sulfide derivatives of coumarins 8a–h:

The diaryl sulfides **8a**–**h** were synthesized according to the procedure described for the synthesis of compounds **4**/**5**.

Methyl 7-bromo-6-hydroxy-2-oxo-5-(phenylthio)-2H-chromene-3-carboxylate (**8a**): Reaction time: 2 min; Yield: 0.170 g (70%) as yellow solid; mp: 179–180 °C; IR (KBr): ν_{max} 3414, 2922, 1771, 1622, 1550, 1415, 1318, 1203, 1041, 806, 617 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.91 (s, 1H), 7.70 (s, 1H), 7.30–7.22 (m, 3H), 7.08 (d, *J* = 7.5 Hz, 2H), 7.04 (s, 1H), 3.92 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (*C*O), 155.6 (*C*O), 152.3 (*C*), 149.5 (C), 146.4 (*C*H), 133.0 (C), 129.8 (*C*H), 127.6 (*C*H), 127.5 (*C*H), 123.5 (*C*H), 120.1 (C), 119.4 (C), 117.0 (C), 115.4 (C), 53.0 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{11}BrO_5SNa$ $[M + Na]^+$: 428.9403, found: 428.9402.

Methyl 7-bromo-6-hydroxy-2-oxo-5-(4-methylphenylthio)-2H-chromene-3-carboxylate (**8b**): Reaction time: 2 min; Yield: 0.184 g (73%) as yellow solid; mp: 167–168 °C; IR (KBr): ν_{max} 3414, 2922, 1771, 1622, 1550, 1415, 1318, 1203, 1041, 806, 617 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.95 (s, 1H), 7.67 (s, 1H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.08 (s, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 3.92 (s, 3H), 2.29 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (*C*O), 155.7 (*C*O), 152.2 (C), 149.4 (C), 146.5 (*C*H), 138.0 (C), 130.6 (*C*H), 129.4 (C), 128.2 (*C*H), 123.2 (*C*H), 120.0 (C), 119.2 (C), 117.0 (C), 116.3 (C), 53.0 (O*C*H$_3$), 21.0 (CH_3) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}BrO_5SNa$ $[M + Na]^+$: 442.9559, found: 442.9559.

Methyl 7-bromo-6-hydroxy-5-(4-methoxyphenylthio)-2-oxo-2H-chromene-3-carboxylate (**8c**): Reaction time: 2 min; Yield: 0.199 g (76%) as yellow solid; mp: 187–188 °C; IR (KBr): ν_{max} 3417, 2924, 1702, 1571, 1498, 1374, 1266, 1028, 803 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): 9.01 (s, 1H), 7.63 (s, 1H), 7.17–7.13 (m, 2H), 6.81 (d, *J* = 9.0 Hz, 2H), 3.94 (s, 3H), 3.76 (s, 3H) ppm;

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (*C*O), 159.7 (*C*O), 155.7 (C), 151.9 (C), 149.4 (C), 146.6 (*C*H), 130.9 (*C*H), 123.3 (C), 123.0 (*C*H), 119.8 (C), 119.0 (C), 117.5 (C), 117.0 (C), 115.5 (*C*H), 55.4 (O*C*H$_3$), 53.0 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}BrO_6SNa$ $[M + Na]^+$: 458.9508, found: 458.9509.

Methyl 7-bromo-6-hydroxy-5-(napthalen-2-ylthio)-2-oxo-2H-chromene-3-carboxylate (**8d**): Reaction time: 2 min; Yield: 0.214 (78%) as yellow solid; mp: 193–194 °C; IR (KBr): ν_{max} 3437, 2928, 1731, 1569, 1486, 1378, 1178, 1026, 800, 635 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.96 (s, 1H), 7.78–7.74 (m, 2H), 7.70–7.65 (m, 2H), 7.52–7.45 (m, 3H), 7.16 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.12 (s, 1H), 3.89 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3 (*C*O), 155.6 (*C*O), 152.4 (C), 149.5 (C), 146.3 (*C*H), 133.6 (C), 132.2 (C), 130.3 (C) 129.8 (*C*H), 127.8 (*C*H), 127.3 (*C*H), 127.2 (*C*H), 126.7 (*C*H), 126.4 (*C*H), 125.0 (*C*H), 123.5 (*C*H), 120.2 (C), 119.3 (C), 117.2 (C), 115.5 (C), 53.0 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{21}H_{13}BrO_5SNa$ $[M + Na]^+$: 478.9559, found: 478.9559.

