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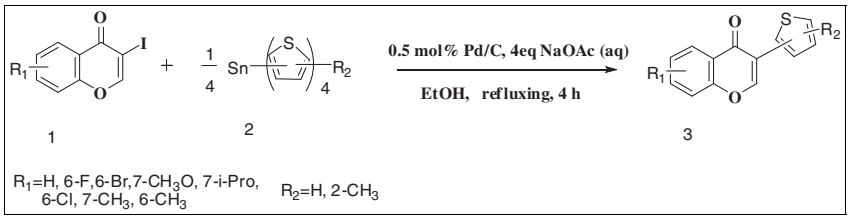
Received January 4, 2013
DOI 10.1002/jhet.2035
Published online 20 May 2014 in Wiley Online Library (wileyonlinelibrary.com).



A new concise, facile, and efficient method for synthesis of 3-thiophenchromone was accomplished in more than over 80% yield starting from formation of the substituted 3-iodochromones and tetrathiophentins by Stille cross-coupling reaction in the presence of palladium on charcoal-catalyzed ligand-free under mild conditions.

J. Heterocyclic Chem., **52**, 310 (2015).

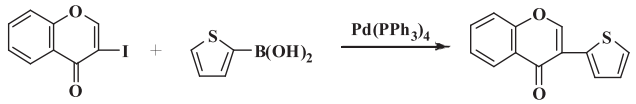
INTRODUCTION

Heteroarylchromones as the derivatives of arylchromones show the activities of antifungal [1], pesticidal [2] and Gastroprotective agents [3]. Yokoe, I. *etal*. [4] reported the synthesis of 3-thiophenchromones by the Suzuki cross-coupling of thiophen-2-ylboronic acid and 3-(thiophen-2-yl)-4H-chromen-4-one (Scheme 1). Stille reaction [5], a palladium-catalyzed cross-coupling between organotin compounds and aryl halides, has been widely used as a synthetic method for functional and bioactive materials including natural products, agrochemicals, pharmaceuticals, and organic electroluminescent polymers [6]. Organostannanes are air-stable and moisture stable and tolerate a wide variety of functional groups [7]. Stille coupling reaction was generally catalyzed by homogenous palladium catalysts together with expensive phosphine ligands. For example, Fu and Littke developed a powerful method for the cross-coupling between aryl chlorides and aryl or alkenyltributyltin compounds using $Pd_2(dba)_3$ and P(n-Bu) [8] as catalysts. Using homogeneous palladium catalysts unfortunately and frequently causes a contamination of the residual metal in the desired product due to the difficulty of its removal [9]. Palladium on charcoal (Pd/C), which has been employed as a common heterogeneous catalyst for hydrogenations, is attracting the interests of organic chemists as a practical catalyst for a variety of bond forming reactions [10] due to the air-stability and non-residual properties. On the basis of our previous cross-coupling of stannanes Ph_4Sn, Ph_3SnCl, Ph_2SnCl_2, and $PhSnCl_3$ with aryl iodides promoted by TBAF/H_2O [11], this inspired us to apply the Stille reaction in the synthesis of 3-thiophenchromone by tetrathiophen-2-ylstannane. We report here an efficient protocol for the ligand-free, Pd/C-catalyzed Stille reaction under atmospheric conditions to give corresponding 3-thiophenchromones (Scheme 2).

RESULTS AND DISCUSSION

As an initial experiment, 3-iodo-4*H*-chromen-4-one **1a** (0.5 mmol) [12] reacting with tetrathiophen-2-ylstannane **2a** (0.15 mmol) in toluene by TBAF (1 M/THF solution containing 5% of water) as base with $Pd_2(dba)_3$ catalyst was tried. Unfortunately, no product **3a** was obtained (Table 1, entry 1). Then, the reaction was carried out in the presence of NaOAc in THF with $Pd(PPh_3)_4$ catalyst by refluxing, 33% of **3a** was obtained (Table 1, entry 2). In order to obtain a good to high yield, we first optimized the palladium catalytic system with $Pd(PPh_3)_4$, Pd/C, $PdCl_2(PPh_3)_2$, and $Pd(OAc)_2$ (Table 1, entries 2–5). It can be seen that 10% Pd(0)/C was the most effective catalyst for the reaction (Table 1, entry 3). Further reaction in different solvents such as THF (Table 1, entry 3), DMF, CH_3CN, and EtOH (Table 1, entries 6–8) revealed EOH as the solvent that yields 92% of **3a** (Table 1, entry 8). And EtOH was an ideal environmentally friendly 'green' synthesis solvent. Third, base NaOAc, Na_2CO_3, NaOH, K_2CO_3, $NaHCO_3$ were tested, and the result indicated that NaOAc was the most effective base for the coupling reaction (Table 1, entries 8–12). Finally, the investigation with different NaOAc equivalents revealed that 16.0 equiv of NaOAc is the most suitable to obtain a high yield (Table 1, entries 13–16). It is interesting to note that the yield is not a significant change that reacted in the air (Table 1, entry 17), although the argon shield could facilitate the yield.

