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Pd(PPh$_3$)$_4$-catalyzed direct *ortho*-fluorination of 2-arylbenzothiazoles with an electrophilic fluoride *N*-fluorobenzenesulfonimide (NFSI)

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ABSTRACT

An efficient protocol was developed for regio-selective Pd-catalyzed direct *ortho*-fluorination of 2-arylbenzo[*d*]thiazoles using *N*-fluorobenzenesulfonimide (NFSI) as the F^+ source, and L-proline as the crucial promoter. The present method offered a practical route to synthesize valuable fluorinated products, which are of potential importance in the pharmaceutical and agrochemical industries.

1. Introduction

2-Arylbenzo[*d*]thiazoles as privileged motifs are present in many natural products and pharmaceuticals that exhibit remarkable biological and therapeutic activities, such as antitumor, antiviral, and antimicrobial activities.[1] Substitution of hydrogen with fluorine can dramatically improve the physical, chemical, and biological activity of organic molecules. Recently, there are more than 20% newly registered pharmaceuticals and 40% agrochemicals containing one or more fluorine atoms. In particular, fluoro-substituted-1,3-benzo[*d*]thiazoles are versatile building blocks found in a broad range of pharmaceutically active molecules.[2] For instance, benzo[*d*]thiazoles **A** and **B** are found to be potent S1P$_1$ agonist (EC_{50}=0.042 and 0.017 μM, respectively, Fig. 1).[2a,b] Benzo[*d*]thiazole **C** could potently inhibit the growth of trypanosomes (Fig. 1).[2c] Benzo[*d*]thiazole **D** has an excellent inhibitory effect on the inflammatory cytokine production (Fig. 1).[2d] In addition, fluoro-substituted-1,3-benzo[*d*]thiazoles have been used as phosphorescent material.[3] Practical methods for the synthesis of functionalized 2-arylbenzo[*d*]thiazoles are well-documented.[4] In contrast, there are only a few protocols have been reported to access fluoro-substituted-1,3-benzo[*d*]thiazoles.[5] In addition, no examples have been reported for the synthesis of these important compounds via direct C–H bond fluorination of 2-arylbenzo[*d*]thiazoles. It seems to be a more practical approach to obtain the highly desired fluoro-substituted-1,3-benzo[*d*]thiazoles if these functionalized 2-arylbenzo[*d*]thiazoles can undergo directed C–H fluorination.

Recently, transition metal-catalyzed C–F bond formation has become an attractive approach to fluorine containing pharmaceuticals and agrochemicals. Although much remarkable achievements have been made in C–F bond formation in the last few years,[6] development of more efficient methods via ligand-directed C–H bond activation/fluorination for the synthesis of fluorine containing arenes is still full of challenge.[7] In 2006, Sanford group reported the pioneering work of pyridine-directed Pd(II)-catalyzed C–H bond fluorination using electrophilic fluorinating reagent (*N*-fluoro-2,4,6-trimethylpyridinium tetrafluoroborate) as F^+ source upon microwave irradiation.[7a] Subsequently, Yu et al. reported two Pd(II)-catalyzed *ortho*-fluorinations of C–H bond using *N*-fluoro-2,4,6-trimethylpyridinium triflate as the F^+ source and NMP as a crucial promoter directed by triflamide and *N*-arylamide groups.[7b,c] Very recently, when we were preparing this manuscript, Xu et al. reported the Pd(OAc)$_2$-catalyzed regio-selective aromatic C–H bond fluorination of quinoxaline, pyrazole, benzo[*d*]oxazole, and pyrazine derivatives promoted by trifluoroacetic acid (TFA).[7d]

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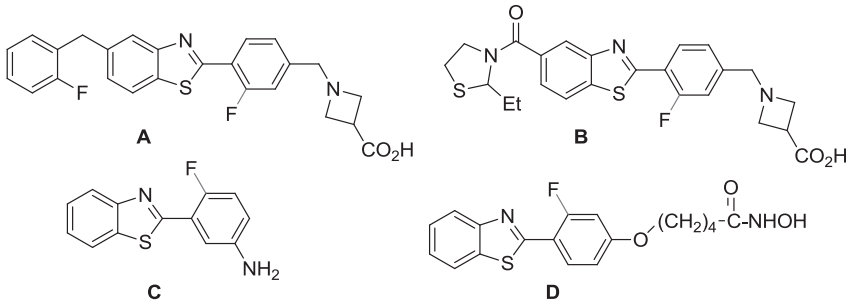


Fig. 1. Potential therapeutic/diagnostic fluoro-substituted-1,3-benzothiazoles.

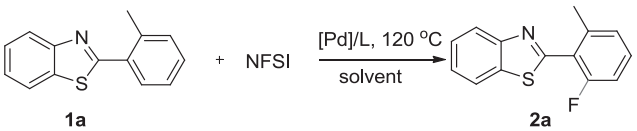
We and others have previously reported the Pd-catalyzed *ortho*-functionalization of 2-arylbenzo[*d*]thiazole to construct various C–C[8] and C–O[9] bonds from C–H bond. Therefore, benzo[*d*]thiazole might be a feasible directing group for C–H bond fluorination. Herein, we reported the simple Pd-catalyzed direct C–H bond fluorination to synthesize fluoro-substituted-1,3-benzothiazoles using an electrophilic fluoride (NFSI) promoted by L-proline.

2. Results and discussions

Based on the Yu's work for the C–H bond fluorination of triflamide-protected benzylamines, we started our research by treating the model substrate 2-(*o*-tolyl)benzo[*d*]thiazole **1a** with NFSI (2.0 equiv) under the NMP/DCE reaction system [NMP (0.5 equiv), DCE (2 mL), $Pd(OAc)_2$ (10 mol %), 120 °C]. However, no desired product was observed under the conditions. In view of the structural similarities between NMP and proline, we retried the reaction in the presence of L-proline (20 mol %) instead of NMP. To our delight, the monofluorinated product **2a** was obtained in 25% yield, with a trace amount of acetoxylated by-product, which indicated that L-proline as an additive can promote the fluorination reaction. Then, we investigated the effects of fluorinating agents, and several commonly used fluorinating agents were utilized in the present work. Unfortunately, when the substrate **1a** was treated with *N*-fluoro-2,4,6-trimethylpyridiniums (**F1** and **F2**) or Selectfluor **F3**, no fluorinated product was observed (Scheme 1). However, the desired fluorinated product **2a** was obtained in 33% isolated yield by using NFSI as the fluorine source catalyzed by $Pd(OAc)_2$ (30 mol %) (Scheme 1). Subsequently, various palladium catalysts including Pd(II) and Pd(0), such as $PdCl_2$, $Pd(PhCN)_2Cl_2$, $Pd(PPh_3)_2Cl_2$, $Pd_2(dba)_3$, and $Pd(PPh_3)_4$ were also screened, and the results indicated that $Pd(PPh_3)_4$ was the best efficient catalyst (Table 1, entries 2–6). The control experiment also showed that L-proline was important for the reaction to proceed (Table 1, entry 7). The reaction was also sensitive to the loading of L-proline, with 0.4 equiv being optimal (Table 1, entries 8–12). The use of 0.05 or 1.0 equiv of L-proline reduced the yield to 20% and 10%, respectively. The reaction still showed high efficiency when the loading of $Pd(PPh_3)_4$ was decreased to 15 mol % (Table 1, entry 14). Finally, a range of solvents were screened, which identified that reactions in polar and aprotic solvents, such as DMF, DMA, or DMSO occurred in low yields (Table 1, entries 16–21), while reaction in the non-polar solvent cyclohexane gave the desired product in good yield (Table 1, entry 24).

