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A FACILE SYNTHESIS OF 2-ARYLTHIOCHROMAN-4-ONES BY THE REACTION OF 3-ARYL-1-(2-HALOPHENYL)PROP-2-EN-1-ONES WITH SODIUM HYDROGENSULFIDE

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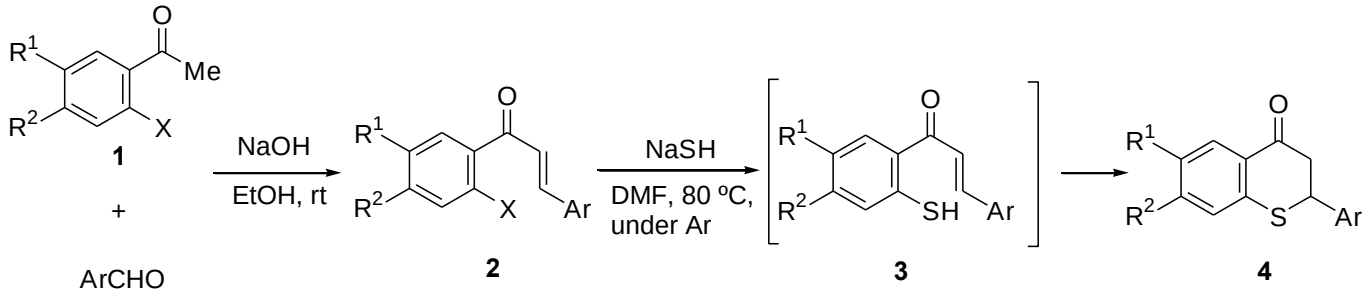
Abstract – An efficient two-step procedure for the preparation of 2-arylthiochroman-4-ones has been developed. Thus, 3-aryl-1-(2-halophenyl)prop-2-en-1-ones, prepared by the condensation between 1-(2-halophenyl)ethanones and aromatic aldehydes in ethanol at room temperature, were treated with sodium hydrogensulfide in DMF at 80 ˚C to give 2-arylthiochroman-4-ones in good overall yields.

The synthesis of thiochroman-4-ones, especially 2-aryl derivatives (thioflavanones), has recently attracted much attention, because a number of compounds having this skeleton have been reported to exhibit a variety of biological activities.[1] Therefore, several efficient methods for the preparation of this class of heterocycles have been developed.[2] For example, Lee has recently reported a synthesis of 2-arylthiochroman-4-ones based on the reaction of 1-(2-sulfanylphenyl)ethanone with aromatic aldehydes.[2b] However, this method cannot allow the preparation of derivatives carrying any substituents on the benzene ring of the thiochroman-4-one structure. Herein, we wish to report a new and facile method for the synthesis of 2-aryl- or 2-heteroaryl-thiochroman-4-ones (**4**), which can allow the preparation of derivatives carrying substituent(s) at the 6- and/or 7-positions of the thiochroman-4-one structure. We have found that the synthesis of these thiochroman-4-ones can be achieved by treatment of 3-aryl- or 3-hetraryl-1-(2-halophenyl)prop-2-en-1-ones (**2**), easily prepared by the condensation of 1-(2-halophenyl)ethanones (**1**) with aromatic or heteroaromatic aldehydes, with sodium hydrogensulfide.

Our preparation of 2-aryl- or 2-heteroaryl-thiochroman-4-ones (**4**) was conducted as illustrated in Scheme 1. 3-Aryl-1-(2-halophenyl)prop-2-en-1-ones (**2a–d**) and (**2h–l**) were readily prepared from commercially or easily available 1-(2-halophenyl)ethanones (**1**) by reacting with aromatic aldehydes using sodium hydroxide as a base in ethanol under the reported conditions[3] in excellent yields as summarized in Table 1 (Entries 1-4 and 8-12). Similar reactions of **1** with heteroaromatic aldehydes, such as thiophene-2-

carboxaldehyde, thiophene-3-carboxaldehyde, 1-methylindole-2-carboxaldehyde, and 1-methylpyrrole-2-carboxaldehyde, in place of aromatic aldehydes gave also excellent yields of the corresponding 1-(2-halophenyl)-3-heterarylprop-2-en-1-ones (**2e-g**) and (**2m**) as summarized in Table 1 (Entries 5-7 and 13) as well.



