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Synthesis of 2-Arylbenzothiazole and 2-Arylthiazole Derivatives via a Ru-Catalyzed *meta*-Selective C−H Nitration Reaction

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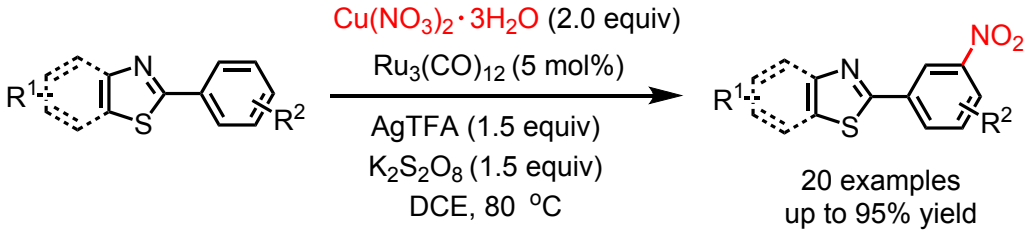


Abstract: A Ru-catalyzed *meta*-selective C−H nitration of 2-arylbenzothiazoles and 2-arylthiazoles has been developed. A wide range of functional groups are tolerated, providing the *meta*-nitrated products in good to excellent yields by using $Cu(NO_3)_2·3H_2O$ as the nitro source. The nitration could be carried out on gram-scale and used to the synthesis of promising therapeutic leads for Human African Trypanosomiasis.

INTRODUCTION

Benzothiazole derivatives are versatile motifs in synthetic chemistry, material chemistry, and the areas related to therapeutic agents, pharmaceuticals, due to their good biological activities and fluorescent properties.[1] In addition, nitroarenes are invaluable building blocks or precursors in organic synthesis, medicinal chemistry

and material science.[2] For example, a series of *meta*-nitro substituted 2-arylbenzothiazole derivatives have been detected as COMT inhibitors, P388 inhibitor, and potential drugs with in vitro antimicrobial activity (Figure 1).[3] Recently, transition-metal catalyzed inert C–H bond activation and directly functionalization offers an attractive strategy for the synthesis of various C–C bond or C–X bonds (X = O, N, S, halogen atoms).[4] Remarkable progress has been made in directing group-assisted *ortho*-selective C–H bond functionalization.[5] Recently, considerable efforts have been devoted to developing various *ortho*-functionalized 2-arylbenzothiazole derivatives by us[1a,6-8] and other groups,[9,10] including amidation,[1a] arylation,[6a] acetoxylation,[6b] halogenations,[6c] sulfonamidation,[7a] acylation,[7b,9a,b] cyanation,[8a] alkylation,[8b,9g] hydroxylation,[10a,b] nitration,[10c] and so on.

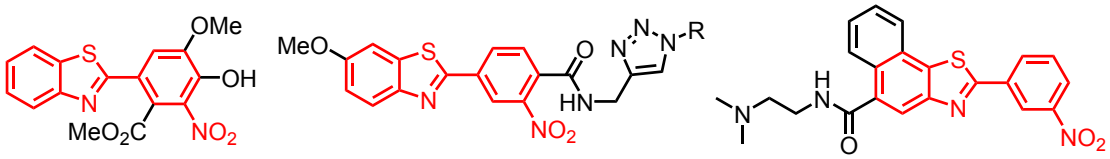


Figure 1. Chemical structures *meta*-nitro substituted 2-arylbenzothiazoles with bioactivities

Although some excellent work[11-15] concerning transition-metal-catalyzed *meta*-C–H bond functionalizations has been reported, study in this area is still in its infancy. Among these, the pioneering work in *meta*-C–H functionalizations mainly reflected in Pd-catalyzed U-shaped nitrile-containing ligand-assisted *meta*-C–H activation or *ortho*-directing group-assisted norbornene-mediated *meta*-C–H functionalizations, which were mainly developed by the Yu,[11,12] Dong[13] and Maiti[14] groups. Additionally, the *meta*-selective functionalizations have been reported by standard Friedel-Crafts