Scheme 1. Synthesis of 3-thiophenchromone by Suzuki cross-coupling reaction.



Scheme 2. Steps for synthesis of 3-thiophenchromones from 1-(2-hydroxyphenyl)ethanones.

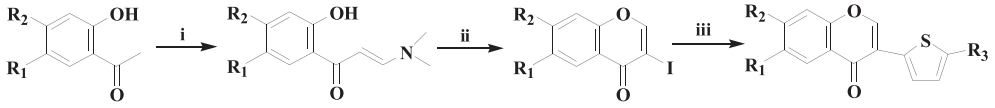
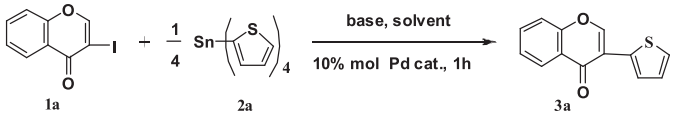


Table 1

Optimization of coupling reaction of 3-iodo-4H-chromen-4-one **1a** with tetrathiophen-2-ylstannane **2a**.[a]



Entry	Solvent	Base	Catalytic	Molar ratios 1a:2a:base	Yield[b] (%)
1	Toluene	TBAF	$Pd_2(dba)_3$	4:1.2:7	NR
2	THF	NaOAc	$Pd(PPh_3)_4$	4:1.2:20	33
3	THF	NaOAc	Pd/C	4:1.2:20	85
4	THF	NaOAc	$PdCl_2(PPh_3)_2$	4:1.2:20	72
5	THF	NaOAc	$Pd(OAc)_2$	4:1.2:20	82
6	DMF	NaOAc	Pd/C	4:1.2:20	71
7	CH_3CN	NaOAc	Pd/C	4:1.2:20	90
8	EtOH[c]	NaOAc	Pd/C	4:1.2:20	92
9	EtOH	Na_2CO_3	Pd/C	4:1.2:20	82
10	EtOH	NaOH	Pd/C	4:1.2:20	N.R.
11	EtOH	K_2CO_3	Pd/C	4:1.2:20	84
12	EtOH	$NaHCO_3$	Pd/C	4:1.2:20	74
13	EtOH	NaOAc	Pd/C	4:1.2:4	75
14	EtOH	NaOAc	Pd/C	4:1.2:12	82
15	EtOH	NaOAc	Pd/C	4:1.2:16	96
16	EtOH	NaOAc	Pd/C	4:1.2:28	86
17	EtOH	NaOAc	Pd/C	4:1.2:16	94[d]

Reaction conditions:
[a]Unless specified, couplings were performed on 0.5 mmol scale of **1a**, 0.15 mmol of **2a** (1a:2a = 4:1.2), with 10% equiv (Pd/1a) Pd catalyst in 10 mL solvent, toluene and DMF at 100 °C, others solvent refluxing, argon shield.
[b]Isolated yield after silica chromatography.
[c]The coupling were performed also at 60°C, 40°C and rt, 78%, 53%, and 0%.
[d]The coupling were performed in the air.

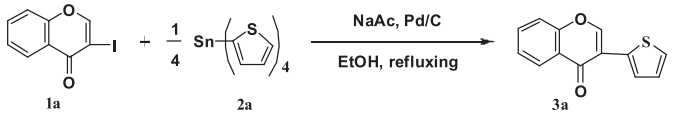
So, all our subsequent studies could be carried out in the air with undistilled solvents and rendered the method exceptionally practicable.

Moreover, the influence of quantity Pd/C and response time was tested. The results indicated that 0.5–10 mol% Pd/C of **1a** can obtain high yield of **3a** in 0.5–4 h (Table 2, entries 1–4). The reaction can also be performed under 0.1 mol% Pd/C of **1a** as catalyst in 15 h, but the yield of **3a** is 68% (Table 2, entry 5). In Table 2, the response time of coupling reactions and the quantity of Pd/C is inversely proportional. Considering the value of Pd/C and yield of **3a**, 0.5 mol% Pd/C of **1a** as the appropriate catalyst was chosen for this reaction (Table 2, entry 4).

