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An Efficient Desulfitative C-C Cross Coupling of Fused Thiazolidine-2-thione with Boronic Acids and Boronic Acid Pinacol esters: Formation of Fused Thiazoles †

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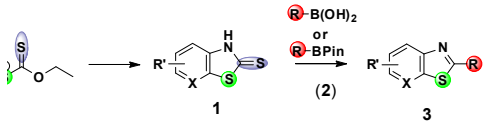
Kandasamy Rajaguru,[a] Arumugam Mariappan,[a] Ramachandran Manjusri,[a] Shanmugam Muthusubramanian,[a]* and Nattamai Bhuvanesh[b]

An efficient Pd(0)-catalyzed Cu(I)-mediated desulfitative C-C cross-coupling of benzofused thiazolidine-2-thione with boronic acids under neutral Liebeskind-Srogl condition is described. The desulfitative cross coupling of boronic acid pinacol esters has also been demonstrated with fused thiazolidine-2-thione under basic condition to afford fused thiazoles with good to excellent yields.

Introduction

The desulfitative cross-coupling reactions involving alkyl thioethers, sulfones, and sulfonyls with organometallic reagents have been largely employed toward the synthesis of diverse molecules including important heterocyclic compounds.[1] In this connection, palladium metal catalyzed - Cu(I) carboxylate mediated - Csp^2-Csp^2 cross coupling of boronic acids and various thioorganic compounds have been explored extensively under non-basic conditions for the construction of diverse cyclic and acyclic motif.[1,2] In this Liebeskind-Srogl cross coupling reaction, the soft Cu(I) carboxylate cofactor has high thiophilicity accelerating the desulfitative C-C cross couplings selectively.[1f,3] The non-basic Liebeskind-Srogl cross coupling reaction has also gained attention, making considerable progress.[1g,2c,4,5] The desulfitative cross-coupling of Sonogashira-Hagihara, Stille, and Suzuki-Miyaura as well as Mizoroki-Heck couplings of sulfonyl chlorides have been explored by Vogel and co-workers.[6] Because of their stability, low toxicity, easy handling, and easy removal of degradable boron derived byproducts, "green" boronic acids[7] are much superior to boronic esters as reactants.[8] Currently, we are focusing on the development of methods for the synthesis of some functionalized heterocyclic compounds.[9] In continuation, herein we report the Pd/Cu(I) mediated desulfitative carbon-carbon cross coupling for the synthesis of fused thiazole derivatives. Over the years, a variety of protocols have been developed for the rapid construction of benzfused or heteroaryl fused thiazoles from prefunctionalized substrates.[10] These highly functionalized thiazoles are found in many pharmaceutical agents[11] and in some diversed materials with potent applications.[12] The synthesis of substituted benzothiazoles has been achieved under Pd mediated Suzuki biaryl coupling of arylboronic acids with 2-halobenzothiazoles,[13] while direct coupling of aryl bromides with benzothiazole[14] is also been known. Direct C-H arylation of heteroarenes via denitrogenative and desulfitative mode of action has also been described.[15,16] Gosmini and co-workers[17] have elaborated the Co(II)-catalyzed synthesis of benzothiazole derivatives through coupling of aryl or benzylzinc reagents and methylsulfanyl-N-heteroarenes. It is pertinent to note that only very few reports are available towards the construction of the heteroaryl fused thiazole and that is the motive to undertake the present investigation.

The starting materials for the present study, fused thiazolidine-2-thiones **1**, have been prepared from cheap and readily available 2-haloanilines and highly reactive potassium ethyl xanthate.[18] At first, the traditional Liebeskind-Srogl coupling reaction of **1** with arylboronic acid **2** with an effective thiophilic reagent - copper(I) thiophene-2-carboxylate (CuTC) and various palladium sources in the presence of phosphine ligands has been investigated (Scheme 1).



Scheme 1. Plan for the synthesis of aryl thiazoles.

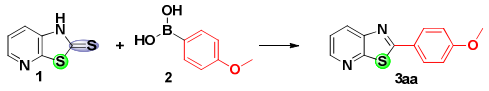
[a] †Department of Organic Chemistry, School of Chemistry, Madurai Kamaraj University, Madurai - 625 021, India..
[b] #X-ray Diffraction Laboratory, Department of Chemistry, Texas A & M University,
[c] College Station, Texas 77842, United States.

† Electronic Supplementary Information (ESI) available: ^1H, ^{13}C NMR & Mass spectra of all the synthesized compounds. ESI and crystallographic data in CIF See DOI: 10.1039/x0xx00000x

Results and Discussion

The screening experiments have been started using a stoichiometric amount of 4-methoxyphenylboronic acid $Pd(dba)_2$ and PPh_3 in the presence of a stoichiometric amount of CuTC. The temperature range studied was 50-100 ^oC, and the solvent tried was dioxane under a nitrogen atmosphere. This resulted in fused thiazoles as the desired product, but the conversion (22-42%) was not effective (Table 1, entries 1-3). Satisfactory results were obtained with $Pd_2(dba)_3$. When the combination of $Pd(OAc)_2$ (10 mol%) - PPh_3 (10 mol%) - $RB(OH)_2$ (1.5 equiv) - CuTC (2 equiv) was tested at 100 ^oC with dioxane as the solvent, the reaction got completed in an hour under nitrogen to get the best result (89%) (Table 1, entry 8). Running the experiment with increased catalyst loading (20 mol%) or lowering the reaction temperature have not increased the yield. The effective conversion has been improved (64-89%, Table 1, entries 9-12) by the sacrificial increment of CuTC as well as arylboronic acid. This can be explained by the low thiophilicity of boron in the organoboron compounds and relatively low nucleophilic reactivity compared to CuTC.[4c,19] The oxidation of Cu(I) cofactor has been avoided under inert atmosphere, promoting the product yield.[1c,2a,20] Phosphine free conditions (Table 1, entry 20) or extending the reaction time does not have any encouraging result.