With the optimized reaction conditions in hand, we next surveyed the substrate scope of benzothiazole-directed *ortho*-C–H bond fluorination. As summarized in Table 2, the protocol can be utilized for the synthesis of diverse fluoro-substituted-1,3-benzothiazoles and is tolerant of many common functional groups, including halogen (F, Cl), methyl, and methyl ether. Substrates containing electron-donating or moderate electron-withdrawing substituents on the *ortho*-position of 2-phenyl ring undergo the fluorination process smoothly under standard conditions to afford the corresponding products in good yields (Table 2, entries 1–4). For instance, substrates **1b** (R^2=*o*-OCH_3) and **1d**

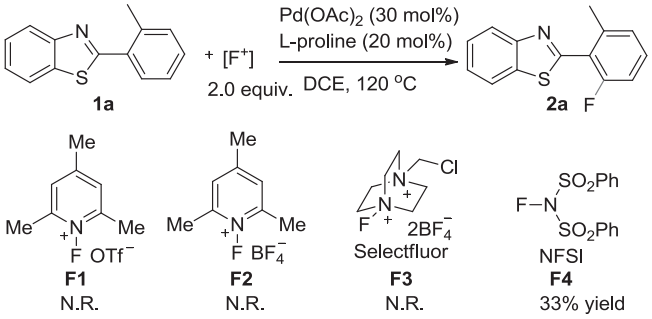
Table 1
Optimization of the reaction conditions[a]



1a 2a

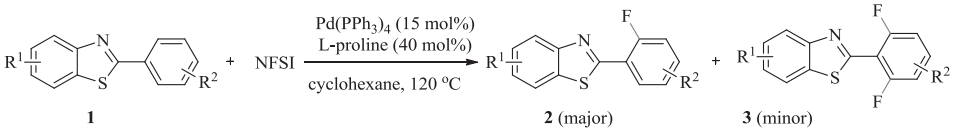
Entry	Solvent	[Pd] (*x* mol %)	L-proline (*y* mol %)	Yield[b] (%)
1	DCE	$Pd(OAc)_2$ (30)	20	33
2	DCE	$PdCl_2$ (30)	20	Trace
3	DCE	$Pd(PhCN)_2Cl_2$ (30)	20	N.R.
4	DCE	$Pd(PPh_3)_2Cl_2$ (30)	20	Trace
5	DCE	$Pd_2(dba)_3$ (30)	20	20
6	DCE	$Pd(PPh_3)_4$ (30)	20	47
7	DCE	$Pd(PPh_3)_4$ (30)	0	16
8	DCE	$Pd(PPh_3)_4$ (30)	5	20
9	DCE	$Pd(PPh_3)_4$ (30)	10	35
10	DCE	$Pd(PPh_3)_4$ (30)	40	54
11	DCE	$Pd(PPh_3)_4$ (30)	50	30
12	DCE	$Pd(PPh_3)_4$ (30)	100	10
13	DCE	$Pd(PPh_3)_4$ (20)	40	54
14	DCE	$Pd(PPh_3)_4$ (15)	40	54
15	DCE	$Pd(PPh_3)_4$ (10)	40	24
16	PhCl	$Pd(PPh_3)_4$ (15)	40	22
17	CH_3CN	$Pd(PPh_3)_4$ (15)	40	33
18	Dioxane	$Pd(PPh_3)_4$ (15)	40	16
19	DMF	$Pd(PPh_3)_4$ (15)	40	25
20	DMA	$Pd(PPh_3)_4$ (15)	40	19
21	DMSO	$Pd(PPh_3)_4$ (15)	40	N.R.
22	Toluene	$Pd(PPh_3)_4$ (15)	40	48
23	DCM	$Pd(PPh_3)_4$ (15)	40	53
24	Cyclohexane	$Pd(PPh_3)_4$ (15)	40	74

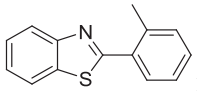
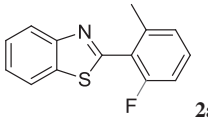
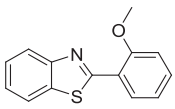
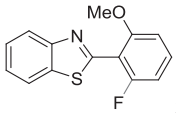
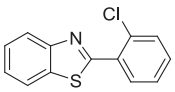
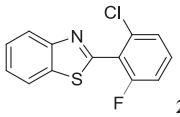
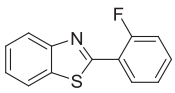
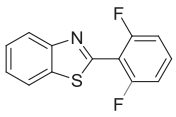
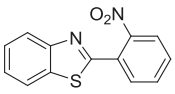
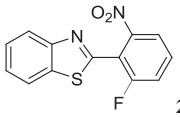
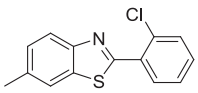
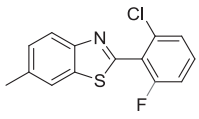
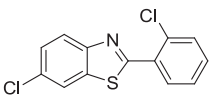
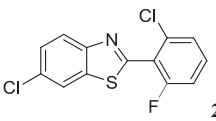
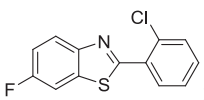
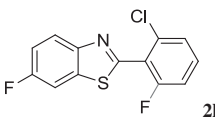
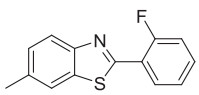
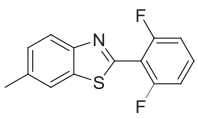
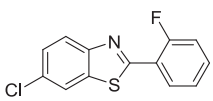
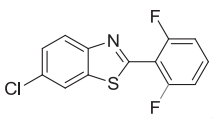
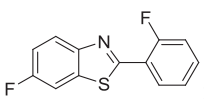
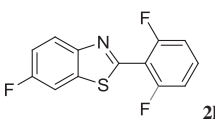
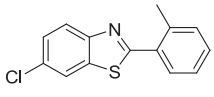
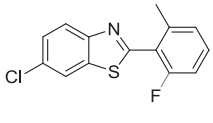
[a] Reaction conditions: 0.3 mmol of 2-arylbenzothiazole **1a**, NFSI (3.0 equiv), 2 mL of solvent, 5 h.
[b] Isolated yield based on **1a**.



Scheme 1. Palladium-catalyzed fluorination of 2-(*o*-tolyl)benzo[*d*]thiazole with F^+ source.

