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Iodine-Mediated Synthesis of 2-(Methylthio)-4*H*-chromen-4-ones and Study of Their Halogenation Reactions

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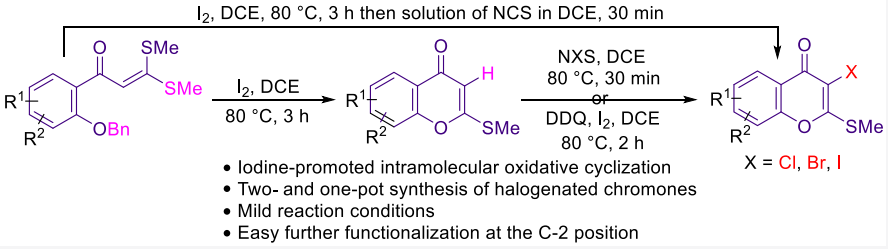

ABSTRACT: An efficient iodine-mediated method is developed for the synthesis of functionalized 2-(methylthio)-4*H*-chromen-4-ones by intramolecular cyclization of easily accessible 1-(2-benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones. The synthesized chromen-4-ones turn out to be a key precursor for various kinds of chemical reactions. Mechanistically, we observed that iodine-mediated intramolecular cyclization of ketene dithioacetal proceeded through a radical pathway. 3-Halo-2-(methylthio)-4*H*-chromen-4-ones were achieved via various two- or one-pot halogenation approaches.

INTRODUCTION

Chromone skeleton is present in many naturally occurring compounds,[1] and its derivatives exhibit a broad range of important biological activities such as anti-inflammatory, antiallergic, antitumor, anticancer, and antimicrobial.[2] Chromones are privileged structures and valuable intermediates in the synthesis of new heterocyclic compounds.[2c,3] The most well-known synthetic routes enclose Claisen condensation,[4] Vilsmeier−Haack reaction,[5] Baker−Venkataraman rearrangement,[6] Simonis and Ruhemann reactions,[3,7] catalytic reactions mediated by palladium,[8] and the oxidative cyclization of 2′-hydroxychalcones,[9] 2′-allyloxychalcones,[10] or 2′-benzyloxy-6′-hydroxychalcone[11] using a catalytic amount of iodine in DMSO. Yang *et al.* reported a green approach for the synthesis of 3-thiocyanated chromones from *o*-hydroxyaryl enaminones under electrochemical thiocyanation conditions.[12] In recent years, C−H activation and annulation methodologies based on salicylaldehyde derivatives have been developed for the synthesis of chromones employing substrates such as alkynes, alkynoic acids, diazo compounds, and sulfoxonium ylides.[13] Larock and co-workers described the successful use of iodine monochloride for the synthesis of chromones, benzo[*b*]furans, and *α*-pyrones via electrophilic cyclization reaction of *o*-alkoxyalkynones, *o*-alkoxyalkynes, and alkynyl ester, respectively.[14]

On the other hand, *α*-aroyl-*α*-bromoketene dithioacetals have been synthesized via direct bromination of the corresponding *α*-aroylketene dithioacetals using NBS in CCl_4.[15] Besides, a study for the synthesis of *α*-bromo-*α*,*β*-unsaturated ketones from *α*,*β*-unsaturated ketones (including 3-bromo-chromone from chromone) has been accomplished using a mixture of DMP and $Et_4N^+Br^-$ or NBS−Et_3N·3HBr and K_2CO_3 in dry DCM.[16,17] However, there is no particular study established for the halogenation of chromone derivatives.

So far, very limited literature studies for the synthesis of 2/3-(methylthio)-4*H*-chromen-4-ones are reported. In 2015, sulfenylation of chromones was first reported by Zheng and co-workers via C−H functionalization.[18] Zhou and co-workers reported another sulfenylation method by using alkyl halides and $Na_2S_2O_3$.[19] These methods provide 3-alkylthio- or 3-arylthio-chromones, while no substitution occurs at the C-2 position even if the reaction site C-3 is blocked. Lee and Pak have reported the one-pot synthesis of 2-(methylthio)-4*H*-chromen-4-ones from 2-hydroxyacetophenones through a ketene dithioacetal intermediate.[20] Although this method provides direct preparation of 2-(methylthio)-4*H*-chromen-4-ones, it requires very low reaction temperature (−78 °C) and the use of strong and moisture sensitive base lithium bis(trimethylsilyl)amide (LiHMDS), and the generality of protocol was not tested. We have tried to obtain the desired product under the same reaction conditions, but we got low yield. Apart from this, there are no other specific methods

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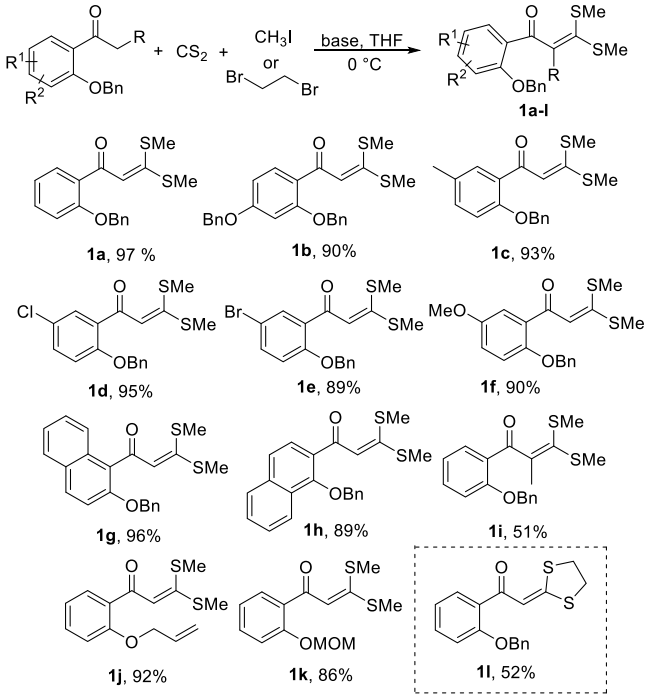
known for the synthesis of 2-(methylthio)-4*H*-chromen-4-ones.

Functionalized ketene dithioacetals are versatile intermediates in the synthesis of various classes of heterocyclic compounds such as furans, thiophenes, pyrroles, pyridines, and lactones.[21] Herein, we reported a synthetic route to 2-(methylthio)-4*H*-chromen-4-ones via iodine-mediated cyclization of α-aroylketene dithioacetals. In addition, a survey for the halogenation of chromones was accomplished.

RESULT AND DISCUSSION

The required precursors **1a**–**k** were synthesized by reaction of functionalized acetophenones, carbon disulfide, and methyl iodide under basic conditions at low temperature (Scheme 1).[22] This method failed to provide precursor **1l** using 1,2-dibromoethane in lieu of methyl iodide under the same reaction conditions. Therefore, we have tried another procedure,[23] and we successfully achieved the desired precursor **1l** in 52% yield (Scheme 1).

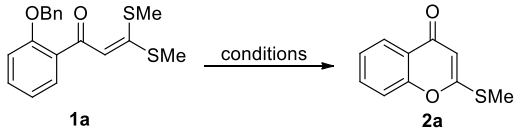
Scheme 1. Synthesis of 1-(2-Benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones 1a–k[a] and 1-(2-(Benzyloxy)phenyl)-2-(1,3-dithiolan-2-ylidene)ethan-1-one 1l[b]



[a]Precursors **1a**–**k** were synthesized by stirring functionalized acetophenones (2.0 mmol), carbon disulfide (2.40 mmol), methyl iodide (4.40 mmol), and NaH (8 mmol) in dry THF (10.0 mL) at 0 °C for 5–6 h. [b]Precursor **1l** was synthesized by stirring 1-(2-(benzyloxy)phenyl)ethan-1-one (2.0 mmol), carbon disulfide (2.40 mmol), 1,2-dibromoethane (4.40 mmol), and potassium *tert*-butoxide (8.0 mmol) in dry THF (8.0 mL) at 0 °C for 6 h.

To find optimal reaction conditions for intramolecular oxidative cyclization, 1-(2-(benzyloxy)phenyl)-3,3-bis-(methylthio)prop-2-en-1-one **1a** was selected as a model substrate. The results are presented in Table 1. Treatment of **1a** with CuI or $Cu(OAc)_2$ as a catalyst in DMSO provided no desired product (entries 1 and 2). The use of (diacetoxyiodo)-

Table 1. Exploration and Optimization Studies for the Synthesis of 2-(Methylthio)-4*H*-chromen-4-one[a]



entry	reagent	solvent, time	yield[b]
1	50 mol % CuI	1 mL DMSO, 24 h	0
2	50 mol % $Cu(OAc)_2$	1 mL DMSO, 24 h	0
3	50 mol % PIDA	1 mL DMSO, 24 h	0
4	50 mol % PIDA	1 mL DCE, 24 h	0
5	10 mol % CuI, 4 equiv TBHP	1 mL DMSO, 24 h	[c]
6	10 mol % CuI, 4 equiv TBHP	1 mL CH_3CN, 24 h	[c]
7	100 mol % DDQ	1 mL CH_3CN, 24 h	0
8[d]	13 mmol TFA	2 mL DCE, 24 h	73%
9	50 mol % I_2	1 mL DMSO, 24 h	[e]
10	50 mol % I_2	1 mL benzene, 3 h	0
11	50 mol % I_2	1 mL THF, 3 h	trace[e]
12	50 mol % I_2	1 mL DCE, 3 h	95%
13[f]	50 mol % I_2	1 mL DCE, 3 h	81%

[a]Unless noted otherwise, reactions were performed on a 0.30 mmol scale using **1a** as a starting material at 80 °C. [b]Isolated yield. [c]Complex mixture formation. [d]The reaction was run at room temperature. [e]Decomposition of the starting material. [f]The reaction was run at 60 °C.

benzene as an oxidizing agent in DMSO or DCE did not produce the compound **2a** (entries 3 and 4). It was also found that using *tert*-butyl hydroperoxide along with CuI in DMSO or CH_3CN gives a complex mixture and the use of DDQ in CH_3CN provided no desired product (entries 5–7). The use of trifluoroacetic acid in DCE at room temperature provides the desired chromone in 73% yield (entry 8), while increasing the temperature up to 80 °C does not provide better yield. The treatment of **1a** with DMSO-I_2 reagent commonly used for the oxidative cyclization of 2′-hydroxychalcones to flavones results in decomposition of the starting material (entry 9). Furthermore, the use of iodine catalyst in benzene and THF provides no product and only a trace amount of **2a**, respectively (entries 10 and 11). When iodine catalyst was used in DCE solvent at 80 °C, the reaction proceeded well and we successfully achieved the desired chromone in 95% yield within 3 h (entry 12). Lowering the temperature from 80 to 60 °C dropped the yield to 81% (entry 13).

To study the effect of a protecting group at the ortho hydroxyl group of α-aroylketene dithioacetal, other protecting groups such as allyl, methoxymethyl, and methyl were used instead of the benzyl group (Scheme 2). When the ortho hydroxyl group was protected with allyl, methoxymethyl, and methyl group, 74%, 70%, and 0% yields of 2-(methylthio)-4*H*-chromen-4-one **2a** were obtained, respectively. Therefore, further synthesis was carried out with 1-(2-benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones as precursor following the optimal condition (entry 12).