Table 1. Optimization of the reaction Conditions[a]

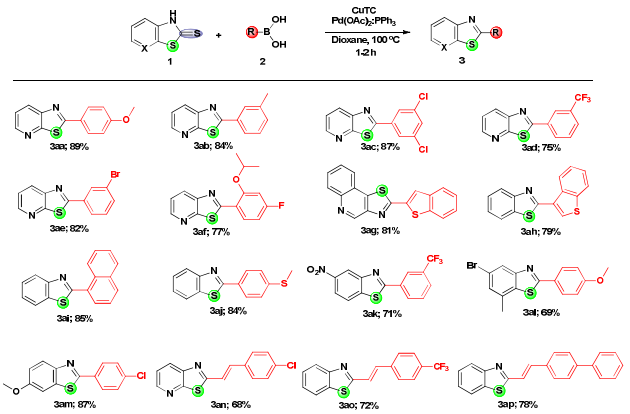


Entry	2 (equvi)/ CuTC (equvi)	Catalyst (mol%)/ligand (mol%)	Solvent	Time (h)	Temp (^oC)	Yield (%) 3aa[b]
1	1/1	$Pd(dba)_2$ (10) /L1 (5)	dioxane	16	50	22
2	1/1	$Pd(dba)_2$ (20)/ L1 (10)	dioxane	12	50	34
3	1/1	$Pd(dba)_2$ (10)/ XPhos (10)	dioxane	8	100	42
4	1.2/1	$Pd_2(dba)_3$. $CHCl_3$ (10)/ L1(10)	dioxane	5	80	55
5	1.5/2	$Pd_2(dba)_3$. $CHCl_3$ (10)/ L1(10)	dioxane	5	100	68
6	1.5/1	$Pd_2(dba)_3$. $CHCl_3$ (10)/ L2 (10)	dioxane	3	100	52
7	1.5/2	$PdCl_2$ (10)/ L2 (10)	dioxane	8	100	22
8	1.5/2	$Pd(OAc)_2$ (10)/ L1(10)	dioxane	1	100	89
9	1.5/2	$Pd(OAc)_2$ (10)/ L1(10)	THF	1	100	72
10	1.5/2	$Pd(OAc)_2$ (20)/ L1(10)	dioxane	1	100	65
11	2/2	$Pd(OAc)_2$ (10)/ L1 (5)	dioxane	1	100	64
12	2/3	$Pd(OAc)_2$ (10)/ L1 10)	dioxane	1	100	82
13	1.5/2	$Pd(OAc)_2$ (10)/ L1(10)	dioxane	1	130	32
14	1.5/2	$Pd(OAc)_2$ (5)/ L1 (10)	THF	1	100	52
15	1.2/1	$Pd(TFA)_2$ (10)/L1 (10)	dioxane	5	100	58
16	1.5/2	$Pd(TFA)_2$ (20)/L2 (10)	dioxane	5	100	66
17	1.5/2	$Pd(OAc)_2$ (10)/ L1(10)	dioxane	24	rt	----[c]
18	1/2	$Pd(MeCN)_2Cl_2$ (10)/ L1 (10)	dioxane	12	100	42
19	2/2	$Pd(MeCN)_2Cl_2$ (10)/ L2 (10)	dioxane	8	100	53
20	1.5/2	$Pd(OAc)_2$ (10 mol %)	dioxane	18	100	----[c]
21	1.5/2	$Pd(PPh_3)_4$ (10mol %)	dioxane	8	100	61

L1=PPh_3; L2=XPhos [a] Experiments were performed in dioxane (5 mL) under N_2 atm. [b] Isolated Yield. [c] No reaction.

Encouraged with this optimised condition, the substrate scope of the reaction has been explored by coupling a range of arylboronic acids and (*E*)-β-styrylboronic acids with **1** to obtain **3** in good yields and the derivatives synthesized are shown in Table 2.

Table 2. Synthesis of aryl thiazolesa **3aa-3ap**[a]



[a] Reaction conditions: In a reaction vessel thiazolidine-2-thione **1** (0.10 mmol), R-$B(OH)_2$ **2** (0.15 mmol), CuTC (0.20 mmol), $Pd(OAc)_2$ (0.01 mmol, 10 mol %) and PPh_3 (0.01 mmol, 10 mol %) in dioxane (5 mL) heated at 100 ^oC for 1-2 h under N_2 atm.

The homocoupling of boronic acids cannot be avoided resulting in biaryls due to the efficiency of copper salt,[21] though the conversion achieved is quite satisfactory. With sterically hindering arylboronic acids or some functionalized boronic acids or alkylboronic acids, the transformation was not successful under the optimized condition. All the synthesized compounds have been characterized by NMR studies and further confirmed by single crystal X-ray analysis of **3ah**[22] as shown in Figure 1.

Having successfully effected the coupling with boronic acid, we wanted to test the efficacy of this protocol with organoboron pinacol esters. However, the neutral Liebeskind-Srogl desulfitative coupling reaction conditions are apparently not suitable in the case of organoboron pinacol esters, even with 3-5 equivalent of CuTC in $Pd(OAc)_2/PPh_3$ system. The base is essential for the cross-coupling with organoboron pinacol esters. Earlier, Yu and Liebeskind[8b] have explored Pd(0)-catalyzed, Cu(I) carboxylate-mediated cross-coupling of thiol esters and B-alkyl-9-BBN under basic condition. We started with oxygen bases such as Na_2CO_3, K_2CO_3, Cs_2CO_3 and K_3PO_4 to accelerate the activation of organoboron pinacol ester in dioxane at 100 ^oC under a nitrogen atmosphere, which resulted in poor yield with undesired side products. Fortunately, clean transformation has been achieved in the

presence of stoichiometric amount of KF with moderate yield, though switching over to CsF (2.0 equiv) ended with the desired product in moderate to excellent yield (Table 3).

