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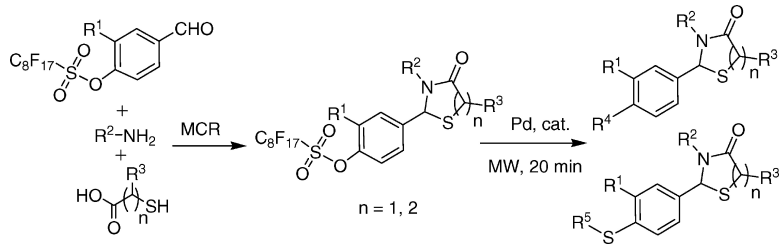

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Microwave-Assisted Fluorous Synthesis of 2-Aryl-Substituted 4-Thiazolidinone and 4-Thiazinanone Libraries

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A straightforward two-step protocol for the synthesis of 2-aryl-substituted 4-thiazolidinone and 4-thiazinanone libraries has been developed. The one-pot, three-component reactions of fluorous benzaldehydes with amines and mercaptoacetic acid or mecaptopropanoic acid produce the heterocyclic systems. Intermediates purified by fluorous solid-phase extraction are subject to microwave-assisted palladium-catalyzed coupling reactions to simultaneously cleave the fluorous tag and introduce the biaryl and thioaryl functional groups to the 2-position of 4-thiazolidinones and 4-thiazinanones.

Introduction

Thiazolidinone and its derivatives are an important class of heterocyclic compounds because of their broad biological activities, such as COX-1 inhibition,[1] anti-inflammatory,[2] antiproliferative,[3,4] antihistaminic,[5] and anti-HIV activities.[6,7] Among those biologically interesting thiazolidinones, the 2-imine-substituted 4-thiazolidinones have shown selective cytotoxicity to both paclitaxel sensitive and resistant lung cancer cells but not to normal human fibroblast.[8–10] To obtain more structurally diverse thiazolidinones and related compounds for quantitative structure–activity relationship (QSAR) studies, we decided to develop a new synthetic methodology for the preparation of 2-aryl-substituted 4-thiazolidinones and the 6-membered analogs, 2-aryl-substituted 4-thiazinanones. Palladium-catalyzed Suzuki and other coupling reactions were introduced to finish the library synthesis. To the best of our knowledge, there is no report on the synthesis of biaryl-substituted 4-thiazinanones in the literature.

Fluorous chemistry is a fast growing synthetic technology, which has demonstrated its value in small molecule library synthesis.[11] The light fluorous tag-attached molecules dissolve well in common organic solvents for conducting solution-phase reactions. The reaction mixtures can be easily separated by fluorous solid-phase extraction (F-SPE).[12] Compared with various fluorous tags such as Boc, Cbz, Fmoc, and trityl,[13] the perfluorooctanesulfonyl is a versatile tag for phenol protection. Phenol-protected benzaldehydes have been used in microwave-assisted multicomponent reactions for construction of heterocyclic skeletons.[14] The perfluorooctanesulfonyl tag can be readily removed by the palladium-catalyzed Suzuki and other coupling reactions to introduce aryl, amine, thiol, and other functionality to the heterocyclic rings.

Reported in this paper is a new application of fluorous benzaldehydes in a two-step reaction sequence for preparation of 4-thiazolidinone and 4-thiazinanone library scaffolds. The 5- and 6-membered heterocyclic rings are assembled by a three-component reaction of fluorous benzaldehydes with amines and mercaptoacetic or mercaptopropanoic acids under mild room-temperature conditions. The second step is a microwave-assisted palladium-catalyzed coupling reaction, which cleaves the fluorous tag and introduces the biaryl or thioaryl functionalities to the 4-thiazolidinone or 4-thiazinanone rings. A total of 60 compounds possess two heterocyclic cores and biaryl- and thioaryl-substitutions have been synthesized.

Results and Discussion

The fluorous benzaldehydes **3** were readily prepared by the reactions of perfluorooctanesulfonyl fluoride **2** with 4-hydroxy benzaldehydes **1** following a literature procedure.[15] Compounds **3** can be purified by flash chromatography with normal silica gel or by F-SPE with fluorous silica gel. The 4-thiazolidinone ring **6** was constructed by a three-component reaction of **3**, amine **4**, and mercaptoacetic acid **5** (Scheme 1). It has been reported in literature that both polymer-supported[16,17] and ionic liquid-supported[18] reactions or one-pot, three-component solution-phase reactions can efficiently assemble **6**.[2–4] The reactions are usually conducted under reflux with a Dean–Stark trap[6] or molecular sieves[16] to remove water and drive the reaction to completion, which may not be a good choice for parallel synthesis. The Katti group[19] developed a room temperature reaction which was promoted by dicyclohexylcarbodiimide (DCC). Following Katti's procedure, we first performed the reaction using **3** as a starting material for a three-component reaction. The reaction did not go completion, and byproducts were generated that complicated the reaction mixture analysis and

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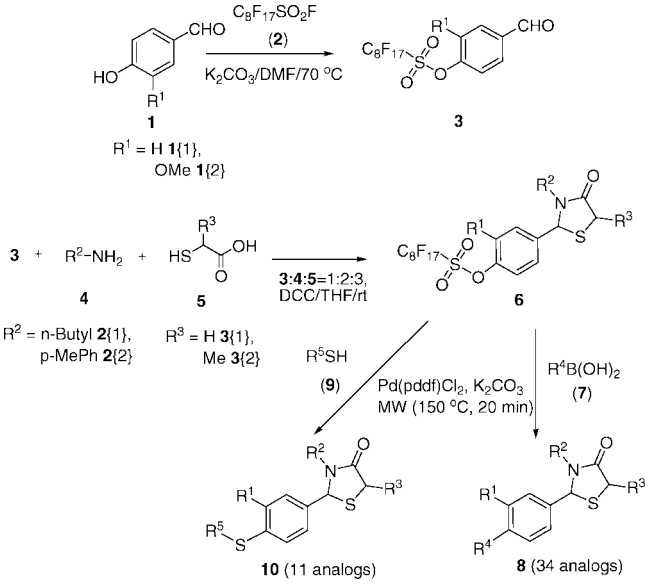
Scheme 1. Synthesis of 2-Aryl-Substituted 4-Thiazolidinones



purification. The alternative approach was to conduct a one-pot, two-step synthesis (Scheme 2). Compound **3** was first reacted with **4** in methanol at room temperature. After the reaction was completed, the solvent was evaporated under reduced pressure, and the resulting imine was dissolved in THF and then reacted with **5** and DCC to give **6**. This two-step, three-component reaction worked well for the other substrates in the synthesis of 4-thiazolidinone derivatives.

For a nonfluorous synthesis of thiazolidinones, the ratio for amine, aldehyde, and mecapatoacetic acid was suggested to be 1:2:3.[16,19] For the fluorous approach, the nonfluorous components were used in excess to consume all fluorous aldehyde, thus no fluorous starting material left over and the fluorous product was easily fished out from the reaction mixture by F-SPE. The three-component reaction for preparation of 4-thiazolidinones was optimized by changing the amount of three starting materials. It was found that a ratio of 1: 2: 3 of aldehyde/amine/mercapto acid gave the best yield. Using the optimized conditions, we prepared seven 4-thizolidinones (Figure 1), which all had purities greater than 90% purity (LC/$UV_{214\ nm}$) after F-SPE. Following the same procedure described above, we employed 3-mercaptopropanoic acid **11** to replace **5** in the synthesis of 4-thiazinanones **12** (Scheme 3).

Six boronic acids **7** and three thiols **9** (Figure 2) were selected for the palladium-catalyzed coupling reactions to introduce new functional group to the heterocyclic systems. The microwave-assisted reactions were carried out using $Pd(dppf)Cl_2$ as a catalyst, K_2CO_3 as a base and 4:4:1 acetone/toluene/water as a cosolvent.[20,21] We tested the different input amount of **7** and **9**. For most reactions, when 0.9 equiv of **7** or **9** and 0.04 equiv of catalyst were used, the yields were between 40 and 90%. After F-SPE, no ligand was found from the final product as analyzed by LC-MS and ^{1}H NMR. When starting materials had a methoxyl group at 3-position, such as in **6**{*2*,*1*,*1*} and **6**{*2*,*2*,*1*}, the reaction activity was reduced. The yields were improved when we doubled the amount of the catalyst. Tables 1 and 2 provide information including yield, purity, and MS of biaryl-substituted 4-thiazolidinones **8** and thioaryl-substituted 4-thiazolidinones **10**. Information for biaryl-substituted 4-thiazinanones **13** and thioaryl-substituted 4-thiazinanones **14** is listed in Tables 3 and 4. All the final compounds are characterized by HPLC-MS at UV_{214nm} and ^{1}H NMR analyses (see Supporting Information). Some compounds were separated as a mixture of diastereomers as detected by ^{1}H and ^{13}C NMR and LC/MS. To ensure the quality of compounds for cell-based screening, all 60 final products were further purified by semipreparative HPLC/MS and analyzed again by HPLC/MS/UV. Diastereomers could not be separated under our purification conditions. Selected compounds were further characterized by HRMS and ^{1}H and ^{13}C NMR (Supporting Information). The anticancer screening of these compounds is in progress.

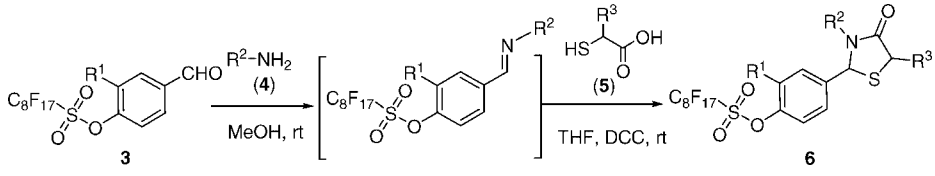
Conclusion

Sixty compounds containing 4-thiazolidinone and 4-thiazinanone cores and biaryl and thioaryl substitution were synthesized using a microwave-assisted fluorous synthesis protocol. Because of the favorable solution-phase reactions and the simple F-SPE for intermediate purifications, this protocol is expected to be easily adopted for production of larger libraries.