Initially, we examined the scope of the oxidative cyclization reaction with respect to various 1-(2-(benzyloxy)aryl)-3,3-bis(methylthio)prop-2-en-1-ones. The reaction proceeded well and the desired chromones were achieved in good to excellent yields as illustrated in Scheme 3. The structure of **2g** was confirmed using single-crystal X-ray diffraction (see Figure S1, Supporting Information (SI)). It was noticed that 1-(2/1-benzyloxy-naphthalen-1/2-yl)-3,3-bis-methylsulfanyl-prope-

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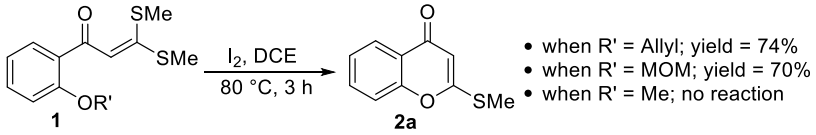
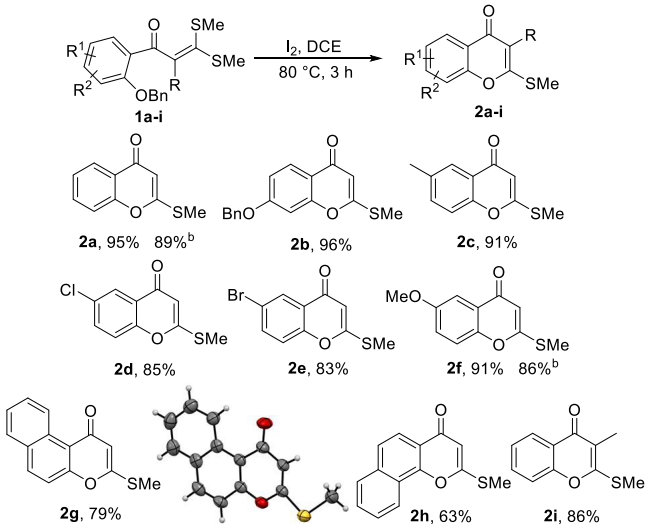
Scheme 2. Examination of Various Protecting Groups for the Synthesis of 2-(Methylthio)-4*H*-chromen-4-one[a]



[a]All reactions were performed by stirring **1** (0.50 mmol) and I_2 (0.25 mmol) in DCE (1 mL) at 80 °C for 3 h.

Scheme 3. Synthesis of 2-(Methylthio)-4*H*-chromen-4-ones from 1-(2-Benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones[a]



[a]All reactions were performed by stirring **1** (1.0 mmol) and I_2 (0.50 mmol) in DCE (2 mL) at 80 °C for 3 h. [b]The procedure was scaled up to a gram scale.

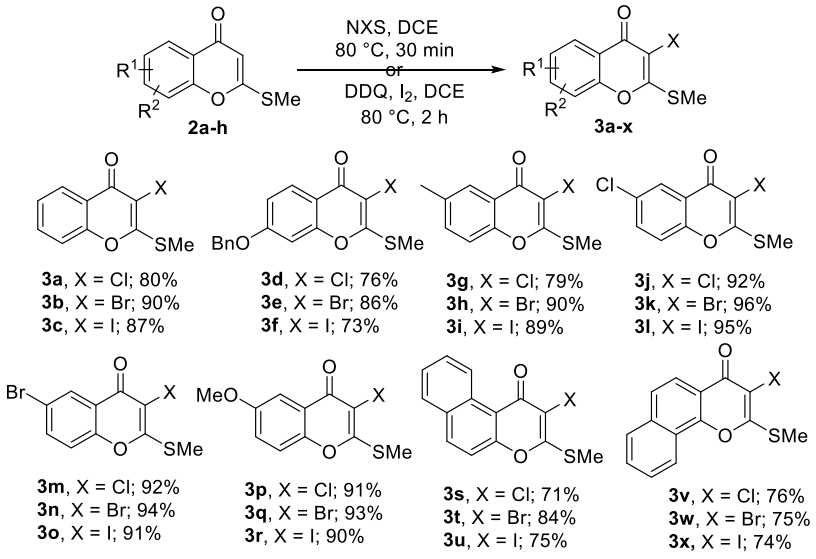
nones **1g** and **1h** provided relatively lower yields of the desired products as compared to 1-(2-benzyloxyphenyl)-3,3-bis-methylsulfanyl-propenones **1a–f** and **1i**, probably due to involvement of an additional electronic factor. Then, we have developed the practical synthesis of some chromone derivatives via conducting scale-up experiments. Thusly, chromone products **2a** and **2f** were obtained in yields of 89% (0.52 g) and 86% (1.06 g), respectively.

Next, we have synthesized 3-chloro/bromo-chromones in high yields using NCS/NBS at 80 °C. A trial using NIS also provides the corresponding iodinated product in a competitive yield. Since NIS is quite an expensive reagent as compared to NCS and NBS, a new method for the synthesis of 3-iodo-chromones was established by heating **2a–h** with DDQ and iodine in DCE for 2 h at 80 °C (Scheme 4).

Further, we investigated the halogenation under a one-pot approach from 1-(2-benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones. After monitoring the complete formation of 2-(methylthio)-4*H*-chromen-4-ones, NBS was added to the reaction mixture under the same reaction condition, and surprisingly, major 3-bromo-chromone along with minor 3-iodo-chromone was observed. An attempt to quench the excess of iodine prior to addition of NBS using sodium thiosulfate was unsuccessful. Moreover, addition of NCS under similar reaction conditions provides 3-iodo-chromone along with a trace of 3-chloro-chromone. However, 3-iodo-chromones were selectively afforded by addition of iodine, followed by dropwise addition of a solution of NCS in DCE (Scheme 5).

In order to study the effect of iodine during one-pot halogenation, we independently carried out the reaction of 6-methyl-2-(methylthio)-4*H*-chromen-4-one **2c** with 1 equiv of iodine and 0.5 equiv of NCS/NBS at room temperature and afforded 3-iodo-6-methyl-2-(methylthio)-4*H*-chromen-4-one **3i** selectively (Scheme 6).

Scheme 4. Scope of Synthesis of 3-Halo-2-(methylthio)-4*H*-chromen-4-ones[a,b]



[a]Bromination and chlorination reactions were performed by stirring **2** (0.30 mmol) and (NBS or NCS) (0.36 mmol) in DCE (1 mL) at 80 °C for 30 min. [b]Iodination reaction was performed by stirring **2** (0.30 mmol), DDQ (0.36 mmol), and I_2 (0.36 mmol) in DCE (1 mL) at 80 °C for 2 h.

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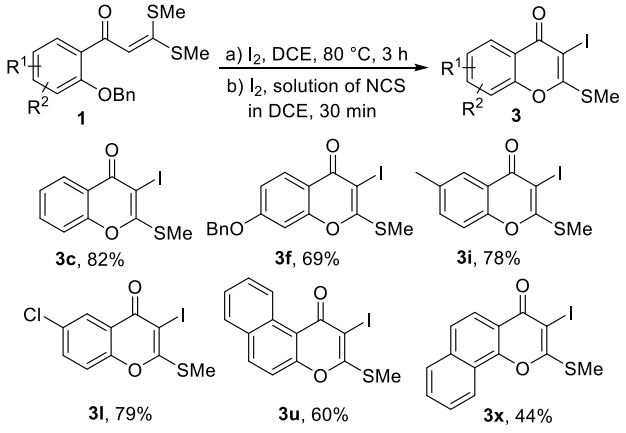
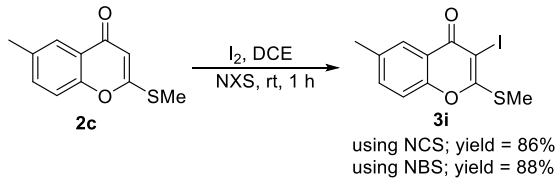
Scheme 5. Scope of One-Pot Synthesis of 3-Iodo-2-(methylthio)-4*H*-chromen-4-ones[a]



[a]The reaction was performed by stirring **1** (0.30 mmol) and I_2 (0.15 mmol) in DCE (1 mL) at 80 °C for 3 h, and subsequent treatment with I_2 (0.15 mmol) and a solution of NCS (0.22 mmol) in DCE (0.5 mL) at 80 °C for 30 min.

Scheme 6. Iodination Using NCS/NBS and Iodine at Room Temperature[a] **(Synthesis of 3-Iodo-6-methyl-2-(methylthio)-4*H*-chromen-4-one)**



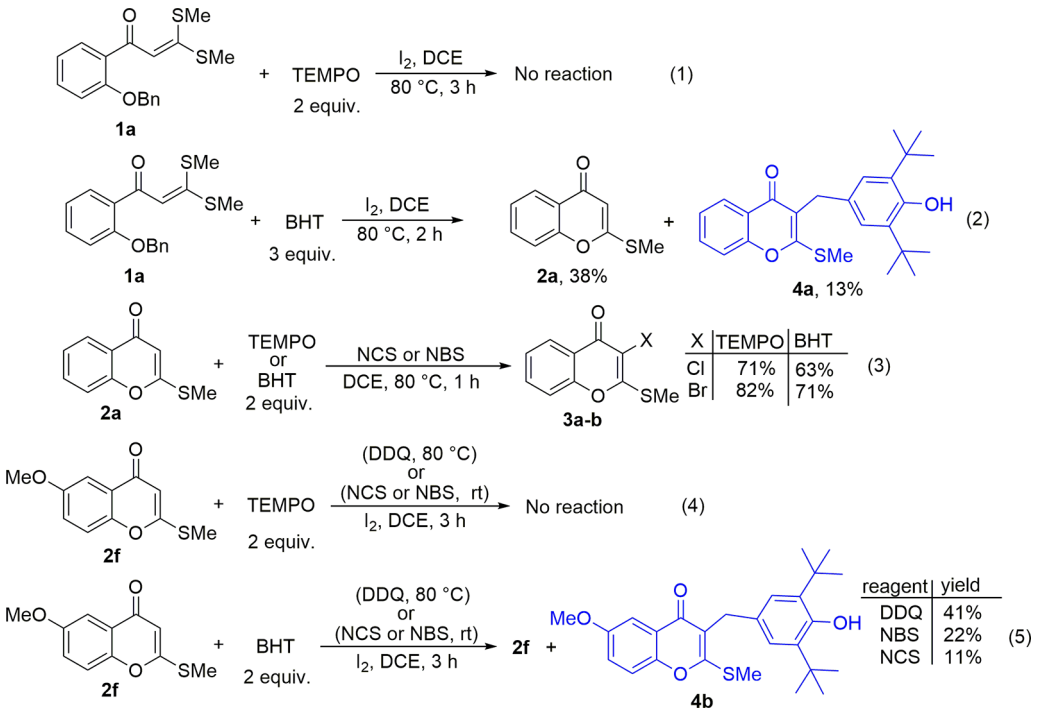
[a]Iodination reaction was performed by stirring **2c** (0.30 mmol), I_2 (0.30 mmol), and NXS (0.15 mmol) in DCE (1 mL) at room temperature for 1 h.