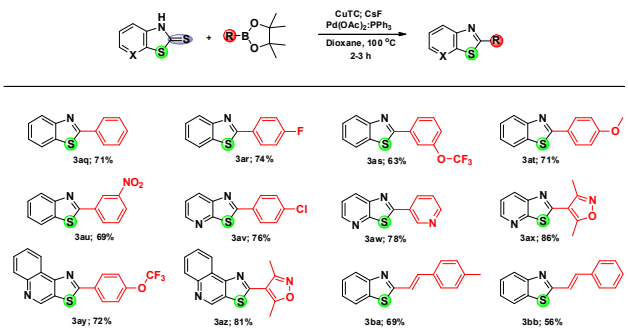
Table 3. Optimization of the reaction Conditions[a]

Entry	**2'** (equvi) /CuTC (equvi)	$Pd(OAc)_2$ (mol %)/ PPh_3 (mol %)	Base (equiv)	Time (h)	Temp (^oC)	Yield (%) **3ai**[b]
1	1.5/3	10/10	Nil	18	100	----[c]
2	1.5/5	10/10	Nil	18	100	----[c]
3	1.5/2	10/10	Na_2CO_3 (1.0)	18	100	trace
4	1.5/2	10/10	K_2CO_3 (1.0)	12	100	12
5	1.5/2	10/10	K_3PO_4 (2.0)	8	100	28
6	1.5/2	10/10	Cs_2CO_3(1.0)	8	100	42
7	1.5/2	10/10	KF (2.0)	5	100	61
8	1.5/2	10/10	CsF (2.0)	2	100	78
9	1.5/1	10/10	CsF (2.0)	8	100	34
10	1.5/2	10/10	CsF (2.0)	24	rt	----[c]
11	1.5/2	10/5	CsF (2.0)	2	100	58
12	1.5/2	$Pd(PPh_3)_4$ (10)	CsF (2.0)	4	100	43
13	1.5/2	Pd(OAc)2 (10)	CsF (2.0)	24	100	----[c]

[a] Experiments were performed in dioxane (5 mL) under N_2 atm. [b] Isolated Yield. [c] No reaction.

No reaction occurred in the absence of the ligand. The additional compounds added to the library of fused thiazole analogues through this protocol are shown in Table 4. It can be noted that under optimized condition, the coupling of thiazolidine-2-thione with the heteroaryl organoboron pinacol ester system seems to be more facile compared to arylboron pinacol esters. Interestingly, homocoupling is not a problem with boronic acid pinacolate ester.

Table 4. Synthesis of aryl thiazoles **3aq**-**3bb**[a]



[a] Reaction conditions: In a reaction vessel thiazolidine-2-thione **1** (0.10 mmol) in dioxane (5 mL), R-BPin **2'** (0.15 mmol), CuTC (0.20 mmol), $Pd(OAc)_2$ (0.01 mmol, 10 mol %), PPh_3 (0.01 mmol, 10 mol %) and CsF (0.20 mmol) in dioxane (5 mL) heated at 100 ^oC for 2-3 h under N_2 atm.

The synthesized compounds were characterized by NMR studies and further confirmed by single crystal X-ray analysis of **3aw**[26] as shown in Figure 1.

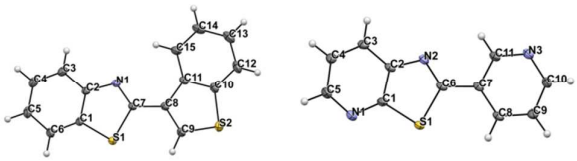
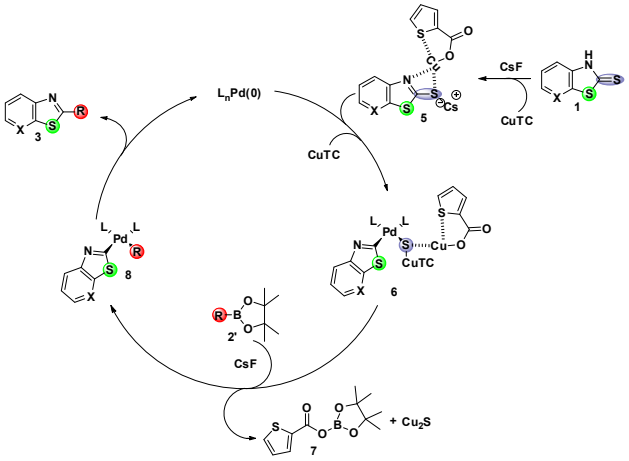


Figure 1. X-ray crystal structures of **3ah** and **3aw.** Thermal ellipsoids are shown at the 50% probability level.

