Synthesis of 2-Aryl-4H-thiochromen-4-one Derivatives via a Cross-Coupling Reaction

Peng Li, Shengnan Li, Gang Li,* and Haihong Huang*

ABSTRACT: A concise and efficient cross-coupling synthetic strategy has been developed to construct 2-aryl-4H-thiochromen-4-one derivatives from 2-sulfonyl-thiochromones and arylboronic acids. This reaction proceeds via a catalyst system of Lewis acid and palladium(II) combined with XPhos as an optimal ligand in moderate to good yields. Besides, this flexible methodology provides a wide scope for the synthesis of different functionally substituted thiochrome scaffolds and can be further exploited to construct diverse thioflavone libraries for pharmaceutical research.

INTRODUCTION

Thioflavones are an important class of sulfur-containing heterocycles in medicinal chemistry due to their structural similarity to flavones, and this scaffold exhibits various biological and pharmacological properties, including antibacterial, anticancer, and anti-HIV activities. However, the synthetic methods for thioflavones via cross-coupling reaction are rarely reported. The major common synthetic routes include synthesizing from benzoylethiosalicylic acid via intramolecular Wittig cyclization (Scheme 1, method A) or coupling of thiophenols with k-ke to ester in the presence of polyphosphoric acid (Scheme 1, method B). Recent synthetic methods of thioflavones mainly rely on the cyclization of various 2-substituted k-phenyl-aromatic ketones (Scheme 1, methods C and D) or intermolecular Michael addition of k-ethyl-aromatic ketones (Scheme 1, methods E and F). However, the preparation of various starting materials for current methods limits the rapid synthesis of large libraries of valuable thioflavone precursors for pharmaceutical studies. To the best of our knowledge, there are no reports of the construction of thioflavones via cross-coupling reactions using sulfinyl as coupling partners.

Organoboron-mediated cross-coupling is a useful C–C bond-forming reaction. The commercial availability of boron reagents, broad functional group tolerance, and general applicability of the reaction make it suitable for derivative expansion. Flavones can be synthesized by organoboron cross-coupling; especially, the synthesis of flavones via transition metal-catalyzed cross-coupling reactions has particularly attracted our attention.

Recently, our group has developed an efficient method to synthesize 2-amino-4H-benzothiopyran-4-ones from 2-sulfonyl-thiochromones via conjugated addition–elimination in which the sulfinyl group worked well as a leaving group (Scheme 2). The use of sulfinyl and sulfonyl groups in Suzuki–Miyaura cross-coupling encouraged us to consider the potential of 2-sulfonyl-thiochromones as substrates for synthesizing thioflavone analogues. Herein, we report a Lewis acid and Pd(II)-catalyzed cross-coupling method for synthesizing 2-aryl-4H-thiochromen-4-one derivatives from 2-sulfonyl-thiochromones in order to expand libraries for biological screening and investigate 2-sulfonyl-thiochromones as important building blocks. This protocol delivers a reliable and concise method for producing thioflavones.