Methyl 7-bromo-5-(4-bromophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**8e**): Reaction time: 2 min; Yield: 0.198 g (68%) as yellow solid; mp: 204–205 °C; IR (KBr): ν_{max} 3414, 2945, 1762, 1622, 1542, 1453, 1244, 1032, 812, 620 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.88 (s, 1H), 7.70 (s, 1H), 7.40 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 3.93 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3 (*C*O), 155.5 (*C*O), 152.3 (C), 149.6 (C), 146.0 (*C*H), 132.9 (*C*H), 132.3 (C), 129.0 (*C*H), 123.7 (*C*H), 121.6 (C), 120.0 (C), 119.6 (C), 117.2 (C), 114.9 (C), 53.0 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{10}Br_2O_5SNa$ $[M + Na]^+$: 506.8508, found: 506.8507.

Methyl 7-bromo-5-(4-chlorophenylthio)-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**8f**): Reaction time: 2 min; Yield: 0.172 g (65%) as yellow solid; mp: 206–207 °C; IR (KBr): ν_{max} 3411, 2925, 1770, 1700, 1622, 1550, 1182, 1035, 797, 617 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.81 (s, 1H), 7.63 (s, 1H), 7.18 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.89 (s, 1H), 3.86 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3 (*C*O), 155.5 (*C*O), 152.2 (C), 149.5 (C), 146.1 (*C*H), 133.6 (C), 131.6 (C), 129.9 (*C*H), 128.8 (*C*H), 123.6 (*C*H), 120.0 (C), 119.4 (C), 117.3 (C), 115.0 (C), 53.1 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{10}BrClO_5SNa$ $[M + Na]^+$: 462.9013, found: 462.9012.

Methyl 5-(benzylthio)-7-bromo-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**8g**): Reaction time: 2 min; Yield: 0.176 g (70%) as yellow solid; mp: 167–168 °C; IR (KBr): ν_{max} 3455, 2925, 1758, 1633, 1553, 1399, 1240, 1140, 1039, 879, 656 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.54 (s, 1H), 7.20 (s, 1H), 7.14–7.12 (m, 3H), 6.89 (d, *J* = 7.0 Hz, 2H), 3.89 (s, 3H), 3.86 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.1 (*C*O), 155.7 (*C*O), 152.2 (C), 148.7 (C), 146.3 (*C*H), 135.6 (C), 128.8 (*C*H), 128.7 (*C*H), 127.9 (*C*H), 122.6 (*C*H), 120.7 (C), 117.8 (C), 116.6 (C), 116.0 (C), 52.7 (O*C*H$_3$), 40.8 (*C*H$_2$) ppm; HRMS (ESI+): *m/z* calcd for $C_{18}H_{13}BrO_5SNa$ $[M + Na]^+$: 442.9559, found: 442.9561.

Methyl 7-bromo-6-hydroxy-5-(3-methoxy-3-oxopropylthio)-2-oxo-2H-chromene-3-carboxylate (**8h**): Reaction time: 2 min; Yield: 0.170 g (68%) as yellow solid; mp: 170–171 °C; IR (KBr): ν_{max} 3248, 2946, 1740, 1697, 1561, 1366, 1161, 1044, 820, 667 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): 9.00 (s, 1H), 7.88 (s, 1H), 7.60 (s, 1H), 3.95 (s, 3H), 3.74 (s, 3H), 3.02 (t, *J* = 6.5 Hz, 2H), 2.60 (t, *J* = 7.0 Hz, 2H) ppm; ^{13}CNMR (125 MHz, $CDCl_3$): δ 172.1 (C), 163.5 (C), 155.8 (C), 152.7 (C), 149.1 (*C*), 146.6 (*C*H), 122.7 (*C*H), 120.0 (C), 118.9 (C), 117.3 (C), 116.9 (C), 52.0 (O*C*H$_3$), 52.3 (O*C*H$_3$), 33.0 (*C*H$_2$), 31.3 (*C*H$_2$) ppm; HRMS (ESI+): *m/z* calcd for $C_{15}H_{13}BrO_7SNa$ $[M + Na]^+$: 438.9458, found: 438.9456.