Experimental Section

The chemical reagents were purchased from Acros Organics (Geel, Belgium) and Sigma-Aldrich (St. Louis, MO) and used without further purification. LC-MS were performed on a Waters system equipped with a Waters 2795 separation module, a Waters 2996 PDA detector, and a Micromass ZQ detector. A C18 column (2.0 μm, 2.0 $\times$ 50 mm) was used for the separation. The mobile phases were methanol and water, both containing 0.05% trifluoroacetic acid. A linear gradient was used to increase from 50:50 v/v methanol/water to 100% methanol over 6.5 min at a flow rate of 0.5 mL/min. The UV detection was at 214 nm. Mass spectra were recorded in positive-ion mode using electrospray ionization. NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer using chloroform-*d* as solvent. Microwave-assisted parallel synthesis was carried out on a Biotage Initiator single-mode microwave reactor equipped with an automatic sample loader. GeneVac HT-12 Series II was used for the evaporation and concentration of samples after F-SPE.

Scheme 2. Optimized Two-Step Three-Component Reaction of 4-Thiazolidinones



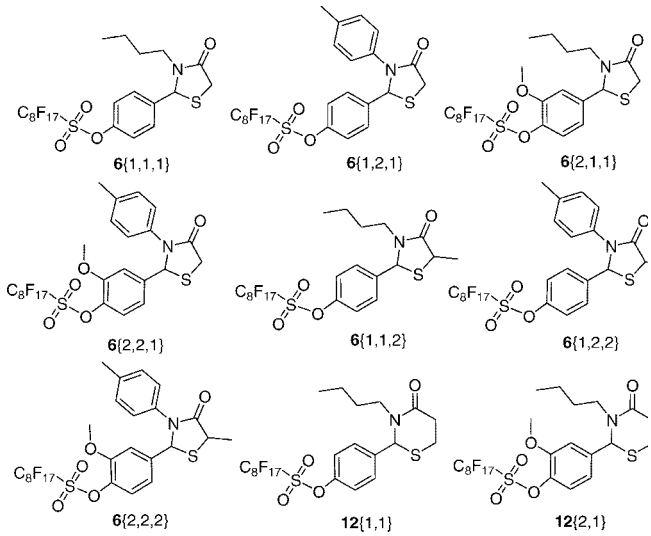
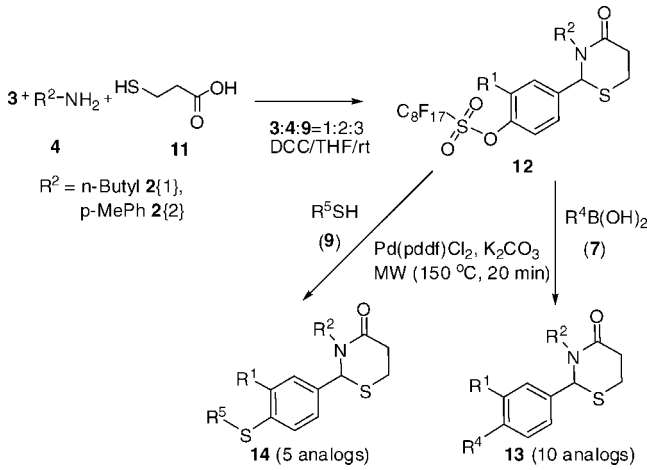


Figure 1. Structures of 4-thiazolidinones **6**{R^1,R^2,R^3} and 4-thiazinanones **12**{R^1,R^2} for Suzuki and Pd-catalyzed coupling reactions.

Scheme 3. Synthesis of 2-Aryl-Substituted 4-Thiazinanones



FluoroFlash SPE cartridges were purchased from Fluorous Technologies, Inc. (Pittsburgh, PA).

General Procedures for F-SPE. A mixture containing fluorous and nonfluorous compounds in a minimum amount of DMF was loaded onto a FluoroFlash cartridge preconditioned with 80:20 MeOH/H_2O. The cartridge was eluted with 80:20 MeOH/H_2O for the nonfluorous fraction followed by the same amount of MeOH for the fluorous fraction. The vacuum was used for elution, allowing the solvent level move at about 4 mL/min. For compounds **6** and **12**, the fluorous fraction was collected. For the final products, the nonfluorous fraction was collected. Both of those fractions were concentrated under reduced pressure using GeneVac HT-12 Series II evaporation system in a 24-plate format. The cartridge was washed thoroughly with acetone or methanol and reused.

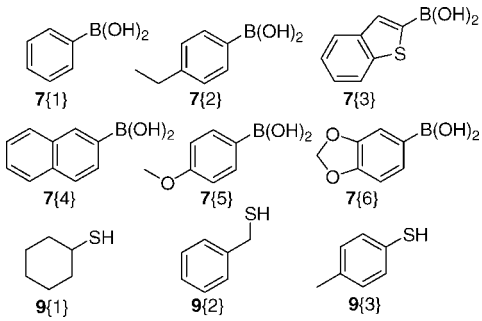


Figure 2. Selected boronic acids and thiols for Pd-catalyzed coupling reaction.

Table 1. Characterization of the Representative Compounds **8**{R^1,R^2,R^3,R^4}

entry	compound	yield[a]	purity[b]	MW (found)[c]
1	**8**{*1,1,1,1*}	94.7	91.1	312 (MH^+)
2	**8**{*1,1,1,2*}	48.3	73.5	340 (MH^+)
3	**8**{*1,1,1,3*}	89.2	86.9	368 (MH^+)
4	**8**{*1,1,1,4*}	81.6	93.5	362 (MH^+)
5	**8**{*1,1,1,6*}	60.0	93.3	356 (MH^+)
6	**8**{*1,2,1,1*}	83.4	90.3	346 (MH^+)
7	**8**{*1,2,1,2*}	72.6	91.6	374 (MH^+)
8	**8**{*1,2,1,3*}	71.8	86.9	402 (MH^+)
9	**8**{*1,2,1,4*}	81.4	87.2	396 (MH^+)
10	**8**{*1,2,1,5*}	76.7	89.1	376 (MH^+)
11	**8**{*1,2,1,6*}	65.3	96.5	390 (MH^+)
12	**8**{*2,1,1,1*}	59.0	74.5	342 (MH^+)
13	**8**{*2,1,1,2*}	95.4	78.8	370 (MH^+)
14	**8**{*2,1,1,4*}	72.9	74.5	392 (MH^+)
15	**8**{*2,1,1,6*}	82.7	90.9	386 (MH^+)
16	**8**{*2,2,1,1*}	58.1	92.0	376 (MH^+)
17	**8**{*2,2,1,2*}	62.4	92.9	404 (MH^+)
18	**8**{*2,2,1,3*}	50.5	75.4	432 (MH^+)
19	**8**{*2,2,1,4*}	71.0	83.9	426 (MH^+)
20	**8**{*2,2,1,6*}	80.0	98.3	420 (MH^+)
21	**8**{*1,1,2,1*}	87.8	88.1	326 (MH^+)
22	**8**{*1,1,2,2*}	96.0	91.3	354 (MH^+)
23	**8**{*1,1,2,4*}	42.8	89.4	376 (MH^+)
24	**8**{*1,1,2,6*}	96.7	84.7	370 (MH^+)
25	**8**{*1,2,2,1*}	84.0	97.3	360 (MH^+)
26	**8**{*1,2,2,2*}	69.3	93.2	388 (MH^+)
27	**8**{*1,2,2,3*}	80.7	96.1	416 (MH^+)
28	**8**{*1,2,2,4*}	69.6	88.4	410 (MH^+)
29	**8**{*1,2,2,6*}	74.8	94.7	404 (MH^+)
30	**8**{*2,2,2,1*}	76.4	100	390 (MH^+)
31	**8**{*2,2,2,2*}	89.0	94.6	418 (MH^+)
32	**8**{*2,2,2,3*}	79.3	92.2	446 (MH^+)
33	**8**{*2,2,2,4*}	76.1	85.0	440 (MH^+)
34	**8**{*2,2,2,6*}	85.7	97.7	434 (MH^+)

[a] The yield (%) was calculated by the weight of the solid obtained after F-SPE. [b] The purity (%) was based on the integration area of HPLC peaks detected at 214 nm. [c] MW (found) was determined by high-performance liquid chromatography−electrospray ionization mass spectrometry (HPLC/ESI MS).

Table 2. Characterization of the Representative Compounds **10**{R^1,R^2,R^3,R^5}

entry	compound	yield[a]	purity[b]	MW (found)[c]
1	**10**{*1,1,1,1*}	70.3	91.6	350 (MH^+)
2	**10**{*1,1,1,2*}	87.1	90.0	358 (MH^+)
3	**10**{*1,2,1,1*}	66.3	100	384 (MH^+)
4	**10**{*1,2,1,2*}	51.9	93.9	392 (MH^+)
5	**10**{*2,1,1,1*}	88.4	91.8	380 (MH^+)
6	**10**{*2,2,1,1*}	85.2	97.7	414 (MH^+)
7	**10**{*1,1,2,1*}	93.3	90.2	364 (MH^+)
8	**10**{*1,2,2,1*}	84.4	96.2	398 (MH^+)
9	**10**{*1,2,2,2*}	78.6	97.6	406 (MH^+)
10	**10**{*2,2,2,1*}	78.2	76.6	428 (MH^+)
11	**10**{*2,2,2,2*}	98.1	94.7	436 (MH^+)

[a] The yield (%) was calculated by the weight of the solid obtained after F-SPE. [b] The purity (%) was based on the integration area of HPLC peaks detected at 214 nm. [c] MW (found) was determined by HPLC/ESI MS.