RESULTS AND DISCUSSION

Initially, 2-(methylsulfonyl)-4H-thiochromen-4-one (1a), which was synthesized according to the reported method, and phenylboronic acid (2a) were chosen as the test substrates for the reaction in the presence of Pd(OAc)2 to investigate the feasibility of our method. However, the reaction only offered a trace amount of the desired product 3a (Table 1, entry 1). Considering that the ligand strongly affects the efficiency of transition-metal catalyzed C–C cross-coupling reactions, we screened several ligands generally used in Pd(II)-catalyzed cross-coupling reactions. First, monodentate phosphine ligands, such as PPh3 (triphenylphosphine) and TFP (tri(2-furyl)phosphine), were investigated, but they showed unsatisfactory yields of 34 and 25%, respectively (Table 1, entries 2 and 3). Next, bidentate phosphine ligands BINAP (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl) and DPEPHOS (bis(2-diphenylphosphinopheny1)ether) were tested, where the yields of 30 and 25% were still not improved significantly (Table 1, entries 4 and 5), though Xantphos (9,9-dimethyl-4,5-...
bis(diphenylphosphino)xanthene) gave the product in moderate yield (50%) (Table 1, entry 6). Gratifyingly, further screening showed that XPhos (2-(dicyclohexylphosphino)-2',4',6'-triisopropylbiphenyl) furnished 3a in relatively good yield (59%) (Table 1, entry 7). With XPhos as a satisfactory ligand, we then focused on the selection of solvents beyond the commonly used DMF. Replacing DMF with toluene, 1,4-dioxane, and acetonitrile resulted in lower yields of 36−31% (Table 1, entries 8−10). Although the reaction in THF proceeded well (yield 56%, entry 11), difficult-to-remove yellow impurities were mixed with the target product 3a. Therefore, DMF was confirmed as the optimal solvent. In addition, we also tried to replace Pd(OAc)$_2$ with Pd(PPh$_3$)$_4$, but it only gave a low yield of 25% (Table 1, entry 12). The aforementioned results provided the proof of concept of using Pd(OAc)$_2$-catalyzed cross-coupling to synthesize thioflavones from 2-sulfonyl-thiochromones.

Based on the reported catalytic effect of Lewis acids in the Pd(II)-catalyzed coupling reaction of arylboronic acids with chromones to form flavanones, subsequently, a variety of Lewis acids were screened to further optimize the reaction condition to construct thioflavones (Table 2). We initially investigated SbCl$_3$, which worked well in the Pd(II)-catalyzed coupling of arylboronic acids with α,β-unsaturated ketones; however, it did not improve the present reaction and gave a yield of 42% only (Table 2, entry 1). We then tested various triflate (OTf)-based Lewis acids. The results displayed that TMSOTf (trimethylsilyl triflate) and Cu(OTf)$_2$ decreased the yields (39−50%) (Table 2, entries 2 and 3), whereas Fe(OTf)$_3$ gave a yield of 59%, which was similar to the yield without using Lewis acid (Table 2, entry 4 vs Table 1, entry 7). To our delight, both In(OTf)$_3$ and Zn(OTf)$_2$ increased the yields to 64 and 67%, respectively (Table 2, entries 5 and 6). Considering the cost and availability, Zn(OTf)$_2$ was chosen as the Lewis acid for this protocol. We further investigated the solvent impact by replacing DMF with THF under the use of Lewis acid, which resulted in a lower yield (Table 2, entries 6 vs 7). Comparing with the reaction without Lewis acid in the absence of the ligand XPhos, Zn(OTf)$_2$ improved the reaction yield significantly, exemplified by entry 8 (yield 18%, Table 2) versus entry 1 (trace product, Table 1), which demonstrated the catalytic effects of Lewis acid. In our previously published work, we compared the difference in the reactivity of sulde, sulfinyl, and sulfonyl groups in the conjugated addition-elimination reaction using 2-sulfinyl-thiochromones to con-

![Scheme 1. Representative Strategies for Constructing Thioflavones](image1)

Scheme 1. Representative Strategies for Constructing Thioflavones

![Scheme 2. Strategy for Constructing 2-Aryl-thiochromones](image2)

Scheme 2. Strategy for Constructing 2-Aryl-thiochromones

![Table 1. Optimization of the Reaction Conditions](image3)