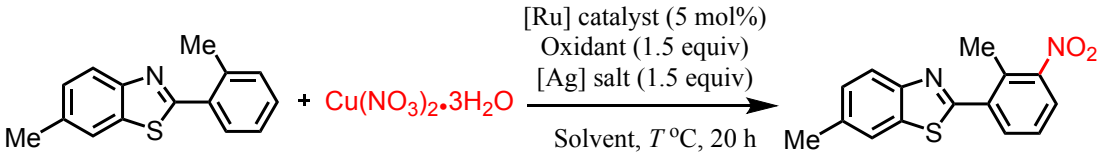
reactions via combination of ligand and electronic effect.[15] Recently, several ruthenium-catalyzed chelation-assisted *meta*-C−H activation in the formation of various C–C, C–S, and C–Br bonds have been well studied.[16] Li described the Ru-catalyzed *meta*-C–H bond alkylation of 2-phenpxypyridines[16a] and azoarenes[16b]. Shi also reported the Ru-catalyzed *meta*-C–H benzylation of pyridyl, pyrimidyl, and pyrazolyl directed arenes with toluene derivatives.[16c] Recently, the methods for regioselective nitration of arenes using various nitro sources also have been developed.[17,18] For instance, Zhang reported the Ru-catalyzed *meta*-C–H nitration of 2-arylpyridines[17a] and oximes[17b] using $Cu(NO_3)_2 \cdot 3H_2O$ as the nitro source. Stimulated by the recent Ru-catalyzed *meta*-selective C–H functionalizations, we wish to find an efficient method for the synthesis of *meta*-nitrated 2-arylbenzothiazole derivatives to examine their bioactivities.

RESULTS AND DISCUSSION

According to Zhang's research,[17] we initially screened the Ru-catalysts using 2-arylbenzothiazole **1a** as the model substrate and $Cu(NO_3)_2 \cdot 3H_2O$ as the nitro source in the presence of oxone and AgTFA (Table 1, entries 1-4). The initial results indicated that $Ru_3(CO)_{12}$ performed better than $[RuCl_2(p\text{-cymene})_2]_2$, affording the desired *meta*-nitrated product **2a** in 64% yield (Table 1, entries 1 vs 2). Using other ruthenium complexes, such as $RuCl_2(PPh_3)_4$ and $RuCl_3$, only trace amounts of desired product was observed (Table 1, entries 3 and 4). Control experiments confirmed that no reaction was observed in the absence of [Ru]-catalyst (Table 1, entry 5), while moderate yield (52%) of product **2a** was obtained in the absence of oxidant (Table 1,

entry 6). Among the oxidants examined, the inexpensive $K_2S_2O_8$ afforded the best results (Table 1, entry 10), whereas $Cu(OAc)_2 \cdot H_2O$, chloranil and $Cu(OAc)_2$ gave the desired product **2a** in moderate yields (Table 1, entries 7-9, 56-68%). We then screened several silver salts as radical initiators, AgTFA exhibited superior results compared to $AgBF_4$, AgOAc and $AgNO_3$ (Table 1, entries 10-13). Only trace amounts of desired product was observed in the absence of silver salts (Table 1, entry 14). Increasing the reaction temperature (T = 100 °C) decreased the yield of desired product **2a** (70%) (Table 1, entry 15). The same result was obtained at 80 °C, and the yield remained satisfactory (86%) at 70 °C (Table 1, entries 16 and 17). However, the yield (51%) of product **2a** declined dramatically when the reaction proceeded at 60 °C (Table 1, entry 18). Among the solvents examined, DCE gave the best results, and toluene afforded inferior yield (64%) (Table 1, entry 19), other solvents such as CH_3CN, EtOH, and DMSO only afforded trace amount of desired product **2a**.

Table 1. Optimization of reaction conditions[a]



1a **2a**

Entry	[Ru] catalyst	Oxidant	[Ag]	Solvent	T/°C	Yield[b]
1	$[RuCl_2(p\text{-cymene})_2]_2$	Oxone	AgTFA	DCE	90	50
2	$Ru_3(CO)_{12}$	Oxone	AgTFA	DCE	90	64
3	$RuCl_2(PPh_3)_4$	Oxone	AgTFA	DCE	90	trace
4	$RuCl_3$	Oxone	AgTFA	DCE	90	trace
5	-	Oxone	AgTFA	DCE	90	0
6	$Ru_3(CO)_{12}$	-	AgTFA	DCE	90	52
7	$Ru_3(CO)_{12}$	$Cu(OAc)_2 \cdot H_2O$	AgTFA	DCE	90	64
8	$Ru_3(CO)_{12}$	Chloranil	AgTFA	DCE	90	56
9	$Ru_3(CO)_{12}$	$Cu(OAc)_2$	AgTFA	DCE	90	68