Methyl 7-bromo-6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**2c′**): mp: 214–215 °C; IR (KBr): ν_{max} 3343, 2920, 1746, 1572, 1348 ,1180, 1038, 760, 670 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.80 (s, 1H), 8.71 (s, 1H), 7.71 (s, 1H), 7.34 (s, 1H) 3.82 (s 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.2 (*C*O), 155.8 (*C*O), 151.0 (C), 148.4 (*C*H), 147.6 (C), 120.4 (*C*H), 117.8 (C), 117.6 (C) 117.5 (C), 114.0 (*C*H), 52.4 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{11}H_7BrO_5Na$ $[M + Na]^+$: 320.9370, found: 320.9370.

4.4 General procedure for the synthesis of aryl sulfide derivatives of alkenyl hydroquinone 9a–h:

The diaryl sulfides **9a**–**h** were synthesized according to the procedure described for the synthesis of compounds **4**/**5**.

Methyl (E)-3-(3,6-dihydroxy-2-(phenylthio)phenyl)acrylate (**9a**): Reaction time: 1 min; Yield: 0.123 g (68%) as brown solid; mp: 205–206 °C; IR (KBr): ν_{max} 3344, 1685, 1626, 1438, 1338, 1265, 1170, 824, 646 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.12 (s, 1H), 9.35 (s, 1H), 8.22 (d, *J* = 16.0 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.00–6.91 (m, 5H), 3.64 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.6 (*C*O), 152.2 (C), 151.5 (C), 140.3 (*C*H), 137.6 (C), 129.0 (*C*H), 125.9 (*C*H), 125.0 (C) 123.6, (*C*H), 121.7 (*C*H), 119.2 (*C*H), 118.7 (*C*H), 117.2 (C), 51.3 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{16}H_{14}O_4SNa$ $[M + Na]^+$: 325.0505, found: 325.0519.

Methyl (E)-3-(3,6-dihydroxy-2-(4-methylthio)phenyl)acrylate (**9b**): Reaction time: 1 min; Yield: 0.132 g (70%) as brown solid; mp: 205–206 °C; IR (KBr): ν_{max} 3326, 2919, 1686, 1628, 1433, 1338, 1264, 1195, 808, 643 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.10 (s, 1H), 9.30 (s, 1H), 8.23 (d, *J* = 16.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.98–6.91 (m, 3H), 6.90–6.86 (m, 2H), 3.65 (s, 3H), 2.20 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.6 (*C*O), 152.0 (C), 151.4 (*C*), 140.4 (*C*H), 134.5 (C), 133.9 (C), 129.6 (*C*H), 126.3 (C), 123.5 (*C*H), 121.5 (*C*H), 119.0 (*C*H), 118.6 (*C*H), 118.0 (C) 51.3 (O*C*H$_3$), 20.4 (*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{17}O_4S$ $[M + H]^+$: 317.0842, found: 317.0853.

Methyl (E)-3-(3,6-dihydroxy-2-(4-methoxyphenylthio)phenyl)acrylate (**9c**): Reaction time: 1 min; Yield: 0.143 g (72%) as light brown solid; mp: 182–183 °C; IR (KBr): ν_{max} 3394, 1679, 1629, 1497, 1436, 1339, 1271, 820, 518 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.00 (s, 1H), 9.24 (s, 1H), 8.31 (d, *J* = 16.0 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.94–6.88 (m, 3H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.68 (s, 3H), 3.67 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.7 (CO), 157.7 (C), 151.9 (C), 151.4 (C), 140.7 (*C*H), 129.0 (*C*H), 127.8 (C), 123.4 (*C*H), 121.4 (C), 119.4 (C), 118.8 (*C*H), 118.6 (*C*H), 114.8 (*C*H), 55.2 (O*C*H$_3$), 51.4 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{17}O_5S$ $[M + H]^+$: 333.0791, found: 333.0811.