Table 1. Optimization of the Reaction Conditions

| entry | catalyst | ligand | solvent | yield (%) |
|-------|----------|--------|---------|-----------|
| 1     | Pd(OAc)$_2$ |        | DMF     | trace     |
| 2     | Pd(OAc)$_2$ | PPh$_3$ | DMF     | 34        |
| 3     | Pd(OAc)$_2$ | TFP    | DMF     | 25        |
| 4     | Pd(OAc)$_2$ | BINAP  | DMF     | 30        |
| 5     | Pd(OAc)$_2$ | DPEPHOS| DMF     | 25        |
| 6     | Pd(OAc)$_2$ | Xantphos | DMF | 50        |
| 7     | Pd(OAc)$_2$ | XPhos  | DMF     | 59        |
| 8     | Pd(OAc)$_2$ | XPhos  | toluene | 36        |
| 9     | Pd(OAc)$_2$ | XPhos  | 1,4-dioxane | 31  |
| 10    | Pd(OAc)$_2$ | XPhos  | acetonitrile | 17  |
| 11    | Pd(OAc)$_2$ | XPhos  | THF     | 56        |
| 12    | Pd(PPh$_3$)$_4$ | XPhos | DMF     | 25        |

$^{a}$1a (0.5 mmol, 1 equiv), 2a (2 equiv), catalyst (0.1 equiv), and ligand (0.1 equiv) in solvent (3.0 mL) were stirred at 80 °C for 6 h. $^b$Isolated yields.
struct 2-amino-4H-benzothiopyran-4-ones.24 Thus, in this present work, we continuously investigated the effect of different substrates on C–C formation via the cross-coupling reaction. Under the same reaction conditions, the sulfuryl group still performed the best with the yield of 67% (Table 2, entries 3–5). Isolated yields. *1a was 2-(methylthio)-4H-thiochromene-4-one. **1a was 2-(methylsulfonyl)-4H-thiochromene-4-one. Pd(OAc)2 (0.1 equiv). #Pd(OAc)2 (0.2 equiv).<ref>

| entry | ligand | Lewis acid | solvent | yield (%) |
|-------|--------|------------|---------|-----------|
| 1     | XPhos  | SnCl4      | DMF     | 42        |
| 2     | XPhos  | TsMTOF     | DMF     | 50        |
| 3     | XPhos  | Cu(OTf)2   | DMF     | 39        |
| 4     | XPhos  | Fe(OTf)2   | DMF     | 59        |
| 5     | XPhos  | In(OTf)3   | DMF     | 64        |
| 6     | XPhos  | Zn(OTf)2   | DMF     | 67        |
| 7     | XPhos  | Zn(OTf)2   | THF     | 31        |
| 8     | XPhos  | Zn(OTf)2   | DMF     | 18        |
| 9     | XPhos  | Zn(OTf)2   | DMF     | 34        |
| 10    | XPhos  | Zn(OTf)2   | DMF     | 12        |
| 11    | XPhos  | Zn(OTf)2   | DMF     | 69        |
| 12    | XPhos  | Zn(OTf)2   | DMF     | 71        |

"1a (0.5 mmol, 1 equiv), 2a (2 equiv), Pd(OAc)2 (0.1 equiv), XPhos (0.1 equiv), and Lewis acid (0.2 equiv) in solvent (3.0 mL) were stirred at 80 °C for 6 h. Isolated yields. *1a was 2-(methylthio)-4H-thiochromene-4-one. **1a was 2-(methylsulfonyl)-4H-thiochromene-4-one. #Pd(OAc)2 (0.1 equiv). #Pd(OAc)2 (0.4 equiv)."
apparatus. Substrates 1 were prepared according to the reported procedures.24

**General Procedure for the Synthesis of Thioflavones 3a–z and 2-Heteroaryl Thioflavone Analogues 4a–d.** To a stirred solution of 1 (0.5 mmol, 1.0 equiv) in DMF (3.0 mL) was added Pd(OAc)2 (0.05 mmol, 0.1 equiv), XPhos (0.05 mmol, 0.1 equiv), Zn(OTf)2 (0.1 mmol, 0.2 equiv), and arylboronic acid 2 (1.0 mmol, 2.0 equiv). The reaction mixture was heated at 80 °C for 6 h. After cooling to room temperature, the solvent was evaporated in vacuo and the residue was purified by column chromatography eluting with ethyl acetate (EA)/petroleum (PE) = 1−20:100 to afford the target products.