Furthermore, with the optimized reaction conditions in hand, a variety of structurally divergent 3-iodochromones (**1**) and tetrathiophentins (**2**) were studied to illustrate this

Table 2

The influence of quantity of catalyst and response time.[a]



Entry	Molar ratios of Pd/C:1a	Time (h)	Yield[b] (%)
1	10%	0.5	94
2	5%	2	92
3	1%	3	91
4	0.5%	4	86
5	0.1%	15	68

Reaction conditions:
[a]All reactions coupling were performed on 0.5 mmol scale of **1a**, 0.15 mmol of **2a**, with NaOAc (2 mmol) in 10 mL EtOH refluxing in the air and until complete disappearance of 1a by TLC.
[b]Isolated yield after silica chromatography.

efficient synthesis of 3-thiophenchromones (**3**) (Table 3). It was shown that all substrates smoothly reacted to give the corresponding 3-thiophenchromones in 4 h to good yields. Products **3** were characterized by IR, ^{1}H-NMR, ^{13}C-NMR, and HRMS. When tetrathiophen-2-ylstannane**(2a)** is coupled with **1a–1g**, the yields of **3** are higher than that of tetrakis(5-methylthiophen-3-yl)stannane **(2b)**. For 3-iodochromone substituted electron-donating groups such as methoxyl, isopropoxide, methyl substituent, the yields of **3** were higher than that of 3-iodochromone substrates with electron-withdrawing groups such as fluorine, bromine, and chloride substituent.

CONCLUSIONS

In conclusion, we have developed a Pd/C-catalyzed free ligand method for synthesis of 3-thiophenchromone from substituted 1-(2-hydroxyphenyl)ethanone and tetrathiophentins. This process has the following significant features: (1) atom-efficient coupling as 4 equiv of 3-iodo-4H-chromen-4-one reacted with 1 equiv of tetrathiophentins provides a high yield of the cross-coupling products; (2) performed in environmentally friendly media EtOH without argon protection; and (3) catalyzed with simple Pd/C in the absence of additional free ligand. The coupling reaction of synthesis of 3-thiophenchromone can greatly reduce the production cost, easy for industrial production.

EXPERIMENTAL

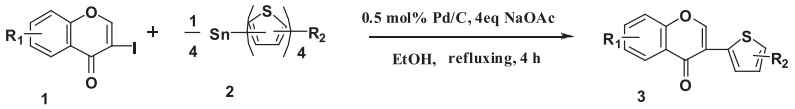
Melting points were measured on X-5 micro melting point apparatus (SanLi Instrument Corporation, Shenzhen, China), which is uncorrected. IR spectra were recorded on FTIR (Nicolet, USA). The ^{1}H-NMR spectra were recorded at 300.00 MHz on Bruker DRX-300 Advance spectrometer (Bruker, USA); chemical shifts (δ scale) are reported in ppm downfield from Me_4Si which was used as the internal standard for all NMR spectra. ^{1}H-NMR spectra are reported in order as follows: multiplicity and approximate coupling constant (*J*-value) in hertz (Hz), number of protons; signals were characterized as s (singlet), d (doublet), t (triplet), m (multiplet), and br (broad signal). The ^{13}C-NMR spectra were recorded at 75.00 MHz; chemical shifts (δ scale) are reported in ppm. The molecular weights were performed with a Bruker MADI-TOF (Bruker, USA). A part of the products are new compounds, but all of the products were characterized by IR, ^{1}H-NMR and ^{13}C-NMR spectra, and MS. 3-Iodochromones were prepared by 1-(2-hydroxyphenyl)ethanones and tetrathiophentins were synthesized by bromothiophene through Grignard reaction[13]. All other commercially obtained reagents were used as received. The silica gel used for the column chromatography was purchased from Qingdao Hailang Chemistry Plant. TLC: silica gel 60 GF_{254} plate; and the eluant of column chromatography is the mixture of petroleum ether and ethyl acetate at volume ratio of 25:1.

