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Efficient synthesis of functionalized 6-substituted-thiosalicylates via microwave-promoted Suzuki cross-coupling reaction



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ABSTRACT

Functionalized 6-substituted-thiosalicylates are key intermediates for the synthesis of pyrimidinyl(thio) salicylic acids, a group of important herbicides targeting plant acetohydroxyacid synthase. Therefore, it is of great interest to develop an efficient method for the syntheses of 6-substituted-thiosalicylates. Herein, we have developed a direct and efficient method for the synthesis of functionalized 6-substituted-thiosalicylates (**4**) from aryl iodide (**1**) by using an improved microwave-assisted Suzuki cross-coupling reaction. Almost all the reactions proceeded smoothly and afforded moderate to excellent yields of products. Moreover, this protocol is obviously superior to the traditional available methods and could be utilized to synthesize pyrimidinyl(thio)salicylic acid and its derivatives.

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1. Introduction

The pyrimidinyl(thio)salicylic acids are an important class of commercial herbicides targeting acetohydroxyacid synthase.¹ As shown in Fig. 1, functionalized 6-substituted-thiosalicylates² are commonly found as a privileged structure in almost all the herbicidal pyrimidinyl(thio)salicylic acids.

Traditionally, these compounds have been prepared by three practical approaches. As shown in Fig. 2, the first pathway has relied on transition-metal-catalyzed³ and metal-free C–S coupling

reactions;⁴ The second method involved formal [3+3]-cyclization of 3-aryloxythio-1-trimethylsilyloxybuta-1,3-dienes with 3alkoxy-2-en-1-ones;⁵ The third synthetic methodology is based on the carbanion-induced ring transformation of 2*H*-pyran-2ones.^{21,6} Although these methods have provided useful access to the substituted 6-substituted-thiosalicylates, there are still noticeable drawbacks, such as relatively harsh reaction conditions, inaccessible substrates, and low yields. Therefore, the development of general and direct strategies for the preparation of functionalized 6-substituted-thiosalicylates would be highly interesting.



Fig. 1. Chemical structures of pyrimidinyl(thio)salicylic herbicides.

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Fig. 2. Three practical approaches for the synthesis of the thiosalicylates.



Not long ago, our laboratory successfully employed microwave irradiation⁷ to synthesize 6-arylsalicylates.⁸ However, application of this strategy to prepare 6-substituted-thiosalicylates has been surprisingly unsuccessful. As shown in Fig. 3, although the optimal conditions have been used on the synthesis of **3a**' with excellent yield, this methodology did not give similar results for the synthesis of **3a**.



Fig. 3. Synthesis of 2,2-dimethyl-5-phenyl-4*H*-benzo[*d*][1,3]oxathiin-4-one and 2,2-dimethyl-5-phenyl-4*H*-benzo[*d*][1,3]dioxin-4-one.

Herein, as a continuation of our research on the synthesis of structurally diverse heterocyclic compounds, we report the synthesis of functionalized 6-substituted-thiosalicylates via an improved Suzuki cross-coupling reaction under microwave irradiation.

2. Result and discussion

The aryl iodide (**1**) was prepared by using a previously reported synthetic strategy.^{8,9} To optimize the conditions for the palladiumcatalyzed Suzuki cross-coupling reaction, we selected the reaction between aryl iodide (**1**) and phenylboronic acids (**2a**) as a model. We initially studied the reaction with the optimal conditions previously established for the synthesis of functionalized 6arylsalicylates.⁸ As shown in Table 1, the reaction was carried out at 110 °C, with 1% of Pd(PPh₃)₄, 2 equiv of NaHCO₃, in a solution of

Table 1

Optimization of the reaction conditions^a

	s	B(OH) ₂		→ S		
		1 2a		3a	I	
No	Temp (°C)	Solvent (v/v)	Pd(PPh ₃) ₄	TBAB ^b	Time (min)	Yield ^c
1	MW:110 ^d	DME/H ₂ O=5:1	1 mol %	0	17	26%
2	MW:110	DME/H ₂ O=5:1	2 mol %	0	6	70%
3	MW:110	DME/H ₂ O=5:1	5 mol %	0	6	62%
4	MW:120	DME/H ₂ O=5:1	2 mol %	0	3	84%
5	MW:120	DMF/H ₂ O=5:1	2 mol %	0	4	35%
6	MW:120	$THF/H_2O=1:1$	2 mol %	0	4	84%
7	MW:120	1,4-Dioxane/H ₂ O=5:1	2 mol %	0	6	37%
8	MW:120	Toluene/H ₂ O=5:1	2 mol %	0	6	89%
9 ^e	MW:120	Toluene/H ₂ O=5:1	2 mol %	0	6	0%
10	MW:120	Toluene/H ₂ O=5:1	2 mol %	0.3 equiv	6	90%
11	MW:120	Toluene/H ₂ O=5:1	2 mol %	0.5 equiv	6	91%
12 ^e	MW:120	Toluene/H ₂ O=5:1	2 mol %	0.5 equiv	13	54%
13	120 ^f	Toluene/H ₂ O=5:1	2 mol %	0.5 equiv	480	75%

^a Unless otherwise noted, all the reactions were carried out at 0.5 mmol scale in a solution of toluene (3 mL) and H_2O (0.6 mL) with 2 mol % of Pd(PPh₃)₄, 2 equiv of NaHCO₃, 0.5 equiv TBAB, protected by N₂.

^b TBAB=tetrabutyl ammonium bromide.

^c Isolated yields.

^d Microwave irradiation.

^e The reaction between aryl iodide (1) and furan-2-ylboronic acid (2s).

^f Conventional heating method.

DME (3 mL), and H₂O (0.6 mL). However, the transformation was incomplete and the yield was only 26% (Table 1, entry 1). During optimization, the stoichiometric ratio of the catalyst and the temperature proved to be important parameters for this reaction (Table 1, entries 2–4). The yield was notably increased to 84% when the reaction was carried out at 120 °C, with 2 mol % of Pd(PPh₃)₄ (Table 1. entry 4). A survey of solvents revealed that toluene/H₂O=5:1 (v/ v) was optimal (Table 1, entries 4–8). Most surprisingly, we observed no conversion of aryl halide into product 3s when the phenylboronic acid was changed to furan-2-ylboronic acid (Table 1, entry 9), indicating that this condition is not generally applicable for different substrates. Therefore, the reaction conditions were further adjusted. As shown in Table 1 (entries 10-12), when we added a small amount of tetrabutyl ammonium bromide (TBAB) into the reaction mixture, the yields of the product were improved markedly. Maybe it is due to that TBAB can facilitate the migration of a reactant from one phase into another phase where reaction occurs. Furthermore, as compared with conventional heating methods, microwave irradiation dramatically accelerated these reactions and increased the reaction yields (Table 1, entry 13).

