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A CONVENIENT SYNTHESIS OF 2-ARYLTHIOCHROMEN-4-ONES (THIOFLAVONES) BY IODINE-MEDIATED CYCLIZATION OF 3-ARYL-1-[2-(1,1-DIMETHYLETHYLSULFANYL)PHENYL]PROP-2-EN-1-ONES

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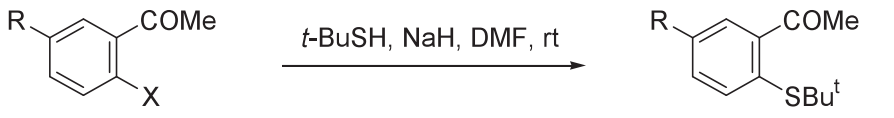
Abstract – A convenient two-step synthesis of 2-arylthiochromen-4-ones (thioflavones) beginning with 1-[2-(1,1-dimethylethylsulfanyl)phenyl]ethanones is described. Thus, 3-aryl-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-ones were prepared by the condensation of 1-[2-(1,1-dimethylethylsulfanyl)phenyl]ethanones with aromatic aldehyde in the presence of sodium hydroxide, and were treated with iodine in refluxing *N*-methylpyrrolidin-2-one (NMP) or propanenitrile to afford the desired products in moderate to fair yields.

Several synthetic approaches to 2-arylthiochromen-4-ones (thioflavones) have recently been reported[1] because of their biological activities.[2] For example, a recent disclosure by Lee and Kim has demonstrated an elegant process based on intramolecular rearrangement of *S*-2-acetophenyl benzothioates.[1d] However this method suffers from limited scope, as it uses 1-(2-sulfanylphenyl)ethanone as the only starting substrate and therefore it cannot allow preparation of the derivatives having substituent(s) on the benzene ring of the thiochromenone structure. In this paper we wish to describe results of our investigation, which offer a new and convenient procedure for the synthesis of 2-arylthiochromen-4-ones (**4**), including derivatives having a substituent, such as chloro or methoxy group, at the 6-position. The method starts with 1-[2-(1,1-dimethylethylsulfanyl)phenyl]ethanones (**2**) and is based on the iodine-mediated cyclization reaction of 3-aryl-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-ones (**3**), derived from **2** and aromatic aldehydes.

In our approach to 2-arylthiochromen-4-ones (**4**), we began with the preparation of 1-[2-(1,1-

dimethylethylsulfanyl)phenyl]ethanones (**2**). The respective 1-(2-halophenyl)ethanones (**1**) were treated with sodium 2-methylpropane-2-thiolate in DMF at room temperature to afford **2** in relatively good yields as shown in Scheme 1.

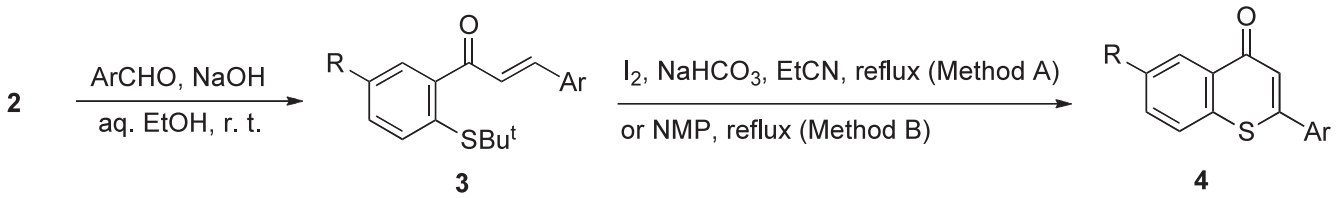


1a R = H, X = Cl
1b R = Cl, X = Cl
1c R = OMe, X = Br

2a R = H 84%
2b R = Cl 84%
2c R = OMe 70%

Scheme 1

Conversion of compounds (**2**) into 3-aryl-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-ones (**3**) was performed by reacting **2** with aromatic aldehydes in the presence of sodium hydroxide in aqueous ethanol at room temperature (Scheme 2). The yields of the products are summarized in Table 1. It indicates that the yields are good and that naphthalene-1-carbaldehyde as well as diversely substituted benzaldehydes are usable in this step.