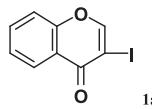
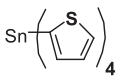
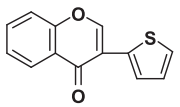
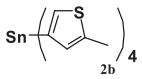
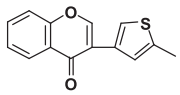
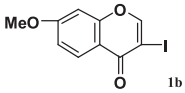
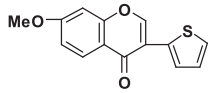
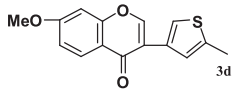
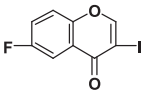
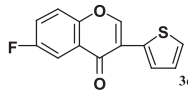
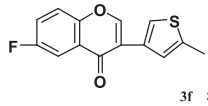
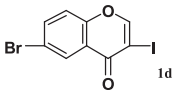
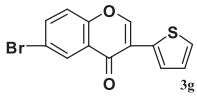
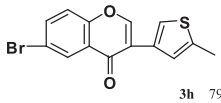
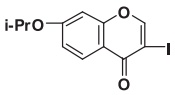
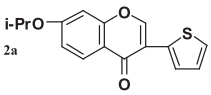
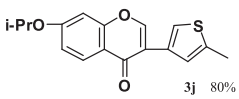
Preparation of 3-iodochromonones 1 [12]. The corresponding 1-(2-hydroxyphenyl)ethanones (2 mmol) and DMF-DMA (8 mmol) were refluxed in DMF (20 mL) at 80°C for 1 h. After completion of the reaction, the mixture was poured into water (40 mL), an orange precipitate appeared, filtered and dried, corresponding 3-dimethylamino-1-(2-hydroxyphenyl)propenones were obtained. Then, 3-dimethylamino-1-(2-hydroxyphenyl)propenones and iodine (4 mmol) were stirred in $CHCl_3$ at room temperature for 2 h. All reactions were monitored by TLC. The solution of 5% $NaHSO_3$ was poured into the reaction mixture to quench I_2, stirred until color of the solution turned to be yellow. After extracted by $CHCl_3$, dried by $MgSO_4$, concentrated by rotary evaporator, and recrystallized by 10 mL ethanol, the pure product corresponding 3-iodochromonones **1** were obtained. The yield of 1a–1g was 89%, 90%, 87%, 88%, 86%, 87%, and 89%.

Preparation of tetrathiophentins 2 [13]. 2-Bromothiophene (0.14 mol) and magnesium turnings (0.28 mol) were added into an oven dried round-bottom flask, along with dry THF (200 mL). The result was an exothermic process and once vigorous reflux had begun, additional dry THF (50 mL) was added, and the mixture was heated at reflux for 3 h. Under an inert atmosphere, the solution was transferred into another round-bottom flask

Table 3

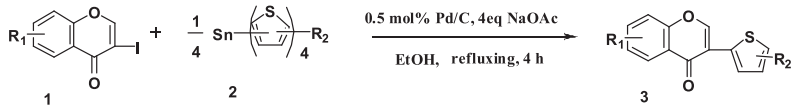
Synthesis of 3-thiophenchromones **3** by coupling of 3-iodochromones **1** with tetrathiophentins **2**.



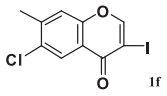
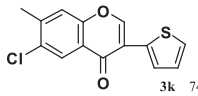
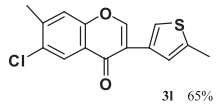
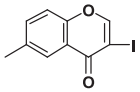
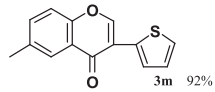
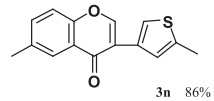
3-Iodochromones	Tetrathiophentins	3-thiophenchromones
1	2	3 Yield[b] (%)
 1a	 2a	 **3a** 94%
	 2b	 **3b** 90%
 1b	**2a**	 **3c** 89%
	2b	 **3d** 87%
 1c	**2a**	 **3e** 86%
	2b	 **3f** 80%
 1d	**2a**	 **3g** 84%
	2b	 **3h** 79%
 1e	**2a**	 **3i** 85%
	2b	 **3j** 80%

(*Continued*)

Table 3
(*Continued*)



1 2 3

3-Iodochromones	Tetrathiophentins	3-thiophenchromones
 1f	**2a**	 **3k** 74%
	2b	 **3l** 65%
 1g	**2a**	 **3m** 92%
	2b	 **3n** 86%

Reaction conditions:
[a]All reactions were carried out in the indicated solvent (10 mL) using 3-iodo-4*H*-chromen-4-ones (**1a–1g**, 0.5 mmol), tetrathiophentins (**2a, 2b**, 0.15 mmol), 0.025 mmol 10% Pd(0)/C, and NaOAc (2 mmol).
[b]Isolated yield after silica chromatography.

containing a magnetic stirrer, leaving any unreacted magnesium behind. The flask was cooled in an ice bath, and tin tetrachloride (0.021 mol) was added drop-wise with rapid stirring via a syringe. The mixture was refluxed for 12 h and cooled. Hydrochloric acid (1 M, 50 mL) was added to the mixture, suspension was appeared and filtered. The residue was washed with methanol (50 mL), hydrochloric acid (1 M, 100 mL), and again with methanol (50 mL) to afford white microcrystal tetrathiophentin **2a** yield in 85%. Using the same method to prepare **2b**, the yield was 80%.