With the optimized conditions defined, we investigated the scope of substrates by employing a variety of arylboronic acids substituted with electron-donating and electron-withdrawing groups. As shown in Table 2, significant structural variations in the arylboronic acid components were well tolerated and afforded the corresponding functionalized 6-substituted-thiosalicylates (3) in moderate to good vields. Both electron-rich and electron-poor arylboronic acids could be successfully utilized in this transformation: methyl, methoxy, tert-butyl, nitro, trifluoromethyl, and acetyl derivatives showed no significant effects on the transformation and afforded good yields of products (Table 2, 3g-1). Even the potentially problematic bromo-substituted arylboronic acid resulted in product 3e with acceptable yields. It should be noted that incorporation of halogen-substituents at the ortho, meta or *para* positions in arylboronic acids did not retard the reaction, demonstrating that steric modification can be accomplished without compromising the efficiency of the process (Table 2, 3b-d).

Table 2

The reaction with aryl iodide (1) and various arylboronic acids or alkenyl boronic acids^a



^a Unless otherwise noted, all the reactions were carried out at 0.5 mmol scale

Very promisingly, polysubstituted phenylboronic acids, furan-2-ylboronic acid, and naphthalen-1-ylboronic acid also reacted with aryl iodide (1) very well and gave moderate to excellent yields of products (Table 2, **3m**-s).

In addition, we also extended the substrates to alkyl and alkenyl boronic acids. Not surprisingly, the process showed good functional group compatibility for the alkenyl reagents (Table 2, **3t**). However, alkyl reagents did not react with 5-iodo-2,2-dimethyl-4*H*-benzo[*d*] [1,3]oxathiin-4-one (**1**) under the investigated conditions.

Finally, we removed the protecting groups of functionalized 6-substituted-thiosalicylates (**3**) successfully to obtain the target compounds 6-substituted-thiosalicylates (**4**). For almost all the substrates **3** with different substituents, deprotection proceeded very smoothly and afforded moderate to excellent yields of products (Table 3).

Table 3





^a Unless otherwise noted, all the reactions were carried out at 1 mmol scale in a solution of CH₃OH (10 mL) with 3.0 eq of NaOH at 50 °C.

3. Conclusion

In summary, we have developed a direct and efficient method for the synthesis of functionalized 6-substituted-thiosalicylates (**4**) from aryl iodide (**1**) by using an improved microwave-assisted Suzuki cross-coupling reaction. Moreover, this protocol is notably superior to the traditionally available methods and could be developed as a general method to synthesize pyrimidinyl(thio) salicylic acid and its derivatives.

4. Experimental section

4.1. General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. Flash column chromatography (FC) was performed using 200–300 mesh silica gel.

¹H NMR spectra were recorded on 400/600 (400/600 MHz) spectrophotometers. Chemical shifts (δ) are reported in parts per million from the solvent resonance as the internal standard (CDCl₃:

7.26 ppm, DMSO: 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, m=multiplet, q=quaternary), coupling constants (Hertz) and integration. ¹³C NMR spectra were recorded on 400/600 (100/150 MHz) spectrophotometers (CDCl₃: 77.0 ppm, DMSO: 39.5 ppm) with complete proton decoupling. Mass spectra were measured on a Trace MS spectrometer. Elemental analysis was determined on an elementary analysis instrument. Microwave irradiation reactions were carried out with a Smith synthesizerTM instrument.

4.2. General procedure for the synthesis of compound 1



To a stirred solution of thiosa¹ icylic acid (5.00 g, 32.5 m¹mol) in TFA (25 mL) was added a solution of acetone (17 mL, 232 mmol) in TFAA (18 mL) at 0 °C and then stirred for 2 d at 5 °C. After this time, the mixture was concentrated, and the residue was redissolved with EtOAc (30 mL) and washed with saturated aqueous NaHCO₃. The organic layer was dried over Na₂SO₄ and concentrated. Purification of the residue by flash column chromatography (petroleum ether/EtOAc=5/1) gave **1**' (2.33 g, 12.0 mmol) in 37% yield.

To a stirred solution of freshly prepared (TMP)2Mg·LiCl (0.42 M in THF, 60 mL, 25.3 mmol) was added to a solution of 1' (1.60 g, 8.25 mmol) in THF at -20 °C. After being stirred for 1 h at -20 °C, a solution of I₂ (10.5 g, 41.3 mmol) in THF (42 mL) was added at 0 °C. The mixture was stirred for additional 4 h at room temperature. The mixture was quenched with saturated aqueous NH₄Cl, and extracted with EtOAc. The organic layer was washed with saturated aqueous Na₂S₂O₃ and brine, dried over Na₂SO₄, and concentrated. Purification of the residue by flash column chromatography (petroleum ether/EtOAc=10/1) gave **1** (1.06 g, 3.30 mmol) in 40% yield as a yellow oil.

4.2.1. 2,2-Dimethyl-4H-benzo[d][1,3]oxathiin-4-one (1'). Yellow solid, 2.33 g, 37% yield; mp: 85–86 °C. ¹H NMR (600 MHz, DMSO) δ 8.08 (dd, *J*=7.8, 0.9 Hz, 1H), 7.64 (td, *J*=7.8, 1.2 Hz, 1H), 7.48 (d, *J*=7.8 Hz, 1H), 7.41 (t, *J*=7.8 Hz, 1H), 1.79 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 163.24, 136.70, 133.73, 131.87, 127.71, 126.12, 123.26, 85.95, 28.91. EI-MS: *m*/*z*=194.17 (M⁺). Anal. Calcd for (C₁₀H₁₀O₂S): C, 61.83; H, 5.19; S, 16.51. Found: C, 61.79; H, 5.20; S, 16.62.