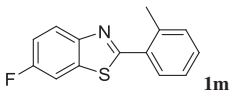
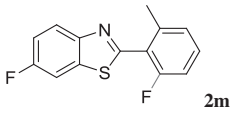
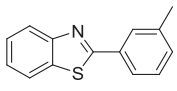
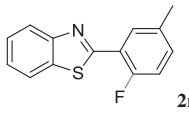
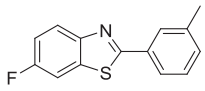
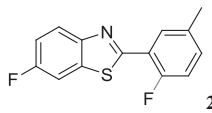
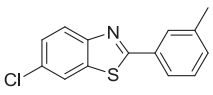
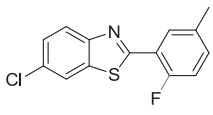
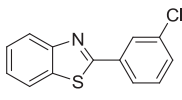
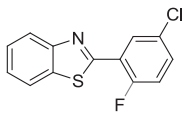
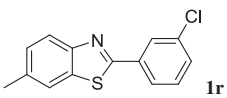
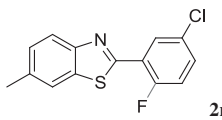
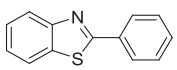
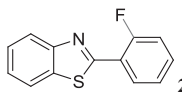
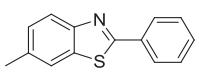
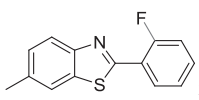
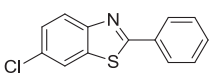
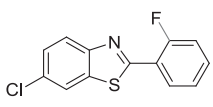
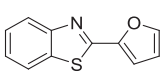
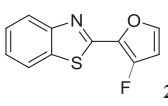
Table 2
Substrate scope of Pd-catalyzed C–H bond fluorination[a]



Entry	Substrate **1**	Product **2**	Yield[b] (%)
1	 **1a**	 **2a**	74
2	 **1b**	 **2b**	68
3	 **1c**	 **2c**	68
4	 **1d**	 **2d**	69
5	 **1e**	 **2e**	Trace
6	 **1f**	 **2f**	54
7	 **1g**	 **2g**	71
8	 **1h**	 **2h**	82
9	 **1i**	 **2i**	35
10	 **1j**	 **2j**	63
11	 **1k**	 **2k**	68
12	 **1l**	 **2l**	65

(*continued on next page*)

Table 2 (*continued*)

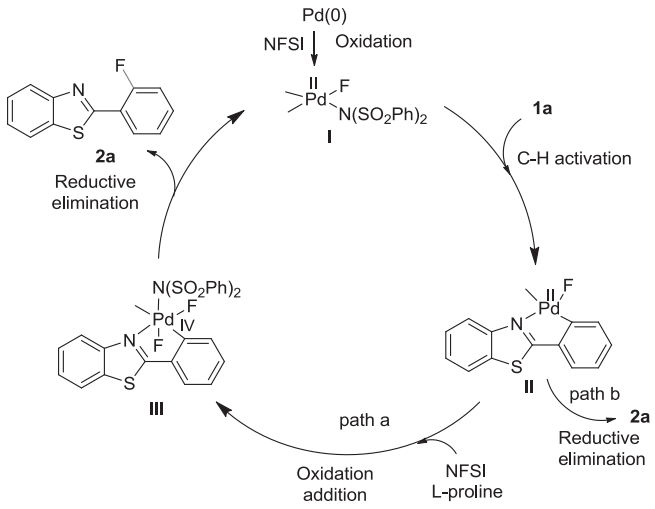
Entry	Substrate **1**	Product **2**	Yield[b] (%)
13	 **1m**	 **2m**	73
14	 **1n**	 **2n**	60/17[c]
15	 **1o**	 **2o**	44/16[c]
16	 **1p**	 **2p**	47/15[c]
17	 **1q**	 **2q**	63/trace[c]
18	 **1r**	 **2r**	34/8[c]
19	 **1s**	 **2s**	79/4 (35/40[c])
20	 **1t**	 **2t**	56/33[c]
21	 **1u**	 **2u**	53/37[c]
22	 **1v**	 **2v**	Trace

[a] Reaction conditions: 0.3 mmol of 2-arylbenzothiazole **1**, $Pd(PPh_3)_4$ (15 mol %), NFSI (3.0 equiv, unless otherwise noted), 2 mL of cyclohexane, 120 °C, 5 h.
[b] Isolated yield of **2** based on 2-arylbenzothiazole **1**.
[c] Isolated yield of difluorinated product **3** (4.0 equiv of NFSI was used).

(R^2=*o*-F) gave the fluorinated products **2b** and **2d** in 68% and 69% yields, respectively (Table 2, entries 2 and 4). Unfortunately, only a trace amount of desired product was detected for the reaction of substrate **1e** bearing a strong electron-withdrawing substituent (R^2=*o*-NO_2) (Table 2, entry 5). Then, effects of substituents on the benzothiazole side were investigated under the present method. Generally, the benzothiazole parts with electron-withdrawing groups were relatively more favorable in this transformation (Table 2, entries 7,8, and 10–13 vs entries 6 and 9). Substrate **1f** bearing a methyl group afforded the product **2f** in 54% yield (Table 2, entry 6). Substrates **1g**, **1h**, and **1j**–**m** bearing electron-withdrawing halogen gave the desired products in yields ranging from 63% to 82% (Table 2, entries 7,8 and 10–13). Furthermore, 2-arylbenzo[*d*]thiazoles **1n**–**r** with substituents at the *meta*-position of 2-phenyl ring were examined under standard conditions. The results showed that monofluorinated products **2n**–**r** were predominant at the less sterically hindered position in moderate yields with a small amount of difluorinated products (Table 2, entries 14–18). For example, a mixture of monofluorinated product **2n** (60%) and difluorinated product **3n** (17%) is obtained, when the fluorination reaction of 2-(*m*-tolyl)benzo[*d*]thiazole **1n** was performed using 4.0 equiv of NFSI (Table 2, entry 14). To those substrates without substituents at the 2-phenyl ring can also undergo the fluorination reaction efficiently to give a mixture of mono- and difluorinated products. The fluorination of 2-phenylbenzo[*d*]thiazole **1s** indicated that monofluorinated product **2s** is obtained predominantly in 79% yield with 4% difluorinated product **3s** when 3.0 equiv of NFSI was utilized, while the similar

amount of mono- and difluorinated products are obtained when 4.0 equiv of NFSI was used (Table 2, entry 19). Unfortunately, 2-position heterocyclic ring substituted benzo[*d*]thiazole **1v** failed to afford the corresponding fluorinated product **2v** (Table 2, entry 22).

Though the detailed role of L-proline remains ambiguous, a plausible reaction mechanism has been proposed in Scheme 2. A Pd(II/IV) catalytic cycle (path a) was proposed based on the previous literature involving high-valent palladium fluoride.[7b,10] The reaction is initiated through oxidation of Pd(0) by NFSI to give Pd(II) fluoride complex **I**,[10d,f] and subsequent C–H activation of **1** offers intermediate **II**, and then oxidation addition of intermediate **II** by NFSI yields the Pd(IV) intermediate **III** promoted by catalytic amount of L-proline, which undergoes reductive elimination to generate the fluorination product **2**. Another possible pathway for this transformation is the reductive elimination of intermediate **II** to give product **2** and Pd(0), which involving a Pd(0)/Pd(II) mechanism (path b).



Scheme 2. Proposed mechanism.