Scheme 2

Table 1. Preparation of 2-Arylthiochromen-4-ones (**4**) *via* chalcone derivatives (**3**)

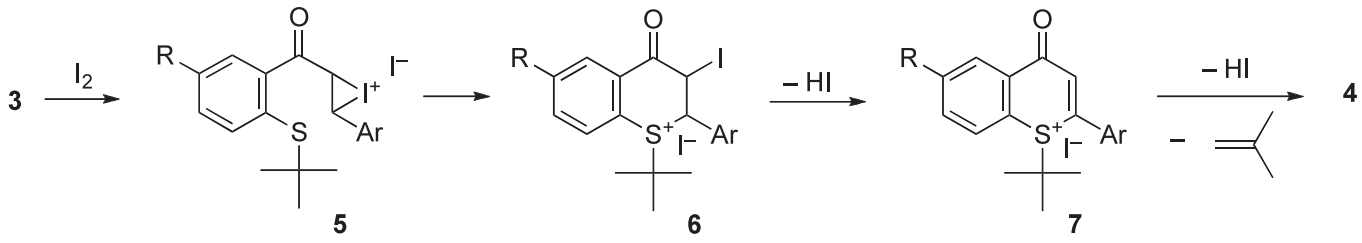
Entry	**2**	Ar in ArCHO	**3** (Yield/%)[a]	Method	**4** (Yield/%)[a]
1	**2a**	Ph	**3a** (88)	B	**4a** (68)
2	**2a**	3,4-$Cl_2C_6H_3$	**3b** (82)	A	**4b** (39)
3	**2a**	2,5-$(MeO)_2C_6H_3$	**3c** (93)	A	**4c** (45)
4	**2a**	3,4-$(OCH_2O)C_6H_3$	**3d** (87)	A	**4d** (45)
5	**2a**	naphthalen-1-yl	**3e** (88)	B	**4e** (65)
6	**2b**	4-MeC_6H_4	**3f** (74)	B	**4f** (63)
7	**2b**	3-$MeOC_6H_4$	**3g** (79)	A	**4g** (43)
8	**2b**	3,4-$(MeO)_2C_6H_3$	**3h** (80)	A	**4h** (46)
9	**2c**	4-MeC_6H_4	**3i** (62)	A	**4i** (45)

[a] Isolated yields.

3-Aryl-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-ones (**3**), thus obtained, were then subjected to cyclization on treatment with iodine to provide the desired 2-arylthiochromen-4-ones (**4**), as illustrated

in Scheme 2. First, compound (**3a**) was treated with iodine in the presence of sodium hydrogencarbonate (three molar equivalents each) in acetonitrile. However, TLC analyses showed that progress of the reaction was very reluctant even at reflux temperature. When it was conducted in refluxing propanenitrile (Method A), the reaction proceeded at an allowable rate and gave, after workup with aqueous sodium thiosulfate followed by purification using column chromatography on silica gel, a somewhat complicated mixture, from which 46% yield of the desired product (**4a**) was isolated. Other eight 3-aryl-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-ones (**3b-i**) gave similar results. Increasing the number of equivalents of iodine did not improve the yields of the products and shorten the reaction times. With less than three equivalents of iodine the reactions did not proceed significantly. Subsequently, we found that when the reaction of **3a**, **3e**, and **3f** was carried out in *N*-methylpyrrolidin-2-one (NMP) at reflux temperature (Method B), much improved yields of the corresponding products (**4a**, **4e**, and **4f**) were obtained. Unfortunately, however, the reactions of the other substrates **3**, which are carrying alkoxy or chloro substituent(s) at the 3-aryl ring or a methoxy substituent at the 1-aryl ring (*i.e.* **3b-d** and **3g-i**) in refluxing NMP gave considerably complex mixtures of the products, from which only low yields (*ca.* 10%) of the corresponding precuts (**4**) were isolated. These disappointing results are attributable to the liability of these substituents under the reaction conditions (especially higher reaction temperature). The best yield of each product is indicated in Table 1.