**2-Phenyl-4H-thiochromen-4-one (3a).** White solid, 80 mg, yield 67%, mp 116−118 °C. 1H NMR (400 MHz, CDCl3): δ 8.56 (dd, J = 8.1, 1.5 Hz, 1H), 7.73−7.68 (m, 2H), 7.68−7.61 (m, 2H), 7.59−7.54 (m, 1H), 7.53−7.49 (m, 1H), 7.28 (s, 1H). 13C NMR (100 MHz, CDCl3): δ 180.9, 153.2, 137.8, 136.6, 131.6, 130.9, 129.3, 128.6, 127.8, 127.0, 126.5, 124.3, 122.7, 19.7. HR-MS (ESI) m/z: [M+H]+ calcd for C15H11OS, 239.0525; found, 239.0529. 1H NMR and 13C NMR spectra are consistent with the literature.15

**2-(p-Tolyl)-4H-thiochromen-4-one (3b).** Off-white solid, 84 mg, yield 67%, mp 112−114 °C. 1H NMR (400 MHz, CDCl3): δ 8.55 (dd, J = 8.0, 1.5 Hz, 1H), 7.69−7.58 (m, 4H), 7.58−7.51 (m, 1H), 7.30 (d, J = 8.2 Hz, 2H), 7.23 (d, J = 1.4 Hz, 1H), 2.43 (s, 3H). 13C NMR (100 MHz, CDCl3): δ 180.9, 153.1, 141.3, 137.7, 133.7, 131.5, 130.9, 130.0, 128.6, 127.7, 126.8, 126.5, 122.9, 21.4. HR-MS (ESI) m/z: [M+H]+ calcd for C16H13OS, 253.0682; found, 253.0687. 1H NMR and 13C NMR spectra are consistent with the literature.14

**2-(3,4-Dimethylphenyl)-4H-thiochromen-4-one (3c).** Off-white solid, 77 mg, yield 58%, mp 130−132 °C. 1H NMR (400 MHz, CDCl3): δ 8.54 (dd, J = 7.8, 1.5 Hz, 1H), 7.68−7.59 (m, 2H), 7.59−7.53 (m, 1H), 7.48 (d, J = 2.1 Hz, 1H), 7.44 (dd, J = 7.8, 2.2 Hz, 1H), 7.24 (d, J = 1.7 Hz, 2H), 2.34 (s, 3H), 2.33 (s, 3H). 13C NMR (100 MHz, CDCl3): δ 180.9, 153.3, 140.1, 137.8, 137.7, 134.1, 131.5, 131.0, 130.5, 128.6, 128.0, 127.6, 126.4, 124.3, 122.7, 19.9, 19.7. HR-MS (ESI) m/z: [M+H]+ calcd for C17H15OS, 267.0838; found, 267.0844.

**2-(2,4-Dimethylphenyl)-4H-thiochromen-4-one (3d).** Off-white solid, 66 mg, yield 50%, mp 80−82 °C. 1H NMR (400 MHz, CDCl3): δ 8.58 (d, J = 8.1 Hz, 1H), 7.64−7.59 (m, 2H), 7.59−7.53 (m, 1H), 7.27−7.22 (m, 1H), 7.13 (s, 1H), 7.10 (d, J = 7.2 Hz, 1H), 2.43 (s, 3H), 2.33 (s, 3H). 13C NMR (100 MHz, CDCl3): δ 180.9, 153.3, 140.1, 137.8, 137.7, 134.1, 131.5, 131.0, 130.5, 128.6, 128.0, 127.6, 126.4, 126.3, 122.7, 19.9, 19.7. HR-MS (ESI) m/z: [M+H]+ calcd for C17H15OS, 267.0838; found, 267.0844.
Table 4. Reaction of Substituted 2-Sulfinyl-thiochromones (1) with Phenylboronic Acid (2a)\(^a\)

\[ \text{R}^2 \text{OH} \quad \text{Pd(OAc)}_2 \quad \text{XPhos} \quad \text{Zn(OTf)}_2 \quad \text{DMF, 80 °C, 6 h} \]

\[ \text{R}^2 \text{H} \]