In summary, we have developed a regio-selective Pd-catalyzed direct *ortho*-fluorination of 2-arylbenzo[*d*]thiazoles using NFSI as the F^+ source, and L-proline as the crucial promoter. The reaction tolerated a range of different substrates with a variety of functional groups. The present protocol offered an efficient route to synthesize valuable fluorinated products, which are of potential importance in the pharmaceutical and agrochemical industries. Further research will focus on the mechanistic studies and synthetic applications of the present transformations.

3. Experimental section

3.1. General experimental procedures and characterizations

2-Arylbenzo[*d*]thiazole (0.3 mmol), NFSI (3 or 4 equiv), $Pd(PPh_3)_4$ (15 mol %), L-proline (40 mol %), cyclohexane (2 mL) were added in a 25 mL sealed tube with a Teflon-lined cap. The mixture was heated at 120 °C for 5 h. After being cooled to room temperature, the volatiles were removed under reduced pressure, and the residue was purified by a flash column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to give the corresponding pure coupling product **2** and **3**.

3.1.1. 2-(2-Fluoro-6-methylphenyl)benzo[d]thiazole ***2a***. Isolated as a yellow solid (53.9 mg, 74% yield), mp: 52–53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 6.96 (t, J=8.8 Hz, 1H), 7.04 (d, J=7.6 Hz, 1H), 7.23–7.30 (m, 1H), 7.37 (t, J=7.6 Hz, 1H), 7.44 (t, J=7.6 Hz, 1H), 7.87 (d, J=8.0 Hz, 1H), 8.06 (d, J=8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 112.1 (d, $^2J_{C-F}$=22 Hz), 120.4, 120.6 (d, $^2J_{C-F}$=15 Hz), 122.5, 124.4, 125.0, 125.2, 130.0 (d, $^3J_{C-F}$=9 Hz), 135.1, 139.3, 152.1, 159.5 (d, $^1J_{C-F}$=248 Hz), 160.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.84; HRMS-ESI (m/z): calcd for $C_{14}H_{11}FNS$ (M+H): 244.0596, found 244.0591.

3.1.2. 2-(2-Fluoro-6-methoxyphenyl)benzo[d]thiazole ***2b***. Isolated as a yellow oil (52.8 mg, 68% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (s, 3H), 6.82–6.89 (m, 2H), 7.36–7.43 (m, 2H), 7.51 (t, J=7.6 Hz, 1H), 7.93 (d, J=7.6 Hz, 1H), 8.16 (d, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.4, 107.0, 108.7 (d, $^2J_{C-F}$=25 Hz), 112.0 (d, $^2J_{C-F}$=15 Hz), 121.2, 123.6, 125.2, 125.9, 131.8 (d, $^3J_{C-F}$=11 Hz), 136.1, 153.0, 158.6, 158.7, 161.0 (d, $^1J_{C-F}$=251 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −110.99; HRMS-ESI (m/z): calcd for $C_{14}H_{11}FNOS$ (M+H): 260.0545, found 260.0540.

3.1.3. 2-(2-Chloro-6-fluorophenyl)benzo[d]thiazole ***2c***.[5c] Isolated as a yellow oil (53.6 mg, 68%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, J=8.4 Hz, 1H), 7.35 (d, J=7.6 Hz, 2H), 7.41 (t, J=7.2 Hz, 1H), 7.47 (t, J=8.0 Hz, 1H), 7.55 (t, J=7.6 Hz, 1H), 7.97 (d, J=8.0 Hz, 1H), 8.18 (d, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 114.6 (d, $^2J_{C-F}$=22 Hz), 121.6, 122.1 (d, $^2J_{C-F}$=18 Hz), 123.9, 125.8, 125.9, 126.3, 131.9 (d, $^3J_{C-F}$=9 Hz), 135.0, 136.3, 153.1, 158.5, 160.9 (d, $^1J_{C-F}$=252 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.12; HRMS-ESI (m/z): calcd for $C_{13}H_8ClFNS$ (M+H): 264.0050, found 264.0045.

3.1.4. 2-(2,6-Difluorophenyl)benzo[d]thiazole ***2d***. Isolated as a yellow oil (51.1 mg, 69%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (t, J=8.4 Hz, 2H), 7.39–7.46 (m, 2H), 7.53 (t, J=8.0 Hz, 1H), 7.95 (d, J=7.6 Hz, 1H), 8.19 (d, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.1 (t, $^2J_{C-F}$=16 Hz), 112.2 (d, $^2J_{C-F}$=26 Hz), 121.3, 123.9, 125.7, 126.3, 131.8 (t, $^2J_{C-F}$=10 Hz), 135.7 (t, $^3J_{C-F}$=2 Hz), 153.0, 155.8 (t, $^3J_{C-F}$=4 Hz), 160.5 (dd, J_{C-F}=6, 254 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.56; HRMS-ESI (m/z): calcd for $C_{13}H_8F_2NS$ (M+H): 248.0346, found 248.0341.

3.1.5. 2-(2-Chloro-6-fluorophenyl)-6-methylbenzo[d]thiazole ***2f***. Isolated as a yellow oil (44.9 mg, 54% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (s, 3H), 7.15 (t, J=8.4 Hz, 1H), 7.34–7.42 (m, 3H), 7.76 (s, 1H), 8.05 (d, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 114.5 (d, $^2J_{C-F}$=22 Hz), 121.1, 122.3 (d, $^2J_{C-F}$=18 Hz), 123.4, 125.8, 127.9, 131.7 (d, $^3J_{C-F}$=9 Hz), 135.1, 136.0, 136.6, 151.3, 157.3, 160.9 (d, $^1J_{C-F}$=252 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.15; HRMS-ESI (m/z): calcd for $C_{14}H_{10}ClFNS$ (M+H): 278.0207, found 278.0201.

3.1.6. 6-Chloro-2-(2-chloro-6-fluorophenyl)benzo[d]thiazole ***2g***. Isolated as a colorless solid (63.0 mg, 71% yield); mp: 80–81 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, J=8.4 Hz, 1H), 7.35 (d, J=8.0 Hz, 1H), 7.40–7.46 (m, 1H), 7.51 (d, J=8.0 Hz, 1H), 7.94 (s, 1H), 8.08 (d, J=8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 114.6 (d, $^2J_{C-F}$=22 Hz), 121.1, 121.7 (d, $^2J_{C-F}$=17 Hz), 124.7, 125.9, 127.2, 131.9, 132.0 (d, $^3J_{C-F}$=9 Hz), 135.0, 137.5, 151.6, 158.9, 160.8 (d, $^1J_{C-F}$=252 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.02; HRMS-ESI (m/z): calcd for $C_{13}H_7Cl_2FNS$ (M+H): 297.9660, found 297.9655.