General Procedure for Preparation of Compounds 3. To a magnetically stirred solution of **1** (1.0 mmol) in DMF (5.0 mL) was added K_2CO_3 powder (1.5 mmol) at room temperature. The mixture was stirred for about 10 min before **2** (1.0 mmol) was added. The mixture was heated at 70 °C

Table 3. Characterization of the Representative Compounds **13**{R^1,R^2,R^4}

entry	compound	yield[a]	purity[b]	MW (found)[c]
1	**13**{*1*,*1*,*1*}	92.2	98.3	326 (MH^+)
2	**13**{*1*,*1*,*2*}	94.3	96.2	354 (MH^+)
3	**13**{*1*,*1*,*3*}	74.3	97.3	382 (MH^+)
4	**13**{*1*,*1*,*4*}	79.9	85.2	376 (MH^+)
5	**13**{*1*,*1*,*6*}	67.7	97.8	370 (MH^+)
6	**13**{*2*,*1*,*1*}	84.8	89.8	356 (MH^+)
7	**13**{*2*,*1*,*3*}	69.9	72.1	412 (MH^+)
8	**13**{*2*,*1*,*4*}	54.0	95.1	406 (MH^+)
9	**13**{*2*,*1*,*5*}	74.6	92.6	386 (MH^+)
10	**13**{*2*,*1*,*6*}	72.0	95.6	400 (MH^+)

[a] The yield (%) was calculated by the weight of the solid obtained after F-SPE. [b] The purity (%) was based on the integration area of HPLC peaks detected at 214 nm. [c] MW (found) was determined by HPLC/ESI MS.

Table 4. Characterization of the Representative Compounds **14**{R^1,R^2,R^5}

entry	compound	yield[a]	purity[b]	MW (found)[c]
1	**14**{*1*,*1*,*1*}	90.0	100	364 (MH^+)
2	**14**{*1*,*1*,*2*}	40.4	91.9	372 (MH^+)
3	**14**{*2*,*1*,*1*}	66.1	72.1	394 (MH^+)
4	**14**{*2*,*1*,*2*}	64.8	94.4	402 (MH^+)
5	**14**{*2*,*1*,*3*}	30.7	92.5	402 (MH^+)

[a] The yield (%) was calculated by the weight of the solid obtained after F-SPE. [b] The purity (%) was based on the integration area of HPLC peaks detected at 214 nm. [c] MW (found) was determined by HPLC/ESI MS.

for 8 h until TLC showed the disappearance of starting materials. The cooled reaction mixture was filtered, and the solid was washed with EtOAc. The filtrate was extracted between EtOAc and water twice, and the combined organic phase was washed with brine and dried by anhydrous Na_2SO_4. After it was concentrated under reduced pressure, the crude product was purified by normal-phase column chromatography (ethyl acetate/petroleum ether = 1:9).

4-Formylphenyl Perfluorooctylsulfonate 3{1}: ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.01 (d, 2H, J = 8.1 Hz), 7.48 (d, 2H, J = 8.0 Hz).

4-Formyl-2-methoxyphenyl Perfluorooctylsulfonate 3{2}: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.58 (s, 1H), 7.52 (d, 1H, J = 8.2 Hz), 7.42 (d, 1H, J = 8.1 Hz), 4.01 (s, 3H).

General Procedure for the Preparation of Compounds 6 (4-Thiazolidinones). Compounds **3** (1.0 mmol) and **4** (2.0 mmol) were stirred in methanol (5.0 mL) at room temperature for 2 h. The solvent was evaporated under reduced pressure. The solid was dissolved in THF (5.0 mL), followed by addition of **5** (3.0 mmol). After 5 min, DCC (2.0 mmol) was added, and the reaction mixture was stirred for additional 1 h at room temperature. After TLC showed the reaction was complete, DCU was removed by filtration, and the product was washed with EtOAc. The filtrate was extracted with 5% $NaHCO_3$ solution and brine and dried over anhydrous Na_2SO_4. After filtration, the organic layer was concentrated to dryness under reduced pressure. The crude product was dissolved in a minimum amount of DMF and purified by F-SPE using a standard procedure.

4-(3-Butyl-4-oxo-1,3-thiazolidin-2-yl)phenyl perfluorooctylsulfonate 6{*1*,*1*,*1*}: yield 72.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, 2H, J = 8.8 Hz), 7.25 (d, 2H, J = 8.7 Hz), 5.57 (s, 1H), 3.75 (d, 1H, J = 15.5 Hz), 3.63 (dd, 2H, J = 7.5 Hz, 15.7 Hz), 2.58 (m, 1H, J = 7.3 Hz), 1.34 (m, 2H, J = 7.3 Hz), 1.18 (m, 2H, J = 8.5 Hz), 0.80 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 171.00, 149.85, 140.42, 128.82, 122.15, 62.53, 42.83, 32.85, 28.87, 19.95, 13.62; ESI-MS m/z 734 (MH^+).

4-(4-Oxo-3-*p*-tolyl-1,3-thiazolidin-2-yl)phenyl Perfluorooctylsulfonate 6{*1*,*2*,*1*}: yield 98.9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, 2H, J = 8.7 Hz), 7.16 (d, 2H, J = 8.0 Hz), 7.02 (d, 2H, J = 8.5 Hz), 6.92 (d, 2H, J = 8.3 Hz),6.00 (s, 1H), 3.91 (d, 1H, J = 15.8 Hz), 3.82 (d, 1H, J = 15.8 Hz), 2.21 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.83, 149.62, 140.15, 137.58, 134.37, 130.01, 129.09, 125.66, 121.85, 64.70, 33.34, 20.99; ESI-MS m/z 768 (MH^+).

4-(3-Butyl-4-oxo-1,3-thiazolidin-2-yl)-2-methoxyphenyl Perfluorooctylsulfonate 6{*2*,*1*,*1*}: yield 44.8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (m, 1H, J = 8.7 Hz), 6.93 (m, 2H), 5.58 (d, 1H, J = 46.1 Hz),3.97 (m, 3H), 3.71 (m, 3H), 2.70 (m, 1H), 1.44 (m, 2H), 1.29 (m, 2H), 0.92 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 171.16, 152.22, 141.32, 139.14, 122.83, 119.24, 111.25, 63.01, 56.44, 42.90, 32.91, 28.89, 19.96, 13.64; ESI-MS m/z 764 (MH^+).

2-Methoxy-4-(4-oxo-3-*p*-tolyl-1,3-thiazolidin-2-yl)phenyl Perfluorooctylsulfonate 6{*2*,*2*,*1*}: yield 53.5%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, 1H, J = 8.8 Hz), 7.14 (d, 1H, J = 8.7 Hz), 7.03 (dd, 2H, J = 7.2 Hz, 14.8 Hz), 6.88 (m, 3H), 5.99 (d, 1H, J = 8.0 Hz), 3.90 (m, 1H), 3.82 (m, 4H), 2.23 (d, 3H, J = 8.0 Hz); ESI-MS m/z 798 (MH^+).

4-(3-Butyl-5-methyl-4-oxo-1,3-thiazolidin-2-yl)phenyl Perfluorooctylsulfonate 6{*1*,*1*,*2*}: yield 66.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, 2H, J = 12.0 Hz), 7.23 (d, 2H, J = 5.2 Hz), 5.50 (d, 1H, J = 9.4 Hz), 3.91 (dq, 1H, J = 7.0 Hz, 32.4 Hz), 3.61 (m, 1H, J = 8.3 Hz), 2.55 (m, 1H), 1.53 (dd, 3H, J = 7.0 Hz, 19.0 Hz), 1.33 (m, 2H), 1.17 (m, 2H), 0.77 (dt, 3H, J = 7.5 Hz, 10.6 Hz); ESI-MS m/z 748 (MH^+).

4-(5-Methyl-4-oxo-3-*p*-tolyl-1,3-thiazolidin-2-yl)phenyl Perfluorooctylsulfonate 6{*1*,*2*,*2*}: yield 83.6%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (t, 2H, J = 8.5 Hz), 7.08 (dd, 2H, J = 8.8 Hz, 12.9 Hz), 6.92 (m, 4H), 5.91 (d, 1H, J = 27.5 Hz), 4.03 (dq, 1H, J = 7.0 Hz, 22.8 Hz), 2.14 (d, 3H, J = 7.9 Hz), 1.59 (dd, 3H, J = 7.0 Hz, 25.0 Hz); ESI-MS m/z 782 (MH^+).

2-Methoxy-4-(5-methyl-4-oxo-3-*p*-tolyl-1,3-thiazolidin-2-yl)phenyl Perfluorooctylsulfonate 6{*2*,*2*,*2*}: yield 66.6%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (m, 4H), 7.02 (d, 1H, J = 8.4 Hz), 6.92 (dd, 2H, J = 8.6 Hz, 10.3 Hz), 6.03 (d, 1H, J = 26.5 Hz), 4.17 (dq, 1H, J = 7.0 Hz, 21.4 Hz), 3.88 (d, 3H, J = 5.8 Hz), 2.33 (dd, 3H, J = 8.6 Hz, 26.6 Hz), 1.73 (dd, 3H, J = 7.0 Hz, 25.3 Hz); ESI-MS m/z 812 (MH^+).

General Procedure for the Preparation of Compounds 12 (4-Thiazinanones). Compounds **3** (1.0 mmol) and **4** (2.0 mmol) were stirred in methanol (5.0 mL) at room temperature for 2 h. The solvent was evaporated under reduced pressure. The solid was dissolved in THF (5 mL), followed by addition of **11** (3.0 mmol). After 5 min, DCC (2.0 mmol) was added, and the reaction mixture was stirred for additional 1 h at room temperature. After TLC showed that the reaction was complete, DCU was removed by filtration and washed with EtOAC. The filtrate was extracted with 5% $NaHCO_3$ solution

and brine and dried over anhydrous Na_2SO_4. After filtration, the organic layer was concentrated to dryness under reduced pressure. The crude product was dissolved in a minimum amount of DMF and purified by F-SPE using standard procedure.

4-(3-Butyl-4-oxo-1,3-thiazinan-2-yl)phenyl Perfluorooctylsulfonate 12{*1,1*}: yield 73.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dt, 4H, J = 9.1 Hz, 18.2 Hz), 5.54 (s, 1H), 4.19 (m, 1H), 2.77 (m, 4H), 2.56 (m, 1H), 1.60 (m, 2H, J = 6.4 Hz), 1.31 (m, 2H), 0.93 (t, 3H, J = 7.3 Hz); ESI-MS m/z 748 (MH^+).