\(^{a}\)1 (0.5 mmol, 1 equiv), 2a (2 equiv), Pd(OAc)$_2$ (0.1 equiv), XPhos (0.1 equiv), and Zn(OTf)$_2$ (0.2 equiv) in DMF (3.0 mL) were stirred at 80 °C for 6 h. Isolated yields are shown in brackets.

\[ J = 7.8 \text{ Hz}, 1H), \delta_{269.0635} \text{ (s, 3H), 2.36 (s, 3H).} \]

\[^{13}\text{C} \text{ NMR (100 MHz, CDCl}_3\):} \delta_{180.6, 153.8, 139.9, 138.5, 135.5, 133.4, 131.7, 131.5, 131.0, 129.0, 128.7, 127.7, 126.8, 126.3, 126.2, 21.2, 19.9. \]

\[^{1}H \text{ NMR and } ^{13}C \text{ NMR spectra are consistent with the literature.}^{31} \]

\[^{2}\text{-4-(Nitrophenyl)-4H-thiochromen-4-one (3h). Yellow,} \text{ off-white solid, 87 mg, yield 61\%, mp 157–177 °C.}^{31} \]

\[^{1}H \text{ NMR (400 MHz, CDCl}_3\):} \delta_{8.57 (d, J = 7.9 \text{ Hz}, 1H), 8.37 (d, J = 8.8 \text{ Hz}, 2H), 7.87 (d, J = 8.8 \text{ Hz}, 2H), 7.71–7.67 (m, 2H), 7.63–7.58 (m, 1H), 7.27 (s, 1H).} \]

\[^{13}C \text{ NMR (100 MHz, CDCl}_3\):} \delta_{180.5, 150.0, 149.1, 142.5, 137.0, 132.1, 130.8, 128.8, 128.3, 128.1, 126.6, 125.0, 124.5. HR-MS (ESI) m/z: [M + H]$^+$ calc for C$_{16}$H$_{15}$NO$_2$S, 284.0376; found, 284.0381. \]

\[^{1}H \text{ NMR and } ^{13}C \text{ NMR spectra are consistent with the literature.}^{31} \]

\[^{2}\text{-4-(Trifluoromethoxy)phenyl)-4H-thiochromen-4-one (3i). Off-white solid, 68 mg, yield 44\%, mp 167–169 °C.}^{31} \]

\[^{1}H \text{ NMR (400 MHz, CDCl}_3\):} \delta_{8.56 (d, J = 8.0 \text{ Hz}, 1H), 7.79 (q, J = 8.3 \text{ Hz}, 4H), 7.70–7.63 (m, 2H), 7.58 (t, J = 7.2 \text{ Hz}, 1H), 7.25 (s, 1H).}^{31} \]

\[^{13}C \text{ NMR (100 MHz, CDCl}_3\):} \delta_{180.6, 151.1, 140.0, 137.3, 132.6 (q, J$_{CF} = 33 \text{ Hz}$), 131.9, 130.9, 128.7, 128.1, 127.5, 126.6, 126.3, 124.4, 123.7 (q, J$_{CF} = 271 \text{ Hz}$). HR-MS (ESI) m/z: [M + H]$^+$ calc for C$_{16}$H$_{15}$O$_2$FOS, 307.0399; found, 307.0406.}^{31} \]

\[^{1}H \text{ NMR and } ^{13}C \text{ NMR spectra are consistent with the literature.}^{31} \]

\[^{2}\text{-4-(Hydroxyphenyl)phenyl)-4H-thiochromen-4-one (3j). Purified by column chromatography with ethyl acetate (EA)/petroleum (PE) = 1–30:100. Off-white solid, 73 mg, yield 57\%, mp 179–181 °C.}^{31} \]