The probable pathway from **3** to **4** is outlined in Scheme 3. The addition of iodine to the alkene moiety of **3** generates the iodonium ion intermediate (**5**). The lone pair of sulfur atom attacks on the carbon atom adjacent to aryl substituent to give the thiochromanium ion intermediate (**6**), from which elimination of hydrogen iodide affords thiochromenium ion intermediate (**7**). Loss of the *t*-butyl moiety as 2-methylpropene and hydrogen iodide provides **4**.



Scheme 3

In conclusion, we have demonstrated that 2-arylthiochromen-4-ones can be prepared by the iodine-mediated cyclization of 3-aryl-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-ones, which are prepared by an easy two-step sequence from readily available 1-(2-halophenyl)ethanones. This method can allow preparation of derivatives carrying a substituent, such as chloro or methoxy, on the

thiochromenone benzene ring, which are hard to prepare by the previous methods.[1] The present method may also find some value in organic synthesis because of the simplicity of operations and the ready availability of the starting materials.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Shimadzu FTIR-8300 spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a Bruker Biospin AVANCE II 600 spectrometer operating at 600 MHz, a JEOL ECP500 FT NMR spectrometer operating at 500 MHz, or a JEOL LA400FT NMR spectrometer operating at 400 MHz. ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a Bruker Biospin AVANCE II 600 spectrometer operating at 150 MHz or a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. Low-resolution MS spectra (EI, 70 eV) were measured by a JEOL JMS AX505 HA spectrometer. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. 1-(2-Bromo-5-methoxyphenyl)ethanone (**1c**)[3] was prepared according to the reported method. All other chemicals used in this study were commercially available.

Typical Procedure for the Preparation of 1-[2-(1,1-Dimethylethylsulfanyl)phenyl]ethanones (2). 1-[2-(1,1-Dimethylethylsulfanyl)phenyl]ethanone (2a). To a stirred suspension of NaH (60% in mineral oil; 0.66 g, 17 mmol) in DMF (20 mL) at 0 ˚C was added *t*-BuSH (1.5 g, 17 mmol) dropwise. After evolution of H_2 gas had ceased, 1-(2-chlorophenyl)ethanone (**1a**) (2.3 g, 15 mmol) was added dropwise and the mixture was stirred for 1 h at the same temperature. Saturated aqueous NH_4Cl (30 mL) was added and the mixture was extracted with AcOEt (3 × 25 mL). The combined extracts were washed with water three times and brine once, dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on silica gel to give **2a** (2.6 g, 84%); a colorless oil; R_f 0.57 (AcOEt–hexane, 1:10). The ^{1}H NMR data of this product was identical to that reported previously.[4]

1-[5-Chloro-2-(1,1-dimethylethylsulfanyl)phenyl]ethanone (2b): a pale-yellow oil; R_f 0.43 (AcOEt–hexane 1:20); IR (neat) 1697 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.23 (s, 9H), 2.62 (s, 3H), 7.35 (dd, J = 8.0, 2.9 Hz, 1H), 7.37 (d, J = 2.9 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H). Anal. Calcd for $C_{12}H_{15}ClOS$: C, 59.37; H, 6.23. Found: C, 59.40; H, 6.50.

1-[2-(1,1-Dimethylethylsulfanyl)-5-methoxyphenyl]ethanone (2c): a colorless oil; R_f 0.60 (AcOEt–hexane 1:10); IR (neat) 1697 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.20 (s, 9H), 2.64 (s, 3H), 3.83 (s, 3H), 6.88 (d, J = 2.9 Hz, 1H), 6.92 (dd, J = 8.8, 2.9 Hz, 1H), 7.46 (d, J = 8.8 Hz, 1H). Anal. Calcd for $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61. Found: C, 65.48; H, 7.67.