Methyl (E)-3-(3,6-dihydroxy-2-(naphthalen-2-ylthio)phenyl)acrylate (**9d**): Reaction time: 1 min; Yield: 0.150 g (71%) as light brown solid; mp: 194–195 °C; IR (KBr): ν_{max} 3387, 2916, 1681, 1625, 1384, 1265, 1179, 1124, 815, 614 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 9.27 (s, 1H), 8.20 (d, *J* = 16.0 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H|), 7.36–7.27 (m, 3H), 7.13 (d, *J* = 6.0 Hz, 1H), 7.03 (s, 1H), 7.00–6.97 (m, 1H), 6.91 (t, *J* = 8.8 Hz 1H), 3.62 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ

168.1 (*C*O), 151.6 (C), 151.0 (C), 139.9 (*C*H), 138.9 (C), 133.3 (C), 131.3 (C), 128.4 (*C*H), 127.3 (*C*H), 126.7 (*C*H), 126.2 (*C*H), 125.3 (*C*H), 124.8 (*C*H), 124.5 (*C*H), 123.9 (C), 122.4 (*C*H), 119.6 (*C*H), 117.1 (*C*H), 51.1 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{20}H_{17}O_4S$ $[M + H]^+$: 353.0842, found: 353.0861.

Methyl (E)-3-(2-(4-bromophenylthio)-3,6-dihydroxyphenyl)acrylate (**9e**): Reaction time: 1 min; Yield: 0.149 g (65%) as light brown solid; mp: 218–219 ^oC; IR (KBr): ν_{max} 3328, 2919, 1690, 1628, 1433, 1338, 1264, 1190, 806, 642 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 10.20 (s, 1H), 9.47 (s, 1H), 8.16 (d, *J* = 16.0 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.01–6.88 (m, 5H), 3.65 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): 167.6 (*C*O), 152.1 (C), 151.5 (C), 140.0 (*C*H), 137.3 (C), 131.8 (*C*H), 127.8 (*C*H), 123.5 (C), 121.8 (*C*H), 119.5 (*C*H), 118.7 (*C*H), 117.8 (C), 116.6 (C), 51.4 (O*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{16}H_{13}BrO_4SNa$ $[M + Na]^+$: 402.9610, found: 402.9533.

Methyl (E)-3-(2-(4-chlorophenylthio)-3,6-dihydroxyphenyl)acrylate (**9f**): Reaction time: 1 min; Yield: 0.131 g (65%) as light brown solid; mp: 216–217 ^oC; IR (KBr): ν_{max} 3412, 2950, 1690, 1624, 1432, 1358, 1193, 1080, 815, 620 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 10.20 (s, 1H), 9.48 (s, 1H), 8.22 (d, *J* = 16.0 Hz, 1H), 7.27 (d, *J* =8.4 Hz, 2H), 7.03–6.93 (m, 5H), 3.65 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.7 (*C*O), 152.2 (C), 151.6 (C), 140.2 (*C*H), 136.8 (C), 129.8 (C), 129.0 (*C*H), 127.6 (*C*H), 123.7 (C), 122.0 (*C*H), 119.6 (*C*H), 118.8 (*C*H), 117.0 (C), 51.4 (*C*H$_3$) ppm; HRMS (ESI+): *m/z* calcd for $C_{16}H_{14}ClO_4S$ $[M + H]^+$: 337.0295, found: 337.0290.

Methyl (E)-3-(2-(benzylthio)-3,6-dihydroxyphenyl)acrylate (**9g**): *Reaction time:* 2 min; Yield: 0.129 g (68%) as light brown solid; mp: 169–170 ^oC; IR (KBr): ν_{max} 3328, 2930, 1689, 1628, 1436 1338, 1264, 1190, 800, 647 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.82 (s, 1H), 9.25 (s, 1H), 8.15 (d, *J* = 16.0 Hz, 1H), 7.21–7.12 (m, 5H), 6.84–6.72 (m, 3H), 3.97 (s, 2H), 3.69 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.8 (*C*O), 151.6 (C), 150.9 (C), 140.8 (*C*H), 138.0 (C), 128.8 (*C*H), 128.2 (*C*H), 126.9 (*C*H), 123.5 (C), 120.9 (*C*H), 120.7 (C), 117.7 (*C*H), 117.5 (*C*H), 51.3 (O*C*H$_3$), 38.4 (*C*H$_2$) ppm; HRMS (ESI+): *m/z* calcd for $C_{17}H_{16}O_4S$ $[M + Na]^+$: 339.0661, found: 339.0657.