4.2.2. 5-Iodo-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4-one (**1**). Yellow oil, 1.06 g, 40% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.95 (d, *J*=7.8 Hz, 1H), 7.30 (d, *J*=7.8 Hz, 1H), 7.05 (t, *J*=7.8 Hz, 1H), 1.81 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 161.33, 140.70, 138.33, 133.03, 128.45, 126.39, 97.70, 85.51, 28.54. EI-MS: *m*/*z*=320.05 (M⁺). Anal. Calcd for (C₁₀H₉IO₂S): C, 37.52; H, 2.83; S, 10.02. Found: C, 37.43; H, 2.78; S, 10.14.

4.3. General procedure for the synthesis of compounds 3a-t

Aryl iodide **1** (160 mg, 0.5 mmol) and **2a** (61 mg, 0.5 mmol) were dissolved in toluene (3 mL) and H₂O (0.6 mL) in a microwave vial under a nitrogen atmosphere. Pd(PPh₃)₄ (0.01 mmol, 11.56 mg), sodium bicarbonate (84 mg, 1 mmol), and tetrabutyl ammonium bromide (80.5 mg, 0.25 mmol) were added, and then the reaction mixture was irradiated in a microwave apparatus at 120 °C for 6–13 min. After the reaction mixture was concentrated, and the crude residue was purified by silica gel column chromatography using

petroleum ether/acetone (20/1 to 10/1) as eluent to give the title compound **3a** (123 mg) in 91% yield.

4.3.1. 2,2-Dimethyl-5-phenyl-4H-benzo[d][1,3]oxathiin-4-one (**3a**). Yellow solid, 123 mg, 91% yield; mp: 109–110 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.46 (t, *J*=7.8 Hz, 1H), 7.41 (t, *J*=7.2 Hz, 2H), 7.37 (d, *J*=7.2 Hz, 1H), 7.29 (d, *J*=7.2 Hz, 3H), 7.23 (d, *J*=7.8 Hz, 1H), 1.92 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.25, 146.57, 141.08, 137.93, 132.11, 129.71, 128.20, 128.09, 127.39, 126.97, 123.55, 85.78, 28.59. EI-MS: *m*/*z*=270.22 (M⁺). Anal. Calcd for (C₁₆H₁₄O₂S): C, 71.08; H, 5.22; S, 11.86. Found: C, 71.23; H, 5.27; S, 11.89.

4.3.2. 5-(4-Chlorophenyl)-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4one (**3b**). Yellow solid, 133 mg, 88% yield; mp: 134–135 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.46 (t, *J*=7.8 Hz, 1H), 7.37 (d, *J*=7.8 Hz Hz, 2H), 7.31 (d, *J*=8.4 Hz, 1H), 7.21 (d, *J*=7.8 Hz, 2H), 7.18 (d, *J*=7.2 Hz, 1H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.17, 145.40, 139.63, 138.28, 133.54, 132.29, 129.58, 129.43, 128.45, 127.37, 123.36, 85.85, 28.62. El-MS: *m*/*z*=304.26 (M⁺). Anal. Calcd for (C₁₆H₁₃ClO₂S): C, 63.05; H, 4.30; S, 10.52. Found: C, 63.25; H, 4.24; S, 10.70.

4.3.3. 5-(3-Chlorophenyl)-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4one (**3c**). White solid, 127 mg, 84% yield; mp: 149–150 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.46 (t, *J*=7.8 Hz, 1H), 7.35–7.29 (m, 3H), 7.27 (s, 1H), 7.18 (d, *J*=7.8 Hz, 1H), 7.14 (d, *J*=6.6 Hz, 1H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 161.95, 145.06, 142.91, 138.21, 133.90, 132.28, 129.56, 129.32, 128.00, 127.50, 127.41, 126.49, 123.26, 85.82, 28.55. EI-MS: *m*/*z*=304.18 (M⁺). Anal. Calcd for (C₁₆H₁₃ClO₂S): C, 63.05; H, 4.30; S, 10.52. Found: C, 63.25; H, 4.39; S, 10.49.

4.3.4. 5-(2-Chlorophenyl)-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4one (**3d**). White solid, 109 mg, 72% yield; mp: 154–155 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.49 (t, *J*=7.6 Hz, 1H), 7.39 (d, *J*=7.6 Hz, 1H), 7.35 (t, *J*=7.2 Hz, 2H), 7.30 (dd, *J*=11.6, 4.4 Hz, 2H), 7.12 (d, *J*=7.6 Hz, 1H), 1.89 (s, 3H), 1.86 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 161.63, 143.31, 140.14, 137.29, 132.40, 131.34, 130.00, 129.77, 128.98, 128.64, 127.89, 126.86, 124.00, 85.67, 29.11, 28.36. EI-MS: *m*/*z*=304.23 (M⁺). Anal. Calcd for (C₁₆H₁₃ClO₂S): C, 63.05; H, 4.30; S, 10.52. Found: C, 63.22; H, 4.34; S, 10.32.

4.3.5. 5-(4-Bromophenyl)-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4-one (**3e**). White solid, 136 mg, 78% yield; mp: 150–151 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.53 (d, *J*=6.6 Hz, 2H), 7.46 (s, 1H), 7.31 (d, *J*=7.8 Hz, 1H), 7.20–7.12 (m, 3H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.09, 145.31, 140.07, 138.23, 132.28, 131.29, 129.71, 129.46, 127.35, 123.21, 121.66, 85.79, 28.56. EI-MS: *m*/*z*=348.21 (M⁺). Anal. Calcd for (C₁₆H₁₃BrO₂S): C, 55.03; H, 3.75; S, 9.18. Found: C, 55.20; H, 3.74; S, 9.21.

4.3.6. 5-(4-Fluorophenyl)-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4one (**3f**). White solid, 124 mg, 86% yield; mp: 158–159 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.46 (t, *J*=7.8 Hz, 1H), 7.29 (d, *J*=7.8 Hz, 1H), 7.24 (d, *J*=4.2 Hz, 2H), 7.19 (d, *J*=7.8 Hz, 1H), 7.09 (t, *J*=7.8 Hz, 2H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 163.48, 162.20, 161.03, 145.48, 138.10, 137.09, 132.20, 129.74, 129.66, 127.15, 123.41, 115.28, 115.06, 85.78, 28.55. EI-MS: *m*/*z*=288.23 (M⁺). Anal. Calcd for (C₁₆H₁₃FO₂S): C, 66.65; H, 4.54; S, 11.12. Found: C, 66.84; H, 4.39; S, 11.22.