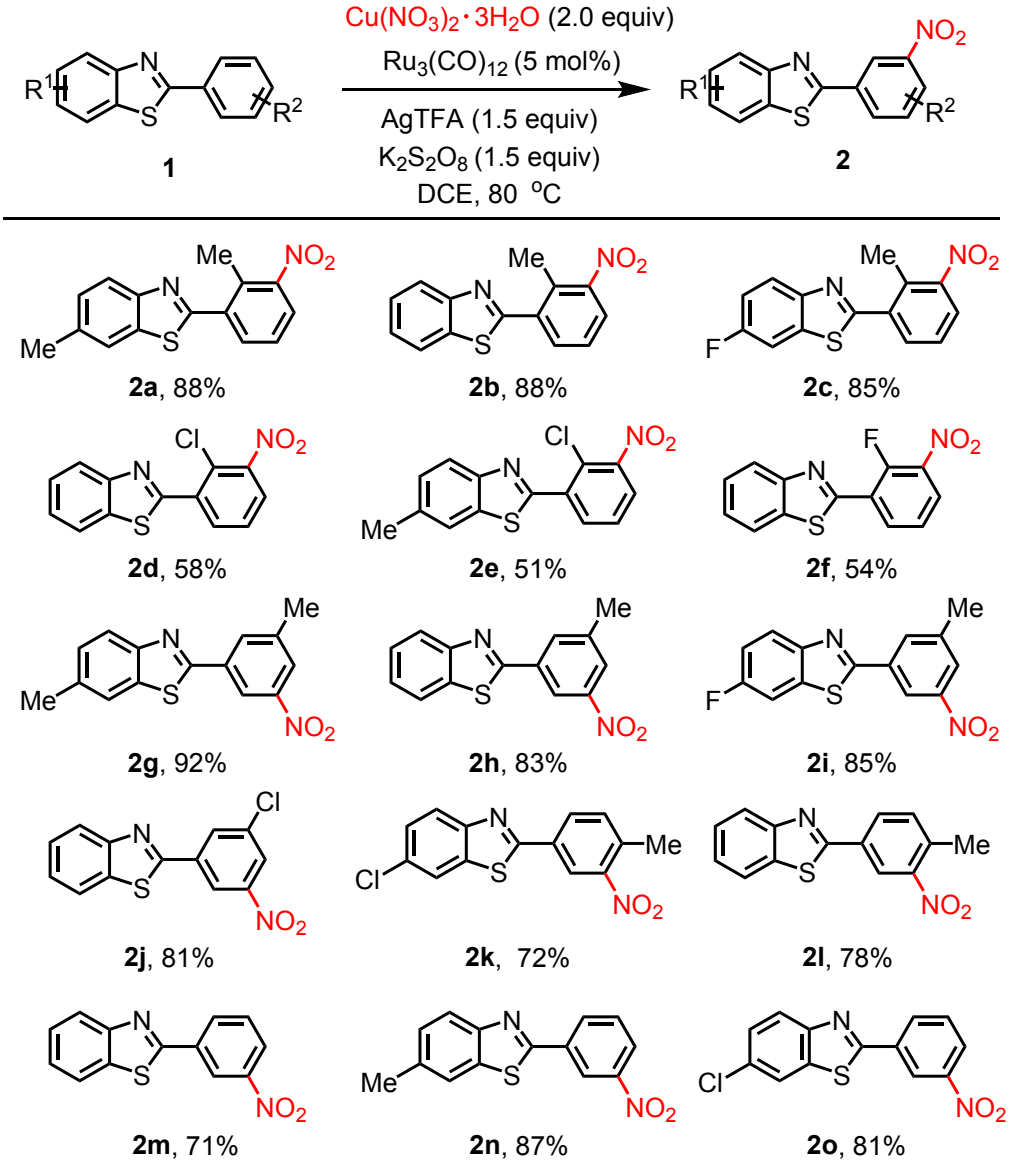
10	$Ru_3(CO)_{12}$	$K_2S_2O_8$	AgTFA	DCE	90	88
11	$Ru_3(CO)_{12}$	$K_2S_2O_8$	$AgBF_4$	DCE	90	50
12	$Ru_3(CO)_{12}$	$K_2S_2O_8$	AgOAc	DCE	90	39
13	$Ru_3(CO)_{12}$	$K_2S_2O_8$	$AgNO_3$	DCE	90	trace
14	$Ru_3(CO)_{12}$	$K_2S_2O_8$	-	DCE	90	trace
15	$Ru_3(CO)_{12}$	$K_2S_2O_8$	AgTFA	DCE	100	70
16	$Ru_3(CO)_{12}$	$K_2S_2O_8$	AgTFA	DCE	80	88
17	$Ru_3(CO)_{12}$	$K_2S_2O_8$	AgTFA	DCE	70	86
18	$Ru_3(CO)_{12}$	$K_2S_2O_8$	AgTFA	DCE	60	51
19	$Ru_3(CO)_{12}$	$K_2S_2O_8$	AgTFA	toluene	80	64