Methyl (E)-3-(2-(benzylthio)-3,6-dihydroxyphenyl)acrylate (**9h**): Reaction time: 2 min; Yield: 0.131 g (70%) as brown solid; mp: 130–131 ^oC; IR (KBr): ν_{max} 3389, 2919, 1684, 1585, 1384, 1269, 1171, 988, 829, 614 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 9.04 (s, 1H), 8.23 (d, *J* = 16.0 Hz, 1H), 7.02 (d, *J* = 16.0 Hz, 1H), 6.89 (s, 1H), 6.82 (dd, *J* = 8.8, 21.6 Hz, 2H), 3.73 (s, 3H), 3.59 (s, 3H), 2.82 (t, *J* = 7.2 Hz, 2H), 2.42 (t, *J* = 6.8 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 171.9 (CO), 168.5 (*C*O), 151.6 (C), 150.9 (C), 140.1 (*C*H), 123.5 (C), 122.5 (*C*H), 119.0 (*C*H), 118.7, 116.5 (*C*H), 51.75 (O*C*H$_3$), 51.40 (O*C*H$_3$), 33.4 (*C*H$_2$), 30.8 (*C*H$_2$) ppm; HRMS (ESI+): *m/z* calcd for $C_{14}H_{17}O_6S$ $[M + H]^+$: 313.0740, found: 313.0737.

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Notes and references

1. (a) Cano, R.; Ramón, D. J.; Yus, M. *J. Org. Chem.* **2011**, *76*, 654. (b) Sach, N. W.; Richter, D. T.; Cripps, S.; Tran-Dubé, M.; Zhu, H.; Huang, B.; Cui, J.; Sutton, S. C. *Org. Lett*. **2012**, *14*, 3886. (c) Mehta, V. P.; Punji, B. *RSC Adv.* **2013**, *3*, 1195.

2. (a) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131.(b) Tietze, L. F. *Chem. Ind. (London)* **1995**, *12*, 453.(c) Tietze, L. F. *Chem. Rev*. **1996**, *96*, 115. (d) Tietze, L. F.; Lieb, M. E. *Curr. Opin. Chem. Biol.* **1998**, *2*, 363. (e) Tietze, L. F.; Brasche, G.; Gericke, K. In Domino Reactions in Organic Synthesis; Wiley-VCH: Weinheim, Germany, **2006**.

3. (a) Ilangovan, A.; Saravanakumar, S.; Malayappasamy, S. *Org. Lett*. **2013**, *15*, 4968. (b) Walker, S. E.; Jordan-Hore, J. A.; Johnson, D. G.; Macgregor, S. A.; Lee, A.-L. *Angew. Chem. Int. Ed*. **2014**, *53*, 13876. (c) Chen, Y.-H.; Cheng, D.-J.; Zhang, J.; Wang, Y.; Liu, X.-Y.; Tan, B. *J. Am. Chem. Soc*. **2015**, *137*, 15062. (b) Mori-Quiroz, L. M.; Clift, M. D. *Org. Lett*. **2016**, *18*, 3446. (c) Hosamani, B.; Ribeiro, M. F.; da Silva Júnior, E. N.; Namboothiri, I. N. N. *Org. Biomol. Chem.* **2016**, *14*, 6913.

4. (a) He, Z.; Liu, T.; Tao, H.; Wang, C.-J. *Org. Lett*. **2012**, *14*, 6230. (b) Rojas-Martín, J.; Veguillas, M.; Ribagorda, M.; Carreño, M. C. *Org. Lett.* **2013**, *15*, 5686. (c) Löbermann, F.; Weisheit, L.; Trauner, D. *Org. Lett*. **2013**, *15*, 4324. (d) Tran, M. Q.; Ermolenko, L.; Retailleau, P.; Nguyen, T. B.; Al-Mourabit, A. *Org. Lett*. **2014**, *16*, 920. (e) Fujii, Y.; Takehara, T.; Suzuki, T.; Fujioka, H.; Shuto, S.; Arisawa, M. *Adv. Synth. Catal*. **2015**, *357*, 4055. (f) Mfuh, A. M.; Zhang, Y.; Stephens, D. E.; Vo, A. X. T.; Arman, H. D.; Larionov, O. V. *J. Am. Chem. Soc.* **2015**, *137*, 8050. (g) Zhou, X.-L.; Wang, P.-S.; Zhang, D.-W.; Liu, P.; Wang, C.-M.; Gong, L.-Z. *Org. Lett*. **2015**, *17*, 5120. (h) Guo, J.; Chaithanya Kiran, I. N.; Reddy, R. S.; Gao, J.; Tang, M.; Liu, Y.; He, Y. *Org. Lett*. **2016**, *18*, 2499. (i) Gelis, C.; Bekkaye, M.; Lebée, C.; Blanchard, F.; Masson, G. *Org. Lett*. **2016**, *18*, 3422.