4-(3-Butyl-4-oxo-1,3-thiazinan-2-yl)-2-methoxyphenyl Perfluorooctylsulfonate 12{*2,1*}: yield 57.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (m, 1H), 6.88 (s, 1H), 6.75 (d, 1H, J = 8.4 Hz), 5.42 (s, 1H), 4.10 (m, 1H), 3.89 (m, 3H), 2.74 (m, 3H), 2.61 (m, 1H), 2.51 (m, 1H), 1.52 (m, 2H, J = 7.5 Hz), 1.24 (m, 2H, J = 8.5 Hz), 0.85 (t, 3H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 169.00, 151.77, 141.49, 138.45, 122.16, 118.65, 111.52, 61.50, 56.37, 48.04, 34.27, 29.61, 22.18, 20.20, 13.84; ESI-MS m/z 778 (MH^+).

General Procedure for the Preparation of Compounds 8 (4-Thiazolidinone-Based Suzuki Reaction with Boronic Acids). To a reaction tube with a stirring bar was added compound **6** (1.0 mmol), **7** (0.9 mmol), Pd(pddf)Cl_2 (0.04 mmol), and K_2CO_3 (2.0 mmol) in 0.6 mL of a 4:4:1 acetone/toluene/H_2O solvent. The reactions took place automatically in a monomode microwave cavity (150 °C, 20 min). HPLC was used to monitor the reaction. The reaction mixture was washed with 0.8 mL of water, and the organic layer was loaded onto a 2 g FluoroFlash cartridge directly and washed with 80:20 MeOH/H_2O. The nonfluorous fractions were concentrated, and the fluorous fraction was eluted by methanol for the reuse of cartridge.

For some compounds, which have a bad activity, such as intermediate **6**{*2,1,1*} and **6**{*2,2,1*}, we doubled the amount of the Pd catalyst for completion of the reaction.

2-(Biphenyl-4-yl)-3-butyl-1,3-thiazolidin-4-one 8{*1,1,1,1*}: yield 94.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (t, 4H, J = 8.3 Hz), 7.48 (dd, 2H, J = 4.8 Hz, 10.2 Hz), 7.38 (m, 3H), 5.70 (s, 1H), 3.79 (m, 3H), 2.73 (m, 1H), 1.48 (m, 2H, J = 8.4 Hz), 1.30 (m, 2H, J = 7.3 Hz), 0.92 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ171.13, 142.14, 140.26, 138.59, 128.89, 128.76, 127.82, 127.71, 127.35, 127.12, 63.30, 42.74, 33.05, 28.89, 20.02, 13.72; ESI-MS m/z 312 (MH^+); HR-MS calcd for $C_{19}H_{22}NOS$ $(M + H)^+$ 312.1422, found 312.1423.

3-Butyl-2-(4′-ethylbiphenyl-4-yl)-1,3-thiazolidin-4-one 8{*1,1,1,2*}: yield 48.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, 2H, J = 8.3 Hz), 7.35 (d, 2H, J = 8.2 Hz), 7.18 (d, 2H, J = 8.3 Hz), 7.12 (d, 2H, J = 8.4 Hz),5.51 (s, 1H), 3.68 (d, 1H, J = 15.5 Hz), 3.56 (md, 2H, J = 15.5 Hz), 2.54 (m, 3H, J = 7.5 Hz), 1.28 (m, 2H), 1.12 (m, 5H, J = 8.6 Hz), 0.71 (t, 3H, J = 7.3 Hz); ESI-MS m/z 340 (MH^+).

2-(4-(Benzo[*b*]thiophen-2-yl)phenyl)-3-butyl-1,3-thiazolidin-4-one 8{*1,1,1,3*}: yield 89.2%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (m, 4H), 7.57 (m, 1H), 7.37 (m, 4H), 5.69 (s, 1H), 3.87 (d, 1H, J = 15.5 Hz), 3.75 (md, 2H, J = 15.5 Hz), 2.73 (m, 1H), 1.48 (m, 2H), 1.28 (m, 2H), 0.91 (t, 3H, J = 7.3 Hz); ESI-MS m/z 368 (MH^+).

3-Butyl-2-(4-(naphthalen-2-yl)phenyl)-1,3-thiazolidin-4-one 8{*1,1,1,4*}: yield 81.6%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.93 (m, 3H), 7.76 (m, 3H), 7.54 (m, 2H), 7.43 (d, 2H, J = 8.3 Hz),5.73 (s, 1H), 3.89 (d, 1H, J = 15.5 Hz), 3.77 (md, 2H, J = 15.5 Hz), 2.75 (m, 1H), 1.51 (m, 2H), 1.32 (m, 2H, J = 7.3 Hz), 0.93 (t, 3H, J = 7.3 Hz); ESI-MS m/z 362 (MH^+).

2-(4-(Benzo[*d*][1,3]dioxol-5-yl)phenyl)-3-butyl-1,3-thiazolidin-4-one 8{*1,1,1,6*}: yield 60.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, 2H, J = 8.3 Hz), 7.15 (t, 2H, J = 8.3 Hz), 6.87 (d, 2H, J = 8.0 Hz), 6.70 (d, 1H, J = 8.0 Hz), 5.82 (m, 3H), 5.47 (s, 1H), 3.67 (d, 1H, J = 15.0 Hz), 3.53 (md, 2H, J = 15.0 Hz), 3.30 (s, 1H), 2.50 (m, 1H), 1.26 (m, 2H, J = 6.6 Hz), 1.07 (m, 2H), 0.68 (t, 4H, J = 7.3 Hz); ESI-MS m/z 356 (MH^+); HR-MS calcd for $C_{20}H_{22}NO_3S$ $(M + H)^+$: 356.1320, found 356.1310.

2-(Biphenyl-4-yl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,1,1*}: yield 83.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (m, 4H), 7.34 (t, 2H, J = 7.5 Hz), 7.27 (m, 3H), 6.99 (t, 4H, J = 5.3 Hz), 6.02 (s, 1H), 3.94 (d, 1H, J = 15.8 Hz), 3.81 (d, 1H, J = 15.8 Hz), 2.18 (s, 3H); ESI-MS m/z 346 (MH^+).

2-(4′-Ethylbiphenyl-4-yl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,1,2*}: yield 72.6%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, 2H, J = 8.3 Hz), 7.49 (d, 2H, J = 8.2 Hz), 7.37 (d, 2H, J = 8.3 Hz), 7.28 (d, 2H, J = 7.7 Hz),7.10 (t, 4H, J = 8.0 Hz), 6.11 (s, 1H), 4.04 (d, 1H, J = 15.8 Hz), 3.91 (d, 1H, J = 15.8 Hz), 2.71 (q, 2H, J = 7.6 Hz), 2.28 (s, 3H), 1.30 (t, 3H, J = 8.0 Hz); ESI-MS: m/z 374 (MH^+).

2-(4-(Benzo[*b*]thiophen-2-yl)phenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,1,3*}: yield 71.8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (m, 3H, J = 8.2 Hz), 7.52 (d, 1H, J = 8.3 Hz), 7.42 (d, 1H, J = 12.7 Hz), 7.21 (m, 4H), 6.93 (m, 4H), 5.97 (s, 1H), 3.84 (dd, 2H, J = 15.8 Hz, 49.2 Hz), 2.14 (s, 3H); ESI-MS m/z 402 (MH^+).

2-(4-(Naphthalen-2-yl)phenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,1,4*}: yield 81.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (m, 4H), 7.70 (m, 2H), 7.53 (m, 3H), 7.43 (d, 2H, J = 8.3 Hz), 7.13 (s, 4H), 6.15 (s, 1H), 4.06 (d, 1H, J = 15.8 Hz), 3.93 (d, 1H, J = 15.8 Hz), 2.29 (s, 3H); ESI-MS m/z 396 (MH^+).

2-(4′-Methoxybiphenyl-4-yl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,1,5*}: yield 76.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, 4H, J = 8.6 Hz), 7.21 (d, 2H, J = 8.2 Hz), 6.96 (s, 3H), 6.84 (d, 3H, J = 8.8 Hz), 5.97 (s, 1H), 3.90 (d, 1H, J = 15.8 Hz), 3.74 (ds, 4H, J = 9.0 Hz, 15.0 Hz), 2.14 (s, 3H); ESI-MS m/z 376 (MH^+).

2-(4-(Benzo[*d*][1,3]dioxol-5-yl)phenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,1,6*}: yield 65.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, 2H, J = 8.0 Hz), 7.17 (d, 2H, J = 8.1 Hz), 6.92 (m, 4H), 6.83 (m, 3H), 6.69 (d, 1H, J = 8.2 Hz), 5.92 (s, 1H), 5.83 (s, 3H), 3.85 (d, 1H, J = 15.8 Hz), 3.72 (d, 1H, J = 15.8 Hz), 2.10 (s, 3H); ESI-MS m/z 390 (MH^+).

3-Butyl-2-(2-methoxybiphenyl-4-yl)-1,3-thiazolidin-4-one 8{*2,1,1,1*}: yield 59.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (m, 2H), 7.24 (m, 5H), 6.73 (m, 1H), 5.51 (s, 1H), 3.67 (m, 6H), 2.60 (m, 1H), 1.32 (m, 2H), 1.09 (m, 2H), 0.73 (t, 4H, J = 7.3 Hz); ESI-MS m/z 342 (MH^+).

3-Butyl-2-(4′-ethyl-2-methoxybiphenyl-4-yl)-1,3-thiazolidin-4-one 8{*2,1,1,2*}: yield 95.4%; ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.39 (dt, 3H, J = 9.4 Hz, 18.8 Hz), 7.20 (m, 3H), 6.83 (m, 2H), 5.59 (s, 1H), 3.73 (m, 6H), 2.66 (m, 3H), 1.41 (m, 2H), 1.20 (m, 5H), 0.83 (m, 3H); ^{13}C NMR ($CDCl_3$) δ171.23, 157.71, 143.32, 139.80, 135.00, 131.24, 128.24, 126.93, 119.31, 109.19, 63.61, 55.74, 42.83, 33.10, 28.96, 28.52, 20.04, 15.60, 13.75; ESI-MS *m*/*z* 370 (MH^+).