Typical Procedure for the Preparation of 3-Aryl-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-ones (3). 1-[2-(1,1-Dimethylethylsulfanyl)phenyl]-3-phenylprop-2-en-1-one (3a). To a stirred solution of **2a** (0.17 g, 0.79 mmol) in EtOH–H_2O (4 mL; 1:1, v/v) containing NaOH (47 mg, 1.2 mmol) at 0 ˚C was added PhCHO (84 mg, 0.79 mmol). The mixture was then stirred for 20 h at rt before saturated aqueous NH_4Cl (10 mL) was added. The mixture was extracted with Et_2O (3 × 10 mL), and the combined extracts were washed with brine, dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on silica gel to give **3a** (0.21 g, 88%); a yellow viscous oil; R_f 0.32 ($CHCl_3$–hexane 1:1); IR (neat) 1651, 1607 cm^{-1}; ^1H NMR (500 MHz) δ 1.23 (s, 9H), 7.14 (d, *J* = 16.0 Hz, 1H), 7.34 (d, *J* = 16.0 Hz, 1H), 7.38–7.39 (m, 3H), 7.45–7.47 (m, 3H), 7.54–7.56 (m, 2H), 7.63–7.64 (m, 1H). Anal. Calcd for $C_{19}H_{20}OS$: C, 76.98; H, 6.80. Found: C, 77.14; H, 7.01.

3-(3,4-Dichlorophenyl)-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-one (3b): a pale-yellow solid; mp 79–80 ˚C (hexane–Et_2O); IR (KBr) 1667, 1604 cm^{-1}; ^1H NMR (500 MHz) δ 1.22 (s, 9H), 7.11 (d, *J* = 16.0 Hz, 1H), 7.24 (d, *J* = 16.0 Hz, 1H), 7.38 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.45–7.48 (m, 4H), 7.61–7.64 (m, 2H). Anal. Calcd for $C_{19}H_{18}Cl_2OS$: C, 62.47; H, 4.97. Found: C, 62.25; H, 5.06.

3-(2,5-Dimethoxyphenyl)-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-one (3c): a yellow viscous oil; R_f 0.54 ($CHCl_3$); IR (neat) 1659, 1645 cm^{-1}; ^1H NMR (500 MHz) δ 1.24 (s, 9H), 3.789 and 3.794 (2s, combined 6H), 6.83 (d, *J* = 8.6 Hz, 1H), 6.91 (dd, *J* = 8.6, 2.9 Hz, 1H), 7.10 (d, *J* = 2.9 Hz, 1H), 7.17 (d, *J* = 16.0 Hz, 1H), 7.42–7.45 (m, 3H), 7.62–7.64 (m, 1H), 7.67 (d, *J* = 16.0 Hz, 1H). Anal. Calcd for $C_{21}H_{24}O_3S$: C, 70.75; H, 6.79. Found: C, 70.63; H, 6.76.

3-(1,3-Benzoxol-5-yl)-1-[2-(1,1-dimethylethylsulfanyl)phenyl]prop-2-en-1-one (3d): a pale-yellow solid; mp 81–83 ˚C (hexane–Et_2O); IR (KBr) 1636, 1603 cm^{-1}; ^1H NMR (500 MHz) δ 1.23 (s, 9H), 6.00 (s, 2H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 16.1 Hz, 1H), 7.00 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.07 (d, *J* = 1.8 Hz, 1H), 7.24 (d, *J* = 16.1 Hz, 1H), 7.41–7.46 (m, 3H), 7.60–7.63 (m, 1H). Anal. Calcd for $C_{20}H_{20}O_3S$: C, 70.56; H, 5.92. Found: C, 70.30; H, 6.07.

1-[2-(1,1-Dimethylethylsulfanyl)phenyl]-3-(naphthalen-1-yl)prop-2-en-1-one (3e): a yellow viscous oil; R_f 0.51 ($CHCl_3$); IR (neat) 1659 cm^{-1}; ^1H NMR (400 MHz) δ 1.25 (s, 9H), 7.24 (d, *J* = 16.1 Hz, 1H),7.45–7.56 (m, 6H), 7.67 (dd, *J* = 8.8, 1.5 Hz, 1H), 7.83–7.90 (m, 3H), 8.10 (d, *J* = 8.3 Hz, 1H), 8.22 (d, *J* = 16.1 Hz, 1H). Anal. Calcd for $C_{23}H_{22}OS$: C, 79.73; H, 6.40. Found: C, 79.62; H, 6.42.