The mechanism of the oxidative cyclization was investigated and established by the control experiments (Scheme 7, eqs 1 and 2). Initially, we performed the cyclization reaction in the presence of a radical scavenger, (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) or butylated hydroxytoluene (BHT), under standard conditions. The reaction was completely inhibited in the presence of TEMPO, whereas the product yield was significantly lowered in the presence of BHT (Scheme 7, eqs 1 and 2). In addition, we have identified the BHT-trapped chromone compound **4a**, indicating that a radical pathway might be involved in this transformation. Therefore, the free radical mechanism starts with abstraction of one electron from the ethereal oxygen lone pair of compound **1** to form intermediate **I**, which undergoes cyclization to generate radical cation **II**, followed by deprotection of the benzyl group to provide radical intermediate **III** and benzyl iodide. The removal of the SMe radical from intermediate **III** results in the formation of chromone **2**, and the SMe radical reacts with benzyl iodide to form benzyl(methyl)sulfane (Scheme 8).

To probe the mechanism, starting material **1l** was used and we have isolated 2-(1,3-dithiolan-2-ylidene)-1-(2-hydroxyphenyl)ethan-1-one **5** in 79% yield within 2 h. Although, when the reaction was carried out for a longer time (12 h), 2-((2-(benzylthio)ethyl)thio)-4*H*-chromen-4-one **2l** was isolated in 19% yield. This result confirms that the SMe group was eliminated as benzyl(methyl)sulfane.

The mechanism of the halogenation reaction was established by the control experiments (Scheme 7, eqs 3–5). Radical scavenger experiment of **2a** with TEMPO or BHT using NXS in DCE at 80 °C provide the desired products **3a–b** in high yields (Scheme 7, eq 3), indicating that radical species is not involved and the reaction proceeds via an electrophilic substitution pathway. The halogenation reactions of compound **2f** using DDQ/I_2 at 80 °C or NXS/I_2 at room

Scheme 7. Control Experiments



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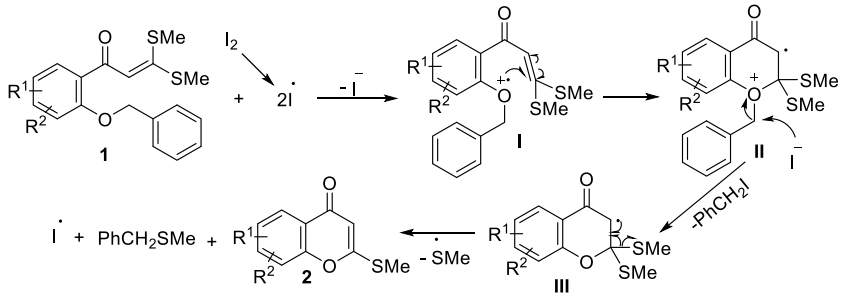
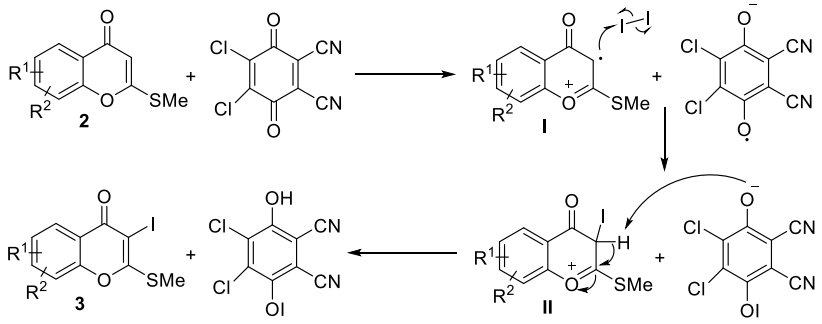
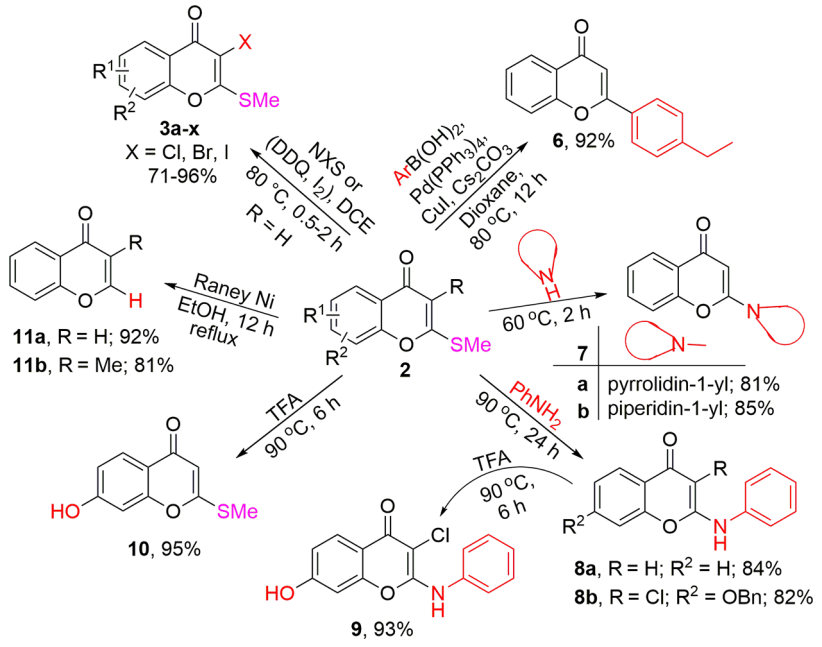
Scheme 8. Proposed Reaction Mechanism for Intramolecular Cyclization of 1-(2-Benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones Using Iodine in DCE



Scheme 9. Proposed Reaction Mechanism for Iodination of 2-(Methylthio)-4*H*-chromen-4-ones Using I_2 and DDQ



Scheme 10. Synthetic Utility of 2-(Methylthio)-4*H*-chromen-4-ones



temperature were totally inhibited in the presence of TEMPO or BHT. We have also identified the BHT-trapped chromone compound in all cases (Scheme 7, eqs 4 and 5), indicating that a radical pathway might be involved in this reaction.

A plausible reaction mechanism for the iodination of 2-(methylthio)-4*H*-chromen-4-ones with DDQ and I_2 is shown in (Scheme 9). A single electron transfer from **2** to DDQ results in the formation of radical cation **I**, which reacts with iodine to generate the cation intermediate **II**, followed by proton transfer to provide product **3**. A similar reaction mechanism is proposed for iodination using NXS and I_2 (see Scheme S1, SI).

To demonstrate the utility of 2-(methylthio)-4*H*-chromen-4-ones, various kinds of chemical reactions were conducted as shown in Scheme 10. Synthesis of halogenated chromones **3a–x** is considered to be an example of an electrophilic substitution reaction at the C-3 position of chromones. The Liebeskind–Srogl coupling reaction was carried out using the previously reported literature[24] to provide 4′-ethylflavone **6** in 92% yield. Nucleophilic substitution reaction at the C-2 position was performed using primary and secondary amines to

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provide the corresponding aminated chromones in very good yields. Deprotection of the benzyl group from compound **8b** and **2b** was carried out in the presence of an excess amount of TFA to give 3-chloro-7-hydroxy-2-(phenylamino)-4*H*-chromen-4-one **9** and 7-hydroxy-2-(methylthio)-4*H*-chromen-4-one **10** in 93% and 95% yields, respectively. On the basis of a previously reported procedure,[25] we have achieved reductive desulfuration of 2-(methylthio)-4*H*-chromen-4-one **2a** and 3-methyl-2-(methylthio)-4*H*-chromen-4-one **2i** in very good yields through refluxing with freshly prepared Raney nickel in ethanol for 12 h.

CONCLUSION

In summary, we have developed an efficient method for the synthesis of 2-(methylthio)-4*H*-chromen-4-ones via oxidative cyclization of easily accessible precursors 1-(2-benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones under mild conditions in high yields. Bromination and chlorination of 4*H*-chromen-4-ones at the C-3 position proceeded through an electrophilic substitution reaction. Iodination was achieved through a free radical pathway. One- and two-pot approaches were developed to access iodinated chromones using I_2/NCS and I_2/DDQ, respectively, at 80 °C. Iodination using I_2/NXS at room temperature was the most interesting finding, where no chlorination or bromination occurs as side reaction and selective iodination was achieved. Various kinds of chemical reactions were conducted to demonstrate the synthetic potential of 2-(methylthio)-4*H*-chromen-4-ones. During synthetic applicability, we have achieved 3-methyl-4*H*-chromen-4-one (CAS No. 85-90-5) in good yield by simple reductive desulfuration, which is an expensive reagent.

EXPERIMENTAL SECTION

General Information. Commercially available reagent and solvent purchased by Sigma-Aldrich and Alfa Aesar were used directly without further purification. Reactions were monitored by analytical thin-layer chromatography (TLC). All reactions were conducted using dried glassware. IR spectra were recorded on an IR spectrophotometer, and stretching frequencies were reported in wavenumber (cm^{-1}). The ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ solution using chloroform peak (7.24 ppm for ^1H and 77.0 ppm for ^{13}C) as reference. Only spectra of compounds **9** and **10** were recorded in DMSO-d_6 solution using the DMSO peak (2.50 ppm for ^1H and 39.52 ppm for ^{13}C) as reference. Compounds **2a**,[26] **6**,[27] **7a,b**,[28] and **11a,b**[29] are known; the remaining compounds are newly synthesized. The coupling constants *J* are reported in Hz, and signal patterns are reported as s, singlet; br, broad; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet doublets. High-resolution mass spectra were recorded on a quadrupole-time-of-flight (Q-TOF) mass spectrometer equipped with an electrospray ion source (ESI-TOF).

General Procedure for the Synthesis of 1-(2-Benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones (1a−k). To a stirred suspension of NaH (8.0 mmol) (previously washed with hexane in order to remove mineral oil) in THF (8.0 mL) was added a solution of functionalized acetophenones (2.0 mmol) in THF (2.0 mL) dropwise within 15 min at 0 °C. The reaction mixture was stirred for 20 min at 0 °C; then carbon disulfide (2.40 mmol) was added dropwise within 15 min at 0 °C. The reaction mixture was stirred for 30 min at 0 °C; then methyl iodide (4.40 mmol) was added dropwise during 15 min at 0 °C. The reaction mixture was stirred for 15 min at 0 °C, then warmed to room temperature, and stirred for 5−6 h. Completion of the reaction was monitored by TLC. After completion, THF was removed under vacuum, and ice-cold water (20.0 mL) was added to the mixture and stirred well. The formed solid was filtered and was washed with water (20.0 mL × 2), dried, and recrystallized from hexane.