Preparation of 3-thiophenchromone 3. 3-Iodo-4H-chromen-4-one **1a** (0.5 mmol), tetrathiophen-2-ylstannane **2a** (0.15 mmol), NaOAc (2 mmol) and 10% Pd/C (0.025 mmol) were refluxed in ethanol (10 mL) for 4 h. The reaction mixture was filtered, and the mother liquid was acidified with 5% HCl/H_2O to the neutral pH. Evaporation of the solvent in vacuo and the residue was partitioned (H_2O/CH_2Cl_2). The organic layer was dried ($MgSO_4$), evaporated, and purified by silica gel column chromatography (petroleum ether-ethyl acetate = 20:1) to the corresponding pure product **3a. 3b–3n** were obtained by the same method as **3a**.

3-(Thiophen-2-yl)-4H-chromen-4-one (3a). White solid; mp 126.6–127.8°C; IR (KBr), ν (cm^{-1}): 3107, 3082, 3003, 1629, 1567, 1463, 1344, 1276, 1225, 834, 756, 726; ^{1}H-NMR [300 MHz, $CDCl_3$/TMS, δ (ppm)]: 8.36 (s, 1H, C_2-H), 8.31 (d, J = 8.6, 1H,C_5-H), 7.69 (t, J = 7.5, 1H,C_4`-H), 7.52–7.39 (m, 4H,$C_7$-H, $C_8$-H, $C_3$`-H, C_5`-H), 7.11 (t, J = 3.8, 1H, C_6-H); ^{13}C-NMR [75 MHz, $CDCl_3$/TMS, δ (ppm)]: 175.1, 155.8, 151.5, 133.7, 132.4, 126.71, 126.6, 126.4, 125.4, 124.5, 123.9, 119.5, 118.1; HRMS(ESI)[M + Na]$^+$ for $C_{13}H_8O_2SNa$, Calcd: 251.0143; found: 251.0140.

3-(5-Methylthiophen-3-yl)-4H-chromen-4-one (3b). White solid; mp: 155.0–156.2°C; IR (KBr), ν (cm^{-1}): 3133, 3067, 3042, 1632, 1616, 1468, 1365, 1219, 857, 751; ^{1}H-NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 8.79 (s, 1H,C_2-H), 8.15 (d, J = 7.4, 1H,C_5-H), 7.92 (s, 1H,C_2`-H), 7.81 (t, $J$ = 7.1, 1H, $C_7$-H), 7.68 (d, $J$ = 8.2, 1H, $C_8$-H), 7.51 (t, $J$ = 7.2, 1H, $C_6$-H), 7.25 (s, 1H, $C_4$`-H), 2.48 (s, 3H, C_5`-CH_3); ^{13}C-NMR [75 MHz, DMSO-d_6 / TMS, δ (ppm)]: 175.4, 155.7, 154.7, 139.0, 134.5, 131.8, 125.9, 125.2, 124.1, 122.4, 119.5, 118.8, 15.3; HRMS(ESI)[M + Na]$^+$ for $C_{14}H_{10}O_2SNa$, Calcd: 265.0299; found: 265.0293.

7-Methoxy-3-(thiophen-2-yl)-4H-chromen-4-one (3c). White solid; mp: 170.6–172.3 °C;IR (KBr), ν (cm^{-1}): 3267, 3257, 3218, 1635, 1598, 1499, 1445, 1321, 1276, 1231, 1219, 1025, 835, 708; ^{1}H-NMR [300 MHz, DMSO-d_6 /TMS, δ (ppm)]: 8.94 (s, 1H, C_2-H), 8.07 (d, J = 8.9, 1H, C_5-H), 7.72–7.53 (m, 2H, C_6-H, C_8-H), 7.27–7.02 (m, 3H, C_3`-H, $C_4$`-H, C_5`-H), 3.92 (s, 3H, C_7-OCH_3); ^{13}C-NMR [75 MHz, DMSO-d_6 /TMS, δ (ppm)]: 173.9, 164.5, 157.6, 153.2, 132.1, 127.5, 127.2, 126.7, 124.5,

118.4, 117.0, 115.6, 101.1, 56.6; HRMS(ESI)[M + Na]$^+$ for $C_{14}H_{10}O_3S$ Na, calcd: 281.0248; found: 281.0242.