3-Butyl-2-(3-methoxy-4-(naphthalen-2-yl)phenyl)-1,3-thiazolidin-4-one 8{*2,1,1,4*}: yield 72.9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, 1H, J = 9.8 Hz), 7.81 (m, 2H), 7.56 (m, 1H), 7.41 (m, 2H, J = 6.2 Hz), 7.33 (m, 2H, J = 9.2 Hz), 7.15 (m, 1H), 6.89 (m, 1H), 5.58 (s, 1H), 3.76 (m, 6H), 2.71 (m, 1H), 1.43 (m, 2H), 1.24 (m, 2H, J = 7.8 Hz), 0.83 (m, 3H); ESI-MS *m*/*z* 392 (MH^+).

2-(4-(Benzo[*d*][1,3]dioxol-5-yl)-3-methoxyphenyl)-3-butyl-1,3-thiazolidin-4-one 8{*2,1,1,6*}: yield 82.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, 1H, J = 8.5 Hz), 7.20 (d, 1H, J = 7.4 Hz), 7.07 (m, 1H), 6.99 (m, 1H), 6.90 (m, 2H, J = 9.1 Hz),5.99 (s, 2H), 5.64 (s, 1H), 3.82 (m, 6H), 2.77 (m, 1H), 1.49 (m, 2H), 1.31 (m, 2H), 0.93 (m, 3H); ESI-MS *m*/*z* 386 (MH^+).

2-(2-Methoxybiphenyl-4-yl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,1,1*}: yield 58.1%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, 1H, J = 7.1 Hz), 7.61 (t, 3H, J = 5.8 Hz), 7.53 (t, 3H, J = 7.3 Hz), 7.42 (m, 3H), 7.09 (d, 1H, J = 7.8 Hz), 7.03 (s, 1H), 6.25 (s, 1H), 4.16 (d, 1H, J = 15.8 Hz), 4.03 (d, 1H, J = 15.7 Hz), 3.90 (s, 3H), 2.42 (s, 3H); ESI-MS *m*/*z* 376 (MH^+).

2-(4′-Ethyl-2-methoxybiphenyl-4-yl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,1,2*}: yield 62.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (m, 1H), 7.45 (m, 3H), 7.25 (m, 4H), 7.08 (m, 3H), 6.90 (m, 1H), 6.12 (s, 1H), 3.92 (m, 5H), 2.73 (m, 2H, J = 7.6 Hz), 2.33 (d, 3H), 1.28 (m, 3H); ^{13}C NMR ($CDCl_3$) δ171.20, 156.88, 143.23, 139.86, 137.14, 134.96, 131.29, 131.06, 129.85, 128.24, 127.56, 126.94, 125.55, 119.27, 109.36, 65.65, 55.65, 33.50, 28.59, 21.06, 15.45; ESI-MS *m*/*z* 404 (MH^+); HR-MS calcd for $C_{25}H_{26}NO_2S$ $(M + H)^+$ 404.1684, found 404.1695.

2-(4-(Benzo[*b*]thiophen-2-yl)-3-methoxyphenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,1,3*}: yield 50.5%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (m, 3H), 7.69 (m, 1H), 7.48 (m, 7H), 7.07 (m, 1H), 6.93 (m, 1H), 6.16 (d, 1H, J = 28.4 Hz), 4.00 (m, 5H), 2.34 (m, 3H); ESI-MS *m*/*z* 432 (MH^+).

2-(3-Methoxy-4-(naphthalen-2-yl)phenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,1,4*}: yield 71.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (m, 5H), 7.77 (m, 1H), 7.65 (d, 1H, J = 8.6 Hz), 7.53 (m, 4H), 7.36 (d, 1H, J = 7.7 Hz), 7.01 (d, 1H, J = 7.8 Hz), 6.95 (s, 1H), 6.10 (s, 1H), 4.06 (d, 1H, J = 15.8 Hz), 3.90 (d, 1H, J = 15.0 Hz), 3.77 (s, 3H), 2.30 (s, 3H); ESI-MS *m*/*z* 426 (MH^+).

2-(4-(Benzo[*d*][1,3]dioxol-5-yl)-3-methoxyphenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,1,6*}: yield 80.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 3H), 7.11 (d, 1H, J = 7.7 Hz), 6.94 (m, 3H), 6.84 (d, 1H, J = 8.0 Hz), 6.76 (m, 2H), 5.92 (m, 4H), 3.84 (dd, 2H, J = 15.0 Hz, 38.0 Hz), 3.69 (s, 3H), 2.22 (s, 3H); ESI-MS *m*/*z* 420 (MH^+).

2-(Biphenyl-4-yl)-3-butyl-5-methyl-1,3-thiazolidin-4-one 8{*1,1,2,1*}: yield 87.8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (m, 3H), 7.28 (dd, 2H, J = 6.8 Hz, 8.1 Hz), 7.19 (m, 3H), 5.46 (d, 1H, J = 8.7 Hz), 3.83 (dt, 1H, J = 7.0 Hz, 21.1 Hz), 3.56 (m, 1H), 2.54 (m, 1H), 1.46 (m, 3H), 1.28 (m, 2H), 1.09 (m, 2H), 0.71 (dq, 3H, J = 7.3 Hz, 10.5 Hz); ^{13}C NMR ($CDCl_3$) diastereomers, δ (174.07, 173.86), 142.13, 140.29, 138.91, 138.14, 128.88, (127.87, 127.82), (127.69, 127.66), (127.12, 127.10), (61.62, 61.20), (42.91, 42.86), (42.47, 41.76), (28.94, 28.81), (20.04, 19.95), (13.75, 13.71); ESI-MS: *m*/*z* 326 (MH^+).

3-Butyl-2-(4′-ethylbiphenyl-4-yl)-5-methyl-1,3-thiazolidin-4-one 8{*1,1,2,2*}: yield 96.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (m, 2H), 7.53 (dt, 2H, J = 4.5 Hz, 11.8 Hz), 7.34 (m, 4H), 5.64 (d, 1H, J = 8.0 Hz), 4.05 (dq, 1H, J = 8.0 Hz, 21.1 Hz), 3.76 (m, 1H), 2.73 (m, 3H), 1.64 (m, 3H), 1.48 (m, 2H), 1.28 (m, 5H), 0.91 (m, 3H); ^{13}C NMR ($CDCl_3$) diastereomers, δ (174.06, 173.87), (143.90, 143.87), (142.09, 141.90), 138.55, 137.65, (128.41, 128.23), 127.84, (127.63, 127.54), (127.03, 126.93), (61.66, 61.23), (42.90, 42.85), (42.46, 41.76), (28.95, 28.81), (20.04, 19.95), 15.56, (13.75, 13.71); ESI-MS *m*/*z* 354 (MH^+); HR-MS calcd for $C_{22}H_{28}NOS$ $(M + H)^+$ 354.1892, found 354.1888.

3-Butyl-5-methyl-2-(4-(naphthalen-2-yl)phenyl)-1,3-thiazolidin-4-one 8{*1,1,2,4*}: yield 42.8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, 1H, J = 53.2 Hz), 7.73 (m, 3H), 7.56 (m, 2H), 7.32 (m, 2H), 7.25 (d, 1H, J = 8.3 Hz), 7.20 (d, 1H, J = 8.3 Hz), 7.09 (m, 1H), 5.47 (d, 1H, J = 8.0 Hz), 3.85 (dq, 1H, J = 7.1 Hz, 21.1 Hz), 3.58 (m, 1H), 2.56 (m, 1H), 1.44 (m,3H), 1.29 (m, 2H), 1.11 (m, 2H), 0.73 (m, 3H); ESI-MS *m*/*z* 376 (MH^+).

2-(4-(Benzo[*d*][1,3]dioxol-5-yl)phenyl)-3-butyl-5-methyl-1,3-thiazolidin-4-one 8{*1,1,2,6*}: yield 96.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 2H), 7.18 (m, 2H), 6.88 (m, 2H), 6.72 (m, 1H), 5.85 (d, 2H, J = 8.0 Hz), 5.45 (d, 1H, J = 8.0 Hz), 3.84 (dq, 1H, J = 7.0 Hz, 21.0 Hz), 3.56 (m, 1H), 2.55 (m, 1H), 1.45 (m, 3H), 1.28 (m, 2H), 1.11 (m, 2H), 0.72 (m, 3H); ESI-MS *m*/*z* 370 (MH^+).

2-(Biphenyl-4-yl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,2,1*}: yield 84.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (m, 10H), 7.03 (m, 3H), 6.00 (d, 1H, J = 33.5 Hz), 4.14 (dq, 1H, J = 8.0 Hz, 32.0 Hz), 2.23 (dd, 3H, J = 12.0 Hz, 31.7 Hz), 1.65 (dt, 3H, J = 7.7 Hz, 15.4 Hz). ^{13}C NMR ($CDCl_3$) diastereomers, δ 173.86, 141.52, 140.23, 139.15, 136.84, 135.36, (129.76, 129.73), (128.82, 128.80), 128.04, 127.62, 127.18, (127.04, 127.00), 125.84, 125.19, (63.44, 63.25), (42.72, 41.78), (21.02, 20.36), 19.24; ESI-MS *m*/*z* 360 (MH^+).

2-(4′-Ethylbiphenyl-4-yl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,2,2*}: yield 69.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 2H), 7.28 (dt, 2H, J = 4.6 Hz, 11.8 Hz), 7.16 (t, 2H, J = 7.3 Hz), 7.08 (m, 3H), 6.92 (m, 3H), 5.88 (d, 1H, J = 33.4 Hz), 4.01 (dq, 1H, J = 7.0 Hz, 42.4 Hz), 2.51 (m, 2H), 2.08 (d, 3H, J = 8.4 Hz), 1.54 (dd, 3H, J = 8.0 Hz, 16.0 Hz), 1.10 (m, 3H); ESI-MS: *m*/*z* 388 (MH^+).