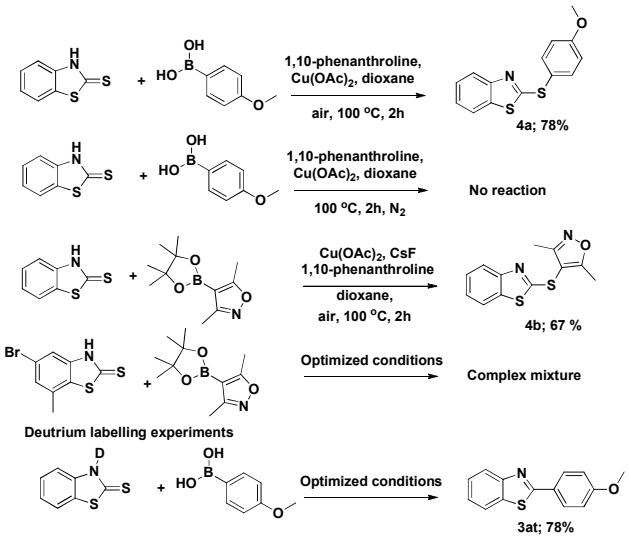
Based on the anticipated interaction between organosulfur and organoboron (thiophilic/borophilic) in the presence of Cu cofactors,[1,2a,8b,23,24] the mechanism for the formation of **3** has been illustrated in Scheme 2. The proposed mechanism for the formation of **3** by the boranepinacol ester strategy starts with the Cu(I) thiolate species **5** obtained by the thione-thiol tautomerization,[25] which undergoes oxidative addition with the Pd(0) catalyst and with an additional equivalent of CuTC cofactor to form an intermediate **6**. In the transmetalation step, the fluoride accelerates the pinacolate deprotection from **2'** to yield **8** with extrusion of **7** and Cu_2S. The subsequent reductive elimination results in the cross-coupled product **3**.



Scheme 2. Mechanism for the formation of fused thiazole **3**

To support the proposed mechanism, some control experiments have been performed (Scheme 3). In the first experiment, a mixture of thiazolidine-2-thione and 4-methoxy phenylboronic acid (2 equiv) (or boronic ester with CsF) was heated under aerobic condition1g at 100 ^oC for 2 h in the presence of Cu(II) acetate (1.5 equiv) and 1,10-phenanthroline (2 equiv) in dioxane, which resulted in the carbon-sulfur cross-coupled product **4a**. This reaction is not proceeding under nitrogen atmosphere indicating that the reaction may go via disulfide formation. Under the optimized condition, Suzuki active bromo substituted thiazolidine-2-thione and 4-methoxy phenylboronic acid (2 equiv), again yielded the anticipated thiazole derivative without traces of the traditional Suzuki coupled product (Table 2), while with boronic acid pinacol esters, a complex mixture was observed with the bromo substituted thiazolidine-2-thione system. Finally, the reaction

of N-deuterium substituted aryl thiazolidine-2-thione and 4-methoxyphenylboronic acid under the same condition furnished the benzothiazole with no deuterium incorporation, proving no hydrogen exchange in the mechanism. From the above observations a chemoselective desulfitative couplings occurred at C=S and no case the C-S-C was affected to yield fused hetero benzothiazoles.



Scheme 3. Control Experiments

In addition, under the optimized condition the same strategy has also been experimented with the controlled amount of water and also performed under the normal condition in the absence of CuTC as well but the desired product was not achieved (Table S1 See ESI).

Conclusions

In summary, we have demonstrated a Pd(0)/Cu(I)-mediated desulfitative C-C cross-coupling of boronic acids with fused thiazolidine-2-thione under neutral condition. We have also performed desulfitative coupling under basic condition with thiazolidine-2-thione and organoboron pinacol esters ending in C-C bond formation. This strategy involves mild reaction conditions towards the synthesis of diversely substituted benzfused thiazoles in good to excellent yields.

Experimental Section

General Remarks: Nuclear Magnetic Resonance (^{1}H and ^{13}C NMR) spectra were recorded on a 300 MHz spectrometer in CDCl3 using TMS as an internal standard. Chemical shifts are reported in parts per million (δ), coupling constants (*J* values) are reported in Hertz (Hz) and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), m (multiplet). ^{13}C NMR spectra were routinely run with broadband decoupling. Pre coated silica gel on aluminium plates (Merck) were used for TLC analysis with a mixture of petroleum ether (60–80 °C) and ethyl acetate as eluent. Elemental analyses were performed on a Perkin Elmer 2400 Series II Elemental CHNS analyser. Mass spectra were recorded in LCQ Fleet mass spectrometer, Thermo Fisher Instruments Limited, US. Electrospray ionisation mass spectrometry (ESI-MS) analysis was performed in the positive ion and negative ion mode on a liquid chromatography ion trap.

General procedure

A typical procedure for the synthesis of fused aryl thiazoles 3: Neutral Condition: To a stirred solution of thiazolidine-2-thione **1** (0.10 mmol) in dioxane (5 mL), R-$B(OH)_2$ **2** (0.15 mmol), CuTC (0.20 mmol), $Pd(OAc)_2$ (0.01 mmol, 10 mol%) and PPh_3 (0.01 mmol, 10 mol%) were added in a reaction vessel, and the reaction mixture heated at 100 °C for 1 h under N_2 atm. The completion of the reaction was monitored by TLC. After cooling to room temperature, the reaction mixture was filtered through Celite. Then, the filtrate was washed with saturated solution of NH_4Cl (3×10 mL) and extracted with EtOAc (2×20 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was then purified by column chromatography on silica gel (hexanes/ethyl acetate 4.5:0.5) to yield arylthiazole **3**.

Basic condition: To a stirred solution of thiazolidine-2-thione **1** (0.10 mmol) in dioxane (5 mL), R-BPin **2'** (0.15 mmol), CuTC (0.20 mmol), $Pd(OAc)_2$ (0.01 mmol, 10 mol%), PPh_3 (0.01 mmol, 10 mol%) and CsF (0.20 mmol) were added in a reaction vessel, and the reaction mixture heated at 100 °C for 2 h under N_2 atm. The completion of the reaction was monitored by TLC. After cooling to room temperature, the reaction mixture was filtered through Celite. Then, the filtrate was washed with saturated solution of NH_4Cl (3×10 mL) and extracted with EtOAc (2×20 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was then purified by column chromatography on silica gel (hexanes/ethyl acetate 4.5:0.5) to yield aryl thiazole **3a**.