4.3.7. 2,2-Dimethyl-5-(p-tolyl)-4H-benzo[d][1,3]oxathiin-4-one (**3g**). White solid, 125 mg, 88% yield; mp: 116–117 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.44 (t, *J*=7.8 Hz, 1H), 7.26 (s, 1H), 7.22 (d, *J*=9.6 Hz, 3H), 7.18 (d, *J*=7.2 Hz, 2H), 2.39 (s, 3H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.34, 146.52, 138.13, 137.83, 137.12, 132.07, 129.65, 128.98, 127.96, 126.71, 123.53, 85.73, 28.56, 21.17. EI-

MS: *m*/*z*=284.23 (M⁺). Anal. Calcd for (C₁₇H₁₆O₂S): C, 71.80; H, 5.67; S, 11.28. Found: C, 71.91; H, 5.69; S, 11.36.

4.3.8. 5-(4-Methoxyphenyl)-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4-one (**3h**). White solid, 118 mg, 79% yield; mp: 166–167 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.43 (t, *J*=7.8 Hz, 1H), 7.24–7.19 (m, 4H), 6.94 (d, *J*=7.8 Hz, 2H), 3.84 (s, 3H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.42, 159.03, 146.08, 137.81, 133.29, 132.03, 129.57, 129.23, 126.48, 123.36, 113.70, 85.69, 55.10, 28.50. EI-MS: *m*/ *z*=300.25 (M⁺). Anal. Calcd for (C₁₇H₁₆O₃S): C, 67.98; H, 5.37; S, 10.68. Found: C, 67.92; H, 5.32; S, 10.74.

4.3.9. 5-(4-(tert-Butyl)phenyl)-2,2-dimethyl-4H-benzo[d][1,3]ox-athiin-4-one (**3i** $). White solid, 152 mg, 93% yield; mp: 153–154 °C. ¹H NMR (600 MHz, CDCl₃) <math>\delta$ 7.43 (m, 3H), 7.24 (m, 4H), 1.91 (s, 6H), 1.35 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 162.33, 150.08, 146.42, 137.97, 137.74, 132.00, 129.64, 127.72, 126.61, 125.11, 123.46, 85.67, 34.39, 31.22, 28.49. EI-MS: m/z=326.28 (M⁺). Anal. Calcd for (C₂₀H₂₂O₂S): C, 73.58; H, 6.79; S, 9.82. Found: C, 73.52; H, 6.85; S, 9.77.

4.3.10. 2,2-Dimethyl-5-(4-(trifluoromethyl)phenyl)-4H-benzo[d][1,3] oxathiin-4-one (**3***j*). White solid, 137 mg, 81% yield; mp: 160–161 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.65 (d, *J*=7.8 Hz, 2H), 7.49 (t, *J*=7.8 Hz, 1H), 7.38 (d, *J*=7.8 Hz, 2H), 7.34 (d, *J*=7.8 Hz, 1H), 7.19 (d, *J*=7.8 Hz, 1H), 1.92 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.01, 145.12, 144.93, 138.40, 133.81, 132.38, 129.49, 129.09, 128.42, 127.73, 125.48, 125.09, 123.23, 122.78, 85.87, 28.51. EI-MS: *m*/*z*=338.28 (M⁺). Anal. Calcd for (C₁₇H₁₃F₃O₂S): C, 60.35; H, 3.87; S, 9.48. Found: C, 60.40; H, 3.82; S, 9.53.

4.3.11. 2,2-Dimethyl-5-(4-nitrophenyl)-4H-benzo[d][1,3]oxathiin-4one (**3k**). Yellow solid, 131 mg, 83% yield; mp: 141–142 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.35–8.17 (m, 2H), 7.51 (d, *J*=7.6 Hz, 1H), 7.46–7.33 (m, 3H), 7.19 (d, *J*=7.6 Hz, 1H), 1.93 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 161.88, 148.10, 146.92, 144.26, 138.73, 132.55, 129.21, 128.98, 128.22, 123.37, 122.94, 85.94, 28.53. EI-MS: *m*/ *z*=315.19 (M⁺). Anal. Calcd for (C₁₆H₁₃NO₄S): C, 60.94; H, 4.16; N, 4.44; S, 10.17. Found: C, 60.81; H, 4.12; N, 4.49; S, 10.26.

4.3.12. 5-(4-Acetylphenyl)-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4-one (**3l** $). White solid, 97 mg, 62% yield; mp: 149–150 °C. ¹H NMR (600 MHz, CDCl₃) <math>\delta$ 8.00 (d, *J*=7.8 Hz, 2H), 7.48 (d, *J*=7.8 Hz, 1H), 7.38 (d, *J*=7.8 Hz, 2H), 7.34 (d, *J*=7.8 Hz, 1H), 7.21 (d, *J*=7.8 Hz, 1H), 2.63 (s, 3H), 1.92 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 197.51, 162.03, 146.08, 145.44, 138.36, 135.83, 132.35, 129.39, 128.34, 128.27, 127.65, 123.26, 85.87, 28.58, 26.56. EI-MS: *m*/*z*=312.22 (M⁺). Anal. Calcd for (C₁₈H₁₆O₃S): C, 69.21; H, 5.16; S, 10.26. Found: C, 69.33; H, 5.06; S, 10.11.

4.3.13. 5-(4-Fluoro-3-methylphenyl)-2,2-dimethyl-4H-benzo[d][1,3] oxathiin-4-one (**3m**). White solid, 136 mg, 90% yield; mp: 133–134 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.44 (t, *J*=7.8 Hz, 1H), 7.28 (d, *J*=7.8 Hz, 1H), 7.18 (d, *J*=7.8 Hz, 1H), 7.10 (d, *J*=7.2 Hz, 1H), 7.07–6.95 (m, 2H), 2.31 (s, 3H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.28, 162.14, 159.70, 145.76, 138.02, 136.80, 132.13, 131.06, 131.01, 129.72, 127.19, 127.11, 127.02, 124.73, 124.55, 123.46, 114.92, 114.70, 85.80, 28.59, 14.68, 14.64. EI-MS: *m*/*z*=302.19 (M⁺). Anal. Calcd for (C₁₇H₁₅FO₂S): C, 67.53; H, 5.00; S, 10.60. Found: C, 67.61; H, 5.09; S, 10.59.