2-(4-(Benzo[*b*]thiophen-2-yl)phenyl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,2,3*}: yield 80.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (m, 2H), 7.63 (dd, 2H, J = 8.3 Hz, 14.2 Hz), 7.53 (t, 1H, J = 9.9 Hz), 7.34 (m, 4H), 7.13 (m, 4H), 6.07 (d, 1H, J = 33.2 Hz), 4.21 (dq, 1H, J = 7.0 Hz, 32.4 Hz), 2.26 (d, 3H, J = 7.9 Hz), 1.74 (dd, 3H, J = 7.0 Hz, 31.5 Hz); ESI-MS *m*/*z* 416 (MH^+).

5-Methyl-2-(4-(naphthalen-2-yl)phenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,2,4*}: yield 69.6%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, 1H, J = 8.1 Hz), 7.82 (m, 3H, J = 6.7 Hz), 7.63 (m, 3H), 7.45 (m, 3H), 7.34 (t, 1H, J = 7.4 Hz), 7.06 (m, 3H), 6.03 (d, 1H, J = 33.7 Hz), 4.16 (dt, 1H, J = 7.0 Hz, 37.1 Hz), 2.22 (t, 3H, J = 14.7 Hz), 1.66 (m, 3H); ESI-MS m/z 410 (MH^+).

2-(4-(Benzo[*d*][1,3]dioxol-5-yl)phenyl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*1,2,2,6*}: yield 74.8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (m, 2H), 7.29 (t, 2H, J = 7.2 Hz), 7.07 (m, 4H), 6.96 (m, 2H), 6.83 (m, 1H), 5.98 (m, 3H), 4.15 (dq, 1H, J = 7.0 Hz, 41.2 Hz), 2.27 (d, 3H, J = 11.3 Hz), 1.69 (dd, 3H, J = 7.0 Hz, 32.4 Hz); ^{13}C NMR ($CDCl_3$) diastereomers, δ (173.86, 173.81), 148.19, 147.33, 141.20, 138.79, (136.91, 136.79), 135.38, 134.59, (129.75, 129.72), 128.75, (127.08, 126.90), 125.80, 125.14, (120.64, 120.31), 108.60, (107.71, 107.51), (101.22, 101.13), (63.38, 63.19), (42.71, 41.76), (21.02, 20.35), (19.23, 18.47); ESI-MS m/z 404 (MH^+); HR-MS calcd for $C_{24}H_{22}NO_3S$ $(M + H)^+$ 404.1320, found 404.1322.

2-(2-Methoxybiphenyl-4-yl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,2,1*}: yield 76.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, 2H, J = 7.2 Hz, 14.1 Hz), 7.40 (dd, 2H, J = 7.3 Hz, 12.3 Hz), 7.33 (t, 1H, J = 9.9 Hz), 7.20 (m, 5H), 6.93 (dd, 2H, J = 8.9 Hz, 19.9 Hz), 6.08 (d, 1H, J = 33.2 Hz), 4.22 (dq, 1H, J = 7.0 Hz, 33.0 Hz), 3.80 (d, 3H, J = 13.8 Hz), 2.30 (dd, 4H, J = 34.3 Hz, 40.4 Hz), 1.76 (dd, 3H, J = 7.0 Hz, 33.7 Hz); ESI-MS m/z 390 (MH^+).

2-(4′-Ethyl-2-methoxybiphenyl-4-yl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,2,2*}: yield 89.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (m, 1H), 7.49 (m, 2H), 7.31 (m, 6H), 7.01 (m, 2H), 6.14 (d, 1H, J = 23.4 Hz), 4.30 (dq, 1H, J = 8.0 Hz, 32.0 Hz), 3.79 (d, 3H, J = 4.0 Hz), 2.79 (m, 2H), 2.35 (dd, 4H, J = 34.0 Hz, 40.4 Hz), 1.84 (dd, 3H, J = 7.0 Hz, 33.0 Hz), 1.36 (m, 4H); ESI-MS m/z 418 (MH^+).

2-(4-(Benzo[*b*]thiophen-2-yl)-3-methoxyphenyl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,2,3*}: yield 79.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dt, 3H, J = 6.0 Hz, 14.3 Hz), 7.61 (m, 1H), 7.33 (dd, 2H, J = 5.9 Hz, 10.2 Hz), 7.14 (m, 4H), 6.96 (m, 2H), 6.08 (d, 1H, J = 32.6 Hz), 4.20 (dq, 1H, J = 8.0 Hz, 33.0 Hz), 3.86 (m, 3H), 2.32 (d, 3H, J = 8.0 Hz), 1.74 (dd, 3H, J = 6.2 Hz, 12.4 Hz); ESI-MS m/z 446 (MH^+).

2-(3-Methoxy-4-(naphthalen-2-yl)phenyl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,2,4*}: yield 76.1%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (m, 5H), 7.76 (dd, 1H, J = 4.5 Hz, 11.5 Hz), 7.64 (m, 3H), 7.45 (m, 1H), 7.32 (d, 1H, J = 8.5 Hz), 7.27 (d, 2H, J = 10.3 Hz), 7.10 (dd, 2H, J = 7.8 Hz, 23.2 Hz), 6.23 (d, 1H, J = 32.5 Hz), 4.35 (dq, 1H, J = 8.0 Hz, 40.0 Hz), 3.92 (m, 3H), 2.42 (m, 3H), 1.89 (dd, 3H, J = 7.0 Hz, 34.1 Hz); ESI-MS m/z 440 (MH^+).

2-(4-(Benzo[*d*][1,3]dioxol-5-yl)-3-methoxyphenyl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 8{*2,2,2,6*}: yield 85.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (t, 1H, J = 7.3 Hz), 6.97 (m, 5H), 6.82 (dd, 1H, J = 6.1 Hz, 9.9 Hz), 6.72 (m, 3H), 5.82 (m, 3H), 4.03 (dq, 1H, J = 8.0 Hz, 32.0 Hz), 3.46 (d, 3H, J = 5.4 Hz), 2.11 (dd, 3H, J = 34.3 Hz, 40.2 Hz), 1.55 (dd, 3H, J = 14.6 Hz, 45.7 Hz); ESI-MS m/z 434 (MH^+).

General Procedure for Preparation of Compounds 10 (4-Thiazolidinone-Based Palladium Coupling Reaction with Thiols). To a reaction tube with a stirring bar was added **6** (1.0 mmol), **9** (0.9 mmol), Pd(pddf)Cl_2 (0.04 mmol), and K_2CO_3 (2.0 mmol) in 0.6 mL of a 4:4:1 acetone/toluene/H_2O solvent. The reactions took place automatically in a monomode microwave cavity (150 °C, 20 min). HPLC was used to monitor the reaction. The reaction mixture was washed with 0.8 mL water, and the organic layer was loaded onto a 2 g FluoroFlash cartridge directly and washed with 80:20 MeOH/H_2O. The nonfluorous fractions were concentrated, and the fluorous fraction was eluted by methanol for the reuse of cartridge.

For some compounds, which have poor activity, such as intermediates **6**{*2,1,1*} and **6**{*2,2,1*}, we doubled the amount of the Pd catalyst for the complete of the reaction.

3-Butyl-2-(4-(cyclohexylthio)phenyl)-1,3-thiazolidin-4-one 10{1,1,1,1}: yield 70.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, 2H, J = 8.0 Hz), 7.00 (d, 2H, J = 8.0 Hz), 5.40 (s, 1H), 3.65 (d, 1H, J = 15.5 Hz), 3.52 (md, 2H, J = 16.0 Hz), 3.00 (m, 1H, J = 8.4 Hz), 2.50 (m, 1H, J = 8.5 Hz), 1.84 (m, 2H), 1.63 (m, 2H), 1.42 (m, 2H), 1.16 (m, 8H), 0.72 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 171.03, 137.53, 137.09, 131.30, 127.37, 63.24, 50.01, 46.17, 42.71, 33.29, 32.89, 28.87, 25.74, 19.99, 13.69; ESI-MS m/z 350 (MH^+).

2-(4-(Benzylthio)phenyl)-3-butyl-1,3-thiazolidin-4-one 10{*1,1,1,2*}: yield 87.1%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 8H), 7.20 (d, 1H, J = 8.4 Hz), 5.55 (s, 1H), 4.19 (s, 2H), 3.73 (m, 3H), 2.64 (m, 1H, J = 8.5 Hz), 1.42 (m, 2H, J = 6.5 Hz), 1.27 (m, 2H), 0.91 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 171.01, 138.12, 137.37, 136.94, 129.50, 128.80, 128.59, 127.47, 127.37, 63.19, 43.31, 42.66, 38.51, 33.02, 28.83, 19.99, 13.70; ESI-MS m/z 358 (MH^+); HR-MS calcd for $C_{20}H_{24}NOS_2$ $(M + H)^+$ 358.1299, found 358.1299.

2-(4-(Cyclohexylthio)Phenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 10{*1,2,1,1*}: yield 66.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, 2H, J = 9.0 Hz), 7.22 (d, 2H, J = 8.3 Hz), 7.09 (d, 2H, J = 8.2 Hz), 7.02 (d, 2H, J = 8.4 Hz), 6.03 (s, 1H), 4.00 (d, 1H, J = 15.8 Hz), 3.88 (d, 1H, J = 15.7 Hz), 3.12 (m, 1H), 2.28 (s, 3H), 1.97 (m, 2H), 1.78 (m, 2H), 1.63 (m, 2H), 1.35 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 170.97, 137.50, 137.19, 136.75, 134.74, 130.98, 129.82, 127.50, 125.76, 65.42, 46.07, 33.45, 33.26, 26.01, 25.72, 21.03; ESI-MS m/z 384 (MH^+); HR-MS calcd for $C_{22}H_{26}NOS_2$ $(M + H)^+$ 384.1456, found 384.1469.

2-(4-(Benzylthio)Phenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 10{*1,2,1,2*}: yield 51.9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 7H), 7.20 (m, 3H), 7.10 (d, 1H, J = 8.1 Hz), 7.03 (t, 2H, J = 7.9 Hz), 6.01 (s, 1H), 4.22 (m, 2H), 3.93 (m, 2H), 2.32 (m, 3H); ESI-MS m/z 392 (MH^+).