2-(4-Methoxyphenyl)thiazolo[5,4-*b*]pyridine (3aa): Isolated as white solid; mp: 120–123 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 4.6, 1.2 Hz, 1H), 8.23 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.05 (d, *J* = 8.8 Hz, 2H), 7.42 (dd, *J* = 8.2, 4.7 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 2H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 162.2, 158.2, 147.2, 146.3, 129.2, 129.0, 125.9, 121.1, 114.3, 55.3. Anal. Calcd for $C_{13}H_{10}N_2OS$: C, 64.44; H, 4.16; N, 11.56%. Found: C, 64.46; H, 4.11; N, 11.59%.

2-(*m*-Tolyl)thiazolo[5,4-*b*]pyridine (3ab): Isolated as white solid; mp: 84–86 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 4.6, 1.4 Hz, 1H), 8.27 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.94 – 7.82 (m, 2H), 7.45 – 7.32 (m, 3H), 2.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 158.2, 147.0, 146.7, 138.8, 133.1, 132.2, 129.7, 128.8, 127.8, 124.7, 121.2, 21.2. Anal. Calcd for $C_{13}H_{10}N_2S$: C, 69.00; H, 4.45; N, 12.38%. Found: C, 69.04; H, 4.41; N, 12.33%.

2-(3,5-Dichlorophenyl)thiazolo[5,4-*b*]pyridine (3ac): Isolated as off–white solid; mp: 172–174 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 – 8.60 (m, 1H), 8.31 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.03 – 7.95 (m, 2H), 7.52 – 7.47 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 163.9, 158.2, 147.7, 146.9, 135.9, 131.1, 130.5,

125.7, 121.8. Anal. Calcd for $C_{12}H_6Cl_2N_2S$: C, 51.26; H, 2.15; N, 9.96%. Found: C, 51.31; H, 2.17; N, 9.92%.

2-(3-(Trifluoromethyl)phenyl)thiazolo[5,4-*b*]pyridine (3ad): Isolated as white solid; mp: 101–103 °C;^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 4.6, 1.3 Hz, 1H), 8.40 (s, 1H), 8.33 (dd, *J* = 8.2, 1.5 Hz, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.49 (dd, *J* = 8.2, 4.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 158.2, 147.5, 146.9, 134.1, 130.7, 130.3, 129.6, 127.8, 125.4, 124.1 ($^1J_{C-F}$ = 272.2), 121.8, 121.6. Anal. Calcd for $C_{13}H_7F_3N_2S$: C, 55.71; H, 2.52; N, 10.00. Found: C, 55.76; H, 2.53; N, 10.04%.

2-(3-Bromophenyl)thiazolo[5,4-*b*]pyridine (3ae)[27]: Isolated as white solid; mp: 121–122 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 4.6, 1.3 Hz, 1H), 8.33 – 8.28 (m, 2H), 8.00 (ddd, *J* = 7.8, 1.6, 1.0 Hz, 1H), 7.66 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1H), 7.47 (dd, *J* = 8.2, 4.7 Hz, 1H), 7.40 (t, *J* = 7.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 158.3, 147.3, 146.9, 135.1, 134.3, 130.5, 130.2, 130.1, 126.2, 123.2, 121.6.

2-(4-Fluoro-2-isopropoxyphenyl)thiazolo[5,4-b]pyridine (3af): Isolated as colorless solid; mp:119–120 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.6 Hz, 1H), 8.24 (d, *J* = 8.2 Hz, 1H), 7.87 (dd, *J* = 11.8, 2.1 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.43 (dd, *J* = 8.2, 4.7 Hz, 1H), 7.06 (t, *J* = 8.4 Hz, 1H), 4.75 – 4.61 (m, 1H), 1.43 (d, *J* = 6.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 158.1, 154.6 ($^1J_{C-F}$ = 245.2), 151.3, 148.6 ($^3J_{C-F}$ = 10.5), 146.5, 129.4, 126.1, 123.8 ($^4J_{C-F}$ = 3.0), 121.2, 115.9 ($^2J_{C-F}$ = 21.0), 114.9, 71.9, 21.7. Anal. Calcd for $C_{15}H_{13}FN_2OS$: C, 62.48; H, 4.54; N, 9.72%. Found: C, 62.50; H, 4.51; N, 9.77%.

2-(Benzo[*b*]thiophen-2-yl)thiazolo[4,5-*c*]quinoline (3ag): Isolated as white solid; mp: 213–214 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.54 (s, 1H), 8.26 (d, *J* = 8.3 Hz, 1H), 8.01 (dd, *J* = 15.8, 7.7 Hz, 2H), 7.94 – 7.83 (m, 2H), 7.77 (t, *J* = 7.7 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.60 – 7.50 (m, 1H), 7.45 – 7.42 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 148.1, 145.9, 144.2, 140.9, 140.4, 139.3, 136.2, 130.5, 129.1, 127.7, 127.6, 126.5, 125.8, 125.1, 124.8, 124.7, 122.6. ESI-MS *m/z* calcd for $C_{18}H_{10}N_2S_2$: $[M+H]^+$ 318.03; found: 319.02. Anal. Calcd for: $C_{18}H_{10}N_2S_2$: C, 67.90; H, 3.17; N, 8.80%. Found: C, 67.95; H, 3.12; N, 8.84%.

2-(Benzo[*b*]thiophen-3-yl)benzo[*d*]thiazole (3ah): Isolated as off–white solid; mp: 79–81 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.97 (dd, *J* = 4.9, 3.9 Hz, 1H), 8.17 – 8.12 (m, 1H), 8.10 (s, 1H), 7.91 (dd, *J* = 8.0, 0.7 Hz, 2H), 7.56 – 7.41 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 153.9, 140.4, 136.1, 134.1, 130.2, 129.9, 126.2, 125.3, 125.3, 125.1, 124.9, 123.3, 122.5, 121.2. ESI-MS *m/z* calcd for $C_{15}H_9NS_2$: $[M+H]^+$ 267.02; Found: 268.11. Anal. Calcd for $C_{15}H_9NS_2$: C, 67.38; H, 3.39; N, 5.24%. Found: C, 67.33; H, 3.37; N, 5.27%.