4.3.14. 5-(3,5-Difluorophenyl)-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4-one (**3n**). Yellow solid, 138 mg, 90% yield; mp: 139–140 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.48 (t, J=7.8 Hz, 1H), 7.34 (d, J=7.8 Hz, 1H), 7.17 (d, J=7.8 Hz, 1H), 6.84–6.80 (m, 1H), 6.78 (d, J=6.0 Hz, 2H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 163.84, 163.72, 161.74, 161.38, 144.26, 138.50, 132.40, 129.25, 127.91, 123.21, 111.43, 111.36, 111.18, 103.00, 102.75, 102.50, 85.91, 28.54. EI-MS: m/z=306.18 (M⁺). Anal. Calcd for (C₁₆H₁₂F₂O₂S): C, 62.73; H, 3.95; S, 10.47. Found: C, 62.68; H, 3.90; S, 10.41.

4.3.15. 5-(3-*Chloro-4-fluorophenyl*)-2,2-*dimethyl*-4H-*benzo*[*d*][1,3] *oxathiin*-4-*one* (**30**). White solid, 129 mg, 80% yield; mp: 147–148 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.46 (t, *J*=7.8 Hz, 1H), 7.31 (t, *J*=7.2 Hz, 2H), 7.16 (t, *J*=7.8 Hz, 2H), 7.11 (s, 1H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 161.97, 158.72, 156.24, 144.18, 138.38, 138.28, 132.36, 130.02, 129.56, 128.09, 128.02, 127.66, 123.15, 120.71, 116.36, 116.15, 85.84, 28.54. EI-MS: *m/z*=322.21 (M⁺). Anal. Calcd for (C₁₆H₁₂CIFO₂S): C, 59.54; H, 3.75; S, 9.93. Found: C, 59.67; H, 3.70; S, 10.02.

4.3.16. 5-(3,5-Dichlorophenyl)-2,2-dimethyl-4H-benzo[d][1,3]oxathiin-4-one (**3p**). Yellow solid, 144 mg, 85% yield; mp: 160–161 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.47 (t, *J*=7.8 Hz, 1H), 7.34 (dd, *J*=7.8, 5.4 Hz, 2H), 7.15 (d, *J*=7.8 Hz, 1H), 7.13 (d, *J*=1.8 Hz, 2H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 161.65, 144.11, 143.71, 138.47, 134.40, 132.40, 129.36, 127.97, 127.28, 126.56, 122.91, 85.83, 28.50. EI-MS: *m*/*z*=338.16 (M⁺). Anal. Calcd for (C₁₆H₁₂Cl₂O₂S): C, 56.65; H, 3.57; S, 9.45. Found: C, 56.67; H, 3.61; S, 9.52.

4.3.17. 2,2-Dimethyl-5-(3,4,5-trimethoxyphenyl)-4H-benzo[d][1,3] oxathiin-4-one (**3q**). Yellow solid, 117 mg, 65% yield; mp: 130–131 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.44 (t, *J*=7.6 Hz, 1H), 7.26 (dd, *J*=14.4, 8.4 Hz, 2H), 6.48 (s, 2H), 3.89 (s, 3H), 3.86 (s, 6H), 1.91 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.15, 152.90, 146.43, 137.95, 137.56, 136.75, 132.04, 129.55, 126.97, 123.55, 105.53, 85.74, 60.82, 55.96, 28.52. EI-MS: *m/z*=360.26 (M⁺). Anal. Calcd for (C₁₉H₂₀O₅S): C, 63.32; H, 5.59; S, 8.90. Found: C, 63.34; H, 5.61; S, 8.88.

4.3.18. 2,2-Dimethyl-5-(naphthalen-2-yl)-4H-benzo[d][1,3]oxathiin-4-one (**3r**). Yellow solid, 144 mg, 90% yield; mp: 165–166 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.85 (dd, *J*=10.0, 6.0 Hz, 3H), 7.80 (s, 1H), 7.49 (dd, *J*=8.8, 6.4 Hz, 3H), 7.32 (dt, *J*=13.2, 10.0 Hz, 3H), 1.95 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.25, 146.49, 138.74, 138.02, 133.28, 132.50, 132.23, 130.06, 128.08, 127.61, 127.50, 127.04, 126.86, 126.44, 126.06, 125.97, 123.45, 85.76, 28.58. EI-MS: *m*/*z*=320.29 (M⁺). Anal. Calcd for (C₂₀H₁₆O₂S): C, 74.97; H, 5.03; S, 10.01. Found: C, 74.94; H, 5.11; S, 10.14.

4.3.19. 5-(*Furan-2-yl*)-2,2-*dimethyl-4H-benzo*[*d*][1,3]oxathiin-4-one (**3s**). White solid, 70 mg, 54% yield; mp: 69–70 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.50 (s, 1H), 7.43 (dd, *J*=15.0, 7.8 Hz, 2H), 7.26 (d, *J*=1.8 Hz, 1H), 6.64 (s, 1H), 6.50 (d, *J*=1.8 Hz, 1H), 1.90 (s, 6H). ¹³C NMR (150 MHz, CDCl₃) δ 162.09, 152.43, 143.07, 138.09, 134.04, 132.25, 127.78, 127.20, 122.54, 111.46, 108.58, 86.02, 28.38. EI-MS: *m*/*z*=260.19 (M⁺). Anal. Calcd for (C₁₄H₁₂O₃S): C, 64.60; H, 4.65; S, 12.32. Found: C, 64.76; H, 4.70; S, 12.34.

4.3.20. (*E*)-2,2-Dimethyl-5-styryl-4H-benzo[d][1,3]oxathiin-4-one (**3t**). Yellow solid, 128 mg, 87% yield; mp: 106–107 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, *J*=16.4 Hz, 1H), 7.58 (dd, *J*=15.2, 7.6 Hz, 3H), 7.43 (t, *J*=7.6 Hz, 1H), 7.36 (t, *J*=7.6 Hz, 2H), 7.29 (d, *J*=7.2 Hz, 1H), 7.22 (d, *J*=7.6 Hz, 1H), 7.04 (d, *J*=16.4 Hz, 1H), 1.83 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.48, 142.42, 137.45, 136.93, 132.49, 131.84, 128.49, 127.90, 127.60, 127.13, 126.90, 125.64, 121.97, 85.44, 28.58. EI-MS: *m*/*z*=296.21 (M⁺). Anal. Calcd for (C₁₈H₁₆O₂S): C, 72.94; H, 5.44; S, 10.82. Found: C, 72.85; H, 5.37; S, 10.90.