[a]Reaction conditions: **1a** (0.2 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.4 mmol), [Ru] catalyst (5 mol%), oxidant (1.5 equiv), [Ag] salt (1.5 equiv), solvent (2 mL), 20 h. [b]Isolated yield by flash column chromatography.

With the optimized conditions in hand, we investigated the substrate scope of 2-arylbenzothiazoles **1**. As shown in Scheme 1, a broad range of 2-arylbenzothiazole derivatives **1** could be smoothly transformed into the corresponding *meta*-selective nitration products **2** in moderate to excellent yields. For instance, *ortho*-electron-donating group (R^2 = *ortho*-Me) substituted substrates 2-(*o*-tolyl)benzo[d]thiazoles **1a–c** delivered the desired *meta*-nitrated products (**2a–c**) in good yields (85-88%). While *ortho*-electron-withdrawing group (R^2 = *ortho*-Cl and F) substituted substrates 2-arylbenzo[d]thiazoles **1d–f** provided the corresponding desired products **2d-f** in moderate yields (51-58%) under the standard conditions. Subsequently, *meta*-electron-donating or -withdrawing groups (R^2 = *meta*-Me and Cl) substituted 2-arylbenzo[d]thiazoles **1g–j** showed good reactivity and provided the desired *meta*-selective nitration products **2g-j** in good to excellent yields (81-92%). The *para*-substituted 2-arylbenzo[d]thiazoles **1k–l** also performed well and gave the corresponding *mono*-nitrated products **2k–l** in good yields. The *meta*-nitration

structure of **2k** was confirmed by single-crystal X-ray analysis. In addition, 2-phenylbenzo[d]thiazoles **1m–o** (R^2 = H) underwent the *meta*-nitration smoothly under standard reaction conditions, leading to the corresponding *mono*-nitrated products **2m–o** in high yields (71-87%).

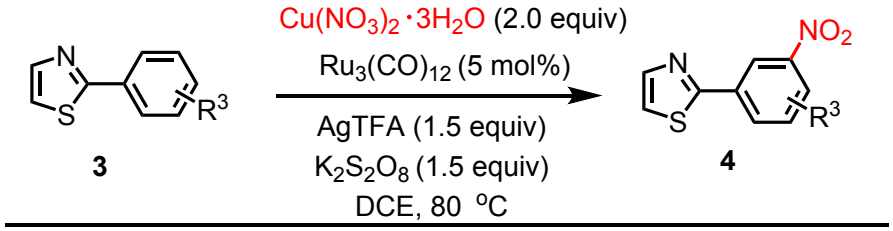
Scheme 1. Scope of 2-arylbenzo[d]thiazoles[a,b]

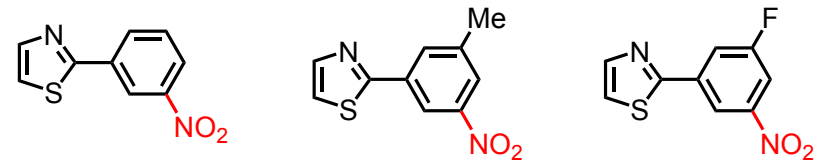


[a]Reaction conditions: 2-arylbenzothiazoles **1** (0.2 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.4 mmol), $Ru_3(CO)_{12}$ (5 mol %), $K_2S_2O_8$ (0.3 mmol), AgTFA (0.3 mmol), DCE (2 mL), 80 °C, 20 h. [b]Isolated yield by flash column chromatography.