7-Methoxy-3-(5-methylthiophen-3-yl)-4H-chromen-4-one (3d). White solid; mp: 175.8–176.2°C; IR (KBr), ν (cm^{-1}): 3171, 3147, 3022, 2975, 2834, 1629, 1594, 1435, 1338, 1275, 1239, 1168, 1097, 838, 789; ^{1}H-NMR [300 MHz, DMSO-d_6 /TMS, δ (ppm)]:8.71 (s, 1H, C_2-H), 8.05 (d, J = 8.8, 1H, C_5-H), 7.91 (s, 1H, C_2`-H), 7.24 (s, 1H, $C_8$-H), 7.17 (s, 1H, $C_4$`-H), 7.09 (d, J = 8.8, 1H, C_6-H), 3.91 (s, 3H, C_7-OCH_3), 2.48 (s, 3H, C_5`-CH_3); ^{13}C-NMR [75 MHz, DMSO-d_6 /TMS, δ (ppm)]: 174.9, 164.3, 157.4, 154.4, 139.2, 131.9, 127.3, 125.4, 122.3, 119.4, 118.2, 115.3, 101.3, 56.5, 15.3; HRMS(ESI)[M + Na]$^+$ for $C_{15}H_{12}O_3SNa$, calcd: 295.0405; found: 295.0394.

6-Fluoro-3-(thiophen-2-yl)-4H-chromen-4-one (3e). Gray solid; mp: 159.3–161.2°C; IR (KBr),ν (cm^{-1}): 3200, 3071, 3032, 3108, 1633, 1625, 1574, 1475, 1425, 1325, 1264, 829,759, 698; ^{1}H-NMR [300 MHz, DMSO-d_6 /TMS, δ (ppm)]: 9.06 (s, 1H, C_2-H), 7.83 (dd, J = 8.1, 3.3, 1H, C_5-H), 7.76(d, J = 3.0, 1H, C_7-H), 7.73 (d, J = 8.7, 1H, C_8-H), 7.67(d, J = 2.7, 1H, C_3`-H), 7.63 (d, $J$ = 4.5, 1H, $C_5$`-H), 7.16 (t, J = 3.9, 1H, C_4`-H); ^{13}C-NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 173.8, 161.3, 157.9, 154.1, 152.3, 132.0, 127.8, 126.9, 124.7, 123.1, 122.8, 121.8, 121.7, 118.3, 110.6, 110.3; HRMS(ESI)[M + Na]$^+$ for $C_{13}H_7FO_2SNa$, calcd: 269.0048; found: 269.0043.

Gray solid; mp: 164.9–166.3°C; IR (KBr),ν (cm^{-1}): 3192, 3128, 3067, 1634, 1478, 1406, 1366, 1259, 1180, 1133, 817, 722; ^{1}H-NMR [300 MHz, $CDCl_3$/TMS, δ (ppm)]:8.11 (s, 1H, C_2-H), 7.87 (d, J = 7.8, 1H, C_5-H), 7.63 (s, 1H, C_2`-H), 7.49(d, $J$ = 3.2, 1H, $C_7$-H), 7.41 (d, $J$ = 6.1, 1H, $C_8$-H), 6.97 (s, 1H, $C_4$`-H), 2.45 (s, 3H, C_5`-CH_3); ^{13}C-NMR [75 MHz, $CDCl_3$/TMS, δ (ppm)]: 161.2, 152.4, 139.9, 130.9, 130.8, 128.7, 124.3, 122.4, 121.9, 121.5, 120.1, 120.0, 111.2, 110.9, 15.2; HRMS(ESI) [M + Na]$^+$ for $C_{14}H_9FO_2SNa$, calcd: 283.0205; found: 283.0198.

6-Bromo-3-(thiophen-2-yl)-4H-chromen-4-one (3g). Gray solid; mp: 189.3–190.7°C; IR (KBr),ν (cm^{-1}): 3151, 3073, 3015, 1633, 1599, 1461, 1320, 1266, 847, 705; ^{1}H-NMR [300 MHz, $CDCl_3$/TMS, δ (ppm)]: 8.43 (s, 1H, C_2-H), 8.33 (s, 1H, C_5-H), 7.70 (d, J = 2.3, 1H, C_7-H), 7.67 (d, J = 2.2, 1H, C_8-H), 7.43 (d, J = 3.4, 1H, C_3`-H), 7.34 (d, $J$ = 4.6, 1H, $C_5$`-H), 7.03 (t, J = 3.7,1H, C_4`-H); ^{13}C-NMR [75 MHz, $CDCl_3$/TMS, δ (ppm)]: 173.2, 151.0, 136.6, 136.1, 128.5, 126.3, 126.2, 126.0, 124.5, 119.5, 119.3, 118.3; HRMS(ESI)[M + Na]$^+$ for $C_{13}H_7BrO_2SNa$, calcd: 328.9248; found: 328.9218.