2-(Naphthalen-1-yl)benzo[*d*]thiazole (3ai)[28]: Isolated as white solid; mp: 124–125°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.95 (d, *J* = 8.3 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H), 8.02 – 7.92 (m, 4H), 7.66 – 7.55 (m, 4H), 7.49 – 7.43 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 153.9, 135.2, 133.8, 130.8, 130.5, 130.4, 129.2, 128.2, 127.4, 126.3, 126.0, 125.7, 125.0, 124.7, 123.3, 121.2. ESI-MS *m/z* calcd for $C_{17}H_{11}NS$: $[M+H]^+$261.06; Found: 261.99.

2-(4-(Methylthio)phenyl)benzo[*d*]thiazole (3aj)[29]: Isolated as white solid; mp: 142–144°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 – 8.02 (m, 1H), 7.98 (d, *J* = 8.6 Hz, 2H), 7.90 – 7.84 (m, 1H), 7.51 – 7.44 (m, 1H), 7.39 – 7.33 (m, 1H), 7.30 (d, *J* = 8.6 Hz, 2H), 2.52 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 154.0, 142.7, 134.7, 129.9, 127.6, 126.2, 125.8, 124.9, 122.9, 121.5, 14.9. ESI-MS *m/z* calcd for $C_{14}H_{11}NS_2$: $[M+H]^+$ 257.03; Found: 258.12.

5-Nitro-2-(3-(trifluoromethyl)phenyl)benzo[*d*]thiazole (3ak): Isolated as pale yellow solid; mp: 124–126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.92 (d, *J* = 2.1 Hz, 1H), 8.37 (s, 1H), 8.32 – 8.26 (m, 2H), 8.06 (d, *J* = 8.8 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.68 (t, *J* = 7.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 153.5, 146.9, 141.3, 133.1, 131.6 ($^2J_{C-F}$ = 33.0), 130.7, 129.8, 128.2 ($^3J_{C-F}$ = 3.7), 124.2 ($^3J_{C-F}$ = 3.0), 123.5 ($^1J_{C-F}$ = 271.5), 122.1, 119.9, 118.6. Anal. Calcd for $C_{14}H_7F_3N_2O_2S$: C, 51.85; H, 2.18; N, 8.64 %. Found: C, 51.88; H, 2.14; N, 8.69%.

5-Bromo-2-(4-methoxyphenyl)-7-methylbenzo[*d*]thiazole (3al): Isolated as white solid; mp: 145–147 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.8 Hz, 2H), 7.82 (s, 1H), 7.38 (s, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H), 2.75 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 161.9, 152.5, 136.1, 134.4, 129.9, 129.0, 126.3, 121.3, 117.9, 114.3, 55.42, 18.20. ESI-MS *m/z* calcd for $C_{15}H_{12}BrNOS$: $[M+H]^+$ 334.98; Found: 334.00. Anal. Calcd for $C_{15}H_{12}BrNOS$: C, 53.90; H, 3.62; N, 4.19%. Found: C, 53.94; H, 3.64; N, 4.13%.

2-(4-Chlorophenyl)-6-methoxybenzo[*d*]thiazole (3am): Isolated as white solid; mp: 129–131 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 3H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 2.5 Hz, 1H), 7.09 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 157.8, 148.5, 136.4, 132.3, 132.1, 129.1, 128.2, 123.7, 115.7, 104.0, 55.7. Anal. Calcd for $C_{14}H_{10}ClNOS$: C, 60.98; H, 3.66; N, 5.08%. Found: C, 60.94; H, 3.69; N, 5.03%.

(*E*)-2-(4-Chlorostyryl)thiazolo[5,4-*b*]pyridine (3an): Isolated as white solid; mp: 172–174°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, *J* = 3.5 Hz, 1H), 8.21 (d, *J* = 8.1 Hz, 1H), 7.55 – 7.50 (m, 3H), 7.43 – 7.37 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$)* δ 167.2, 157.9, 147.2, 137.4, 135.7, 133.7, 129.7, 129.3*, 128.7, 122.8, 121.5. Anal. Calcd for $C_{14}H_9ClN_2S$: C, 61.65; H, 3.33; N, 10.27%. Found: C, 61.68; H, 3.31; N, 10.23%. *Two carbons are merged.

(*E*)-2-(4-(Trifluoromethyl)styryl)benzo[*d*]thiazole (3ao): Isolated as white solid; mp: 161–163 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.67 (s, 4H), 7.51 (d, *J* = 8.3 Hz, 2H), 7.50 – 7.38 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 153.7, 138.6, 135.5, 134.4, 130.7 ($^2J_{C-F}$ = 32.2), 127.3, 126.4, 125.8, 125.7 ($^3J_{C-F}$ = 3.7), 124.3 ($^1J_{C-F}$ = 270.6), 123.1, 122.1, 121.5. Anal. Calcd for $C_{16}H_{10}F_3NS$: C, 62.94; H, 3.30; N, 4.59%. Found: C, 62.97; H, 3.35; N, 4.53%.