3-Butyl-2-(4-(cyclohexylthio)-3-methoxyphenyl)-1,3-thiazolidin-4-one 10{*2,1,1,1*}: yield 88.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, 1H, J = 8.0 Hz), 6.84 (d, 1H, J = 8.0 Hz), 6.77 (s, 1H), 5.56 (s, 1H), 3.91 (m, 3H), 3.75 (m, 3H), 3.24 (m, 1H), 2.71 (m, 1H), 2.03 (m, 2H), 1.79 (s, 2H), 1.61 (m, 2H), 1.35 (m, 8H), 0.89 (t, 3H, J = 7.6 Hz); ESI-MS m/z 380 (MH^+).

2-(4-(Cyclohexylthio)-3-methoxyphenyl)-3-*p*-tolyl-1,3-thiazolidin-4-one 10{*2,2,1,1*}: yield 85.2%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (m, 2H), 7.07 (dd, 4H, J = 8.3 Hz, 23.0 Hz), 6.82 (m, 2H), 6.04 (s, 1H), 3.92 (m, 5H), 3.19 (m, 1H), 2.29 (s, 3H), 1.95 (m, 1H), 1.80 (m, 1H), 1.63 (m, 2H), 1.34 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 171.06, 157.83, 138.52, 137.20, 134.81, 130.40, 129.82, 125.65, 125.23, 119.64, 108.90, 65.64, 55.90, 50.01, 43.88, 33.51, 33.14, 32.89, 26.04, 25.72, 21.03; ESI-MS: *m/z* 414 (MH^+).

3-Butyl-2-(4-(cyclohexylthio)phenyl)-5-methyl-1,3-thiazolidin-4-one 10{*1,2,2,1*}: yield 93.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.15 (d, 1H, J = 8.3 Hz), 7.10 (d, 1H, J = 8.3 Hz), 5.46 (d, 1H, J = 8.0 Hz), 3.90 (dq, 1H, J = 6.3 Hz, 14.1 Hz), 3.59 (m, 1H), 3.08 (m, 1H), 2.59 (m, 1H), 1.92 (d, 2H, J = 11.4 Hz), 1.71 (d, 2H, J = 5.6 Hz), 1.53 (m, 5H), 1.24 (m, 8H), 0.80 (tt, 3H, J = 7.3 Hz, 10.8 Hz); ESI-MS *m/z* 364 (MH^+).

2-(4-(Cyclohexylthio)Phenyl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 10{*1,2,2,1*}: yield 84.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, 2H, J = 7.8 Hz), 7.13 (m, 2H, J = 7.6 Hz), 6.99 (m, 3H), 6.91 (d, 1H, J = 8.4 Hz), 5.90 (d, 1H, J = 30.7 Hz), 4.09 (dq, 1H, J = 8.0 Hz, 31.0 Hz), 3.02 (m, 1H), 2.21 (d, 3H, J = 8.0 Hz), 1.89 (d, 2H, J = 10.2 Hz), 1.65 (m, 5H), 1.23 (m, 6H); ^{13}C NMR ($CDCl_3$) diastereomers, δ 173.74, 138.10, 136.87, 136.41, 135.26, (131.15, 130.85), 129.73, (128.14, 127.10), (125.92, 125.27), (63.37, 63.20), 50.01, 46.05, (42.63, 41.78), (33.28, 32.89), (26.02, 25.73), (21.02, 20.25), 19.32; ESI-MS *m/z* 398 (MH^+); HR-MS calcd for $C_{23}H_{28}NOS_2$ $(M + H)^+$ 398.1612, found 398.1623.

2-(4-(Benzylthio)Phenyl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 10{*1,2,2,2*}: yield 78.6%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 6H), 7.19 (t, 4H, J = 8.7 Hz), 7.06 (dt, 4H, J = 8.3 Hz, 20.3 Hz), 5.98 (d, 1H, J = 31.4 Hz), 4.18 (m, 3H), 2.33 (d, 3H, J = 27.0 Hz), 1.72 (dd, 3H, J = 7.0 Hz, 26.8 Hz); ^{13}C NMR ($CDCl_3$) diastereomers, δ 173.72, 138.03, 137.58, 136.99, 135.23, (129.74, 129.58), (129.44, 129.38), (128.79, 128.51), 128.21, (127.45, 127.31), 127.21, (125.87, 128.30), (63.29, 63.17), (43.32, 42.63), 41.83, 38.63, (21.04, 20.22), 19.40; ESI-MS *m/z* 406 (MH^+).

2-(4-(Cyclohexylthio)-3-methoxyphenyl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 10{*2,2,2,1*}: yield 78.2%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (m, 5H), 6.82 (m, 2H), 6.00 (d, 1H, J = 4.6 Hz), 4.18 (dq, 1H, J = 8.0 Hz, 32.0 Hz), 3.80 (dd, 3H, J = 6.5 Hz, 24.1 Hz), 3.19 (m, 1H), 2.28 (d, 3H, J = 6.6 Hz), 2.06 (d, 2H, J = 8.9 Hz), 1.78 (m, 5H), 1.31 (m, 6H); ^{13}C NMR ($CDCl_3$) diastereomers, δ 173.81, 157.95, 139.19, 136.88, 135.53, (130.67, 130.27), 129.70, (125.80, 125.04), (120.27, 119.16), (109.45, 108.56), (60.60, 60.32), (55.90, 55.28), 50.01, (43.94, 43.87), (42.62, 41.87), (33.20, 32.89), (26.04, 25.73), (21.02, 20.22), 19.33; ESI-MS *m/z* 428 (MH^+).

2-(4-(Benzylthio)-3-methoxyphenyl)-5-methyl-3-*p*-tolyl-1,3-thiazolidin-4-one 10{*2,2,2,2*}: yield 98.1%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (m, 5H), 7.07 (dt, 5H, J = 8.1 Hz, 18.9 Hz), 6.78 (dt, 2H, J = 4.2 Hz, 6.5 Hz), 6.00 (d, 1H, J = 32.0 Hz), 4.12 (m, 3H), 3.84 (m, 3H), 2.34 (dd, 3H, J = 5.3 Hz, 29.0 Hz), 1.73 (dd, 3H, J = 7.0 Hz, 26.7 Hz); ESI-MS *m/z* 436 (MH^+).

General Procedure for the Preparation of Compounds 13 (4-Thiazinanone-Based Suzuki Reaction with Boronic Acids). To a reaction tube with a stirring bar was added **12** (1.0 mmol), **7** (0.9 mmol), Pd(pddf)Cl_2 (0.04 mmol), and K_2CO_3 (2.0 mmol) in 0.6 mL of a 4:4:1 acetone/toluene/H_2O solvent. The reactions took place automatically in a monomode microwave cavity (150 °C, 20 min). HPLC was used to monitor the reaction. The reaction mixture was washed with 0.8 mL water, and the organic layer was loaded onto a 2 g FluoroFlash cartridge directly and washed with 80:20 MeOH/H_2O. The nonfluorous fractions were concentrated, and the fluorous fraction was eluted by methanol for reuse of cartridge.

2-(Biphenyl-4-yl)-3-butyl-1,3-thiazinan-4-one 13{*1,1,1*}: yield 92.2%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (m, 4H), 7.48 (dd, 2H, J = 7.5 Hz, 14.7 Hz), 7.37 (m, 3H), 5.58 (s, 1H), 4.20 (m, 1H), 2.87 (m, 3H), 2.67 (m, 2H), 1.64 (m, 2H), 1.34 (m, 2H), 0.94 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 169.14, 147.28, 141.06, 140.27, 138.63, 128.88, 127.62, 127.32, 127.09, 126.98, 61.89, 47.88, 34.44, 29.65, 21.96, 20.24, 13.88; ESI-MS *m/z* 326 (MH^+); HR-MS calcd for $C_{20}H_{24}NOS$ $(M + H)^+$ 326.1579, found 326.1584.

3-Butyl-2-(4′-ethylbiphenyl-4-yl)-1,3-thiazinan-4-one 13{*1,1,2*}: yield 94.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, 2H, J = 8.3 Hz), 7.53 (d, 2H, J = 8.3 Hz), 7.30 (m, 4H), 5.58 (s, 1H), 4.20 (m, 1H), 2.87 (m, 3H), 2.68 (m, 4H), 1.63 (m, 2H), 1.33 (m, 5H), 0.94 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 169.15, 143.82, 141.02, 138.26, 137.63, 128.41, 127.14, 127.00, 126.93, 61.73, 47.87, 34.44, 28.54, 21.97, 20.25, 15.56, 13.89; ESI-MS *m/z* 354 (MH^+).

2-(4-(Benzo[*b*]thiophen-2-yl)phenyl)-3-butyl-1,3-thiazinan-4-one 13{*1,1,3*}: yield 74.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, 1H, J = 7.9 Hz), 7.71 (d, 1H, J = 6.8 Hz), 7.64 (d, 2H, J = 8.3 Hz), 7.48 (d, 1H, J = 6.1 Hz), 7.27 (m, 4H), 5.47 (s, 1H), 4.10 (m, 1H), 2.76 (m, 3H), 2.56 (m, 2H), 1.54 (m, 2H), 1.25 (m, 2H, J = 6.2 Hz), 0.84 (t, 3H, J = 7.3 Hz); ESI-MS *m/z* 382 (MH^+).

3-Butyl-2-(4-(naphthalen-2-yl)phenyl)-1,3-thiazinan-4-one 13{*1,1,4*}: yield 79.9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (m, 4H), 7.77 (dd, 2H, J = 6.8 Hz, 9.8 Hz), 7.54 (m, 3H), 7.39 (d, 2H, J = 8.1 Hz), 5.58 (s, 1H), 4.23 (m, 1H), 2.89 (m, 3H), 2.69 (m, 2H), 1.65 (m, 2H), 1.35 (m, 2H), 0.94 (t, 3H, J = 8.0 Hz); ESI-MS *m/z* 376 (MH^+).