Scheme 1

Table 1. Preparation of 3-aryl- or 3-heteroaryl-thiochroman-4-ones (**4**)

Entry	**1**	Ar in ArCHO	**2**	Yield/%[a]	**4**	Yield/%[a]
1	**1a** (R^1 = R^2 = H, X = Br)	Ph	**2a**	95	**4a**	71
2	**1a**	3-ClC_6H_4	**2b**	99	**4b**	76
3	**1a**	3-$MeOC_6H_4$	**2c**	94	**4c**	70
4	**1b** (R^1 = X = Cl, R^2 = H)	Ph	**2d**	90	**4d**	77
5	**1b**	thiophen-2-yl	**2e**	95	**4e**	80
6	**1b**	thiophen-3-yl	**2f**	95	**4f**	83
7	**1b**	1-methylindol-2-yl	**2g**	91	**4g**	79
8	**1c** (R^1 = OMe, R^2 = H, X = Br)	Ph	**2h**	91	**4h**	66
9	**1c**	4-MeC_6H_4	**2i**	98	**4i**	74
10	**1c**	naphthalen-1-yl	**2j**	95	**4j**	75
11	**1d** (R^1 = R^2 = OMe, X = Br)	Ph	**2k**	96	**4k**	84
12	**1d**	3,4-$(OCH_2O)C_6H_3$	**2l**	91	**4l**	89
13	**1d**	1-methylpyrrol-2-yl	**2m**	99	**4m**	87

[a] Yields of isolated products.

These chalcone derivatives (**2a–d**) and (**2h–l**) were then subjected to treatment with sodium hydrogensulfide. Thus, argon gas was bubbled through solutions of these precursors and sodium hydrogensulfide in DMF in order to remove oxygen, which may oxidize intermediate 3-aryl-1-(2-sulfanylphenyl)propenones (**3**) to the corresponding disulfides. These solutions were then heated at 80 ˚C. Substitution of the 2-halogen of **2** with a sulfanyl group giving **3** followed by intramolecular conjugate addition of the resulting 2-sulfanyl group to the enone moiety of **3** proceeded smoothly and completed within 10 min. After usual aqueous workup and subsequent purification by column chromatography on silica gel or recrystallization, the desired 2-arylthiochroman-4-ones (**4a–d**) and (**4h–l**) were obtained in good yields as summarized in Table 1 (Entries 1-4 and 8-12). Although we have no firm evidences, this order of the reaction sequence seems to be preferable to the reverse one.

Treatment of heteroaryl chalcone analogues (**2e-g**) and (**2m**) with sodium hydrogensulfide in DMF was conducted in a similar manner as described for the preparation of 2-arylthiochroman-4-ones (**4a–d**) and (**4h–l**) to give also the corresponding 2-heteroarylthiochroman-4-ones (**4e-g**) and (**4m**) in yields comparable to those of (**4a–d**) and (**4h–l**) as summarized in Table 1 as well (Entries 5-7 and 13).

The results described in this paper demonstrate that 2-arylthiochroman-4-ones (thioflavanones) can be produced from readily available 1-(2-halophenyl)ethanones and aromatic aldehydes *via* an easy two-step sequence. This procedure has proved to be applicable to the synthesis of 2-heteroarylthiochroman-4-ones using heteroaromatic aldehydes in place of aromatic aldehydes. We believe that the present procedure is advantageous over the previous methods[2] especially in the ease of operations, the readily availability of the starting materials, and the wide scope.

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. The ^{1}H NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz. The ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with 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 a 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**)[4] and 1-(2-bromo-4,5-dimethoxyphenyl)ethanone (**1d**)[5] were prepared by the appropriate reported procedures. All other chemicals used in this study were commercially available.

(*E*)-3-Aryl-1-(2-halophenyl)prop-2-en-1-ones (2). These compounds were prepared from 1-(2-halophenyl)ethanones **1** and aromatic or heteroaromatic aldehydes under the reported conditions.[3] Physical, spectral, and analytical data for new compounds follow.