(*E*)-2-(2-([1,1'-Biphenyl]-4-yl)vinyl)benzo[*d*]thiazole (3ap): Isolated as white solid; mp: 192–193 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.1 Hz, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 10.5 Hz, 6H), 7.54 (s, 1H), 7.52 – 7.33 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 153.8, 141.9, 140.1, 137.0, 134.3, 134.2, 128.8, 127.8, 127.6, 127.4, 126.9, 126.2, 125.2, 122.8, 121.9, 121.4. ESI-MS *m/z* calcd for $C_{21}H_{15}NS$ $[M+H]^+$ 313.09; Found: 314.14. Anal. Calcd for $C_{21}H_{15}NS$: C, 80.48; H, 4.82; N, 4.47 %. Found: C, 80.45; H, 4.88; N, 4.43%.

2-Phenylbenzo[*d*]thiazole (3aq)[29]: Isolated as white solid; mp: 110–111 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 – 7.99 (m,

3H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.45 – 7.37 (m, 4H), 7.33 – 7.27 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 153.9, 134.9, 133.4, 130.8, 128.8, 127.4, 126.1, 125.0, 123.0, 121.4.

2-(4-Fluorophenyl)benzo[*d*]thiazole (3ar)[28]: Isolated as white solid; mp:101–103 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 – 8.04 (m, 3H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.41 – 7.35 (m, 1H), 7.21 – 7.14 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 165.9, 162.6 ($^1J_{C\text{-}F}$ = 250.5), 153.9, 134.9, 129.3 ($^3J_{C\text{-}F}$ = 8.2), 126.3, 125.1, 123.1, 121.5, 116.0 ($^2J_{C\text{-}F}$ = 21.7).

2-(3-(Trifluoromethoxy)phenyl)benzo[*d*]thiazole (3as)[30]: Isolated as off–white solid; mp: 100–102 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.1 Hz, 1H), 7.99 (d, *J* = 6.6 Hz, 2H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.53 (dd, *J* = 11.6, 4.7 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.35 (dd, *J* = 8.3, 1.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 153.9, 149.7, 141.6, 135.3, 130.3, 126.5, 125.7 ($^1J_{C\text{-}F}$ = 248.2), 125.4, 123.4, 122.9, 121.6, 119.3, 119.7. ESI-MS *m/z* calcd for $C_{14}H_8F_3NOS$ $[M+H]^+$ 295.03; Found: 295.02

2-(4-Methoxyphenyl)benzo[*d*]thiazole (3at)[31]: Isolated as white solid; mp: 111–114 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.8 Hz, 3H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 161.7*, 154.1, 134.7, 128.9, 126.0, 124.6, 122.7, 121.4, 114.2, 55.2. *Two quartnary carbons are merged.

2-(3-Nitrophenyl)benzo[*d*]thiazole (3au)[28]: Isolated as pale yellow solid; mp: 141–143 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.41 (d, *J* = 7.7 Hz, 1H), 8.33 (d, *J* = 8.1 Hz, 1H), 8.11 (d, *J* = 8.1 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.69 (t, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 153.8, 148.6, 135.1, 135.0, 132.9, 130.0, 126.7, 125.9, 125.0, 123.6, 122.1, 121.7. ESI-MS *m/z* calcd for $C_{13}H_8N_2O_2S$: $[M+H]^+$ 256.03; found 257.02.

2-(4-Chlorophenyl)thiazolo[5,4-*b*]pyridine (3av): Isolated as white solid; mp: 157–158 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.6, 1.4 Hz, 1H), 8.27 (dd, *J* = 8.2, 1.5 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 2H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.46 – 7.42 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0, 158.3, 147.11, 147.06, 137.6, 131.8, 129.9, 129.3, 128.6, 121.5. Anal. Calcd for $C_{12}H_7ClN_2S$: C, 58.42; H, 2.86; N, 11.35%. Found: C, 58.46; H, 2.82; N, 11.39%.

2-(Pyridin-3-yl)thiazolo[5,4-*b*]pyridine (3aw): Isolated as colorless solid; mp: 168–169 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.34 – 9.30 (m, 1H), 8.76 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.62 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.38 (ddd, *J* = 8.0, 2.2, 1.7 Hz, 1H), 8.33 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.51 – 7.45 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 158.0, 151.9, 148.4, 147.4, 146.8, 134.5, 130.2, 129.3, 123.7, 121.6. ESI-MS *m/z* calcd for $C_{11}H_7N_3S$ $[M+H]^+$ 213.04; Found: 214.00. Anal. Calcd for $C_{11}H_7N_3S$: C, 61.95; H, 3.31; N, 19.70%. Found: C, 61.91; H, 3.34; N, 19.73%.

3,5-Dimethyl-4-(thiazolo[5,4-*b*]pyridin-2-yl)isoxazole (3ax): Isolated as colorless solid; mp: 154–155 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.5 Hz, 1H), 8.27 (d, *J* = 8.2 Hz, 1H), 7.47 (dd, *J* = 8.2, 4.7 Hz, 1H), 2.82 (s, 3H), 2.64 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 158.6, 158.5, 157.6, 146.9, 146.1, 129.8, 121.5, 111.7, 13.3, 12.1. ESI-MS *m/z* calcd for $C_{11}H_9N_3OS$: $[M+H]^+$ 231.05; Found: 232.06.Anal. Calcd for $C_{11}H_9N_3OS$: C, 57.13; H, 3.92; N, 18.17%. Found: C, 57.17; H, 3.95; N, 18.19%.

2-(4-(Trifluoromethoxy)phenyl)thiazolo[5,4-*c*]quinoline (3ay): Isolated as white solid; mp: 171–172 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.55 (s, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 8.7 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$)* δ 166.6, 153.1, 151.3, 148.5, 146.0, 144.2, 140.4, 131.4, 130.5, 129.1, 127.7, 124.8, 123.2 ($^1J_{C\text{-}F}$ = 264.0), 121.3. ESI-MS *m/z* calcd for $C_{17}H_9F_3N_2OS$: $[M+H]^+$ 346.04; Found: 346.95. Anal. Calcd for $C_{17}H_9F_3N_2OS$: C, 58.96; H, 2.62; N, 8.09%. Found: C, 58.98; H, 2.65; N, 8.04%. *one quartnary carbon not picked up.