We subsequently explored the generality of the *meta*-selective nitration using 2-arylthiazoles **3** as substrates under the standard conditions. As illustrated in Scheme 2, various substituted 2-arylthiazoles **3** were proceeded *meta*-selective nitration in good to excellent yields. The reactivity is similar to that of 2-arylbenzo[d]thiazoles. Among these, the nitration of *meta*-methyl substituted substrate **3b** gave the desired product **4b** in excellent yield (95%). Furthermore, the reaction of 2-(naphthalen-2-yl)thiazole **3d** occurred smoothly, providing the desired product **4d** in 66% yield. Unfortunately, no desired product **4f** was observed when 2-(2-methoxyphenyl)thiazole **3f** was used as substrate, which was possibly caused by the strong electron donation of the methoxy group.[19]

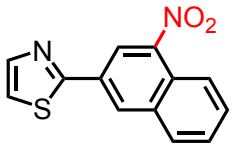
Scheme 2. Scope of 2-Arylthiazoles[a,b]

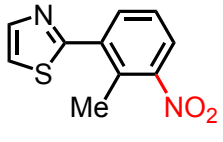


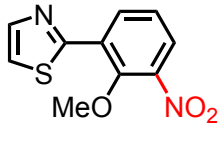

4a, 71%

4b, 95%

4c, 71%


4d, 66%

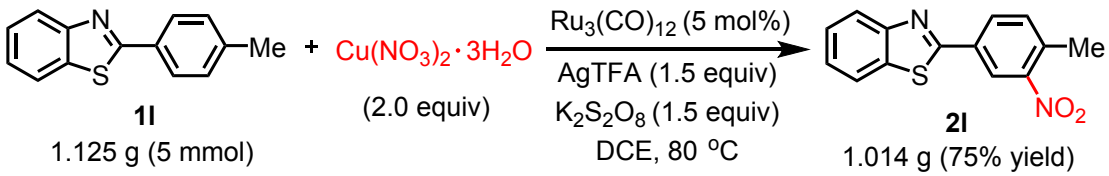

4e, 74%


4f, ND

[a]Reaction conditions: 2-arylthiazoles **3** (0.2 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.4 mmol), $Ru_3(CO)_{12}$ (5 mol %), $K_2S_2O_8$ (0.3 mmol), AgTFA (0.3 mmol), DCE (2 mL), 80 °C, 20 h. [b]Isolated yield by flash column chromatography.

To demonstrate the efficiency of the present method, we tried the nitration of **1l** at the gram-scale. Predictably, nitrated product **2l** was obtained in 75% yield (Scheme 3). According to previous work, nitroarenes are versatile aromatic building blocks, which could be easily undergone various functionalization by transition metal-catalyzed denitration-cross coupling reactions,[20] such as arylation, amination, etherification, and thioetherification. In addition, the selective reduction nitro group of **2l** to amine **5** was achieved in 92% yield in the presence of $SnCl_2 \cdot 2H_2O$ (5.0 equiv) (Scheme 4).[21] Amine **5** was previously converted into compound **6** by amidation reaction, which was reported as promising therapeutic leads for Human African Trypanosomiasis, which also displayed suitable physiochemical characteristics and microsomal stability.[21] Furthermore, 2-(3-aminophenyl)-benzothiazole derivatives could be effectively synthesized from the corresponding reduction products. Recently, Zhang and co-workers described that 2-(3-aminophenyl)-benzothiazoles displayed good in vitro antiproliferative activity against various human cancer cell lines, such as A549, HeLa, HepG2, MCF-7, and so on.[22]

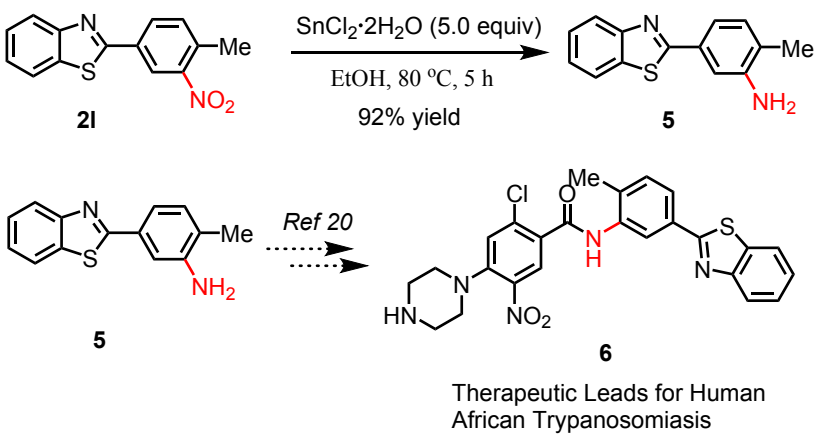
Scheme 3. Gram-Scale Nitration of 1l



1l
1.125 g (5 mmol)