(*E*)-1-(2-Bromophenyl)-3-(3-chlorophenyl)prop-2-en-1-one (2b): a white solid; mp 95–98 ˚C (hexane); IR (KBr) 1670, 1607 cm^{-1}; ^{1}H NMR δ 7.10 (d, J = 16.0 Hz, 1H), 7.33–7.45 (m, 7H), 7.54 (s, 1H), 7.66 (d, J = 8.2 Hz, 1H). Anal. Calcd for $C_{15}H_{10}BrClO$: C, 56.02; H, 3.13. Found: C, 55.74; H 3.16.

(*E*)-1-(2-Bromophenyl)-3-(3-methoxyphenyl)prop-2-en-1-one (2c): a yellow oil; R_f 0.34 (AcOEt–hexane 1:10); IR (neat) 1651, 1603 cm^{-1}; ^{1}H NMR δ 3.83 (s, 3H), 6.97 (dd, J = 8.2, 2.3 Hz, 1H), 7.08 (d, J = 16.4 Hz, 1H), 7.07 (dd, J = 2.3, 1.8 Hz, 1H), 7.15 (d, J = 7.3 Hz, 1H), 7.30–7.44 (m, 5H), 7.65 (d, J = 7.8 Hz, 1H). Anal. Calcd for $C_{16}H_{13}BrO_2$: C, 60.59; H, 4.13. Found: C, 60.56; H, 4.38.

(*E*)-1-(2,5-Dichlorophenyl)-3-phenylprop-2-en-1-one (2d): a white solid; mp 61–63 ˚C (hexane–Et_2O). IR (KBr) 1668, 1607 cm^{-1}; ^{1}H NMR δ 7.10 (d, J = 16.5 Hz, 1H), 7.40–7.49 (m, 7H), 7.57–7.59 (m, 2H).

Anal. Calcd for $C_{15}H_{10}Cl_2O$: C, 65.01; H 3.64. Found: C, 65.01; H, 3.55.

(*E*)-1-(2,5-Dichlorophenyl)-3-(thiophen-2-yl)prop-2-en-1-one (2e): a yellow solid; mp 64–66 ˚C (hexane–Et_2O); IR (KBr) 1659 cm^{-1}; ^1H NMR δ 6.89 (d, *J* = 16.0 Hz, 1H), 7.10 (dd, *J* = 5.0, 4.1 Hz, 1H), 7.34 (d, *J* = 4.1, 1H); 7.39 (s, 2H), 7.44 (t, *J* = 0.9 Hz, 1H), 7.48 (d, *J* = 5.0 Hz, 1H), 7.60 (d, *J* = 16.0 Hz, 1H). Anal. Calcd for $C_{13}H_8Cl_2OS$: C, 55.14; H, 2.85. Found: C, 55.34; H, 2.66.

(*E*)-1-(2,5-Dichlorophenyl)-3-(thiophen-3-yl)prop-2-en-1-one (2f): a white solid; mp 50–52 ˚C (hexane–Et_2O); IR (KBr) 1663 cm^{-1}; ^1H NMR δ 6.90 (d, *J* = 16.0 Hz, 1H), 7.35–7.39 (m, 4H), 7.42 (s, 1H), 7.44 (d, *J* = 16.0 Hz, 1H), 7.59 (t, *J* = 0.9 Hz, 1H). Anal. Calcd for $C_{13}H_8Cl_2OS$: C, 55.14; H, 2.85. Found: C, 55.09; H, 2.91.

(*E*)-1-(2,5-Dichlorophenyl)-3-(1-methylindol-2-yl)prop-2-en-1-one (2g): a yellow solid; mp 107–108 ˚C (hexane–Et_2O); IR (KBr) 1663 cm^{-1}; ^1H NMR δ 3.84 (s, 3H), 7.11 (s, 1H), 7.13 (ddd, *J* = 7.8, 7.3, 1.4, Hz, 1H), 7.19 (d, *J* = 16.0 Hz, 1H), 7.30 (ddd, *J* = 8.2, 7.3, 0.9 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.40–7.41 (m, 2H), 7.53 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.73 (d, *J* = 16.0 Hz, 1H). Anal. Calcd for $C_{18}H_{13}Cl_2NO$: C, 65.47; H, 3.97; N, 4.24. Found: C, 65.27; H, 3.25; N, 4.26.