3.1.7. 2-(2-Chloro-6-fluorophenyl)-6-fluorobenzo[d]thiazole ***2h***. Isolated as a colorless solid (69.1 mg, 82% yield), mp: 120–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, J=8.4 Hz, 1H), 7.29 (d, J=8.8 Hz, 1H), 7.36 (d, J=8.4 Hz, 1H), 7.40–7.46 (m, 1H), 7.65 (d, J=8.0 Hz, 1H), 8.10–8.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 107.6 (d, $^2J_{C-F}$=27 Hz), 114.6 (d, $^2J_{C-F}$=22 Hz), 115.2 (d, $^2J_{C-F}$=25 Hz), 121.7 (d, $^2J_{C-F}$=17 Hz), 125.0 (d, $^3J_{C-F}$=9 Hz), 125.9, 132.0 (d, $^3J_{C-F}$=10 Hz),

135.0, 137.4 (d, $^{3}J_{C-F}$=11 Hz), 158.2, 160.8 (d, $^{1}J_{C-F}$=245 Hz), 160.9 (d, $^{1}J_{C-F}$=253 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.11, −114.77; HRMS-ESI (*m*/*z*): calcd for $C_{13}H_7ClF_2NS$ (M+H): 281.9956, found 281.9950.

3.1.8. 2-(2-Chloro-6-fluorophenyl)-6-methylbenzo[d]thiazole ***2i***. Isolated as a colorless solid (27.4 mg, 35% yield), mp: 71–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (s, 3H), 7.08 (t, *J*=8.4 Hz, 2H), 7.35 (d, *J*=8.4 Hz, 1H), 7.39–7.47 (m, 1H), 7.75 (s, 1H), 8.06 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 112.2 (d, $^{2}J_{C-F}$=26 Hz), 120.9, 123.3, 128.0, 131.59, 131.6 (d, $^{2}J_{C-F}$=21 Hz), 135.9, 136.0, 151.2, 154.6, 161.8 (d, $^{1}J_{C-F}$=254 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.86; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_{10}F_2NS$ (M+H): 262.0502, found 262.0497.

3.1.9. 6-Chloro-2-(2,6-difluorophenyl)benzo[d]thiazole ***2j***. Isolated as a colorless solid (53.1 mg, 63% yield), mp: 127–128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (t, *J*=8.4 Hz, 2H), 7.42–7.51 (m, 2H), 7.93 (s, 1H), 8.09 (d, *J*=8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.6 (t, $^{2}J_{C-F}$=15 Hz), 112.3 (d, $^{2}J_{C-F}$=26 Hz), 120.8, 124.6, 127.2, 131.8, 132.1 (t, $^{3}J_{C-F}$=11 Hz), 136.8, 151.5, 156.3, 160.5 (d, $^{1}J_{C-F}$=254 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.24; HRMS-ESI (*m*/*z*): calcd for $C_{13}H_7ClF_2NS$ (M+H): 281.9956, found 281.9950.

3.1.10. 2-(2,6-Difluorophenyl)-6-fluorobenzo[d]thiazole ***2k***. Isolated as a colorless solid (54.0 mg, 68% yield), mp: 91–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (t, *J*=8.8 Hz, 2H), 7.27 (t, *J*=8.8 Hz, 1H), 7.41–7.49 (m, 1H), 7.63 (d, *J*=8.0 Hz, 1H), 8.11–8.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 107.4 (d, $^{2}J_{C-F}$=27 Hz), 111.7 (t, $^{2}J_{C-F}$=16 Hz), 112.3 (d, $^{2}J_{C-F}$=26 Hz), 115.2 (d, $^{2}J_{C-F}$=25 Hz), 124.9 (d, $^{3}J_{C-F}$=9 Hz), 132.0 (t, $^{3}J_{C-F}$=11 Hz), 136.7 (d, $^{3}J_{C-F}$=14 Hz), 149.7, 155.5, 160.5 (d, $^{1}J_{C-F}$=254 Hz), 160.8 (d, $^{2}J_{C-F}$=245 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.54, −114.78; HRMS-ESI (*m*/*z*): calcd for $C_{13}H_7F_3NS$ (M+H): 266.0251, found 266.0255.

3.1.11. 6-Chloro-2-(2-fluoro-6-methylphenyl)benzo[d]thiazole ***2l***. Isolated as a colorless solid (54.0 mg, 65% yield), mp: 103–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.04 (t, *J*=8.8 Hz, 1H), 7.13 (d, *J*=7.6 Hz, 1H), 7.32–7.38 (m, 1H), 7.48 (d, *J*=8.8 Hz, 1H), 7.92 (s, 1H), 8.03 (d, *J*=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 113.3 (d, $^{2}J_{C-F}$=22 Hz), 121.0, 121.3 (d, $^{2}J_{C-F}$=14 Hz), 124.3, 126.4, 127.0, 131.3 (d, $^{3}J_{C-F}$=9 Hz), 131.4, 137.4, 140.3, 151.7, 160.6 (d, $^{1}J_{C-F}$=246 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.80; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_{10}ClFNS$ (M+H): 278.0207, found 278.0203.

3.1.12. 6-Fluoro-2-(2-fluoro-6-methylphenyl)benzo[d]thiazole ***2m***. Isolated as a colorless solid (57.1 mg, 73% yield), mp: 70–71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.04 (t, *J*=8.8 Hz, 1H), 7.13 (d, *J*=7.6 Hz, 1H), 7.26 (t, *J*=8.8 Hz, 1H), 7.32–7.37 (m, 1H), 7.63 (d, *J*=8.0 Hz, 1H), 8.05–8.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 107.6 (d, $^{2}J_{C-F}$=27 Hz), 113.3 (d, $^{2}J_{C-F}$=22 Hz), 114.9 (d, $^{2}J_{C-F}$=24 Hz), 121.4 (d, $^{2}J_{C-F}$=14 Hz), 124.6 (d, $^{3}J_{C-F}$=10 Hz), 126.4, 131.2 (d, $^{3}J_{C-F}$=9 Hz), 137.2 (d, $^{3}J_{C-F}$=11 Hz), 140.3, 149.8, 160.6 (d, $^{1}J_{C-F}$=260 Hz), 160.7 (d, $^{1}J_{C-F}$=259 Hz), 161.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −113.02, −115.51; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_{10}F_2NS$ (M+H): 262.0502, found 262.0497.

3.1.13. 2-(2-Fluoro-5-methylphenyl)benzo[d]thiazole ***2n***. Isolated as a yellow solid (43.7 mg, 60% yield), mp: 61–62 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 7.11 (t, *J*=9.2 Hz, 1H), 7.23–7.26 (m, 1H), 7.40 (t, *J*=8.0 Hz, 1H), 7.51 (t, *J*=8.4 Hz, 1H), 7.93 (d, *J*=8.0 Hz, 1H), 8.12 (d, *J*=8.0 Hz, 1H), 8.21 (d, *J*=6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 116.1 (d, $^{2}J_{C-F}$=22 Hz), 120.9 (d, $^{2}J_{C-F}$=11 Hz), 121.5, 123.2, 125.2, 126.3, 129.7, 132.8 (d, $^{3}J_{C-F}$=9 Hz), 134.3, 135.8, 152.5, 158.9 (d, $^{1}J_{C-F}$=250 Hz), 161.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ −116.92; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_1FNS$ (M+H): 244.0596, found 244.0591.