Synthetic Procedure for 1-(2-(Benzyloxy)phenyl)-2-(1,3-dithiolan-2-ylidene)ethan-1-one 1l. To a stirred suspension of potassium *tert*-butoxide (898 mg, 8.0 mmol) in dry THF (3.0 mL) at 0 °C was dropwise added a dry THF solution (3.0 mL) of 1-(2-(benzyloxy)phenyl)ethan-1-one (453 mg, 2.0 mmol) and carbon disulfide (145 mg, 2.40 mmol). The reaction mixture was vigorously stirred at 0 °C for 90 min. To this suspension was added a dry THF solution (2 mL) of 1,2-dibromoethane (379 mg, 4.40 mmol) dropwise within 10 min at 0 °C. The reaction mixture was stirred for 6 h. After completion of the reaction, the mixture was poured into a saturated aqueous solution of ammonium chloride with crushed ice. Then, the aqueous solution was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with brine (1 × 20 mL), dried, and then concentrated under vacuum to obtain the crude product. Pure product was obtained by silica gel column chromatography using 10% EtOAc/hexane.

General Procedure for the Synthesis of 2-(Methylthio)-4*H*-chromen-4-ones (2a−i). A 10 mL Schlenk tube equipped with a magnetic stirring bar was charged with 1-(2-benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones **1a−i** (1 mmol) and DCE (2 mL), followed by addition of iodine (0.50 mmol). The reaction mixture was stirred at 80 °C (oil bath) for 3 h. After completion, the reaction mixture was quenched with 3% $Na_2S_2O_3$ (5 mL), diluted with brine (10 mL), and extracted with DCM (15 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified through silica gel column chromatography using 10% EtOAc/hexane to afford the desired chromones.

Gram-Scale Procedure for the Synthesis of 2-(Methylthio)-4*H*-chromen-4-ones 2a. A 50 mL round-bottom flask equipped with a magnetic stirring bar was charged with 1-(2-(benzyloxy)-phenyl)-3,3-bis(methylthio)prop-2-en-1-one **1a** (1 g, 3.02 mmol) and DCE (6 mL), followed by addition of iodine (1.5 mmol). The reaction mixture was stirred at 80 °C (oil bath) for 4−5 h. After completion, the reaction mixture was quenched with 3% $Na_2S_2O_3$ (50 mL), diluted with brine (50 mL), and extracted with DCM (50 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified through silica gel column chromatography using 10% EtOAc/hexane to afford the desired chromone **2a** in 89% yield (0.52 g).

Gram-Scale Procedure for the Synthesis of 6-Methoxy-2-(methylthio)-4*H*-chromen-4-one 2f. A 50 mL round-bottom flask equipped with a magnetic stirring bar was charged with 1-(2-(benzyloxy)-5-methoxyphenyl)-3,3-bis(methylthio)prop-2-en-1-one **1f** (2 g, 5.5 mmol) and DCE (10 mL), followed by addition of iodine (2.7 mmol). The reaction mixture was stirred at 80 °C (oil bath) for 4−5 h. After completion, the reaction mixture was quenched with 6% $Na_2S_2O_3$ (100 mL), diluted with brine (100 mL), and extracted with DCM (75 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified through silica gel column chromatography using 10% EtOAc/hexane to afford the desired chromone **2f** in 86% yield (1.06 g).

General Procedure for the Synthesis of 3-Chloro/bromo-2-(methylthio)-4*H*-chromen-4-ones (3a,b, 3d,e, 3g,h, 3j,k, 3m,n, 3p,q, 3s,t, and 3v,w). A solution of 2-(methylthio)-4*H*-chromen-4-ones **2a−h** (0.30 mmol) in DCE (1 mL) was treated with NBS or NCS (0.36 mmol) and then stirred at 80 °C (oil bath) for 30 min. Completion of the reaction was monitored by TLC. After completion, DCE was removed under vacuum, and the crude 3-chloro and 3-bromo-chromones were purified by column chromatography using 5% EtOAc/hexane.

General Procedure for the Synthesis of 3-Iodo-2-(methylthio)-4*H*-chromen-4-ones (3c, 3f, 3i, 3l, 3o, 3r, 3u, and 3x) Using I_2/DDQ. A solution of 2-(methylthio)-4*H*-chromen-4-ones **2a−h** (0.30 mmol) in DCE (1 mL) was treated with DDQ (0.36 mmol) and I_2 (0.36 mmol) in sequence and then stirred at 80 °C (oil bath) for 2 h. After completion, the reaction mixture was quenched with 5% $Na_2S_2O_3$ (5 mL), diluted with brine (10 mL), and extracted with DCM (15 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified through silica gel

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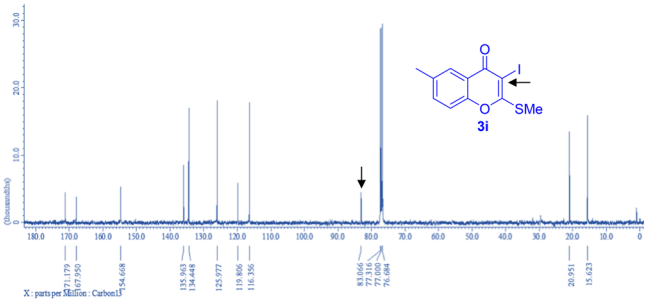
column chromatography using 5% EtOAc/hexane to afford 3-iodo-2-(methylthio)-4*H*-chromen-4-ones.

General Procedure for the One-Pot Synthesis of 3-Iodo-2-(methylthio)-4*H*-chromen-4-ones (3c, 3f, 3i, 3l, 3u, and 3x). A solution of 1-(2-benzyloxy-aryl)-3,3-bis-methylsulfanyl-propenones **1** (0.30 mmol) in DCE (1 mL) was treated with iodine (0.15 mmol) and then stirred at 80 °C (oil bath) for 3 h. The complete formation of chromones **2** was monitored by TLC. Thereafter, I_2 (0.15 mmol) was added to the reaction mixture, followed by dropwise addition of a solution of NCS (0.22 mmol) in DCE (0.5 mL) at 80 °C (oil bath). The reaction mixture was stirred for 30 min. Upon completion, it was quenched with 3−5% $Na_2S_2O_3$ (5 mL), diluted with brine (10 mL), and extracted with DCM (15 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified through silica gel column chromatography using 5% EtOAc/hexane to afford the desired products.

Synthetic Procedure for 3-Iodo-6-methyl-2-(methylthio)-4*H*-chromen-4-one (3i) Using NXS and Iodine at Room Temperature. A solution of 6-methyl-2-(methylthio)-4*H*-chromen-4-one **2c** (62 mg, 0.30 mmol) in DCE (1 mL) was treated with I_2 (76 mg, 0.30 mmol), followed by addition of NCS or NBS (0.5 equiv, 0.15 mmol), and then stirred at room temperaturefor 1 h. After completion, the reaction mixture was quenched with 5% $Na_2S_2O_3$ (5 mL), diluted with brine (10 mL), and extracted with DCM (15 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified through silica gel column chromatography using 5% EtOAc/hexane to afford compound **3i**.

The presence of only the iodinated product was confirmed using a ^{13}C NMR spectrum to prove the selectivity of this method.



General Procedure for the Synthesis of 2-*sec*-Amino-4*H*-chromen-4-ones (7a,b). A mixture of 2-(methylthio)-4*H*-chromen-4-one **2a** (0.20 mmol) and pyrrolidine/piperidine (0.15 mL) was stirred at 60 °C (oil bath) for 2 h. Completion of the reaction was monitored by TLC. After completion, the excess of secondary amine was removed under vacuum and recrystallized from methanol to afford 2-*sec*-amino-4*H*-chromen-4-ones.

General Procedure for the Synthesis of 2-(Phenylamino)-4*H*-chromen-4-ones (8a,b). A mixture of 2-(methylthio)-4*H*-chromen-4-one/7-(benzyloxy)-3-chloro-2-(methylthio)-4*H*-chromen-4-one **2a**/**3d** (0.20 mmol) and aniline (1 mL) was stirred at 90 °C (oil bath) for 24 h. Completion of the reaction was monitored by TLC. After completion, the excess of aniline was removed through silica gel column chromatography using DCM; then the desired product was collected using 20% MeOH/DCM.

General Procedure for the Synthesis of 7-Hydroxy-4*H*-chromen-4-ones (9 and 10). A mixture of 7-(benzyloxy)-2-(methylthio)-4*H*-chromen-4-one/7-(benzyloxy)-3-chloro-2-(phenylamino)-4*H*-chromen-4-one **2b**/**8b** (0.20 mmol) and TFA (1 mL) was stirred at 90 °C (oil bath) for 6 h. Completion of the reaction was monitored by TLC. After completion, the excess of TFA was removed under vacuum and the obtained precipitate was washed with water, filtered, and dried to afford the desired products without further purification.

*1-(2-(Benzyloxy)phenyl)-3,3-bis(methylthio)prop-2-en-1-one (**1a**).* Yield: 97% (641 mg), yellow solid (recrystallized from hexane), mp: 126−128 °C; IR (KBr): 3030, 2918, 1585, 1476, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.84 (d, 1H, J = 7.6 Hz), 7.42−7.29 (m, 6H), 7.04−6.99 (m, 2H), 6.91 (s, 1H), 5.06 (s, 2H), 2.44 (s, 3H), 1.88 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 185.4, 163.9, 156.7, 136.2, 132.5, 131.4, 129.5, 128.5, 128.2, 128.0, 121.1, 114.9, 112.5, 70.6, 16.3, 15.0; HRMS (ESI) m/z calcd for $C_{18}H_{19}O_2S_2$ $[M + H]^+$ 331.0821, found 331.0825.

*1-(2,4-Bis(benzyloxy)phenyl)-3,3-bis(methylthio)prop-2-en-1-one (**1b**).* Yield: 90% (812 mg), white solid (recrystallized from hexane), mp: 135−137 °C; IR (KBr): 3031, 2921, 1589, 1478, 757 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.94 (d, 1H, J = 8.8 Hz), 7.43−7.33 (m, 10H), 6.95 (s, 1H), 6.64 (d, 1H, J = 8.8 Hz), 6.62 (s, 1H), 5.08 (s, 2H), 5.01 (s, 2H), 2.43 (s, 3H), 1.78 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 184.1, 163.0, 162.6, 158.5, 136.3, 136.0, 133.5, 128.6, 128.5, 128.4, 128.1, 127.5, 122.6, 115.1, 106.4, 100.2, 70.8, 70.1, 16.2, 15.1; HRMS (ESI) m/z calcd for $C_{25}H_{25}O_3S_2$ $[M + H]^+$ 437.1240, found 437.1237.

*1-(2-(Benzyloxy)-5-methylphenyl)-3,3-bis(methylthio)prop-2-en-1-one (**1c**).* Yield: 93% (640 mg), white solid (recrystallized from hexane), mp: 117−119 °C; IR (KBr): 3030, 1593, 1483, 762 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.65 (s, 1H), 7.42−7.31 (m, 5H), 7.19 (d, 1H, J = 7.6 Hz), 6.92−6.89 (m, 2H), 5.04 (s, 2H), 2.46 (s, 3H), 2.29 (s, 3H), 1.91 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 185.7, 163.8, 154.7, 136.5, 133.0, 131.8, 130.6, 129.3, 128.6, 128.2, 128.0, 115.0, 112.8, 70.9, 20.3, 16.4, 15.1; HRMS (ESI) m/z calcd for $C_{19}H_{21}O_2S_2$ $[M + H]^+$ 345.0977, found 345.0968.