6-Bromo-3-(5-methylthiophen-3-yl)-4H-chromen-4-one (3h). Gray solid; mp: 193.2–194.5°C; IR (KBr),ν (cm^{-1}): 3169, 3064, 1605, 1557, 1438, 1275, 8151, 593; ^{1}H- NMR [300 MHz, $CDCl_3$/TMS, δ (ppm)]:8.42 (s, 1H, C_2-H), 8.17 (s, 1H, C_5-H), 7.75 (d, J = 8.7, 1H, C_7-H), 7.70 (s, 1H, C_2`-H), 7.37 (d, $J$ = 8.9, 1H, $C_8$-H), 7.02 (s, 1H, $C_4$`-H), 2.52 (s, 3H, C_5`-CH_3); ^{13}C-NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 173.7, 154.5, 138.7, 136.6, 131.0, 128.63, 127.5, 125.1, 124.7, 122.2, 121.1, 119.3, 118.2, 14.9; HRMS(ESI)[M + Na]$^+$ for $C_{14}H_9BrO_2SNa$, calcd: 342.9404; found: 342.9387.

7-Isopropoxy-3-(thiophen-2-yl)-4H-chromen-4-one (3i). White solid; mp: 123.4–124.5°C; IR (KBr),ν (cm^{-1}): 3014, 2950, 2926, 1626, 1444, 1284, 1261, 1110, 847, 691; ^{1}H-NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 8.95 (s, 1H, C_2-H), 8.05 (d, J = 8.8, 1H, C_5-H), 7.71–7.51 (m, 2H, C_3`-H, $C_5$`-H), 7.20 (s, 1H, C_8-H), 7.14 (t, J = 5.7, 1H C_4`-H), 7.08 (d, J = 8.7, 1H, C_6-H),4.87–4.82 (m, 1H, C_7-OCH), 1.34 (d, J = 5.7, 6H,C_7-$OCH(CH_3)_2$); ^{13}C-NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 173.8, 162.6, 157.7, 153.1, 149.7, 132.5, 127.6, 127.5, 126.8, 124.3, 118.5, 117.0, 116.4, 102.3, 71.0, 22.0; HRMS(ESI)[M + Na]$^+$ for $C_{16}H_{14}O_3SNa$, calcd: 309.0561; found: 309.0541.

7-Isopropoxy-3-(5-methylthiophen-3-yl)-4H-chromen-4-one (3j). White solid; mp: 119.6–120.7°C; IR (KBr),ν (cm^{-1}): 3177, 3106, 2977, 1632, 1601, 1573, 1441, 1238, 1201, 824, 782; ^{1}H-NMR [300 MHz, DMSO-d_6/TMS, δ (ppm)]: 8.69 (s, 1H C_2-H), 8.03 (d, J = 8.8, 1H, C_5-H), 7.90 (s, 1H, C_8-H), 7.24 (s, 1H, C_2`-H), 7.15 (s, 1H, $C_4$`-H), 7.05 (d, J = 8.7, 1H, C_6-H), 4.97–4.75 (m, 1H, C_7-OCH), 2.48 (s, 3H, C_5`-CH_3), 1.33 (d, J = 5.7, 6H, C_7-$OCH(CH_3)_2$); ^{13}C-NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 174.8, 162.4, 157.7, 154.7, 139.3, 132.35, 128.0, 125.1, 122.8, 119.5, 118.2, 115.8, 102.2, 70.7, 22.0, 15.3; HRMS(ESI)[M + Na]$^+$ for $C_{17}H_{16}O_3SNa$, calcd: 323.0718; found: 323.0701.