3.1.14. 2-(2,6-Difluoro-3-methylphenyl)benzo[d]thiazole ***3n***. Isolated as a yellow oil (13.3 mg, 17% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 6.98 (t, *J*=8.8 Hz, 1H), 7.27–7.32 (m, 1H), 7.45 (t, *J*=8.0 Hz, 1H), 7.54 (t, *J*=8.4 Hz, 1H), 7.96 (d, *J*=8.0 Hz, 1H), 8.19 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3 (d, $^{3}J_{C-F}$=4 Hz), 111.4 (dd, $^{2}J_{C-F}$=4, 22 Hz), 121.3, 121.6 (dd, $^{2}J_{C-F}$=2, 18 Hz), 123.8, 125.6, 126.2, 128.8, 130.9, 133.0 (dd, $^{3}J_{C-F}$=7, 10 Hz), 153.0, 158.4 (dd, $^{1}J_{C-F}$=6, 254 Hz), 158.7 (dd, $^{1}J_{C-F}$=6, 252 Hz), 167.7 (d, $^{3}J_{C-F}$=4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.44, −113.77; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_{10}F_2NS$ (M+H): 262.0502, found 262.0506.

3.1.15. 6-Fluoro-2-(2-fluoro-5-methylphenyl)benzo[d]thiazole ***2o***. Isolated as a colorless solid (34.4 mg, 44% yield), mp: 122–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 7.02 (t, *J*=9.6 Hz, 1H), 7.11–7.22 (m, 2H), 7.51 (d, *J*=6.4 Hz, 1H), 7.94–7.98 (m, 1H), 8.08 (d, *J*=6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 107.5 (d, $^{2}J_{C-F}$=27 Hz), 115.1 (d, $^{2}J_{C-F}$=24 Hz), 116.1 (d, $^{2}J_{C-F}$=22 Hz), 120.6 (d, $^{2}J_{C-F}$=11 Hz), 124.2 (d, $^{3}J_{C-F}$=9 Hz), 129.5, 132.8 (d, $^{3}J_{C-F}$=8 Hz), 134.4, 136.8, 149.2, 158.8 (d, $^{1}J_{C-F}$=249 Hz), 160.5 (d, $^{1}J_{C-F}$=244 Hz), 161.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.62, −117.15; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_{10}F_2NS$ (M+H): 262.0502, found 262.0499.

3.1.16. 2-(2,6-Difluoro-3-methylphenyl)-6-fluorobenzo[d]thiazole ***3o***. Isolated as a colorless solid (13.4 mg, 16% yield), mp: 176–177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 6.98 (t, *J*=8.8 Hz, 1H), 7.26–7.32 (m, 2H), 7.63 (d, *J*=7.6 Hz, 1H), 8.11–8.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3 (d, $^{3}J_{C-F}$=4 Hz), 107.4 (d, $^{2}J_{C-F}$=26 Hz), 111.5 (d, $^{2}J_{C-F}$=22 Hz), 115.1 (d, $^{2}J_{C-F}$=25 Hz), 121.6 (d, $^{2}J_{C-F}$=19 Hz), 124.8 (d, $^{3}J_{C-F}$=10 Hz), 128.8 (d, $^{3}J_{C-F}$=4 Hz), 130.9, 133.1 (d, $^{3}J_{C-F}$=9 Hz), 136.8 (d, $^{3}J_{C-F}$=11 Hz), 149.7, 156.0 (d, $^{3}J_{C-F}$=4 Hz), 158.3 (d, $^{1}J_{C-F}$=247 Hz), 158.6 (d, $^{1}J_{C-F}$=253 Hz), 160.8 (d, $^{1}J_{C-F}$=245 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.40, −113.72, −114.99; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_9F_3NS$ (M+H): 280.0408, found 280.0405.

3.1.17. 6-Chloro-2-(2-fluoro-5-methylphenyl)benzo[d]thiazole ***2p***. Isolated as a colorless solid (39.1 mg, 47% yield), mp: 152–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.10 (dd, *J*=8.4, 11.2 Hz, 1H), 7.21–7.27 (m, 1H), 7.45 (d, *J*=10.4 Hz, 1H), 7.88 (s, 1H), 7.99 (d, *J*=8.8 Hz, 1H), 8.17 (d, *J*=6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 115.0 (d, $^{2}J_{C-F}$=22 Hz), 119.4 (d, $^{2}J_{C-F}$=11 Hz), 119.9, 122.8, 126.1, 128.5, 130.1, 132.0 (d, $^{3}J_{C-F}$=8 Hz), 133.3, 135.9 (d, $^{3}J_{C-F}$=8 Hz), 150.0, 157.9 (d, $^{1}J_{C-F}$=250 Hz), 160.8 (d, $^{3}J_{C-F}$=6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −116.64; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_{10}ClFNS$ (M+H): 278.0207, found 278.0205.

3.1.18. 6-Chloro-2-(2,6-difluoro-3-methylphenyl)benzo[d]thiazole ***3p***. Isolated as a colorless solid (13.3 mg, 15% yield), mp: 132–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 6.99 (t, *J*=9.2 Hz, 1H), 7.31 (t, *J*=8.0 Hz, 1H), 7.50 (d, *J*=8.8 Hz, 1H), 7.94 (s, 1H), 8.08 (d, *J*=8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3 (d, $^{3}J_{C-F}$=4 Hz), 111.1 (t, $^{3}J_{C-F}$=6 Hz), 111.6 (dd, J_{C-F}=4, 22 Hz), 120.9, 121.7 (dd, J_{C-F}=4, 18 Hz), 124.5, 127.1, 131.7, 133.3 (dd, J_{C-F}=8, 10 Hz), 136.8 (t, $^{3}J_{C-F}$=4 Hz), 151.5, 156.9 (t, J_{C-F}=4 Hz), 158.3 (dd, J_{C-F}=6, 253 Hz), 158.6 (dd, J_{C-F}=4, 256 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.05, −113.36; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_9ClF_2NS$ (M+H): 296.0112, found 296.0116.

3.1.19. 2-(5-Chloro-2-fluorophenyl)benzo[d]thiazole ***2q***. Isolated as a colorless solid (49.7 mg, 63% yield), mp: 97–97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J*=10.0 Hz, 1H), 7.39–7.46 (m, 2H), 7.54 (t, *J*=7.2 Hz, 1H), 7.95 (d, *J*=7.6 Hz, 1H), 8.13 (d, *J*=8.0 Hz, 1H), 8.44

(dd, J=2.8, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.7 (d, $^2J_{C-F}$=24 Hz), 121.5, 122.8 (d, $^3J_{C-F}$=11 Hz), 123.5, 125.7, 126.5, 129.2, 130.2, 131.7 (d, $^3J_{C-F}$=9 Hz), 135.9, 152.4, 159.0 (d, $^1J_{C-F}$=252 Hz), 159.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.65; HRMS-ESI (m/z): calcd for $C_{13}H_8ClFNS$ (M+H): 264.0050, found 264.0045.

3.1.20. 2-(5-Chloro-2-fluorophenyl)-6-methylbenzo[d]thiazole ***2r***. Isolated as a colorless solid (28.2 mg, 34% yield), mp: 165–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (s, 3H), 7.16 (t, J=9.6 Hz, 1H), 7.33 (d, J=8.4 Hz, 1H), 7.35–7.39 (m, 1H), 7.71 (s, 1H), 7.99 (d, J=8.0 Hz, 1H), 8.39–8.42 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 117.7 (d, $^2J_{C-F}$=24 Hz), 121.1, 122.8, 123.0, 128.2, 129.1, 130.2, 131.5 (d, $^3J_{C-F}$=9 Hz), 136.0 (d, $^3J_{C-F}$=8 Hz), 136.1 (d, $^3J_{C-F}$=8 Hz), 150.5, 158.4, 158.9 (d, $^1J_{C-F}$=252 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.86; HRMS-ESI (m/z): calcd for $C_{14}H_{10}ClFNS$ (M+H): 278.0207, found 278.0209.