1-[5-Chloro-2-(1,1-dimethylethylsulfanyl)phenyl]-3-(4-methylphenyl)prop-2-en-1-one (3f): a white solid; mp 85–86 ˚C (hexane–Et_2O); IR (KBr) 1638, 1607 cm^{-1}; ^1H NMR (400 MHz) δ 1.23 (s, 9H), 2.38 (s, 3H), 7.04 (d, *J* = 16.1 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 16.1 Hz, 1H), 7.38–7.45 (m, 4H), 7.55 (dd, *J* = 7.4, 0.9 Hz, 1H). Anal. Calcd for $C_{20}H_{21}ClOS$: C, 69.65; H, 6.14. Found: C, 69.60; H, 6.18.

1-[5-Chloro-2-(1,1-dimethylethylsulfanyl)phenyl]-3-(3-methoxyphenyl)prop-2-en-1-one (3g): a white solid; mp 58–60 ˚C (hexane–Et_2O); IR (KBr) 1655, 1620, 1601 cm^{-1}; ^1H NMR (400 MHz) δ 1.23 (s, 9H),

3.83 (s, 3H), 6.95 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.06 (dd, *J* = 2.0, 1.5 Hz, 1H), 7.07 (d, *J* = 16.1 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 16.1 Hz, 1H), 7.30 (dd, *J* = 8.3, 7.8 Hz, 1H), 7.40–7.46 (m, 2H), 7.55 (dd, *J* = 7.8, 1.5 Hz, 1H). Anal. Calcd for $C_{20}H_{21}ClO_2S$: C, 66.56; H, 5.87. Found: C, 66.43; H, 6.02.

1-[5-Chloro-2-(1,1-dimethylethylsulfanyl)phenyl]-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (3h): colorless needles; mp 132–133 ˚C (hexane–Et_2O); IR (KBr) 1636, 1616 cm^{-1}; ^1H NMR (400 MHz) δ 1.24 (s, 9H), 3.915 and 3.920 (2s, combined 6H), 6.87 (d, *J* = 8.3 Hz, 1H), 6.95 (d, *J* = 16.1 Hz, 1H), 7.07 (d, *J* = 1.5 Hz, 1H), 7.12 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.22 (s, 1H), 7.39–7.42 (m, 2H), 7.56 (d, *J* = 9.2 Hz, 1H). Anal. Calcd for $C_{21}H_{23}ClO_3S$: C, 64.52; H, 5.93. Found: C, 64.46; H, 5.97.

1-[2-(1,1-Dimethylethylsulfanyl)-5-methoxyphenyl]-3-(4-methylphenyl)prop-2-en-1-one (3i): a yellow solid; mp 80–81 ˚C (hexane–Et_2O); IR (KBr) 1634, 1607 cm^{-1}; ^1H NMR (400 MHz) δ 1.19 (s, 9H), 2.37 (s, 3H), 3.85 (s, 3H), 6.96–6.99 (m, 2H), 7.08 (d, *J* = 16.1 Hz, 1H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 16.1 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.51 (dd, *J* = 8.8, 2.0 Hz, 1H). Anal. Calcd for $C_{21}H_{24}O_2S$: C, 74.08; H, 7.10. Found: C, 74.03; H, 7.24.

General Procedure for the Preparation of 2-Arylthiochromen-4-ones (4). A stirred solution of **3** (0.5 mmol) in EtCN (Method A) or NMP (Method B) (4 mL) containing I_2 (0.19 g, 1.5 mmol) and $NaHCO_3$ (0.13 g, 1.5 mmol) was heated at reflux temperature until an almost complete consumption of the starting material (ca. 4 h) had been confirmed by TLC analyses. To the cooled reaction mixture was added 10% aqueous $Na_2S_2O_3$ under stirring until the color of I_2 had appeared. The mixture was extracted with AcOEt (3 × 10 mL), and the combined extracts were washed with saturated aqueous $NaHCO_3$ twice, water twice, and brine once. After drying (Na_2SO_4), the solvent was removed by evaporation to give a residue, purification of which by column chromatography on silica gel ($CHCl_3$–hexane 1:1) afforded **4**.