2-(4-(Benzo[*d*][1,3]dioxol-5-yl)phenyl)-3-butyl-1,3-thiazinan-4-one 13{*1,1,6*}: yield 67.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, 2H, J = 8.3 Hz), 7.11 (d, 2H, J = 8.0 Hz), 6.89 (d, 2H, J = 8.0 Hz), 6.72 (d, 1H, J = 8.0 Hz), 5.86 (m, 2H), 5.38 (s, 1H), 4.00 (m, 1H), 2.67 (m, 3H), 2.47 (m, 2H), 1.44 (m, 2H), 1.15 (m, 2H), 0.75 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 169.12, 148.24, 147.36, 140.75, 138.26, 134.61, 127.01, 126.95 120.66, 108.68, 107.54, 101.25, 61.68, 47.85, 34.44, 29.64, 21.95, 20.24, 13.88; ESI-MS *m/z* 370 (MH^+).

3-Butyl-2-(2-methoxybiphenyl-4-yl)-1,3-thiazinan-4-one 13{*2,1,1*}: yield 84.8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, 2H, J = 7.2 Hz), 7.25 (dd, 2H, J = 6.5 Hz, 13.8 Hz), 7.14 (m, 2H), 6.70 (m, 2H), 5.35 (d, 1H, J = 23.1 Hz), 4.01 (m, 1H), 3.65 (m, 3H), 2.70 (m, 3H), 2.50 (m, 2H),

1.45 (m, 2H, J = 6.4 Hz), 1.17 (m, 2H, J = 7.0 Hz), 0.76 (t, 3H, J = 7.3 Hz); ESI-MS m/z 356 (MH^+).

2-(4-(Benzo[*b*]thiophen-2-yl)-3-methoxyphenyl)-3-butyl-1,3-thiazinan-4-one 13{*2,1,3*}: yield 69.9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, 1H, J = 7.5 Hz), 7.61 (m, 2H), 7.51 (d, 1H, J = 7.8 Hz), 7.17 (dd, 2H, J = 7.9 Hz, 15.3 Hz), 6.72 (d, 2H, J = 8.0 Hz), 5.34 (d, 1H, J = 19.6 Hz), 4.01 (m, 1H), 3.77 (m, 3H), 2.69 (m, 3H), 2.51 (m, 2H), 1.44 (m, 3H, J = 6.5 Hz), 1.16 (m, 2H), 0.75 (t, 3H, J = 7.4 Hz); ESI-MS m/z 412 (MH^+).

3-Butyl-2-(3-methoxy-4-(naphthalen-2-yl)phenyl)-1,3-thiazinan-4-one 13{*2,1,4*}: yield 54.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (m, 9H), 6.94 (d, 1H, J = 4.6 Hz), 5.60 (s, 1H), 4.22 (m, 1H), 3.93 (m, 3H), 2.92 (m, 3H), 2.73 (m, 2H), 1.66 (m, 2H, J = 6.5 Hz), 1.45 (m, 2H), 0.96 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 169.31, 157.03, 140.40, 135.42, 133.39, 132.56, 131.01, 130.71, 128.18, 127.82, 127.63, 127.35, 126.38, 126.05, 125.90, 118.91, 109.68, 62.00, 55.80, 48.02, 34.43, 29.70, 22.20, 20.28, 13.92; ESI-MS m/z 406 (MH^+).

3-Butyl-2-(2,4′-dimethoxybiphenyl-4-yl)dihydro-2H-thiazinan-4-one 13{*2,1,5*}: yield 74.6%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (m, 3H), 7.30 (d, 1H, J = 8.3 Hz), 6.98 (dd, 2H, J = 1.3 Hz, 8.9 Hz), 6.87 (d, 1H, J = 4.6 Hz), 5.56 (s, 1H), 4.20 (m, 1H), 3.88 (m, 6H), 2.89 (m, 3H), 2.68 (m, 2H), 1.65 (m, 2H), 1.36 (d, 2H, J = 7.1 Hz), 0.95 (t, 3H, J = 7.3 Hz); ESI-MS m/z 386 (MH^+).

2-(4-(Benzo[*d*][1,3]dioxol-5-yl)-3-methoxyphenyl)-3-butyl-1,3-thiazinan-4-one 13{*2,1,6*}: yield 72.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (d, 1H, J = 8.3 Hz), 6.78 (s, 1H), 6.70 (d, 1H, J = 8.1 Hz), 6.60 (d, 3H, J = 10.5 Hz), 5.73 (s, 2H), 5.27 (s, 1H), 3.92 (m, 1H), 3.56 (s, 3H), 2.59 (m, 3H), 2.40 (s, 2H), 1.35 (d, 2H, J = 8.3 Hz), 1.08 (d, 2H, J = 8.5 Hz), 0.67 (t, 3H, J = 8.0 Hz); ESI-MS m/z 400 (MH^+).

General Procedure for Preparation of Compounds 14 (4-Thiazinanone-Based Palladium Coupling Reaction with Thiols). To a reaction tube with a stirring bar was added **12** (1.0 mmol), **9** (0.9 mmol), Pd(pddf)Cl_2 (0.04 mmol), and K_2CO_3 (2.0 mmol) in 0.6 mL of a 4:4:1 acetone/toluene/H_2O solvent. The reactions took place automatically in a monomode microwave cavity (150 °C, 20 min). HPLC was used to monitor the reaction. The reaction mixture was washed with 0.8 mL of water, and the organic layer was loaded onto a 2 g FluoroFlash cartridge directly and washed with 80:20 MeOH/H_2O. The nonfluorous fractions were concentrated, and the fluorous fraction was eluted by methanol for reuse of cartridge.

3-Butyl-2-(4-(cyclohexylthio)phenyl)-1,3-thiazinan-4-one 14{*1,1,1*}: yield 90.0%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, 2H, J = 10.1 Hz), 7.17 (d, 2H, J = 8.4 Hz), 5.49 (s, 1H), 4.15 (m, 1H), 3.16 (m, 1H), 2.81 (m, 3H), 2.63 (m, 2H), 2.01 (d, 2H, J = 10.9 Hz), 1.80 (d, 2H, J = 5.4 Hz), 1.60 (m, 2H), 1.35 (m, 6H), 0.92 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 169.05, 137.74, 135.71, 131.08, 126.95, 61.62, 50.00, 47.82, 46.28, 34.38, 33.33, 32.88, 29.62, 26.02, 25.74, 21.97, 20.22, 13.86; ESI-MS m/z 364 (MH^+); HR-MS calcd for $C_{20}H_{30}NOS_2$ $(M + H)^+$ 364.1769, found 364.1777.

2-(4-(Benzylthio)phenyl)-3-butyl-1,3-thiazinan-4-one 14{*1,1,2*}: yield 40.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (m, 7H), 6.95 (d, 2H, J = 8.2 Hz), 5.28 (s, 1H), 3.94 (m, 3H), 2.61 (m, 3H), 2.42 (m, 2H), 1.37 (m, 2H), 1.12 (m, 2H, J = 7.5 Hz), 0.72 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 169.06, 137.58, 137.04, 136.78, 129.43, 129.26, 128.82, 128.57, 127.34, 127.01, 61.60, 47.81, 43.31, 38.66, 34.37, 29.61, 21.92, 20.22, 13.86; ESI-MS m/z 372 (MH^+).

3-Butyl-2-(4-(cyclohexylthio)-3-methoxyphenyl)-1,3-thiazinan-4-one 14{*2,1,1*}: yield 66.1%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 1H), 6.82 (m, 2H), 5.50 (s, 1H), 4.15 (m, 1H), 3.91 (dd, 3H, J = 19.5 Hz, 37.6 Hz), 3.24 (s, 1H), 2.82 (m, 3H), 2.66 (m, 2H), 2.03 (dd, 2H, J = 10.1 Hz, 22.1 Hz), 1.80 (s, 2H), 1.62 (m, 4H), 1.35 (m, 6H), 0.92 (t, 3H, J = 7.8 Hz); ESI-MS: m/z 394 (MH^+).

2-(4-(Benzylthio)-3-methoxyphenyl)-3-butyl-1,3-thiazinan-4-one 14{*2,1,2*}: yield 64.8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 5H), 7.19 (d, 1H, J = 7.9 Hz), 6.74 (dd, 2H, J = 4.7 Hz, 13.5 Hz), 5.49 (s, 1H), 4.13 (m, 3H), 3.91 (s, 3H), 2.81 (m, 3H), 2.64 (m, 2H), 1.60 (m, 2H), 1.33 (m, 2H), 0.93 (t, 3H, J = 7.3 Hz). ^{13}C NMR ($CDCl_3$) δ 169.11, 157.44, 139.04, 137.07, 128.90, 128.47, 127.44, 127.22, 125.21, 118.98, 108.77, 61.92, 55.96, 47.87, 43.31, 34.37, 29.66, 22.17, 20.24, 13.88; ESI-MS m/z 402 (MH^+); HR-MS calcd for $C_{22}H_{28}NO_2S_2$ $(M + H)^+$ 402.1561, found 402.1570.

3-Butyl-2-(3-methoxy-4-(*p*-tolylthio)phenyl)-1,3-thiazinan-4-one 14{*2,1,3*}: yield 30.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, 2H, J = 8.1 Hz), 7.21 (d, 2H, J = 7.9 Hz), 6.79 (dd, 2H, J = 4.7 Hz, 12.4 Hz), 6.67 (d, 1H, J = 8.1 Hz), 5.48 (s, 1H), 4.12 (m, 1H), 3.92 (s, 3H), 2.80 (m, 3H), 2.63 (m, 2H), 2.40 (s, 3H), 1.59 (m, 2H), 1.32 (m, 2H, J = 6.5 Hz), 0.92 (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 169.05, 156.09, 138.60, 138.57, 134.06, 130.32, 128.43, 127.14, 119.16, 108.81, 61.87, 56.03, 47.84, 34.36, 29.64, 22.18, 21.25, 20.23, 13.87; ESI-MS m/z 402 (MH^+); HR-MS calcd for $C_{22}H_{28}NO_2S_2$ $(M + H)^+$ 402.1561, found 402.1559.

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Supporting Information Available. Library characterization data (LC/MS and NMR) of selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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