*1-(2-(Benzyloxy)-5-chlorophenyl)-3,3-bis(methylthio)prop-2-en-1-one (**1d**).* Yield: 95% (693 mg), yellow solid (recrystallized from hexane), mp: 112−113 °C; IR (KBr): 3032, 2918, 1606, 1485, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.80 (d, 1H, J = 2.4 Hz), 7.41−7.30 (m, 6H), 6.93 (d, 1H, J = 8.8 Hz), 6.84 (s, 1H), 5.04 (s, 2H), 2.45 (s, 3H), 1.88 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 183.7, 165.7, 155.2, 135.9, 131.9, 131.2, 130.9, 128.7, 128.4, 128.1, 126.5, 114.3, 114.2, 71.2, 16.4, 15.1; HRMS (ESI) m/z calcd for $C_{18}H_{18}ClO_2S_2$ $[M + H]^+$ 365.0431, found 365.0435.

*1-(2-(Benzyloxy)-5-bromophenyl)-3,3-bis(methylthio)prop-2-en-1-one (**1e**).* Yield: 89% (729 mg), yellow solid (recrystallized from hexane), mp: 106−108 °C; IR (KBr): 3057, 2910, 1573, 1456, 746 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.94 (d, 1H, J = 2.0 Hz), 7.45 (dd, 1H, J = 8.4, 2.0 Hz), 7.40−7.31 (m, 5H), 6.88 (d, 1H, J = 8.4 Hz), 6.83 (s, 1H), 5.04 (s, 2H), 2.45 (s, 3H), 1.90 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 183.6, 165.6, 155.7, 135.8, 134.8, 134.0, 131.3, 128.7, 128.4, 128.1, 114.7, 114.3, 113.8, 71.2, 16.5, 15.1; HRMS (ESI) m/z calcd for $C_{18}H_{18}BrO_2S_2$ $[M + H]^+$ 408.9926, found 408.9920.

*1-(2-(Benzyloxy)-5-methoxyphenyl)-3,3-bis(methylthio)prop-2-en-1-one (**1f**).* Yield: 90% (649 mg), yellow solid (recrystallized from hexane), mp: 96−98 °C; IR (KBr): 3032, 2914, 1597, 1479, 1278, 1037, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.43−7.29 (m, 6H), 6.98 (s, 1H), 6.94 (s, 2H), 5.00 (s, 2H), 3.78 (s, 3H), 2.46 (s, 3H), 1.91 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 184.9, 164.4, 154.0, 151.2, 136.6, 130.3, 128.5, 128.2, 128.1, 119.3, 115.0, 114.9, 114.7, 71.9, 55.7, 16.5, 15.1; HRMS (ESI) m/z calcd for $C_{19}H_{21}O_3S_2$ $[M + H]^+$ 361.0927, found 361.0933.

*1-(2-(Benzyloxy)naphthalen-1-yl)-3,3-bis(methylthio)prop-2-en-1-one (**1g**).* Yield: 96% (728 mg), white solid (recrystallized from hexane), mp: 113−115 °C; IR (KBr): 3028, 2922, 1623, 1469, 748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.83 (d, 1H, J = 8.4 Hz), 7.72 (d, 1H, J = 8.4 Hz), 7.68 (d, 1H, J = 7.6 Hz), 7.38−7.17 (m, 8H), 6.35 (s, 1H), 5.13 (s, 2H), 2.47 (s, 3H), 2.15 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 189.0, 163.7, 152.8, 137.0, 131.5, 130.8, 129.2, 128.4, 127.8, 127.7, 127.1, 127.0, 126.8, 124.7, 124.1, 116.1, 115.1, 71.5, 16.9, 14.9; HRMS (ESI) m/z calcd for $C_{22}H_{21}O_2S_2$ $[M + H]^+$ 381.0977, found 381.0987.

*1-(1-(Benzyloxy)naphthalen-2-yl)-3,3-bis(methylthio)prop-2-en-1-one (**1h**).* Yield: 89% (676 mg), brown viscous liquid (recrystallized from hexane); IR (KBr): 3060, 2922, 1613, 1476, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.29 (m, 1H), 7.89−7.82 (m, 2H), 7.66 (d, 1H, J = 8.8 Hz), 7.55−7.48 (m, 4H), 7.42−7.33 (m, 3H), 7.13 (s, 1H), 4.96 (s, 2H), 2.53 (s, 3H), 2.11 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 186.0, 165.0, 154.0, 136.6, 136.1, 129.3, 128.4, 128.2, 128.1, 128.0, 127.8, 127.6, 126.5, 126.3, 124.2, 122.9, 114.0, 78.3, 16.6, 14.9; HRMS (ESI) m/z calcd for $C_{22}H_{21}O_2S_2$ $[M + H]^+$ 381.0977, found 381.0962.

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*1-(2-(Benzyloxy)phenyl)-2-methyl-3,3-bis(methylthio)prop-2-en-1-one (**1i**).* Yield: 51% (348 mg), yellow viscous liquid (recrystallized from hexane); IR (KBr): 3030, 2919, 1593, 1449, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.75 (d, 1H, J = 7.6 Hz), 7.42−7.29 (m, 6H), 7.03−6.95 (m, 2H), 5.04 (s, 2H), 2.21 (s, 3H), 2.00 (s, 3H), 1.89 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 196.7, 157.7, 147.1, 136.0, 133.3, 132.3, 131.6, 128.7, 128.6, 128.2, 127.8, 120.8, 112.4, 70.7, 20.1, 16.9, 16.1; HRMS (ESI) m/z calcd for $C_{19}H_{21}O_2S_2$ $[M + H]^+$ 345.0977, found 345.0972.

*1-(2-(Allyloxy)phenyl)-3,3-bis(methylthio)prop-2-en-1-one (**1j**).* Yield: 92% (516 mg), white solid (recrystallized from hexane), mp: 50−52 °C; IR (KBr): 3072, 2920, 1598, 1478, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.73 (d, 1H, J = 8.0 Hz), 7.35 (t, 1H, J = 7.6 Hz), 6.98 (t, 1H, J = 7.6 Hz), 6.91 (s, 1H), 6.88 (d, 1H, J = 8.4 Hz), 6.08−5.98 (m, 1H), 5.39 (d, 1H, J = 17.2 Hz), 5.26 (d, 1H, J = 10.4 Hz), 4.55 (d, 2H, J = 5.2 Hz), 2.47 (s, 3H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 185.9, 163.5, 156.3, 132.8, 132.2, 131.1, 130.0, 121.0, 117.9, 114.9, 112.6, 69.2, 17.1, 15.0; HRMS (ESI) m/z calcd for $C_{14}H_{17}O_2S_2$ $[M + H]^+$ 281.0664, found 281.0651.

*1-(2-(Methoxymethoxy)phenyl)-3,3-bis(methylthio)prop-2-en-1-one (**1k**).* Yield: 86% (488 mg), white solid (recrystallized from hexane), mp: 55−57 °C; IR (KBr): 2921, 1597, 1479, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.68 (d, 1H, J = 7.2 Hz), 7.35 (s, 1H), 7.13−7.02 (m, 2H), 6.82 (s, 1H), 5.20 (s, 2H), 3.46 (s, 3H), 2.49 (s, 3H), 2.46 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 186.1, 163.9, 154.9, 132.1, 130.9, 130.6, 122.1, 115.3, 114.5, 95.1, 56.3, 17.2, 15.0; HRMS (ESI) m/z calcd for $C_{13}H_{17}O_3S_2$ $[M + H]^+$ 285.0614, found 285.0611.

*1-(2-(Benzyloxy)phenyl)-2-(1,3-dithiolan-2-ylidene)ethanone (**1l**).* Yield: 52% (342 mg), white solid, eluent (hexane/EtOAc = 9:1), mp: 101−102 °C; IR (KBr): 3065, 2924, 1595, 1483, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.80 (dd, 1H, J = 7.8, 1.8 Hz), 7.49 (s, 1H), 7.44−7.29 (m, 6H), 7.03−6.96 (m, 2H), 5.15 (s, 2H), 3.42 (t, 2H, J = 6.2 Hz), 3.32 (t, 2H, J = 6.2 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 186.3, 165.5, 157.0, 136.4, 132.6, 131.2, 129.1, 128.6, 127.8, 127.1, 121.1, 113.8, 113.0, 70.6, 38.8, 35.3; HRMS (ESI) m/z calcd for $C_{18}H_{17}O_2S_2$ $[M + H]^+$ 329.0664, found 329.0657.

*2-(Methylthio)-4H-chromen-4-one (**2a**).* Yield: 95% (182 mg), eluent (hexane/EtOAc = 9:1); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.13 (d, 1H, J = 8.0 Hz), 7.60 (t, 1H, J = 7.8 Hz), 7.36 (t, 2H, J = 8.8 Hz), 6.19 (s, 1H), 2.52 (s, 3H); HRMS (ESI) m/z calcd for $C_{10}H_9O_2S$ $[M + H]^+$ 193.0318, found 193.0320.

*7-(Benzyloxy)-2-(methylthio)-4H-chromen-4-one (**2b**).* Yield: 96% (286 mg), white solid, eluent (hexane/EtOAc = 9:1), mp: 150−152 °C; IR (KBr): 2925, 1622, 1548, 1439, 1337, 1163, 757 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.03 (dd, 1H, J = 8.8 Hz), 7.42−7.32 (m, 5H), 6.97 (dd, 1H, J = 8.8, 1.6 Hz), 6.84 (d, 1H, J = 1.6 Hz), 6.10 (s, 1H), 5.10 (s, 2H), 2.47 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 175.2, 169.5, 162.9, 158.3, 135.6, 128.7, 128.3, 127.4, 127.1, 117.2, 114.7, 107.1, 101.0, 70.5, 13.8; HRMS (ESI) m/z calcd for $C_{17}H_{15}O_3S$ $[M + H]^+$ 299.0736, found 299.0747.

*6-Methyl-2-(methylthio)-4H-chromen-4-one (**2c**).* Yield: 91% (188 mg), white solid, eluent (hexane/EtOAc = 9:1), mp: 96−98 °C; IR (KBr): 2924, 1651, 1548, 1463, 1356, 1131, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.92 (s, 1H), 7.40 (d, 1H, J = 8.4 Hz), 7.27 (d, 1H, J = 8.4 Hz), 6.17 (s, 1H), 2.51 (s, 3H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 175.8, 169.8, 155.0, 135.2, 134.5, 125.1, 123.0, 116.9, 107.1, 20.8, 13.7; HRMS (ESI) m/z calcd for $C_{11}H_{11}O_2S$ $[M + H]^+$ 207.0474, found 207.0482.