2-Phenylthiochromen-4-one (4a): a beige solid; mp 120–122 ˚C (lit.,[5] 122–123 ˚C). The spectral (IR and ^1H NMR) data of this product was identical to those reported previously.[5]

2-(3,4-Dichlorophenyl)thiochromen-4-one (4b): a white solid; mp 198–200 ˚C (hexane–CH_2Cl_2); IR (KBr) 1634 cm^{-1}; ^1H NMR (600 MHz) δ 7.19 (s, 1H), 7.53 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.56–7.60 (m, 2H), 7.64–7.67 (m, 2H), 7.79 (d, *J* = 2.2 Hz, 1H), 8.54 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (150 MHz) δ 123.99, 126.06, 126.52, 128.12, 128.72, 128.83, 130.82, 131.30, 131.92, 133.79, 135.27, 136.40, 137.08, 150.11, 180.58; MS *m/z* 306 (M^+, 100). Anal. Calcd for $C_{15}H_8Cl_2OS$: C, 58.65; H, 2.62. Found: C, 58.49; H, 2.67.

2-(2,5-Dimethoxyphenyl)thiochromen-4-one (4c): a beige solid; mp 115–117 ˚C (hexane–Et_2O); IR (KBr) 1626 cm^{-1}; ^1H NMR (500 MHz) δ 3.811 and 3.814 (2s, combined 6H), 6.95 (d, *J* = 8.6 Hz, 1H), 6.97–7.00 (m, 2H), 7.16 (s, 1H), 7.53 (ddd, *J* = 8.6, 7.4, 1.7 Hz, 1H), 7.59–7.63 (m, 2H), 8.55 (d, *J* = 8.6, 1.1 Hz, 1H); ^{13}C NMR (125 MHz) δ 55.87, 56.44, 113.24, 115.64, 116.60, 126.08, 126.22, 126.72, 127.48, 128.52, 130.89, 131.35, 138.68, 150.10, 150.64, 153.66, 180.76; MS *m/z* 298 (M^+, 100). Anal. Calcd for $C_{17}H_{14}O_3S$: C, 68.44; H, 4.73. Found: C, 68.45; H, 4.80.

2-(1,3-Benzoxol-5-yl)thiochromen-4-one (4d): a beige solid; mp 180–182 ˚C (hexane–CH_2Cl_2); IR (KBr) 1622 cm^{-1}; ^1H NMR (500 MHz) δ 6.06 (s, 2H), 6.91 (d, *J* = 8.0 Hz, 1H), 7.155 (s, 1H), 7.157 (d, *J* = 1.8 Hz, 1H), 7.23 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.53 (ddd, *J* = 8.1, 7.4, 1.8 Hz, 1H), 7.57–7.65 (m, 2H), 8.52 (d, *J* = 8.1, 1.8 Hz, 1H); ^{13}C NMR (125 MHz) δ 101.87, 107.16, 108.90, 121.51, 122.66, 126.36, 127.71, 128.55, 130.58, 130.89, 131.55, 137.53, 148.60, 150.00, 152.62, 180.85; MS *m/z* 282 (M^+, 100). Anal. Calcd for $C_{16}H_{10}O_3S$: C, 68.07; H, 3.57. Found: C, 67.99; H, 3.49.