5. (a) Suzuki, T.; Kubomura, K.; Takayama, H. *Chem. Pharm. Bull*. **1991**, *39*, 2164. (b) Canto, M.; March, P.; de Figueredo, M. J.; Font Rodríguez, S.; Alvarez-Larena, A.; Piniella, J. F. *Tetrahedron: Asymmetry* **2002**, *13*, 455. (c) Sankararaman, S.; Srinivasan, M. *Org. Biomol. Chem*. **2003**, *1*, 2388. For examples, see: (d) Furusaki, A.; Watanabe, T. *Chem. Pharm. Bull*. **1973**, *21*, 931. (e) Nagoaka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873. (f) Maddaford, S. P.; Andersen, N. G.; Cristofoli, W. A.; Keay, B. A. *J. Am. Chem. Soc*. **1996**, *118*, 10766

6. (a) Errante, G.; Motta, G. L.; Lagana, C.; Wittebolle, V.; Sarciron, M.-É.; Barret, R. *Eur J Med Chem* **2006**, 41, 773. (b) Lagorio, S. H.; Bianchi, D. A.; Sutich, E. G.; Kaufman, T. S. *Eur J Med Chem.* **2006**; *41*, 1333.

7. (a) Yadav, J. S.; Swamy, T.; Reddy, B. V. S.; Rao, D. K., *J. Mol. Catal. A: Chem.* **2007**, *274*, 116. (b) da Rocha**,** D. R.; de Souza, A. C. G.; Resende, J. A. L. C.; Santos, W. C.; dos Santos, E. A.; Pessoa, C.; de Moraes, M. O.; Costa-Lotufo, L. V.; Montenegro, R. C.; Ferreira, V. F. *Org. Biomol. Chem.* **2011**, *9*, 4315.

8. Noland, W. E.; Kedrowski, B. L. *J. Org. Chem.* **2002**, *67*, 8366.

9. Tremblay, M. S.; Sames, D. *Org. Lett.* **2005**, *7*, 2417.

10. Review: Medina, F. G.; Marrero, J. G.; Macías-Alonso, M.; Gonzalez, M. C.; Córdova-Guerrero, I.; García, A. G. T.; Osegueda-Roblesa, S. *Nat. Prod. Rep*. **2015**, *32*, 1472. (b) Widelski, J.; Melliou, E.; Fokialakis, N.; Magiatis, P.; Glowniak, K.; Chinou, I. *J. Nat. Prod*. **2005**, *68*, 1637.

11. (a) Murata, M.; Buchwald, S. L. *Tetrahedron* **2004**, *60*, 7397. (b) Fernndez Rodrguez, M. A.; Shen, Q.-L.; Hartwig, J. F. *J. Am. Chem. Soc*. **2006**, *128*, 2180. (c) Wang, L.; Zhou, W.-Y.; Chen,

S.-C.; He, M.-Y.; Chen, Q. *Synlett* **2011**, 3041. d) Guan, P.; Cao, C.; Liu, Y.; Li, Y.; He, P.; Chen, Q.; Liu, G.; Shi, Y. *Tetrahedron Lett*. **2012**, *53*, 5987. For review see: (e) Lee, C.-F.; Liu, Y.-C.; Badsara, S. S. *Chem. Asian J.* **2014**, *9*, 706. (f) Kazemi, M.; Shiri, L.; Kohzadi, H. *Phosphorus, Sulfur, and Silicon* **2015**, *190*, 978. (g) Chauhan, P.; Mahajan, S.; Enders, D. *Chem. Rev*. **2014**, *114*, 8807.

12. Review: (a) Grover, J.; Jachak, S. M. *RSC Adv*. **2015**, *5*, 38892. (b) Gaudino, E. C.; Tagliapietra, S.; Martina, K.; Palmisanob, G.; Cravotto, G. *RSC Adv*. **2016**, *6*, 46394. (c) Cravotto, G.; Nano, G. M.; Palmisano, G.; Pilati, T.; Tagliapietra, S. *J. Heterocycl. Chem.* **2001**, *38*, 965. (d) Bhat, M. A.; Al-Omar, M. A.; Siddiqui, N. *Med. Chem. Res.* **2013**, *22*, 4455. (e) Nasr, T.; Bondock, S.; Youns, M. *Eur. J. Med. Chem*. **2014**, *76*, 539.