6-Chloro-7-methyl-3-(thiophen-2-yl)-4H-chromen-4-one (3k). White solid; mp: 186.6–189.2°C; IR (KBr),ν (cm^{-1}): 3322, 3266, 3243, 1650, 1632, 1615, 1566, 1455, 1416, 1373, 1251, 1128, 844, 692; ^{1}H-NMR [300 MHz, $CDCl_3$/TMS, δ (ppm)]: 8.30 (s, 1H, C_2-H), 8.25 (s, 1H, C_5-H), 7.50 (s, 1H, C_8-H), 7.40 (d, J = 5.0, 1H, C_3`-H), 7.35 (d, $J$ = 8.4, 1H, $C_5$`-H), 7.11 (t, J = 3.8, 1H, C_4`-H), 2.51(s, 3H, C_7-CH_3); ^{13}C-NMR [75 MHz, $CDCl_3$/TMS, δ (ppm)]: 173.3, 156.9, 153.6, 150.8, 142.7, 131.83, 126.2, 126.1, 125.5, 123.9, 122.3, 119.6, 118.9, 20.2; HRMS(ESI) [M + Na]$^+$ for $C_{14}H_9ClO_2SNa$, calcd: 299.9909; found: 298.9885.

6-Chloro-7-methyl-3-(5-methylthiophen-3-yl)-4H-chromen-4-one (3l). White solid; mp: 193.3–194.9°C; IR (KBr),ν (cm^{-1}): 3209, 3174, 3148, 2992, 2923, 2806, 1636, 1618, 1450, 1412, 1373, 1352, 1216, 1149, 1127, 897, 820, 632; ^{1}H-NMR [300 MHz, $CDCl_3$/TMS, δ (ppm)]:8.24 (s, 1H, C_2-H), 8.12 (s, 1H, C_5-H), 7.69 (s, 1H, C_2`-H), 7.34 (s, 1H, $C_8$-H), 7.02 (s, 1H, $C_4$`-H), 2.51 (d, J = 6.5, 6H, C_7-CH_3, C_5`-CH_3); ^{13}C-NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 174.8, 154.3, 153.6, 138.5, 135.3, 134.9, 131.5, 124.8, 124.4, 123.3, 123.1, 121.8, 119.2, 118.0, 20.4, 15.1; HRMS(ESI)[M + Na]$^+$ for $C_{15}H_{11}ClO_2S$ calcd: 313.0066; found: 313.0059.

6-Methyl-3-(thiophen-2-yl)-4H-chromen-4-one (3m). White solid; mp: 169.2–170.5°C; IR (KBr),ν (cm^{-1}): 3140, 3119, 3073, 2916, 1634, 1568, 1483, 1424, 1365, 1327, 1272, 1231, 844, 817, 686; ^{1}H-NMR [300 MHz, $CDCl_3$/TMS, δ (ppm)]: 8.25 (s, 1H, C_2-H), 8.02 (s, 1H, C_5-H), 7.41 (dd, J = 6.36, 3.36, 2H, C_7-H, C_8-H), 7.32 (dd, J = 3.0, 1H, C_3`-H), 7.27 (d, $J$ = 9.1, 1H, $C_5$`-H), 7.03 (t, J = 3.87, 1H, C_4`-H), 2.47 (s, 3H, C_6-CH_3); ^{13}C-NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 174.6, 159.4, 154.2, 153.4, 136.0, 135.8, 132.5, 127.3, 126.5, 125.2, 124.2, 123.2, 118.8, 20.9; HRMS(ESI)[M + Na]$^+$ for $C_{14}H_{10}O_2SNa$, calcd: 265.0299; found: 265.0279.

6-Methyl-3-(5-methylthiophen-3-yl)-4H-chromen-4-one (3n). White solid; mp: 138.6–139.4°C; IR (KBr),ν (cm^{-1}):3215, 3280, 3119, 1633, 1614, 1548, 1485, 1354, 1268, 1224, 1173, 1150, 841, 813, 799, 717; ^{1}H-NMR [300 MHz, $CDCl_3$/TMS, δ (ppm)]: 8.11 (s, 1H,C_2-H), 8.08(s, 1H, C_5-H),7.69 (s, 1H, C_2`-H), 7.46 (d, $J$ = 8.1, 1H, $C_7$-H), 7.35 (d, $J$ = 8.3, 1H, $C_8$-H), 7.04 (s, 1H, $C_4$`-H), 2.49 (d, J = 16.7, 6H, C_6-CH_3, C_5`-CH_3); ^{13}C-NMR [75 MHz, DMSO-d_6/TMS, δ (ppm)]: 175.3, 154.0, 153.5, 138.4, 135.0, 131.8, 124.6, 123.3, 121.8, 119.3, 118.9, 118.0, 20.46, 15.13; HRMS(ESI)[M + Na]$^+$ for $C_{15}H_{12}O_2SNa$, calcd: 279.0456; found: 279.0438.

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