*6-Chloro-2-(methylthio)-4H-chromen-4-one (**2d**).* Yield: 85% (193 mg), white solid, eluent (hexane/EtOAc = 9:1), mp: 126−128 °C; IR (KBr): 2920, 1647, 1541, 1429, 1323, 1143, 723 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.08 (d, 1H, J = 2.8 Hz), 7.53 (dd, 1H, J = 8.8, 2.8 Hz), 7.32 (d, 1H, J = 8.8 Hz), 6.16 (s, 1H), 2.51 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 174.3, 170.5, 155.0, 133.5, 131.2, 125.3, 124.5, 118.9, 107.2, 13.8; HRMS (ESI) m/z calcd for $C_{10}H_8ClO_2S$ $[M + H]^+$ 226.9928, found 226.9936.

*6-Bromo-2-(methylthio)-4H-chromen-4-one (**2e**).* Yield: 83% (225 mg), pale yellow solid, eluent (hexane/EtOAc = 9:1), mp: 113−115 °C; IR (KBr): 2926, 1656, 1544, 1460, 1327, 1141, 765 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.29 (d, 1H, J = 2.0 Hz), 7.71 (dd, 1H, J = 8.8, 2.0 Hz), 7.30 (d, 1H, J = 8.8 Hz), 6.21 (s, 1H), 2.56 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 174.1, 170.4, 155.5, 136.2, 128.5, 124.9, 119.1, 118.6, 107.3, 13.8; HRMS (ESI) m/z calcd for $C_{10}H_8BrO_2S$ $[M + H]^+$ 270.9423, found 270.9425.

*6-Methoxy-2-(methylthio)-4H-chromen-4-one (**2f**).* Yield: 91% (202 mg), yellow solid, eluent (hexane/EtOAc = 9:1), mp: 100−101 °C; IR (KBr): 2943, 1612, 1544, 1427, 1338, 1134, 1244, 1070, 805 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.50 (d, 1H, J = 2.8 Hz), 7.29 (d, 1H, J = 9.2 Hz), 7.17 (dd, 1H, J = 9.2, 2.8 Hz), 6.16 (s, 1H), 3.86 (s, 3H), 2.51 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 175.4, 169.3, 156.8, 151.5, 124.0, 122.8, 118.5, 106.7, 105.2, 55.8, 13.7; HRMS (ESI) m/z calcd for $C_{11}H_{11}O_3S$ $[M + H]^+$ 223.0423, found 223.0428.

*3-(Methylthio)-1H-benzo[f]chromen-1-one (**2g**).* Yield: 79% (192 mg), white solid, eluent (hexane/EtOAc = 9:1), mp: 144−146 °C; IR (KBr): 2923, 1630, 1561, 1438, 1317, 1139, 955, 823, 755 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.98 (d, 1H, J = 8.8 Hz), 8.00 (d, 1H, J = 9.2 Hz), 7.84 (d, 1H, J = 7.6 Hz), 7.71 (t, 1H, J = 7.6 Hz), 7.57 (t, 1H, J = 7.6 Hz), 7.41 (d, 1H, J = 9.2 Hz), 6.32 (s, 1H), 2.53 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 177.8, 166.7, 157.9, 135.0, 130.6, 130.5, 129.1, 128.1, 127.1, 126.5, 116.8, 116.6, 110.5, 13.8; HRMS (ESI) m/z calcd for $C_{14}H_{11}O_2S$ $[M + H]^+$ 243.0474, found 243.0482.

*2-(Methylthio)-4H-benzo[h]chromen-4-one (**2h**).* Yield: 63% (152 mg), yellow solid, eluent (hexane/EtOAc = 9:1), mp: 100−102 °C; IR (KBr): 2924, 1621, 1548, 1437, 1343, 1164, 914, 824, 757 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.31 (d, 1H, J = 7.2 Hz), 8.06 (d, 1H, J = 8.4 Hz), 7.85 (d, 1H, J = 7.2 Hz), 7.70−7.60 (m, 3H), 6.34 (s, 1H), 2.63 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 175.5, 168.6, 153.8, 135.5, 129.0, 127.9, 127.0, 125.1, 123.1, 121.7, 120.5, 119.4, 108.6, 13.8; HRMS (ESI) m/z calcd for $C_{14}H_{11}O_2S$ $[M + H]^+$ 243.0474, found 243.0478.

*3-Methyl-2-(methylthio)-4H-chromen-4-one (**2i**).* Yield: 86% (178 mg), white solid, eluent (hexane/EtOAc = 9:1), mp: 100−102 °C; IR (KBr): 3012, 1617, 1551, 1466, 1366, 1216, 751 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.18 (dd, 1H, J = 7.6, 1.2 Hz), 7.57 (t, 1H, J = 7.8 Hz), 7.38−7.33 (m, 2H), 2.62 (s, 3H), 2.05 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 175.0, 162.7, 156.5, 132.6, 126.2, 125.0, 122.6, 116.8, 116.3, 13.2, 10.3; HRMS (ESI) m/z calcd for $C_{11}H_{11}O_2S$ $[M + H]^+$ 207.0474, found 207.0476.

*2-((2-(Benzylthio)ethyl)thio)-4H-chromen-4-one (**2l**).* Yield: 19% (62 mg), viscous liquid, eluent (hexane/EtOAc = 9:1); IR (KBr): 2923, 1649, 1550, 1461, 1348, 1130, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.12 (dd, 1H, J = 8.4, 2.0 Hz), 7.49 (t, 1H, J = 8.0 Hz), 7.32−7.06 (m, 8H), 3.85 (s, 2H), 3.40 (t, 2H, J = 7.6 Hz), 2.93 (t, 2H, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 174.8, 162.3, 156.3, 139.1, 133.1, 128.7, 128.3, 126.4, 126.2, 125.3, 122.9, 121.7, 116.7, 38.6, 31.0, 30.1; HRMS (ESI) m/z calcd for $C_{18}H_{17}O_2S_2$ $[M + H]^+$ 329.0664, found 329.0671.

*3-Chloro-2-(methylthio)-4H-chromen-4-one (**3a**).* Yield: 80% (55 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 144−146 °C; IR (KBr): 2925, 2854, 1644, 1525, 1463, 1353, 1320, 1215, 960, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, 1H, J = 8.0 Hz), 7.63 (t, 1H, J = 7.8 Hz), 7.40 (t, 2H, J = 4.4 Hz), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.5, 164.8, 156.0, 133.3, 126.4, 125.7, 122.3, 116.7, 115.0, 13.3; HRMS (ESI) m/z calcd for $C_{10}H_8ClO_2S$ $[M + H]^+$ 226.9928, found 226.9930.

*3-Bromo-2-(methylthio)-4H-chromen-4-one (**3b**).* Yield: 90% (73 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 175−177 °C; IR (KBr): 2924, 2854, 1646, 1516, 1463, 1352, 1320, 950, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, 1H, J = 7.2 Hz), 7.62 (t, 1H, J = 7.4 Hz), 7.39 (t, 2H, J = 7.2 Hz), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.7, 166.0, 156.1, 133.3, 126.6, 125.9, 121.9, 116.8, 105.7, 14.1; HRMS (ESI) m/z calcd for $C_{10}H_8BrO_2S$ $[M + H]^+$ 270.9423, found 270.9426.

*3-Iodo-2-(methylthio)-4H-chromen-4-one (**3c**).* Yield: 87% (83 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 200−202 °C; IR (KBr): 2924, 2852, 1637, 1504, 1463, 1347, 1317, 938, 757 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.20 (dd, 1H, J = 8.4, 1.6 Hz), 7.64

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(t, 1H, J = 7.2 Hz), 7.43−7.40 (m, 2H), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 171.2, 168.2, 156.2, 133.3, 126.8, 125.9, 119.9, 116.6, 83.2, 15.7; HRMS (ESI) m/z calcd for $C_{10}H_8IO_2S$ $[M + H]^+$ 318.9284, found 318.9284.

7-(Benzyloxy)-3-chloro-2-(methylthio)-4H-chromen-4-one (**3d**). Yield: 76% (76 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 162−164 °C; IR (KBr): 2925, 2854, 1644, 1620, 1436, 1311, 1268, 1101, 763 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.05 (d, 1H, J = 8.8 Hz), 7.43−7.32 (m, 5H), 6.99 (dd, 1H, J = 8.8, 1.6 Hz), 6.85 (d, 1H, J = 1.6 Hz), 5.11 (s, 2H), 2.60 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.0, 163.9, 162.7, 157.4, 135.4, 128.7, 128.4, 127.5, 127.5, 116.1, 115.1, 114.7, 100.6, 70.6, 13.3; HRMS (ESI) m/z calcd for $C_{17}H_{14}ClO_3S$ $[M + H]^+$ 333.0347, found 333.0350.

7-(Benzyloxy)-3-bromo-2-(methylthio)-4H-chromen-4-one (**3e**). Yield: 86% (97 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 143−144 °C; IR (KBr): 2925, 2855, 1642, 1618, 1436, 1308, 1271, 1099, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.11 (d, 1H, J = 9.2 Hz), 7.43−7.33 (m, 5H), 7.04 (dd, 1H, J = 9.2, 2.4 Hz), 6.89 (d, 1H, J = 2.4 Hz), 5.13 (s, 2H), 2.62 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.2, 165.0, 162.7, 157.5, 135.4, 128.7, 128.4, 127.8, 127.5, 115.7, 115.1, 105.5, 100.6, 70.6, 14.1; HRMS (ESI) m/z calcd for $C_{17}H_{14}BrO_3S$ $[M + H]^+$ 376.9847, found 376.9858.

7-(Benzyloxy)-3-iodo-2-(methylthio)-4H-chromen-4-one (**3f**). Yield: 73% (93 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 152−154 °C; IR (KBr): 2923, 2854, 1617, 1585, 1493, 1434, 1304, 1270, 1092, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.09 (d, 1H, J = 9.2 Hz), 7.43−7.33 (m, 5H), 7.02 (dd, 1H, J = 9.2, 2.4 Hz), 6.88 (d, 1H, J = 2.4 Hz), 5.13 (s, 2H), 2.61 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 170.7, 167.3, 162.8, 157.9, 135.5, 128.8, 128.5, 128.2, 127.5, 115.1, 114.1, 100.5, 83.3, 70.8, 15.6; HRMS (ESI) m/z calcd for $C_{17}H_{14}IO_3S$ $[M + H]^+$ 424.9703, found 424.9696.

3-Chloro-6-methyl-2-(methylthio)-4H-chromen-4-one (**3g**). Yield: 79% (57 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 154−155 °C; IR (KBr): 2925, 2852, 1644, 1527, 1481, 1317, 1102, 963, 762 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.99 (s, 1H), 7.44 (dd, 1H, J = 8.8, 2.0 Hz), 7.32 (d, 1H, J = 8.8 Hz), 2.64 (s, 3H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.6, 164.7, 154.4, 135.9, 134.4, 125.7, 122.0, 116.7, 114.8, 20.9, 13.3; HRMS (ESI) m/z calcd for $C_{11}H_{10}ClO_2S$ $[M + H]^+$ 241.0085, found 241.0091.