(*E*)-1-(2-Bromo-5-methoxyphenyl)-3-phenylprop-2-en-1-one (2h): a white solid; mp 112–114 ˚C (hexane–CH_2Cl_2); IR (KBr) 1651, 1620 cm^{-1}; ^1H NMR δ 3.82 (s, 3H), 6.89 (dd, *J* = 8.7, 3.2 Hz, 1H), 6.95 (d, *J* = 3.2 Hz, 1H), 7.09 (d, *J* = 16.0 Hz, 1H), 7.39–7.47 (m, 4H), 7.52 (d, *J* = 8.7 Hz, 1H), 7.56–7.58 (m, 2H). Anal. Calcd for $C_{16}H_{13}BrO_2$: C, 60.59; H, 4.13. Found: C, 60.40; H, 4.14.

(*E*)-1-(2-Bromo-5-methoxyphenyl)-3-(4-methylphenyl)prop-2-en-1-one (2i): a white solid; mp 74–76 ˚C (hexane–Et_2O); IR (KBr) 1641, 1605 cm^{-1}; ^1H NMR δ 2.39 (s, 3H), 3.82 (s, 3H), 6.89 (dd, *J* = 9.2, 3.2 Hz, 1H), 6.94 (d, *J* = 3.2 Hz, 1H), 7.04 (d, *J* = 16.0 Hz, 1H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 16.0 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 2H), 7.51 (d, *J* = 9.2 Hz, 1H). Anal. Calcd for $C_{17}H_{15}BrO_2$: C, 61.65; H, 4.56. Found: C, 61.58; H, 4.72.

(*E*)-1-(2-Bromo-5-methoxyphenyl)-3-(naphthalen-1-yl)prop-2-en-1-one (2j): a pale-yellow solid; mp 90–92 ˚C (hexane–Et_2O); IR (KBr) 1647, 1609 cm^{-1}; ^1H NMR δ 3.85 (s, 3H), 6.93 (dd, *J* = 9.2, 3.2 Hz, 1H), 7.04 (d, *J* = 3.2 Hz, 1H), 7.20 (d, *J* = 15.6 Hz, 1H), 7.51–7.59 (m, 4H), 7.87 (dd, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 8.35 (d, *J* = 15.6 Hz, 1H). Anal. Calcd for $C_{20}H_{15}BrO_2$: C, 65.41; H, 4.12. Found: C, 65.40; H, 4.07.

(*E*)-1-(2-Bromo-4,5-dimethoxyphenyl)-3-phenylprop-2-en-1-one (2k): a pale-yellow solid; mp 153–155 ˚C (hexane–Et_2O); IR (KBr) 1638, 1624 cm^{-1}; ^1H NMR δ 3.90 (s, 3H), 3.94 (s, 3H), 7.04 (s, 1H), 7.08 (s, 1H), 7.22 (d, *J* = 16.0 Hz, 1H), 7.40–7.43 (m, 3H), 7.55 (d, *J* = 16.0 Hz, 1H), 7.58–7.61 (m, 2H). Anal. Calcd for $C_{17}H_{15}BrO_3$: C, 58.81; H, 4.35. Found: C, 58.80; H, 4.42.

(*E*)-3-(1,3-Benzodioxol-5yl)-1-(2-bromo-4,5-dimethoxyphenyl)prop-2-en-1-one (2l): a pale-yellow solid; mp 186–188 ˚C (hexane–CH_2Cl_2); IR (KBr) 1640 cm^{-1}; ^1H NMR δ 3.90 (s, 3H), 3.94 (s, 3H), 6.03 (s, 2H), 6.84 (d, *J* = 8.2 Hz, 1H), 7.02–7.07 (m, 4H), 7.11 (d, *J* = 0.9 Hz, 1H), 7.46 (d, *J* = 16.0 Hz, 1H).

Anal. Calcd for $C_{18}H_{15}BrO_5$: C, 55.26; H, 3.86. Found: C, 55.25; H, 3.86.