4.4. General procedure for the synthesis of compounds 4a-t

To a stirred solution of **3a** (270 mg, 1 mmol) in MeOH (10 mL) was added NaOH (120 mg, 3.0 mmol) at room temperature. The

resulting mixture was stirred at 50 °C for 1–10 h and then allowed to cool to room temperature. The solvent was evaporated in vacuo. The mixture was quenched with saturated aqueous NH₄Cl and 1 N aqueous HCl, and extracted with ethyl acetate. The organic layer was dried over Na₂SO₄ and concentrated. Purification of the residue by flash column chromatography (hexane/acetone=5/1) gave **4a** (114 mg, 0.47 mmol) in 47% yield.

4.4.1. Methyl 3-mercapto-[1,1'-biphenyl]-2-carboxylate (**4a**). Yellow oil, 115 mg, 47% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.45–7.29 (m, 6H), 7.27 (d, *J*=13.6 Hz, 1H), 7.19 (d, *J*=7.2 Hz, 1H), 3.94 (s, 1H), 3.57 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.08, 141.81, 140.40, 132.45, 130.30, 129.87, 129.75, 128.29, 127.95, 127.58, 127.45, 52.09. EI-MS: *m*/*z*=244.16 (M⁺). Anal. Calcd for (C₁₄H₁₂O₂S): C, 68.83; H, 4.95; S, 13.12. Found: C, 68.79; H, 4.89; S, 13.26.

4.4.2. Methyl 4'-chloro-3-mercapto-[1,1'-biphenyl]-2-carboxylate (**4b**). Yellow oil, 225 mg, 81% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.37 (dd, *J*=7.8, 3.6 Hz, 3H), 7.32 (t, *J*=7.8 Hz, 1H), 7.26 (d, *J*=2.4 Hz, 2H), 7.15 (d, *J*=7.8 Hz, 1H), 3.94 (s, 1H), 3.62 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.80, 140.51, 138.84, 133.74, 132.25, 130.67, 130.07, 129.97, 129.29, 128.49, 127.29, 52.22. EI-MS: *m/z*=278.13 (M⁺). Anal. Calcd for (C₁₄H₁₁ClO₂S): C, 60.32; H, 3.98; S, 11.50. Found: C, 60.41; H, 3.97; S, 11.46.

4.4.3. *Methyl 3'-chloro-3-mercapto-[1,1'-biphenyl]-2-carboxylate* (**4c**). Yellow oil, 239 mg, 86% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.38 (d, *J*=8.0 Hz, 1H), 7.36–7.28 (m, 4H), 7.24–7.18 (m, 1H), 7.17 (d, *J*=7.6 Hz, 1H), 3.95 (s, 1H), 3.62 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.60, 142.10, 140.26, 134.11, 132.10, 130.80, 130.20, 129.95, 129.46, 128.02, 127.64, 127.19, 126.14, 52.12. EI-MS: *m/z*=278.16 (M⁺). Anal. Calcd for (C₁₄H₁₁ClO₂S): C, 60.32; H, 3.98; S, 11.50. Found: C, 60.33; H, 4.07; S, 11.57.

4.4.4. *Methyl 2'-chloro-3-mercapto-[1,1'-biphenyl]-2-carboxylate* (**4d**). Yellow oil, 245 mg, 88% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.46–7.42 (m, 1H), 7.40 (d, *J*=7.8 Hz, 1H), 7.33 (t, *J*=7.8 Hz, 1H), 7.28 (dd, *J*=7.2, 3.0 Hz, 2H), 7.22–7.19 (m, 1H), 7.12 (d, *J*=7.8 Hz, 1H), 4.05 (s, 1H), 3.52 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 167.88, 139.83, 139.33, 132.58, 132.09, 131.44, 130.37, 129.84, 129.22, 128.83, 127.98, 126.30, 119.27, 51.90. EI-MS: *m/z*=278.14 (M⁺). Anal. Calcd for (C₁₄H₁₁ClO₂S): C, 60.32; H, 3.98; S, 11.50. Found: C, 60.36; H, 4.07; S, 11.64.

4.4.5. *Methyl* 4'-bromo-3-mercapto-[1,1'-biphenyl]-2-carboxylate (**4e**). Yellow oil, 268 mg, 83% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.52 (d, *J*=8.4 Hz, 2H), 7.37 (d, *J*=7.8 Hz, 1H), 7.31 (t, *J*=7.8 Hz, 1H), 7.20 (d, *J*=8.4 Hz, 2H), 7.15 (d, *J*=7.8 Hz, 1H), 3.94 (s, 1H), 3.62 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.79, 140.54, 139.33, 132.19, 131.46, 130.74, 130.11, 130.00, 129.62, 127.25, 121.96, 52.25. EI-MS: *m*/*z*=324.24 (M⁺). Anal. Calcd for (C₁₄H₁₁BrO₂S): C, 52.03; H, 3.43; S, 9.92. Found: C, 52.07; H, 3.51; S, 9.76.

4.4.6. Methyl 4'-fluoro-3-mercapto-[1,1'-biphenyl]-2-carboxylate (**4f**). Yellow oil, 234 mg, 92% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.37 (d, *J*=7.8 Hz, 1H), 7.31 (ddd, *J*=8.4, 7.8, 4.8 Hz, 3H), 7.16 (d, *J*=7.8 Hz, 1H), 7.09 (t, *J*=9.0 Hz, 2H), 3.92 (s, 1H), 3.61 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.91, 163.59, 161.14, 140.67, 136.38, 132.50, 130.42, 129.90, 129.70, 129.62, 127.40, 115.36, 115.15, 52.15. EI-MS: *m*/*z*=262.18 (M⁺). Anal. Calcd for (C₁₄H₁₁FO₂S): C, 64.11; H, 4.23; S, 12.22. Found: C, 64.23; H, 4.20; S, 12.11.