\[^{1}H \text{ NMR (400 MHz, CDCl}_3\):} \delta_{8.99 (s, 1H), 8.37 (d, J = 8.1 \text{ Hz}, 1H), 7.95 (d, J = 8.2 \text{ Hz}, 1H), 7.79 (t, J = 7.6 \text{ Hz}, 1H), 7.66 (t, J = 7.6 \text{ Hz}, 1H), 7.38 (t, J = 7.9 \text{ Hz}, 1H), 7.24 (d, J = 7.8 \text{ Hz}, 1H), 7.18 (s, 1H), 7.16 (t, J = 2.1 \text{ Hz}, 1H), 6.99 (dd, J = 8.1, 2.7 \text{ Hz}, 1H).}^{31} \]

\[^{13}C \text{ NMR (100 MHz, CDCl}_3\):} \delta_{179.3, 158.0, 152.1, 136.9, 136.7, 132.1, 130.6, 130.1, 128.1, 127.6, 127.1, 122.2, 118.0, 117.3, 113.2. HR-MS (ESI) \]

\[^{14659} \text{https://doi.org/10.1021/acsomega.1c01778} \text{ ACS Omega 2021, 6, 14655–14663} \]
Table 5. Synthesis of 2-Aryl-4H-thiochromen-4-one Derivatives

| R2 | 3v (33%) | 3w (41%) | 3x (44%) | 3y (54%) | 3z (37%) | 4a (48%) | 4b (41%) | 4c (54%) | 4d (51%) |
|-----|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|     | ![Image](image1.png) | ![Image](image2.png) | ![Image](image3.png) | ![Image](image4.png) | ![Image](image5.png) | ![Image](image6.png) | ![Image](image7.png) | ![Image](image8.png) | ![Image](image9.png) |

“1 (0.5 mmol, 1 equiv), arylboronic acid 2 (2 equiv), Pd(OAc)2 (0.1 equiv), XPhos (0.1 equiv), and Zn(OTf)2 (0.2 equiv) in DMF (3.0 mL) were stirred at 80 °C for 6 h. Isolated yields are shown in brackets.

Scheme 3. Proposed Mechanism of the Reaction

**2-(4-Methoxycarbonylphenyl)-4H-thiochromen-4-one (3l).** Off-white solid, 86 mg, yield 58%, mp 144–146 °C. 1H NMR (400 MHz, CDCl3): δ 8.56 (d, J = 7.3 Hz, 1H), 8.17 (d, J = 8.7 Hz, 2H), 7.77 (d, J = 8.8 Hz, 2H), 7.69–7.62 (m, 2H), 7.60–7.55 (m, 1H), 7.28 (s, 1H), 3.97 (s, 3H). 13C NMR (100 MHz, CDCl3): δ 180.7, 166.2, 151.6, 140.7, 137.4, 132.1, 131.8, 130.9, 130.5, 130.2, 128.7, 128.0, 127.3, 127.0, 126.6, 124.2, 52.5. HR-MS (ESI) m/z: [M + H]⁺ calcd for C17H13O3S, 297.0580; found, 297.0587.

6-Methyl-2-phenyl-4H-thiochromen-4-one (3m). Off-white solid, 66 mg, yield 52%, mp 143–145 °C. 1H NMR (400 MHz, CDCl3): δ 8.37 (d, J = 1.9 Hz, 1H), 7.72–7.68 (m, 2H), 7.31–7.26 (m, 2H), 7.25–7.20 (m, 1H), 7.17–7.12 (m, 2H), 7.08–7.03 (m, 1H), 3.87 (s, 3H). 13C NMR (100 MHz, CDCl3): δ 180.4, 166.2, 151.6, 140.7, 137.4, 132.1, 131.8, 130.9, 130.5, 130.2, 128.7, 128.0, 127.3, 127.0, 126.6, 124.2, 52.5. HR-MS (ESI) m/z: [M + H]⁺ calcd for C15H14O3S, 272.0540; found, 272.0542.
Yellow solid, 63 mg, yield 41%, mp 191–193 °C. 1H NMR (400 MHz, CDCl3): δ 7.48 (d, J = 2.0 Hz, 1H), 7.52–7.58 (m, 3H), 7.61–7.67 (m, 2H), 7.82 (s, 1H). 13C NMR (100 MHz, CDCl3): δ 179.9, 153.2, 141.2, 136.0, 131.3, 131.0, 130.1 (q, 1J_{CF} = 33 Hz), 129.5, 127.6, 127.5, 127.0, 126.1, 126.3, 126.5 (q, 1J_{CF} = 271 Hz). HR-MS (ESI) m/z: [M + H]^+ calc for C16H14Cl2OS, 306.0739; found, 306.0739.