3.1.21. 2-(3-Chloro-2,6-difluorophenyl)-6-methylbenzo[d]thiazole ***3r***. Isolated as a colorless solid (7.0 mg, 8% yield), mp: 108–109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 7.05 (t, J=8.8 Hz, 1H), 7.37 (d, J=7.6 Hz, 1H), 7.47–7.53 (m, 1H), 7.76 (s, 1H), 8.07 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 112.7 (dd, J_{C-F}=4, 23 Hz), 117.8 (dd, J_{C-F}=4, 7 Hz), 121.0, 123.5, 128.2, 128.8 (d, $^3J_{C-F}$=4 Hz), 130.9, 131.8 (d, $^3J_{C-F}$=10 Hz), 136.3, 151.2, 152.4 (dd, J_{C-F}=4, 252 Hz), 155.8 (dd, J_{C-F}=4, 256 Hz), 167.7 (d, $^3J_{C-F}$=4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.27, −110.62; HRMS-ESI (m/z): calcd for $C_{14}H_9ClF_2NS$ (M+H): 296.0112, found 296.0109.

3.1.22. 2-(2-Fluorophenyl)benzo[d]thiazole ***2s***.[5e,9] Isolated as a colorless solid (54.2 mg, 79% yield), mp: 97–97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, J=9.6 Hz, 1H), 7.26 (t, J=7.6 Hz, 1H), 7.35–7.44 (m, 2H), 7.48 (t, J=7.6 Hz, 1H), 7.89 (d, J=7.6 Hz, 1H), 8.11 (d, J=8.0 Hz, 1H), 8.39 (t, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.4 (d, $^2J_{C-F}$=22 Hz), 121.4, 121.5, 123.3, 124.7, 125.3, 126.3, 129.8, 132.1 (d, $^3J_{C-F}$=7 Hz), 135.8 (d, $^3J_{C-F}$=7 Hz), 152.6, 160.6 (d, $^1J_{C-F}$=252 Hz), 161.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.65; HRMS-ESI (m/z): calcd for $C_{13}H_9FNS$ (M+H): 230.0440, found 230.0434.

3.1.23. 2-(2-Fluorophenyl)-6-methylbenzo[d]thiazole ***2t***.[9] Isolated as a colorless solid (40.8 mg, 56% yield), mp: 111–112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 7.15–7.29 (m, 3H), 7.37–7.42 (m, 1H), 7.65 (s, 1H), 7.97 (d, J=8.4 Hz, 1H), 8.37 (dt, J=1.6, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 116.3 (d, $^2J_{C-F}$=22 Hz), 121.1, 121.6 (d, $^3J_{C-F}$=11 Hz), 122.8, 124.6, 128.0, 129.7, 131.9 (d, $^3J_{C-F}$=9 Hz), 135.5, 136.0 (d, $^3J_{C-F}$=8 Hz), 150.7, 160.0, 160.5 (d, $^1J_{C-F}$=252 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.01; HRMS-ESI (m/z): calcd for $C_{14}H_{11}FNS$ (M+H): 244.0596, found 244.0591.

3.1.24. 6-Chloro-2-(2-fluorophenyl)benzo[d]thiazole ***2u***.[9] Isolated as a colorless solid (41.8 mg, 53% yield), mp: 148–149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (t, J=9.2 Hz, 1H), 7.30 (t, J=6.8 Hz, 1H), 7.43–7.46 (m, 1H), 7.88 (s, 1H), 7.99 (d, J=8.0 Hz, 1H), 8.35–8.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.4 (d, $^2J_{C-F}$=22 Hz), 121.0, 121.1, 124.0, 124.8, 127.2, 129.7, 131.2, 132.4 (d, $^3J_{C-F}$=9 Hz), 136.9 (d, $^3J_{C-F}$=8 Hz), 151.1, 160.6 (d, $^1J_{C-F}$=252 Hz), 161.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.65; HRMS-ESI (m/z): calcd for $C_{13}H_8ClFNS$ (M+H): 264.0050, found 264.0047.

3.1.25. 6-Chloro-2-(2,6-difluorophenyl)benzo[d]thiazole ***3u***. Isolated as a colorless solid (31.2 mg, 37% yield), mp: 127–128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (t, J=8.4 Hz, 2H), 7.42–7.51 (m, 2H), 7.93 (s, 1H), 8.09 (d, J=8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.6 (t, $^2J_{C-F}$=15 Hz), 112.3 (d, $^2J_{C-F}$=26 Hz), 120.8, 124.6, 127.2, 131.8, 132.1 (t, $^3J_{C-F}$=11 Hz), 136.8, 151.5, 156.3, 160.5 (dd, $^3J_{C-F}$=6 Hz, $^1J_{C-F}$=254 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.24; HRMS-ESI (m/z): calcd for $C_{13}H_7ClF_2NS$ (M+H): 281.9956, found 281.9950.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.11.034.