4.4.7. Methyl 3-mercapto-4'-methyl-[1,1'-biphenyl]-2-carboxylate (**4g**). Yellow oil, 230 mg, 89% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.34 (d, *J*=7.8 Hz, 1H), 7.32–7.26 (m, 1H), 7.23 (d, *J*=8.4 Hz, 2H), 7.19 (dd, *J*=7.8, 4.8 Hz, 3H), 3.91 (s, 1H), 3.61 (s, 3H), 2.38 (s, 3H). ¹³C

NMR (100 MHz, CDCl₃) δ 169.12, 141.60, 137.35, 137.27, 132.47, 129.98, 129.76, 129.50, 128.98, 127.76, 127.41, 52.03, 21.04. EI-MS: m/z=258.23 (M⁺). Anal. Calcd for (C₁₅H₁₄O₂S): C, 69.74; H, 5.46; S, 12.41. Found: C, 69.72; H, 5.32; S, 12.58.

4.4.8. Methyl 3-mercapto-4'-methoxy-[1,1'-biphenyl]-2-carboxylate (**4h**). Yellow oil, 238 mg, 87% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.33 (d, *J*=7.8 Hz, 1H), 7.30 (d, *J*=7.8 Hz, 1H), 7.26 (s, 2H), 7.18 (d, *J*=7.8 Hz, 1H), 6.92 (d, *J*=8.4 Hz, 2H), 3.89 (s, 1H), 3.84 (s, 3H), 3.63 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.21, 159.11, 141.21, 132.64, 132.51, 129.89, 129.75, 129.33, 129.06, 127.38, 113.72, 55.11, 52.09. EI-MS: *m/z*=274.19 (M⁺). Anal. Calcd for (C₁₅H₁₄O₃S): C, 65.67; H, 5.14; S, 11.69. Found: C, 65.79; H, 5.21; S, 11.53.

4.4.9. *Methyl* 4'-(*tert-butyl*)-3-*mercapto-[1,1'-biphenyl]-2-carboxylate* (**4i**). Yellow oil, 273 mg, 91% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.41 (d, *J*=7.8 Hz, 2H), 7.34 (d, *J*=7.8 Hz, 1H), 7.30 (t, *J*=7.8 Hz, 1H), 7.28-7.25 (m, 2H), 7.20 (d, *J*=7.8 Hz, 1H), 3.91 (s, 1H), 3.59 (s, 3H), 1.34 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 169.12, 150.41, 141.56, 137.29, 132.46, 129.99, 129.74, 129.45, 127.57, 127.36, 125.13, 51.91, 34.40, 31.19. EI-MS: *m/z*=300.27 (M⁺). Anal. Calcd for (C₁₈H₂₀O₂S): C, 71.96; H, 6.71; S, 10.67. Found: C, 71.93; H, 6.64; S, 10.62.

4.4.10. Methyl 3-mercapto-4'-(trifluoromethyl)-[1,1'-biphenyl]-2carboxylate (**4j**). Yellow oil, 265 mg, 85% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.66 (d, *J*=7.8 Hz, 2H), 7.45 (d, *J*=7.8 Hz, 2H), 7.41 (d, *J*=7.8 Hz, 1H), 7.36 (d, *J*=7.8 Hz, 1H), 7.18 (d, *J*=7.8 Hz, 1H), 3.98 (s, 1H), 3.59 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.62, 144.14, 140.50, 132.15, 131.20, 130.51, 130.12, 129.61, 128.41, 127.33, 125.28, 122.72, 109.73, 52.21. EI-MS: *m*/*z*=312.18 (M⁺). Anal. Calcd for (C₁₅H₁₁F₃O₂S): C, 57.69; H, 3.55; S, 10.27. Found: C, 57.66; H, 3.60; S, 10.38.

4.4.11. Methyl 3-mercapto-4'-nitro-[1,1'-biphenyl]-2-carboxylate (**4k**). Yellow oil, 260 mg, 90% yield. ¹H NMR (600 MHz, CDCl₃) δ 8.30–8.23 (m, 2H), 7.52–7.47 (m, 2H), 7.47–7.41 (m, 1H), 7.37 (t, *J*=7.8 Hz, 1H), 7.21–7.16 (m, 1H), 4.01 (s, 1H), 3.61 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.24, 147.17, 139.70, 131.87, 131.62, 130.93, 130.23, 128.91, 127.10, 125.18, 123.50, 52.28. EI-MS: *m*/*z*=289.18 (M⁺). Anal. Calcd for (C₁₄H₁₁NO₄S): C, 58.12; H, 3.83; N, 4.84; S, 11.08. Found: C, 58.23; H, 3.85; N, 4.80; S, 11.13.

4.4.12. Methyl 4'-acetyl-3-mercapto-[1,1'-biphenyl]-2-carboxylate (**4l**). Yellow oil, 263 mg, 92% yield. ¹H NMR (600 MHz, CDCl₃) δ 8.00 (d, *J*=7.8 Hz, 2H), 7.42 (dd, *J*=15.0, 7.8 Hz, 3H), 7.35 (t, *J*=7.8 Hz, 1H), 7.19 (d, *J*=7.8 Hz, 1H), 3.98 (s, 1H), 3.59 (s, 3H), 2.64 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 197.50, 168.60, 145.19, 140.70, 136.03, 131.91, 131.10, 130.36, 130.03, 128.31, 128.18, 127.18, 52.15, 26.55. EI-MS: *m/z*=286.23 (M⁺). Anal. Calcd for (C₁₆H₁₄O₃S): C, 67.11; H, 4.93; S, 11.20. Found: C, 67.02; H, 4.86; S, 11.33.

4.4.13. Methyl 4'-fluoro-3-mercapto-3'-methyl-[1,1'-biphenyl]-2carboxylate (**4m**). Yellow oil, 221 mg, 80% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.35 (d, J=7.8 Hz, 1H), 7.30 (t, J=7.8 Hz, 1H), 7.16 (d, J=7.8 Hz, 2H), 7.10 (s, 1H), 7.01 (t, J=9.0 Hz, 1H), 3.90 (s, 1H), 3.62 (s, 3H), 2.30 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.94, 162.11, 159.67, 140.76, 136.06, 132.46, 131.09, 131.04, 130.20, 129.78, 129.71, 127.32, 126.88, 126.80, 124.83, 124.65, 114.90, 114.68, 52.04, 14.43. EI-MS: *m*/*z*=276.20 (M⁺). Anal. Calcd for (C₁₅H₁₃FO₂S): C, 65.20; H, 4.74; S, 11.60. Found: C, 65.27; H, 4.79; S, 11.53.