2-(Naphthalen-1-yl)thiochromen-4-one (4e): a beige solid; mp 144–145 ˚C (hexane–Et_2O); IR (KBr) 1624 cm^{-1}; ^1H NMR (600 MHz) δ 7.15 (s, 1H), 7.51–7.56 (m, 3H), 7.58–7.61 (m, 2H), 7.63–7.67 (m, 2H), 7.92 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 8.07 (d, *J* = 8.3 Hz, 1H), 8.63 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (150 MHz) δ 124.93, 125.01, 126.23, 126.60, 127.16, 127.22, 127.38, 127.85, 128.50, 128.76, 130.43, 130.53, 131.13, 131.63, 133.72, 134.08, 138.60, 152.27, 180.38; MS *m/z* 288 (M^+, 100). Anal. Calcd for $C_{19}H_{12}OS$: C, 79.14; H, 4.19. Found: C, 79.08; H, 4.15.

6-Chloro-2-(4-methylphenyl)thiochromen-4-one (4f): a beige solid; mp 165–167 ˚C (hexane–Et_2O); IR (KBr) 1618, 1609 cm^{-1}; ^1H NMR (500 MHz) δ 2.43 (s, 3H), 7.23 (s, 1H), 7.31 (d, *J* = 7.4 Hz, 2H), 7.57–7.62 (m, 4H), 8.52 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR (125 MHz) δ 21.35, 122.59, 126.75, 127.87, 128.16, 130.02, 131.88, 132.07, 133.36, 134.21, 135.79, 141.60, 153.28, 179.66; MS *m/z* 286 (M^+, 100). Anal. Calcd for $C_{16}H_{11}ClOS$: C, 67.01; H, 3.87. Found: C, 66.85; H, 4.04.

6-Chloro-2-(3-methoxyphenyl)thiochromen-4-one (4g): a beige solid; mp 150–151 ˚C (hexane–Et_2O); IR (KBr) 1620 cm^{-1}; ^1H NMR (500 MHz) δ 3.88 (s, 3H), 7.06 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.18 (t, *J* = 1.7 Hz, 1H), 7.24 (s, 1H), 7.26 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.57–7.61 (m, 2H), 8.52 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR (125 MHz) δ 55.47, 112.33, 116.74, 119.27, 123.25, 127.91, 128.20, 130.41, 131.99, 132.10, 134.33, 135.79, 137.56, 153.12, 160.18, 179.64; MS *m/z* (%) 302 (M^+, 100). Anal. Calcd for $C_{16}H_{11}ClO_2S$: C, 63.47; H, 3.66. Found: C, 63.45; H, 3.89.

6-Chloro-2-(3,4-dimethoxyphenyl)thiochromen-4-one (4h): a beige solid; mp 170–172 ˚C (hexane–CH_2Cl_2); IR (KBr) 1634 cm^{-1}; ^1H NMR (600 MHz) δ 3.96 (s, 3H), 3.97 (s, 3H), 6.97 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 1.8 Hz, 1H), 7.22 (s, 1H), 7.31 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.57–7.61 (m, 2H), 8.51 (d, *J* = 1.3 Hz, 1H); ^{13}C NMR (150 MHz) δ 56.11, 56.13, 109.65, 111.47, 120.05, 122.12, 127.81, 128.21, 128.80, 131.92, 132.14, 134.27, 135.72, 149.63, 151.70, 153.06, 179.68; MS *m/z* 332 (M^+, 100). Anal. Calcd for $C_{17}H_{13}ClO_3S$: C, 61.35; H. 3.94. Found: C, 61.17; H, 3.89.

6-Methoxy-2-(4-methylphenyl)thiochromen-4-one (4i): a pale-yellow solid; mp 156–157 ˚C (hexane–Et_2O); IR (KBr) 1613 cm^{-1}; ^1H NMR (500 MHz) δ 2.42 (s, 3H), 3.95 (s, 3H), 7.24 (s, 1H), 7.25 (dd, *J* = 8.6, 2.9 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.99 (d, *J* = 2.9 Hz, 1H); ^{13}C NMR (125 MHz) δ 21.33, 55.73, 108.84, 122.00, 122.08, 126.78, 127.74, 129.74,

129.94, 132.33, 133.80, 141.19, 153.10, 159.54, 180.55; MS *m/z* 282 (M^+, 100). Anal. Calcd for $C_{17}H_{14}O_2S$: C, 72.31; H. 5.00. Found: C, 72.16; H, 5.08.

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