5-Chloro-2-(4-chlorophenyl)-4H-thiochromen-4-one (3w). Yellow solid, 63 mg, yield 39%, mp 184–186 °C. 1H NMR (400 MHz, CDCl3): δ 7.49–7.55 (m, 3H), 7.61–7.67 (m, 2H), 7.82 (s, 1H). 13C NMR (100 MHz, CDCl3): δ 180.2, 153.2, 139.7, 136.3, 131.4, 131.7, 129.6, 128.1, 125.6, 124.8, 116.8. HR-MS (ESI) m/z: [M + H]^+ calc for C16H15Cl3O3S, 309.0924; found, 309.0924.

6-Methyl-2-(4-(trifluoromethyl)phenyl)-4H-thiochromen-4-one (3y). Off-white solid, 87 mg, yield 38%, mp 152–154 °C. 1H NMR (400 MHz, CDCl3): δ 7.48–7.55 (m, 3H), 7.61–7.67 (m, 2H), 7.82 (s, 1H). 13C NMR (100 MHz, CDCl3): δ 179.9, 153.2, 141.2, 136.0, 131.3, 131.0, 130.1 (q, 1J_{CF} = 33 Hz), 129.5, 127.6, 127.5, 127.0, 126.1, 126.3, 126.5 (q, 1J_{CF} = 271 Hz). HR-MS (ESI) m/z: [M + H]^+ calc for C16H14Cl2OS, 306.0739; found, 306.0739.
\[ \delta 180.7, 165.8, 149.8, 145.5, 137.3, 136.9, 131.7, 130.9, 128.7, 127.9, 126.4, 125.9, 122.8, 111.6, 54.0. \]

HR-MS (ESI) \( m/z: [M + H]^+ \) calcd for \( \text{C}_{13}\text{H}_{12}\text{NO}_2\text{S}, 303.0838 \); found, 303.0846.

7.35 (s, 1H), 6.99 (d, \( J = 8.1 \) Hz, 1H). 13C NMR (100 MHz, CDCl\(_3\))

\[ \delta 126.0, 123.5 (q, \( J_{\text{C,F}} = 33 \) Hz), 127.6, 127.4, 126.0, 123.5 (q, \( J_{\text{C,F}} = 270 \) Hz), 118.9, 112.9, 112.1. \]

HR-MS (ESI) \( m/z: [M + H]^+ \) calcd for \( \text{C}_{13}\text{H}_2\text{F}_3\text{O}_2\text{S}, 297.0192 \); found, 297.0197.

6-Methyl-2-(naphthalen-1-yl)-4H-thiochromen-4-one (4c).

Yellow solid, 81 mg, yield 54\%, mp 158–160 °C. \( ^1\)H NMR (400 MHz, CDCl\(_3\))

\[ \delta 7.93 (s, 1H), 7.89 (d, \( J = 8.4 \) Hz, 1H), 7.79 (d, \( J = 8.4 \) Hz, 1H), 7.76 (m, 6H), 7.61 (s, 1H), 2.54 (s, 3H).13C NMR (100 MHz, CDCl\(_3\))

\[ \delta 179.4, 148.5, 145.8, 140.8, 139.9, 131.2, 130.1. \]

HR-MS (ESI) \( m/z: [M + H]^+ \) calcd for \( \text{C}_{20}\text{H}_{15}\text{OS}, 303.0838 \); found, 303.0846.

- The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c01778.

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