(*E*)-1-(2-Bromo-4,5-dimethoxyphenyl)-3-(1-methylpyrrol-2-yl)prop-2-en-1-one (2m): a yellow solid; mp 112–114 ˚C (hexane–Et_2O); IR (KBr) 1649 cm^{-1}; ^1H NMR δ 3.74 (s, 3H), 3.90 (s, 3H), 3.93 (s, 3H), 6.22 (dd, *J* = 4.1, 2.3 Hz, 1H), 6.79 (dd, *J* = 4.1, 1.4 Hz, 1H), 6.83 (dd, *J* = 2.3, 1.4 Hz, 1H), 6.95 (d, *J* = 15.1 Hz, 1H), 7.03 (s, 1H), 7.06 (s, 1H), 7.56 (d, *J* = 15.1 Hz, 1H). Anal. Calcd for $C_{16}H_{16}BrNO_3$: C, 54.87; H, 4.61; N, 4.00, Found: C, 54.85; H, 4.82; N, 4.00.

Typical Procedure for the Preparation of 2-Aryl- or 2-Heteroaryl-thiochromanones (4). 2-Phenylthiochroman-4-one (4a). A mixture of **2a** (0.19 g, 0.65 mmol) and NaSH (70%; 52 mg, 0.65 mmol) in DMF (5 mL) was bubbled with Ar gas and was heated at 80 ˚C for 10 min. After cooling, sat. aq. NH_4Cl (20 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL). The combined extracts were washed with water (2 × 10 mL) and then brine (10 mL), and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was purified by column chromatography on silica gel (AcOEt–hexane 1:15) to give **4a** (0.11 g, 71%) as a yellow solid; mp 57–59 ˚C (hexane) (lit.,[2b] mp 56–57 ˚C). The spectral data (IR, ^1H NMR) of this product were identical to those reported previously.[2b]

2-(3-Chlorophenyl)thiochroman-4-one (4b): a yellow solid; mp 43–45 ˚C (pentane); IR (KBr) 1682 cm^{-1}; ^1H NMR δ 3.19 (dd, *J* = 16.0, 3.2 Hz, 1H), 3.28 (dd, *J* = 16.0, 12.8 Hz, 1H), 4.68 (dd, *J* = 12.8, 3.2 Hz, 1H), 7.21–7.33 (m, 5H), 7.41–7.44 (m, 2H), 8.15 (dd, *J* = 8.2, 1.4 Hz, 1H); ^{13}C NMR δ 44.88, 46.40, 125.42, 125.58, 127.21, 127.70, 128.67, 129.24, 130.25, 130.31, 133.75, 134.79, 140.37, 141.47, 193.77; MS *m/z* 274 (M^+, 100). Anal. Calcd for $C_{15}H_{11}ClOS$: C, 65.57; H, 4.04. Found: C, 65.48; H, 4.14.

2-(3-Methoxyphenyl)thiochroman-4-one (4c): a yellow solid; mp 45–47 ˚C (pentane); IR (KBr) 1678 cm^{-1}; ^1H NMR δ 3.20 (dd, *J* = 16.5, 3.2 Hz, 1H), 3.30 (dd, *J* = 16.5, 12.8 Hz, 1H), 3.82 (s, 3H), 4.69 (dd, *J* = 12.8, 3.2 Hz, 1H), 6.88 (dd, *J* = 8.2, 2.7 Hz, 1H), 6.97 (dd, *J* = 2.3, 1.8 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 7.21 (dd, *J* = 7.8, 7.3 Hz, 1H), 7.28–7.31 (m, 2H), 7.41 (ddd, *J* = 7.8, 7.3, 1.4 Hz, 1H), 8.14 (dd, *J* = 7.8, 1.4 Hz, 1H); ^{13}C NMR δ 45.47, 46.71, 55.27, 113.22, 113.78, 119.61, 125.21, 127.21, 129.19, 130.03, 130.37, 133.63, 139.91, 142.03, 159.91, 194.33; MS *m/z* 270 (M^+, 100). Anal. Calcd for $C_{16}H_{14}O_2S$: C, 71.08; H, 5.22. Found: C, 68.87; H, 5.45.