References and notes

1. (a) Mortimer, C. G.; Wells, G.; Crochard, J. P.; Stone, E. L.; Bradshaw, T. D.; Stevens, M. F. G.; Westwell, A. D. *J. Med. Chem.* **2006**, *49*, 179; (b) McKee, M. L.; Kerwin, S. M. *Bioorg. Med. Chem.* **2008**, *16*, 1775; (c) Kiumars, K.; Khodaei, M. M.; Naali, F. *J. Org. Chem.* **2008**, *73*, 6835; (d) Sun, Q.; Wu, R.; Cai, S.; Lin, Y.; Sellers, L.; Sakamoto, K.; He, B.; Peterson, B. R. *J. Med. Chem.* **2011**, *54*, 1126; (e) Lim, C. S.; Masanta, G.; Kim, H. J.; Han, J. H.; Kim, H. M.; Cho, B. R. *J. Am. Chem. Soc.* **2011**, *133*, 11132; (f) Konig, J.; Wyllie, S.; Wells, G.; Stevens, M. F.; Wyatt, P. G.; Fairlamb, A. H. *J. Biol. Chem.* **2011**, *286*, 8523; (g) Cellier, M.; Fabrega, O. J.; Fazackerley, E.; James, A. L.; Orenga, S.; Perry, J. D.; Salwatura, V. L.; Stanforth, S. P. *Bioorg. Med. Chem.* **2011**, *19*, 2903; (h) Alavez, S.; Vantipalli, M. C.; Zucker, D. J. S.; Klang, I. M.; Lithgow, G. J. *Nature* **2011**, *472*, 226.
2. (a) Lanman, B. A.; Cee, V. J.; Cheruku, S. R.; Frohn, M.; Golden, J.; Lin, J.; Lobera, M.; Marantz, Y.; Muller, K. M.; Neira, S. C.; Pickrell, A. J.; Rivenzon-Segal, D.; Schutz, N.; Sharadendu, A.; Yu, X.; Zhang, Z.; Buys, J.; Fiorino, M.; Gore, A.; Horner, M.; Itano, A.; McElvain, M.; Middleton, S.; Schrag, M.; Vargas, H. M.; Xu, H.; Xu, Y.; Zhang, X.; Siu, J.; Bürli, R. W. *ACS Med. Chem. Lett.* **2011**, *2*, 102; (b) Frohn, M.; Cee, V. J.; Lanma, B. A.; Pickrell, A. J.; Rivenzon-Segal, J. G. D.; Middleton, S.; Fiorino, M.; Xu, H.; Schrag, M.; Xu, Y.; McElvain, M.; Muller, K.; Siu, J.; Bürli, R. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 628; (c) Hwang, J. Y.; Smithson, D. C.; Holbrook, G.; Zhu, F.; Connelly, M. C.; Kaiser, M.; Brun, R.; Guy, R. K. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 4127; (d) Kiyoshi, N.; Masamichi, T.; Makoto, A. PCT Int. Appl., 2007, WO 2007091313 A1 20070816.
3. (a) Li, Y. *J. Lumin.* **2011**, *131*, 1821; (b) Zhang, J.; Li, Y.; Hui, C.; Zhu, J. *Synth. Met.* **2011**, *161*, 1166; (c) Chang, W.; Yang, P.-Y. *J. Lumin.* **2012**, *132*, 403; (d) Cui, X.; Zhang, H. M.; Wu, T. F.; Li, M. *Spectrochim. Acta, Part A* **2011**, *82*, 126.
4. For selected examples, see: (a) Benedi, C.; Bravo, F.; Uriz, P.; Fernandez, E.; Claver, C.; Castillon, S. *Tetrahedron Lett.* **2003**, *44*, 6073; (b) Evindar, G.; Batey, R. A. *J. Org. Chem.* **2006**, *71*, 1802; (c) Itoh, T.; Mase, T. *Org. Lett.* **2007**, *9*, 3687; (d) Do, H.; Daugulis, O. *J. Am. Chem. Soc.* **2007**, *129*, 12404; (e) Zhao, D.; Wang, W.; Yang, F.; Lan, J.; Yang, L.; Gao, G.; You, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 3296; (f) Huang, J.; Chan, J.; Chen, Y.; Borths, C.; Kyle, K.; Larsen, R.; Margaret, M. *J. Am. Chem. Soc.* **2010**, *132*, 3674; (g) Ranjit, S.; Liu, X. *Chem.—Eur. J.* **2011**, *17*, 1105; (h) Wang, Z.; Li, K.; Zhao, D.; Lan, J.; You, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 5365; (i) Zhu, M.; Fujita, K.; Yamaguchi, R. *Chem. Commun.* **2011**, 12876; (j) Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 6993; (k) Liao, Y.; Qi, H.; Chen, S.; Jiang, P.; Zhou, W.; Deng, G.-J. *Org. Lett.* **2012**, *14*, 6004; (l) Yu, D.; Lu, L.; Shen, Q. *Org. Lett.* **2013**, *15*, 940.
5. (a) Mettey, Y.; Michaud, S.; Vierfond, J. M. *Heterocycles* **1994**, *38*, 1001; (b) Sharghi, H.; Asemani, O. *Synth. Commun.* **2009**, *39*, 860; (c) Xie, K.; Yang, Z.; Zhou, X.; Li, X.; Wang, S.; Tan, Z.; An, X.; Guo, C.-C. *Org. Lett.* **2010**, *12*, 1564; (d) Kalkhambkar, R. G.; Laali, K. K. *Tetrahedron Lett.* **2012**, *53*, 4212; (e) Yang, Z.; Chen, X.; Wang, S.; Liu, J.; Xie, K.; Wang, A.; Tan, Z. *J. Org. Chem.* **2012**, *77*, 7086.
6. For selected examples, see: (a) Furuya, T.; Kaiser, H. M.; Ritter, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 5993; (b) Furuya, T.; Ritter, T. *Org. Lett.* **2009**, *11*, 2860; (c) Watson, D. A.; Su, M.; Teverovskiy, G.; Zhang, Y.; García-Fortanet, J.; Kinzel, T.; Buchwald, S. L. *Science* **2009**, *325*, 1661; (d) Tang, P.; Furuya, T.; Ritter, T. *J. Am. Chem. Soc.* **2010**, *132*, 12150; (e) Furuya, T.; Strom, A. E.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 1662; (f) Tang, P.; Ritter, T. *Tetrahedron* **2011**, *67*, 4449; (g) Fier, P. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2012**, *134*, 10795; (h) Lee, E.; Hooker, J. M.; Ritter, T. *J. Am. Chem. Soc.* **2012**, *134*, 17456; (i) Fier, P. S.; Luo, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 2552; (j) Ye, Y.; Sanford, M. S. *J. Am. Chem. Soc.* **2013**, *135*, 4648.
7. (a) Hull, K. L.; Anani, W. Q.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 7134; (b) Wang, X.; Mei, T.-S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 7520; (c) Chan, K. S. L.; Wasa, M.; Wang, X.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2011**, *50*, 9081; (d) Lou, S.-J.; Xu, D.-Q.; Xia, A.-B.; Wang, Y.-F.; Liu, Y.-K.; Du, X.-H.; Xu, Z.-Y. *Chem. Commun.* **2013**, 6218.
8. (a) Ding, Q.; Ji, H.; Wang, D.; Lin, Y.; Yu, W.; Peng, Y. *J. Organomet. Chem.* **2012**, *711*, 62; (b) Hashimoto, Y.; Ortloff, T.; Hirano, K.; Satoh, T.; Bolm, C.; Miura, M. *Chem. Lett.* **2012**, *41*, 151; (c) Zhang, Q.; Li, C.; Yang, F.; Li, J.; Wu, Y. *Tetrahedron*

2013, *69*, 320; (d) Zhang, Q.; Yang, F.; Wu, Y. *Tetrahedron* **2013**, *69*, 4908; (e) Reddy, V. P.; Qiu, R.; Iwasaki, T.; Kambe, N. *Org. Lett.* **2013**, *15*, 1290.
9. Ding, Q.; Ji, H.; Nie, Z.; Yang, Q.; Peng, Y. *J. Organomet. Chem.* **2013**, *739*, 33.
10. For mechanistic studies on C–F reductive elimination from high-valent palladium fluoride, see: (a) Furuya, T.; Ritter, T. *J. Am. Chem. Soc.* **2008**, *130*, 10060; (b) Ball, N. D.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 3796; (c) Furuya, T.; Benitez, D.; Tkatchouk, E.; Strom, A. E.; Tang, P.; Goddard, W. A., III; Ritter, T. *J. Am. Chem. Soc.* **2010**, *132*, 3793; (d) Qiu, S.; Xu, T.; Zhou, J.; Guo, Y.; Liu, G. *J. Am. Chem. Soc.* **2010**, *132*, 2856; (e) Engle, K. M.; Mei, T.-S.; Wang, X.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2011**, *50*, 1478; (f) Peng, H.; Yuan, Z.; Wang, H.-Y.; Guo, Y.-L.; Liu, G. *Chem. Sci.* **2013**, *4*, 3172.