4.4.14. Methyl 3',5'-difluoro-3-mercapto-[1,1'-biphenyl]-2-carboxylate (**4n**). Yellow oil, 249 mg, 89% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.41 (d, J=7.8 Hz, 1H), 7.33 (t, J=7.8 Hz, 1H), 7.15

(d, *J*=7.8 Hz, 1H), 6.87 (d, *J*=6.0 Hz, 2H), 6.81 (t, *J*=9.0 Hz, 1H), 3.96 (s, 1H), 3.67 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.23, 163.85, 163.72, 161.37, 161.24, 143.55, 143.46, 139.33, 131.85, 131.12, 130.54, 129.98, 126.89, 111.15, 111.08, 110.97, 110.90, 103.12, 102.87, 102.62, 52.10. EI-MS: *m*/*z*=280.16 (M⁺). Anal. Calcd for (C₁₄H₁₀F₂O₂S): C, 59.99; H, 3.60; S, 11.44. Found: C, 60.05; H, 3.55; S, 11.34.

4.4.15. *Methyl* 3'-chloro-4'-fluoro-3-mercapto-[1,1'-biphenyl]-2carboxylate (**4o**). Yellow oil, 276 mg, 93% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.37 (dd, *J*=7.2, 5.4 Hz, 2H), 7.28 (dd, *J*=13.8, 6.0 Hz, 1H), 7.21–7.07 (m, 3H), 3.94 (s, 1H), 3.64 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.46, 158.77, 156.29, 139.28, 137.43, 132.13, 130.86, 130.27, 130.09, 129.95, 127.79, 127.72, 127.16, 120.88, 120.70, 116.43, 116.22, 52.15. EI-MS: *m/z*=296.14 (M⁺). Anal. Calcd for (C₁₄H₁₀CIFO₂S): C, 56.66; H, 3.40; S, 10.81. Found: C, 56.77; H, 3.45; S, 10.76.

4.4.16. Methyl 3',5'-dichloro-3-mercapto-[1,1'-biphenyl]-2carboxylate (**4p**). Yellow oil, 253 mg, 81% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.41 (d, *J*=7.6 Hz, 1H), 7.38–7.34 (m, 1H), 7.32 (d, *J*=7.6 Hz, 1H), 7.23 (d, *J*=6.8 Hz, 2H), 7.14 (d, *J*=7.6 Hz, 1H), 3.96 (s, 1H), 3.67 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.28, 143.27, 139.07, 134.80, 131.92, 131.39, 130.75, 130.12, 127.65, 127.08, 126.52, 52.26. El-MS: *m*/*z*=312.11 (M⁺). Anal. Calcd for (C₁₄H₁₀Cl₂O₂S): C, 53.69; H, 3.22; S, 10.24. Found: C, 53.52; H, 3.24; S, 10.26.

4.4.17. *Methyl* 3-*mercapto*-3',4',5'-*trimethoxy*-[1,1'-*biphenyl*]-2*carboxylate* (**4q**). Yellow oil, 294 mg, 88% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.36 (d, J=7.8 Hz, 1H), 7.31 (t, J=7.8 Hz, 1H), 7.22 (d, J=7.8 Hz, 1H), 6.57 (s, 2H), 3.88 (s, 3H), 3.86 (s, 6H), 3.66 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.18, 152.98, 141.45, 137.43, 135.86, 132.63, 129.99, 129.77, 127.13, 105.16, 60.78, 55.98, 52.29. EI-MS: *m*/ *z*=334.20 (M⁺). Anal. Calcd for (C₁₇H₁₈O₅S): C, 61.06; H, 5.43; S, 9.59. Found: C, 60.91; H, 5.54; S, 9.55.

4.4.18. *Methyl* 2-mercapto-6-(*naphthalen-2-yl*)*benzoate* (**4***r*). Yellow oil, 253 mg, 86% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.86 (dd, *J*=8.4, 4.2 Hz, 3H), 7.82 (s, 1H), 7.54–7.48 (m, 2H), 7.46 (d, *J*=8.4 Hz, 1H), 7.40 (d, *J*=7.8 Hz, 1H), 7.36 (t, *J*=7.8 Hz, 1H), 7.30 (d, *J*=7.2 Hz, 1H), 3.98 (s, 1H), 3.52 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.13, 141.76, 137.87, 133.17, 132.52, 130.58, 129.95, 129.83, 128.08, 127.96, 127.78, 127.61, 126.89, 126.37, 126.19, 126.15, 52.17. EI-MS: *m*/*z*=294.19 (M⁺). Anal. Calcd for (C₁₈H₁₄O₂S): C, 73.44; H, 4.79; S, 10.89. Found: C, 73.46; H, 4.71; S, 10.92.

4.4.19. Methyl 2-(furan-2-yl)-6-mercaptobenzoate (**4s**). Yellow oil, 210 mg, 90% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.47 (s, 2H), 7.31 (dd, *J*=12.0, 7.8 Hz, 2H), 6.57 (d, *J*=3.0 Hz, 1H), 6.47 (s, 1H), 3.89 (s, 3H), 3.80 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 169.12, 151.44, 142.91, 130.58, 130.27, 129.77, 129.51, 129.38, 124.45, 111.68, 107.91, 52.53. EI-MS: *m*/*z*=234.13 (M⁺). Anal. Calcd for (C₁₂H₁₀O₃S): C, 61.52; H, 4.30; S, 13.69. Found: C, 61.41; H, 4.25; S, 13.64.

4.4.20. (*E*)-Methyl 2-mercapto-6-styrylbenzoate (**4t**). Yellow oil, 240 mg, 89% yield. ¹H NMR (600 MHz, CDCl₃) δ 7.50 (d, *J*=6.6 Hz, 1H), 7.47 (d, *J*=7.8 Hz, 2H), 7.36 (t, *J*=7.2 Hz, 2H), 7.29 (t, *J*=8.4 Hz, 3H), 7.14 (d, *J*=16.2 Hz, 1H), 7.03 (d, *J*=16.2 Hz, 1H), 3.98 (s, 3H), 3.72 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 168.58, 136.83, 136.67, 132.17, 132.00, 130.15, 129.98, 128.60, 128.05, 126.65, 125.26, 123.52, 52.33. EI-MS: *m*/*z*=270.21 (M⁺). Anal. Calcd for (C₁₆H₁₄O₂S): C, 71.08; H, 5.22; S, 11.86. Found: C, 71.09; H, 5.30; S, 11.89.

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