6-Chloro-2-phenylthiochroman-4-one (4d): colorless needles; mp 80–83 ˚C (hexane–Et_2O); IR (KBr) 1682 cm^{-1}; ^1H NMR δ 3.22 (dd, *J* = 16.5, 3.2 Hz, 1H), 3.31 (dd, *J* = 16.5, 12.8 Hz, 1H), 4.71 (dd, *J* = 12.8, 3.2 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 1H), 7.34–7.43 (m, 6H), 8.12 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR δ 45.46, 46.25, 127.37 (2C), 128.62, 128.80, 129.04, 131.41, 131.44, 133.59, 137.97, 140.37, 193.21; MS *m/z* 274 (M^+, 100). Anal. Calcd for $C_{15}H_{11}ClOS$: C, 65.57; H 4.04. Found: C, 65.41; H, 4.01.

6-Chloro-2-(thiophen-2-yl)thiochroman-4-one (4e): a beige viscous oil; R_f 0.50 (THF–hexane 1:5); IR (KBr) 1682 cm^{-1}; ^1H NMR δ 3.33 (dd, *J* = 17.0, 10.5 Hz, 1H), 3.37 (dd, *J* = 17.0, 4.1 Hz, 1H), 4.96 (ddd, *J* = 10.5, 4.1, 0.9 Hz, 1H), 6.97 (dd, *J* = 5.1, 3.7 Hz, 1H), 7.06 (dt, *J* = 2.8, 1.3 Hz, 1H), 7.23 (*d*, *J* = 8.2 Hz, 1H), 7.27 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.39 (dd, *J* = 8.2, 2.3 Hz, 1H), 8.10 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR

δ 40.58, 47.03, 125.65, 125.99, 127.00, 128.72, 128.74, 131.38, 131.64, 133.67, 139.30, 141.59, 192.32; MS *m/z* 280 (M^+, 100). Anal. Calcd for $C_{13}H_9ClOS_2$: C, 55.61; H, 3.23. Found: C, 55.56; H, 3.38.

6-Chloro-2-(thiophen-3-yl)thiochroman-4-one (4f): a pale-yellow viscous oil; R_f 0.29 ($CHCl_3$–hexane 1:2); IR (KBr) 1682 cm^{-1}; ^1H NMR δ 3.28 (dd, *J* = 16.5, 6.9 Hz, 1H), 3.29 (dd, *J* = 16.5, 8.2 Hz, 1H), 4.79 (dd, *J* = 8.2, 6.9 Hz, 1H), 7.14 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.25–7.26 (m, 2H), 7.34–7.38 (m, 2H), 8.10 (d, *J* = 2.7 Hz, 1H); ^{13}C NMR δ 40.59, 46.11, 122.81, 126.52, 126.87, 128.76 (2C), 131.47, 131.51, 133.61, 138.87, 139.75, 192.94; MS *m/z* 280 (M^+, 100). Anal. Calcd for $C_{13}H_9ClOS_2$: C, 55.61; H, 3.23. Found: C, 55.38; H, 3.18.

6-Chloro-2-(1-methylindol-2-yl)thiochroman-4-one (4g): a white solid; mp 177–180 ˚C (hexane–CH_2Cl_2); IR (KBr) 1682 cm^{-1}; ^1H NMR δ 3.41 (dd, *J* = 16.9, 3.7 Hz, 1H), 3.49 (dd, *J* = 16.9, 10.0 Hz, 1H), 3.81 (s, 3H), 4.84 (dd, *J* = 10.0, 3.7 Hz, 1H), 6.47 (s, 1H), 7.11 (ddd, *J* = 8.2, 7.8, 0.9 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 7.24 (t, *J* = 8.2, 7.8 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 1H), 7.37 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.57 (d, *J* = 8.7 Hz, 1H), 8.17 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR δ 29.87, 37.43, 44.45, 101.32, 109.16, 120.02, 120.85, 122.49, 126.95, 128.81, 129.03, 131.60, 131.86, 133.71, 135.76, 137.83, 138.44, 192.79; MS *m/z* 327 (M^+, 100). Anal. Calcd for $C_{18}H_{14}ClNOS$: C, 65.95; H, 4.30; N, 4.27. Found: C, 65.94; H, 4.30; N, 4.29.