3-Bromo-6-methyl-2-(methylthio)-4H-chromen-4-one (**3h**). Yield: 90% (78 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 167−169 °C; IR (KBr): 2924, 2855, 1642, 1520, 1478, 1312, 1095, 950, 764 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.98 (d, 1H, J = 2.0 Hz), 7.43 (dd, 1H, J = 8.8, 2.0 Hz), 7.31 (d, 1H, J = 8.8 Hz), 2.63 (s, 3H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.8, 166.0, 154.5, 136.2, 134.6, 125.9, 121.7, 116.6, 105.5, 20.9, 14.1; HRMS (ESI) m/z calcd for $C_{11}H_{10}BrO_2S$ $[M + H]^+$ 284.9579, found 284.9586.

3-Iodo-6-methyl-2-(methylthio)-4H-chromen-4-one (**3i**). Yield: 89% (89 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 174−175 °C; IR (KBr): 2924, 2854, 1640, 1512, 1467, 1307, 1086, 942, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.95 (s, 1H), 7.43 (dd, 1H, J = 8.4, 2.0 Hz), 7.29 (d, 1H, J = 8.8 Hz), 2.62 (s, 3H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 171.2, 168.0, 154.7, 136.0, 134.5, 126.0, 119.8, 116.4, 83.1, 21.0, 15.6; HRMS (ESI) m/z calcd for $C_{11}H_{10}IO_2S$ $[M + H]^+$ 332.9441, found 332.9431.

3,6-Dichloro-2-(methylthio)-4H-chromen-4-one (**3j**). Yield: 92% (72 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 196−198 °C; IR (KBr): 2961, 2918, 1645, 1514, 1423, 1340, 1303, 1207, 956, 763 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.16 (d, 1H, J = 2.8 Hz), 7.57 (dd, 1H, J = 8.8, 2.8 Hz), 7.38 (d, 1H, J = 8.8 Hz), 2.65 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.3, 165.4, 154.3, 133.5, 131.8, 125.8, 123.5, 118.6, 115.1, 13.4; HRMS (ESI) m/z calcd for $C_{10}H_7Cl_2O_2S$ $[M + H]^+$ 260.9538, found 260.9545.

3-Bromo-6-chloro-2-(methylthio)-4H-chromen-4-one (**3k**). Yield: 96% (88 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 220−222 °C; IR (KBr): 2927, 2848, 1641, 1510, 1417, 1311, 1307, 1298, 937, 767 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, 1H, J = 2.4 Hz), 7.58 (dd, 1H, J = 9.2, 2.4 Hz), 7.38 (d, 1H, J = 9.2 Hz), 2.65 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.5, 166.4, 154.4, 133.5, 131.8, 126.0, 122.9, 118.6, 105.6, 14.2; HRMS (ESI) m/z calcd for $C_{10}H_7BrClO_2S$ $[M + H]^+$ 304.9033, found 304.9024.

6-Chloro-3-iodo-2-(methylthio)-4H-chromen-4-one (**3l**). Yield: 95% (101 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 218−220 °C; IR (KBr): 2927, 2850, 1635, 1498, 1456, 1334, 1298, 1242, 937, 767 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.16 (d, 1H, J = 2.4 Hz), 7.58 (dd, 1H, J = 9.2, 2.4 Hz), 7.38 (d, 1H, J = 9.2 Hz), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 170.0, 168.6, 154.7, 133.5, 131.8, 126.2, 121.1, 118.4, 83.0, 15.7; HRMS (ESI) m/z calcd for $C_{10}H_7ClIO_2S$ $[M + H]^+$ 352.8894, found 352.8899.

6-Bromo-3-chloro-2-(methylthio)-4H-chromen-4-one (**3m**). Yield: 92% (84 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 195−197 °C; IR (KBr): 2951, 2920, 1649, 1510, 1429, 1340, 1301, 1205, 954, 765 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.32 (d, 1H, J = 2.4 Hz), 7.71 (dd, 1H, J = 9.2, 2.4 Hz), 7.32 (d, 1H, J = 9.2 Hz), 2.65 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.2, 165.4, 154.7, 136.2, 129.0, 123.8, 119.2, 118.9, 115.1, 13.4; HRMS (ESI) m/z calcd for $C_{10}H_7BrClO_2S$ $[M + H]^+$ 304.9033, found 304.9039.

3,6-Dibromo-2-(methylthio)-4H-chromen-4-one (**3n**). Yield: 94% (99 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 224−225 °C; IR (KBr): 2929, 2854, 1645, 1504, 1417, 1336, 1296,1203, 948, 763 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.33 (d, 1H, J = 2.4 Hz), 7.72 (dd, 1H, J = 9.2, 2.4 Hz), 7.32 (d, 1H, J = 9.2 Hz), 2.65 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 168.4, 166.5, 154.9, 136.3, 129.1, 123.2, 119.3, 118.8, 105.6, 14.2; HRMS (ESI) m/z calcd for $C_{10}H_7Br_2O_2S$ $[M + H]^+$ 348.8528, found 348.8537.

6-Bromo-3-iodo-2-(methylthio)-4H-chromen-4-one (**3o**). Yield: 91% (108 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 200−202 °C; IR (KBr): 3007, 2912, 1635, 1494, 1456, 1379, 1338, 1292, 931, 763 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.32 (d, 1H, J = 2.4 Hz), 7.72 (dd, 1H, J = 8.4, 2.4 Hz), 7.31 (d, 1H, J = 8.4 Hz), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.9, 168.6, 155.2, 136.3, 129.3, 121.5, 119.2, 118.6, 83.0, 15.7; HRMS (ESI) m/z calcd for $C_{10}H_7BrIO_2S$ $[M + H]^+$ 396.8389, found 396.8382.

3-Chloro-6-methoxy-2-(methylthio)-4H-chromen-4-one (**3p**). Yield: 91% (70 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 196−170 °C; IR (KBr): 2956, 2929, 1633, 1514, 1438, 1333, 1307, 1240, 1095, 950, 744 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.55 (d, 1H, J = 3.2 Hz), 7.34 (d, 1H, J = 9.2 Hz), 7.20 (dd, 1H, J = 9.2, 3.2 Hz), 3.87 (s, 3H), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.4, 164.5, 157.3, 151.0, 123.2, 123.0, 118.3, 114.5, 105.7, 56.0, 13.3; HRMS (ESI) m/z calcd for $C_{11}H_{10}ClO_3S$ $[M + H]^+$ 257.0034, found 257.0040.

3-Bromo-6-methoxy-2-(methylthio)-4H-chromen-4-one (**3q**). Yield: 93% (84 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 164−166 °C; IR (KBr): 2999, 2933, 1624, 1506, 1471, 1328, 1301, 1290, 1193, 1020, 948, 736 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.46 (d, 1H, J = 3.2 Hz), 7.27 (d, 1H, J = 9.2 Hz), 7.14 (dd, 1H, J = 9.2, 3.2 Hz), 3.83 (s, 3H), 2.59 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.4, 165.5, 157.2, 150.9, 122.8, 122.4, 118.2, 105.7, 104.9, 55.9, 14.0; HRMS (ESI) m/z calcd for $C_{11}H_{10}BrO_3S$ $[M + H]^+$ 300.9529, found 300.9525.

3-Iodo-6-methoxy-2-(methylthio)-4H-chromen-4-one (**3r**). Yield: 90% (94 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 180−182 °C; IR (KBr): 2999, 2924, 1610, 1502, 1467, 1325, 1294, 1259, 1020, 941, 732 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.51 (d, 1H, J = 3.2 Hz), 7.31 (d, 1H, J = 9.2 Hz), 7.17 (dd, 1H, J = 9.2, 3.2 Hz), 3.85 (s, 3H), 2.61 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 171.0, 167.8, 157.3, 151.3, 122.9, 120.8, 118.0, 106.1, 82.6, 55.9, 15.6; HRMS (ESI) m/z calcd for $C_{11}H_{10}IO_3S$ $[M + H]^+$ 348.9390, found 348.9394.

2-Chloro-3-(methylthio)-1H-benzo[f]chromen-1-one (**3s**). Yield: 71% (59 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 158−160 °C; IR (KBr): 2924, 2855, 1629, 1540, 1461, 1384, 1262, 1010, 757 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 10.01 (d, 1H, J = 8.8 Hz), 8.04 (d, 1H, J = 8.8 Hz), 7.87 (d, 1H, J = 8.4 Hz), 7.75 (t, 1H, J = 8.0 Hz), 7.61 (t, 1H, J = 7.6 Hz), 7.44 (d, 1H, J = 9.2 Hz), 2.68 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 171.2, 161.7, 157.2, 135.2, 130.8, 130.4, 129.5, 128.2, 127.2, 126.9, 117.7, 116.3, 115.6, 13.3;

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HRMS (ESI) m/z calcd for $C_{14}H_{10}ClO_2S$ $[M + H]^+$ 277.0085, found 277.0094.

2-Bromo-3-(methylthio)-1H-benzo[f]chromen-1-one (**3t**). Yield: 84% (81 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 196−198 °C; IR (KBr): 2923, 2855, 1629, 1530, 1461, 1377, 1288, 990, 813, 759 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 10.01 (d, 1H, J = 8.8 Hz), 8.05 (d, 1H, J = 8.8 Hz), 7.87 (d, 1H, J = 7.6 Hz), 7.74 (t, 1H, J = 8.0 Hz), 7.61 (t, 1H, J = 7.6 Hz), 7.45 (d, 1H, J = 9.2 Hz), 2.68 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 171.2, 163.0, 157.2, 135.2, 130.7, 130.2, 129.3, 128.2, 127.2, 126.8, 116.1, 114.8, 108.8, 14.0; HRMS (ESI) m/z calcd for $C_{14}H_{10}BrO_2S$ $[M + H]^+$ 320.9585, found 320.9594.

2-Iodo-3-(methylthio)-1H-benzo[f]chromen-1-one (**3u**). Yield: 75% (83 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 209−210 °C; IR (KBr): 2925, 2855, 1626, 1518, 1438, 1377, 1288, 979, 810, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.99 (d, 1H, J = 8.4 Hz), 8.02 (d, 1H, J = 8.8 Hz), 7.85 (d, 1H, J = 7.6 Hz), 7.72 (t, 1H, J = 7.6 Hz), 7.59 (t, 1H, J = 7.6 Hz), 7.42 (d, 1H, J = 9.2 Hz), 2.66 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 172.6, 165.5, 157.5, 135.2, 130.8, 130.1, 129.4, 128.2, 127.3, 126.8, 116.0, 113.3, 87.7, 15.6; HRMS (ESI) m/z calcd for $C_{14}H_{10}IO_2S$ $[M + H]^+$ 368.9441, found 368.9439.

3-Chloro-2-(methylthio)-4H-benzo[h]chromen-4-one (**3v**). Yield: 76% (63 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 208−209 °C; IR (KBr): 2924, 2854, 1637, 1530, 1436, 1218, 979, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.31 (d, 1H, J = 8.8 Hz), 8.14 (d, 1H, J = 8.8 Hz), 7.93 (d, 1H, J = 7.6 Hz), 7.79−7.62 (m, 3H), 2.85 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.7, 163.6, 153.3, 135.5, 129.4, 128.3, 127.5, 125.9, 123.2, 121.3, 121.1, 118.7, 116.4, 13.6; HRMS (ESI) m/z calcd for $C_{14}H_{10}ClO_2S$ $[M + H]^+$ 277.0085, found 277.0087.