3,5-Dimethyl-4-(thiazolo[5,4-*c*]quinolin-2-yl)isoxazole (3az): Isolated as off–white solid; mp: 242–243 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.53 (s, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 2.87 (s, 3H), 2.69 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 158.4, 158.1, 147.8, 145.9, 144.2, 139.2, 130.5, 128.9, 127.7, 124.8, 123.1, 111.4, 13.4, 12.1. ESI-MS *m/z* calcd for $C_{15}H_{11}N_3OS$: $[M+H]^+$ 281.06; found: 282.03 Anal. Calcd for $C_{15}H_{11}N_3OS$: C, 64.04; H, 3.94; N, 14.94%. Found: C, 64.08; H, 3.96; N, 14.99%.

(*E*)-2-(4-Methylstyryl)benzo[*d*]thiazole (3ba)[32]: Isolated as white solid; mp: 139–140 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 1H), 7.77 – 7.67 (m, 1H), 7.50 – 7.44 (m, 4H), 7.39 (s, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 153.8, 139.6, 137.6, 134.2, 129.6, 128.3, 127.3, 126.2, 125.1, 122.7, 121.4, 121.0, 21.4. ESI-MS *m/z* calcd for $C_{16}H_{13}NS$ $[M+H]^+$ 251.08; Found: 252.09.

(*E*)-2-Styrylbenzo[*d*]thiazole (3bb)[28]: Isolated as white solid; mp 110–112 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.1 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.58 (dd, *J* = 9.7, 3.1 Hz, 2H), 7.52 – 7.47 (m, 2H), 7.45 – 7.37 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 153.8, 137.6, 135.3, 134.3, 129.4, 128.9, 127.3, 126.2, 125.3, 122.9, 122.0, 121.4.

2-((4-Methoxyphenyl)thio)benzo[*d*]thiazole (4a)[33]: Isolated as off–white solid; mp: 79–81 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.8 Hz, 1H), 7.60-7.69 (m, 3H), 7.43 – 7.36 (m, 1H), 7.28 – 7.22 (m, 1H), 7.01 (d, *J* = 8.9 Hz, 2H), 3.88 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 161.5, 154.0, 137.4, 135.2, 125.9, 123.9, 121.5, 120.6, 119.9, 115.3, 55.3. ESI-MS *m/z* calcd for $C_{14}H_{11}NOS_2$$[M+H]^+$ 273.03; Found; 274.06.

4-(Benzo[*d*]thiazol-2-ylthio)-3,5-dimethylisoxazole (4b): Isolated as colorless solid; mp 102–104 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 2.41 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.9, 167.8, 161.7, 154.1, 134.9, 126.2, 124.3, 121.7, 120.7, 102.5, 11.5, 9.9. ESI-MS *m/z* calcd for $C_{12}H_{10}N_2OS_2$: $[M+H]^+$ 262.02; Found: 262.98. Anal. Calcd for $C_{12}H_{10}N_2OS_2$: C, 54.94; H, 3.84; N, 10.68%. Found: C, 54.98; H, 3.86; N, 10.65%.

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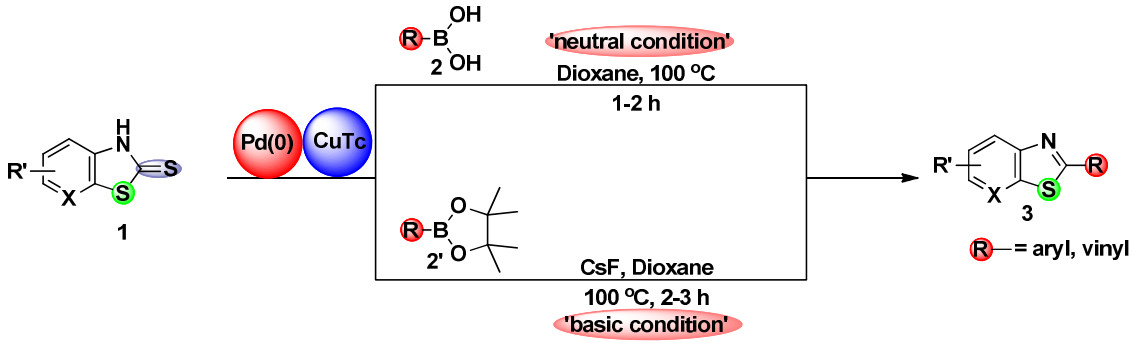
An Efficient Desulfitative C-C Cross Coupling of Fused aryl Thiazolidine-2-thione with Boronic acids and Boronic acid Pinacol esters: Formation of Fused aryl Thiazoles

Kandasamy Rajaguru,[a] Arumugam Mariappan,[a] Ramachandran Manjusri,[a] Shanmugam Muthusubramanian,[a]* and Nattamai Bhuvanesh[b]

[a]*Department of Organic Chemistry, School of Chemistry, Madurai Kamaraj University, Madurai - 625 021, India*

[b]*X-ray Diffraction Laboratory, Department of Chemistry, Texas A & M University, College Station, Texas 77842, USA.*

E-mail: muthumanian2001@yahoo.com



In this study, an efficient Pd(0)-catalyzed Cu(I)-mediated desulfitative C-C cross-coupling of benzfused thiazolidine-2-thione with boronic acids under neutral Liebeskind-Srogl condition is described. The desulfitative cross coupling of boronic acid pinacol esters has also been demonstrated with fused thiazolidine-2-thione under basic condition to afford fused thiazoles with good to excellent yields.