6-Methoxy-2-phenylthiochroman-4-one (4h): an orange solid; mp 111–113 ˚C (hexane–Et_2O); IR (KBr) 1682 cm^{-1}; ^1H NMR δ 3.21 (dd, *J* = 16.5, 3.2 Hz, 1H), 3.31 (dd, *J* = 16.5, 12.8 Hz, 1H), 3.84 (*s*, 3H), 4.69 (dd, *J* = 12.8, 3.2 Hz, 1H), 7.05 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 1H), 7.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 7.38 (dd, *J* = 7.8, 7.3 Hz, 2H), 7.43 (dd, *J* = 7.8, 1.4 Hz, 2H), 7.66 (d, *J* = 2.7 Hz, 1H); ^{13}C NMR δ 45.72, 46.73, 55.58, 111.30, 122.62, 127.38, 128.39, 128.52, 128.93, 131.20, 133.49, 138.52, 157.57, 194.38; MS *m/z* 270 (M^+, 100). Anal. Calcd for $C_{16}H_{14}O_2S$: C, 71.08; H 5.22. Found: C, 71.01; H, 5.31.

6-Methoxy-2-(4-methylphenyl)thiochroman-4-one (4i): pale-yellow needles; mp 104–106 ˚C (hexane–Et_2O); IR (KBr) 1676 cm^{-1}; ^1H NMR δ 2.36 (s, 3H), 3.18 (dd, *J* = 16.5, 2.7 Hz, 1H), 3.29 (dd, *J* = 16.5, 13.3 Hz, 1H), 3.84 (s, 3H), 4.65 (dd, *J* = 13.3, 2.7 Hz, 1H), 7.04 (dd, *J* = 8.7, 3.2 Hz, 1H), 7.17–7.20 (m, 3H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.65 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR δ 21.13, 45.44, 46.78, 55.56, 111.23, 122.59, 127.23, 128.50, 129.57 (2C), 131.17, 135.50, 138.24, 157.50, 194.56; MS *m/z* 284 (M^+, 100). Anal. Calcd for $C_{17}H_{16}O_2S$: C, 71.80; H, 5.67. Found: C, 71.75; H, 5.93.

6-Methoxy-2-(naphthalen-1-yl)thiochroman-4-one (4j): yellow needles; mp 132–134 ˚C (hexane–Et_2O); IR (KBr) 1670 cm^{-1}; ^1H NMR δ 3.36 (dd, *J* = 16.5, 2.7 Hz, 1H), 3.52 (dd, *J* = 16.5, 12.8 Hz, 1H), 3.88 (s, 3H), 5.48 (dd, *J* = 12.8, 2.7 Hz, 1H), 7.08 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.23 (d, *J* = 8.7 Hz, 1H), 7.49–7.59 (m, 3H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.72 (d, *J* = 2.7 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 8.18 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR δ 41.26, 46.36, 55.62, 111.41, 122.62, 122.81, 124.50, 125.35, 126.04, 126.67, 128.66, 129.03, 129.10, 130.73, 131.24, 133.75, 133.99, 134.00, 157.68, 194.83; MS *m/z* 320 (M^+, 100). Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03. Found: C, 75.01; H, 5.04.

6,7-Dimethoxy-2-phenylthiochroman-4-one (4k): a yellow solid; mp 171–174 ˚C (hexane–CH_2Cl_2); IR (KBr) 1653 cm^{-1}; ^1H NMR δ 3.16 (dd, *J* = 16.5, 3.2 Hz, 1H), 3.27 (dd, *J* = 16.5, 12.8 Hz, 1H), 3.92 (s, 6H), 4.70 (dd, *J* = 12.8, 3.2 Hz, 1H), 6.69 (s, 1H), 7.34 (tt, *J* = 7.3, 1.4 Hz, 1H), 7.39 (dd, *J* = 7.8, 7.3 Hz, 2H), 7.43 (dd, *J* = 7.8, 1.4 Hz, 2H), 7.65 (s, 1H); ^{13}C NMR δ 46.09, 46.17, 56.05, 56.23, 108.58, 110.38, 123.69, 127.39, 128.38, 128.93, 135.91, 138.53, 147.35, 153.90, 193.17; MS *m/z* 300 (M^+, 100). Anal. Calcd for $C_{17}H_{16}O_3S$: C, 67.98; H, 5.37. Found: C, 67.93; H, 5.41.