3-Bromo-2-(methylthio)-4H-benzo[h]chromen-4-one (**3w**). Yield: 75% (72 mg), yellow solid, eluent (hexane/EtOAc = 19:1), mp: 194−196 °C; IR (KBr): 2927, 2856, 1634, 1524, 1436, 1215, 978, 759 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.27 (d, 1H, J = 8.0 Hz), 8.11 (d, 1H, J = 8.4 Hz), 7.90 (d, 1H, J = 7.6 Hz), 7.76−7.61 (m, 3H), 2.82 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 169.7, 164.6, 153.2, 135.7, 129.3, 128.3, 127.5, 125.9, 123.2, 121.4, 121.3, 118.2, 107.1, 14.4; HRMS (ESI) m/z calcd for $C_{14}H_{10}BrO_2S$ $[M + H]^+$ 320.9585, found 320.9581.

3-Iodo-2-(methylthio)-4H-benzo[h]chromen-4-one (**3x**). Yield: 74% (82 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 204−205 °C; IR (KBr): 2928, 2856, 1631, 1518, 1429, 1211, 975, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.23 (d, 1H, J = 7.6 Hz), 8.08 (d, 1H, J = 8.8 Hz), 7.90 (d, 1H, J = 8.0 Hz), 7.73−7.61 (m, 3H), 2.80 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 171.2, 167.1, 153.5, 135.6, 129.4, 128.4, 127.5, 126.0, 123.0, 121.6, 121.4, 116.4, 85.0, 16.0; HRMS (ESI) m/z calcd for $C_{14}H_{10}IO_2S$ $[M + H]^+$ 368.9441, found 368.9449.

3-(3,5-Di-tert-butyl-4-hydroxybenzyl)-2-(methylthio)-4H-chromen-4-one (**4a**). Yield: 13% (26 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 180−181 °C; IR (KBr): 3435, 2919, 2865, 1723, 1619, 1546, 1490, 1340, 1219, 1025, 768 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.18 (dd, 1H, J = 8.0, 1.6 Hz), 7.60−7.55 (m, 1H), 7.37−7.32 (m, 4H), 5.00 (s, 1H), 3.82 (s, 2H), 2.63 (s, 3H), 1.39 (s, 18H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 174.8, 163.6, 157.1, 152.4, 135.8, 133.3, 130.4, 126.0, 125.7, 124.0, 122.8, 120.9, 118.5, 34.6, 31.2, 30.6, 13.7; HRMS (ESI) m/z calcd for $C_{25}H_{31}O_3S$ $[M + H]^+$ 411.1988, found 411.1982.

3-(3,5-Di-tert-butyl-4-hydroxybenzyl)-6-methoxy-2-(methylthio)-4H-chromen-4-one (**4b**). Yield: 41% (54 mg), white solid, eluent (hexane/EtOAc = 19:1), mp: 175−177 °C; IR (KBr): 3426, 2926, 2872, 1718, 1612, 1552, 1487, 1355, 1232, 1029, 779 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.57 (d, 1H, J = 2.8 Hz), 7.30 (d, 1H, J = 9.2 Hz), 7.25 (s, 2H), 7.16 (dd, 1H, J = 9.2, 2.8 Hz), 5.01 (s, 1H), 3.87 (s, 3H), 3.83 (s, 2H), 2.62 (s, 3H), 1.40 (s, 18H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 174.5, 163.3, 156.7, 152.1, 151.4, 135.4, 130.1, 125.7, 123.7, 122.5, 120.5, 118.2, 105.6, 55.9, 34.2, 30.9, 30.3, 13.5; HRMS (ESI) m/z calcd for $C_{26}H_{33}O_4S$ $[M + H]^+$ 441.2094, found 441.2089.

2-(1,3-Dithiolan-2-ylidene)-1-(2-hydroxyphenyl)ethanone (**5**). Yield: 79% (188 mg), yellow solid, eluent (hexane/EtOAc = 9:1), mp: 90−92 °C; IR (KBr): 2924, 2856, 1620, 1492, 1206, 1041, 759 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 12.79 (s, 1H), 7.68 (d, 1H, J = 7.6 Hz), 7.41−7.35 (m, 2H), 6.95 (d, 1H, J = 8.8 Hz), 6.84 (t, 1H, J = 7.2 Hz), 3.50 (t, 2H, J = 6.4 Hz), 3.39 (t, 2H, J = 6.4 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 189.5, 170.0, 163.0, 135.2, 128.4, 119.7, 118.6, 118.4, 107.1, 39.2, 35.5; HRMS (ESI) m/z calcd for $C_{11}H_{11}O_2S_2$ $[M + H]^+$ 239.0195, found 239.0186.

2-(4-Ethylphenyl)-4H-chromen-4-one (**6**). Yield: 92% (46 mg), eluent (hexane/EtOAc = 19:1); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.20 (dd, 1H, J = 8.0, 1.6 Hz), 7.82 (d, 2H, J = 8.0 Hz), 7.68−7.64 (m, 1H), 7.53 (d, 1H, J = 8.4 Hz), 7.38 (t, 1H, J = 7.2 Hz), 7.32 (d, 2H, J = 8.4 Hz), 6.77 (s, 1H), 2.70 (q, 2H, J = 7.6 Hz), 1.25 (t, 3H, J = 7.6 Hz); HRMS (ESI) m/z calcd for $C_{17}H_{15}O_2$ $[M + H]^+$ 251.1067, found 251.1062.

2-(Pyrrolidin-1-yl)-4H-chromen-4-one (**7a**). Yield: 81% (35 mg) (recrystallized from methanol); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.09 (dd, 1H, J = 7.6, 1.6 Hz), 7.46−7.42 (m, 1H), 7.26−7.19 (m, 2H), 5.24 (s, 1H), 3.44 (br, 4H), 1.98 (t, 4H, J = 6.8 Hz); HRMS (ESI) m/z calcd for $C_{13}H_{14}NO_2$ $[M + H]^+$ 216.1019, found 216.1025.

2-(Piperidin-1-yl)-4H-chromen-4-one (**7b**). Yield: 85% (39 mg) (recrystallized from methanol); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.05 (dd, 1H, J = 7.6, 1.2 Hz), 7.47−7.43 (m, 1H), 7.26−7.19 (m, 2H), 5.55 (s, 1H), 3.45 (br, 4H), 1.62 (br, 6H); HRMS (ESI) m/z calcd for $C_{14}H_{16}NO_2$ $[M + H]^+$ 230.1176, found 230.1159.

2-(Phenylamino)-4H-chromen-4-one (**8a**). Yield: 84% (40 mg), white solid, eluent (DCM/MeOH = 4:1), mp: 205−207 °C; IR (KBr): 3165, 2926, 1615, 1553, 1240, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.14 (d, 1H, J = 8.0 Hz), 7.56−7.51 (m, 2H), 7.38−7.27 (m, 6H), 7.19 (t, 1H, J = 7.2 Hz), 5.79 (s, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 177.5, 161.4, 153.9, 136.3, 132.5, 129.6, 125.8, 125.7, 124.9, 123.3, 122.9, 116.3, 88.0; HRMS (ESI) m/z calcd for $C_{15}H_{12}NO_2$ $[M + H]^+$ 238.0863, found 238.0871.

7-(Benzyloxy)-3-chloro-2-(phenylamino)-4H-chromen-4-one (**8b**). Yield: 82% (101 mg), white solid, eluent (DCM/MeOH = 4:1), mp: 179−181 °C; IR (KBr): 2925, 2857, 1610, 1554, 1423, 1275, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.10 (d, 1H, J = 8.8 Hz), 7.44−7.26 (m, 11H), 6.99 (dd, 1H, J = 8.8, 2.0 Hz), 6.80 (d, 1H, J = 2.0 Hz), 5.08 (s, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 170.3, 162.4, 156.4, 153.4, 136.0, 135.6, 129.4, 128.7, 128.4, 127.5, 127.3, 125.6, 122.3, 116.3, 114.1, 101.1, 95.2, 70.5; HRMS (ESI) m/z calcd for $C_{22}H_{17}ClNO_3$ $[M + H]^+$ 378.0891, found 378.0890.

3-Chloro-7-hydroxy-2-(phenylamino)-4H-chromen-4-one (**9**). Yield: 93% (54 mg), white solid, mp: 238−240 °C; IR (KBr): 2925, 2857, 1609, 1556, 1432, 1250, 761 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 10.66 (s, 1H), 9.70 (s, 1H), 7.82 (d, 1H, J = 8.4 Hz), 7.45−7.39 (m, 4H), 7.24−7.20 (m, 1H), 6.86 (dd, 1H, J = 8.8, 2.0 Hz), 6.61 (d, 1H, J = 2.0 Hz); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz): δ 169.5, 161.8, 156.6, 153.4, 136.9, 129.0, 128.0, 126.6, 125.1, 123.4, 114.5, 101.8, 93.8; HRMS (ESI) m/z calcd for $C_{15}H_{11}ClNO_3$ $[M + H]^+$ 288.0422, found 288.0426.

7-Hydroxy-2-(methylthio)-4H-chromen-4-one (**10**). Yield: 95% (40 mg), white solid, mp: 200−202 °C; IR (KBr): 2926, 2857, 1612, 1567, 1375, 764 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 7.81 (d, 1H, J = 8.4 Hz), 6.88 (d, 1H, J = 8.4 Hz), 6.82 (s, 1H), 6.13 (s, 1H), 4.77 (br, 1H), 2.56 (s, 3H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz): δ 173.9, 169.1, 162.6, 158.0, 126.7, 115.5, 114.8, 106.4, 102.0, 13.4; HRMS (ESI) m/z calcd for $C_{10}H_9O_3S$ $[M + H]^+$ 209.0267, found 209.0278.

4H-Chromen-4-one (**11a**). Yield: 92% (27 mg), eluent (hexane/EtOAc = 9:1); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, 1H, J = 7.6 Hz), 7.83 (d, 1H, J = 6.0 Hz), 7.65 (t, 1H, J = 7.6 Hz), 7.44−7.36 (m, 2H), 6.32 (d, 1H, J = 6.0 Hz); HRMS (ESI) m/z calcd for $C_9H_7O_2$ $[M + H]^+$ 147.0441, found 147.0436.

3-Methyl-4H-chromen-4-one (**11b**). Yield: 81% (26 mg), eluent (hexane/EtOAc = 9:1); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.21 (d, 1H, J = 8.4 Hz), 7.77 (s, 1H), 7.61 (t, 1H, J = 6.8 Hz), 7.41−7.34 (m, 2H), 2.01 (s, 3H); HRMS (ESI) m/z calcd for $C_{10}H_9O_2$ $[M + H]^+$ 161.0597, found 161.0602.

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■ ASSOCIATED CONTENT

Supporting Information

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Spectral data for all new compounds (PDF)

Accession Codes

CCDC 1969715 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

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