13. (a) Pérez-Cruz, F.; Vazquez-Rodriguez, S.; Matos, M. J.; Herrera-Morales, A.; Villamena, F. A.; Das, A.; Gopalakrishnan, B.; Olea-Azar, C.; Santana, L.; Uriarte, E. *J. Med. Chem.* **2013**, *56*, 6136. (b) Witaicenis, A.; Seito, L. N.; Chagas, A.; Da, S.; De Almeida Junior, L. D.; Luchini, A. C.; Rodrigues-Orsi, P.; Cestari, S. H.; Di Stasi, L. C. *Phytomedicine* **2014**, *21*, 240.

14. (a) Nielsen, S. F.; Nielsen, E. O.; Oslen, G. M.; Liljefors, T.; Peters, D. *J. Med. Chem*. **2000**, *43*, 2217. (b) Liu, G.; Huth, J. R.; Olejniczak, E. T.; Mendoza, R.; De Vries, P.; Leitza, S.; Reilly, E. B.; Okasinski, G. F.; Fesik, S. W.; von Geldern, T. W. *J. Med. Chem*. **2001**, *44*, 1202. (c) Parveen, S.; Khan, M. O. F.; Austin, S. E.; Croft, S. L.; Yardly, V.; Rock, P.; Douglas, K. T. *J. Med. Chem.* **2005**, *48*, 8087. (d) Beletskaya, I. P.; Ananikov, V. P. *Chem. Rev*. **2011**, *111*, 1596.

15. Chen, Y.; Clouthier, C. M.; Tsao, K.; Strmiskova, M.; Lachance, H.; Keillor, J. W. *Angew. Chem. Int. Ed*. **2014**, *53*, 13785.

16. (a) Peng, Y.-Y.; Wen, Y.; Qiu, X. G. *Tetrahedron Lett.* **2009**, *50*, 2405. (b) Rajesha, G.; Mahadevan, K. M.; Satyanarayan, N. D.; Bhojya Naik, H. S. *Phosphorus, Sulfur, and Silicon* **2011**, *186*, 1733.(c) Paul, N.; Muthusubramanian, S. *Med. Chem. Res.* **2014**, *23*, 1612. (d) Tian, H.; Zhu, C.; Yanga, H.; Fu, H. *Chem. Commun.* **2014**, *50*, 8875.

17. (a) Parumala, S. K. R.; Peddinti, R. K. *Org. Lett.* **2013**, *15*, 3546. (b) Surasani, S. R.; Parumala, S. K. R.; Peddinti, R. K. *Org. Biomol. Chem*. **2014**, 12, 5656. (c) Sharma, S.; Naganaboina, R. T.; Peddinti, R. K. *RSC Adv*. **2015**, *5*, 100060.

18. (a) Parumala, S. K. R.; Surasani, S. R.; Peddinti, R. K. *New J. Chem.* **2014**, *38*, 5268. (b) Parumala, S. K. R.; Peddinti, R. K. *Green Chem.* **2015**, *17*, 4068.

19. Jacob, P.; Callery, P. S.; Shulgin, A. T.; Castagnoli, N. *J. Org. Chem.* **1976**, *41*, 3627.

20. (a) **4e**: CCDC No. 1489675. (b) **5e**: CCDC No. 1511658.

21. (a) Tundo, P.; Rossi, L.; Loris, A. *J. Org. Chem.* **2005**, *70*, 2219. (b) Navarro, R.; Pérez, M.; Rodriguez, G.; Reinecke, H. *Eur. Polym. J.*, **2007**, *43*, 4516. (c) Azizi, N.; Khajeh-Amiri, A.; Ghafuri, H.; Bolourtchian. M. *Green Chem. Lett. Rev.*, **2009**, *2*, 43.

22. (a) Domingo, L. R.; Aurell, M. J. *J. Org. Chem*. **2002**, *67*, 959. (b) Bultinck, P.; Carbó-Dorca, R. Langenaeker, W. J. Chem. Phys. **2003**, *118*, 4349. (c) Gayatri, G.; Sastry, N. *J. Chem. Sci.*, **2005**, *117*, 573.