2-(1,3-Benzodioxol-5-yl)-6,7-dimethoxythiochroman-4-one (4l): a yellow solid; mp 198–200 ˚C (hexane–CH_2Cl_2); IR (KBr) 1649 cm^{-1}; ^1H NMR δ 3.12 (dd, *J* = 16.5, 3.2 Hz, 1H), 3.20 (dd, *J* = 16.5, 12.8 Hz, 1H), 3.919 (s, 3H), 3.924 (s, 3H), 4.63 (dd, *J* = 12.8, 3.2 Hz, 1H), 5.99 (s, 2H), 6.68 (s, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.88 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.93 (d, *J* = 1.8 Hz, 1H), 7.64 (s, 1H); ^{13}C NMR δ 45.98, 46.49, 56.05, 56.24, 101.33, 107.76, 108.49, 108.55, 110.37, 120.95, 123.64, 132.31, 135.90, 147.35, 147.61, 147.97, 153.91, 193.16; MS *m/z* 344 (M^+, 100). Anal. Calc for $C_{18}H_{16}O_5S$: C, 62.78; H, 4.68. Found: C, 62.70; H, 4.81.

6,7-Dimethoxy-2-(1-methylpyrrol-2-yl)thiochroman-4-one (4m): a pale-yellow solid; mp 173–175 ˚C (hexane–CH_2Cl_2); IR (KBr) 1655 cm^{-1}; ^1H NMR δ 3.23 (dd, *J* = 16.9, 3.2 Hz, 1H), 3.31 (dd, *J* = 16.9, 11.5 Hz, 1H), 3.69 (*s*, 3H), 3.92 (s, 6H), 4.68 (dd, *J* = 11.5, 3.2 Hz, 1H), 6.09 (t, *J* = 2.7 Hz, 1H), 6.15 (s, 1H), 6.63 (s, 1H), 6.67 (s, 1H), 7.66 (s, 1H); ^{13}C NMR δ 33.85, 38.11, 44.85, 56.04, 56.19, 107.27, 107.74, 108.89, 110.37, 123.50, 123.94, 129.00, 134.96, 147.43, 153.81, 193.28; MS *m/z* 303 (M^+, 100). Anal. Calcd for $C_{16}H_{17}NO_3S$: C, 63.34; H, 5.65; N, 4.62. Found: C, 63.21; H, 4.71; N, 4.82.

REFERENCES

1. For recent reports: (a) Z. Huang, D. Lui, X. Han, Z. Zhang, and J. Wang, PCT. Int. Pat. Appl. WO 2000, 004901 (*Chem. Abstr.*, 2000, **132**, 117566); (b) J. F. Delhomel, R. Hanf, and K. Caumont-Bertrand, PCT. Int. Pat. Appl. WO 2007, 147879 (*Chem. Abstr.*, 2007, **148**, 100385); (c) A. M. Chinnaiyan, S. Lnu, and Q. Cao, PCT. Int. Pat. Appl. WO 2009, 006577 (*Chem. Abstr.*, 2009, **150**, 128895).
2. For an excellent review: (a) S. Bondock and M. A. Metwally, *J. Sulfur Chem.*, 2008, **29**, 623. For recent reports: (b) J. I. Lee, *Bull. Korean Chem. Soc.*, 2008, **29**, 1263; (c) W. Konieczny and M. Konieczny, *Synthesis*, 2009, 1811; (d) B. Willy, W. Frank, and T. J. J. Thomas, *Org. Biomol. Chem.*, 2010, **8**, 90.
3. A. Minatti, X. Zheng, and S. L. Buchwald, *J. Org. Chem.*, 2007, **72**, 9253.
4. I. Fleming and M. Woolias, *J. Chem. Soc., Perkin Trans. 1*, 1979, 829.
5. R. Beugelmans, M. Bois-Choussy, and Q. Tang, *J. Org. Chem.*, 1987, **52**, 3880.