2l
1.014 g (75% yield)

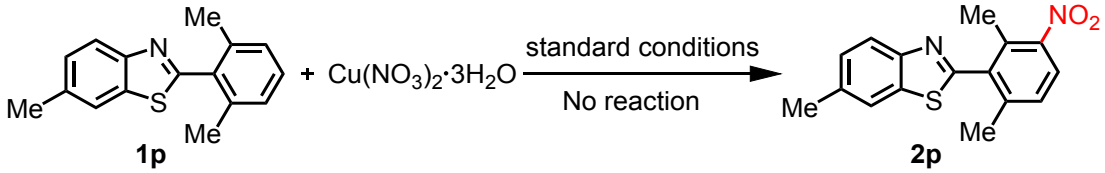
Scheme 4. Reduction and the Application of 2l



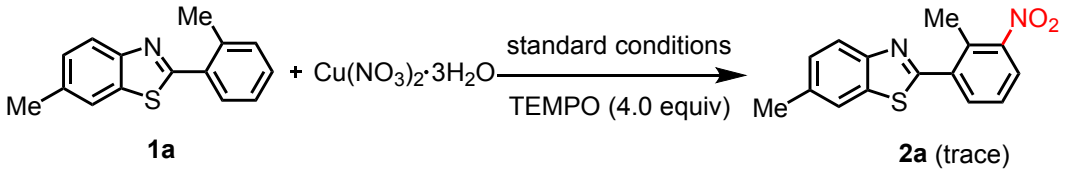
To explore the reaction mechanism, two control experiments were performed. 2-(2,6-Dimethylphenyl)-6-methylbenzo[d]thiazole **1p** bearing two methyl groups to block the two *ortho* positions of the phenyl ring was used as the substrate, resulting in no conversion. This result confirms that the initial ruthenium-mediated *ortho*-C–H bond activation to form a cyclometalated complex is a key step (Scheme 5-1). Subsequently, we found that no desired product **2a** was obtained when the reaction was carried out in the presence of radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, 4.0 equiv), suggesting that this *meta*-nitration reaction may involve a radical process (Scheme 5-2). Based on our control experiments and the recent Ru-catalyzed *meta*-C−H functionalization, the possible catalytic pathway may similar to that of Ru-catalyzed chelation-assisted *meta*-selective C−H nitration of arenes bearing derecting group, such as vrious *N*-heterocycles or oximido.[17]

Scheme 5. Preliminary mechanistic studies

(1) 2-(2,6-Dimethylphenyl)-6-methylbenzo[d]thiazole (**1p**) as substrate:



(2) Radical Mechanism Experiment:



Conclusion

In summary, we have successfully obtained a series of *meta*-nitrated 2-arylbenzothiazole and 2-arylthiazole derivatives via ruthenium-catalyzed *meta*-selective C-H nitration using $Cu(NO_3)_2 \cdot 3H_2O$ as the nitro source. The reaction shows a wide range of functional groups tolerance giving the desired *meta*-nitrated products in good to excellent yields. In addition, the nitration could be carried out on gram-scale and used to the synthesis of promising therapeutic leads for Human African Trypanosomiasis. The reaction may involve the Ru−C(sp^2) σ-bond assisted electrophilic aromatic substitution and a silver-mediated radical process. The biological and therapeutic activities of the *meta*-nitrated products are underway in our laboratory.

EXPERIMENTAL SECTION:

Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on a Bruker AV-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. High resolution mass spectrometry (HRMS) spectra were obtained on a

micrOTOF II instrument.

*Synthesis of starting substrates **1** and **3**.*

2-Arylbenzothiazoles **1**[23] *and 2-arylthiazoles* **3**[24] were synthesized according to the reported procedures. [23,24] All the starting substrates **1** and **3** are known compounds, and their NMR data were identical with those in literature.[23,24] The reactions were carried out on a1.0 mmol scale.

6-methyl-2-(o-tolyl)benzo[d]thiazole (**1a**), 196.0 mg (82% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.75-7.71 (m, 2H), 7.36-7.30 (m, 4H), 2.65 (s, 3H), 2.51 (s, 3H). ^{1}H NMR data were identical with those in literature.[23a] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{15}H_{14}NS^+$: 240.0841; found: 240.0845.

2-(o-tolyl)benzo[d]thiazole (**1b**), 180.0 mg (80 % yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.80 (s, 1H), 7.80-7.76 (m, 1H), 7.55-7.50 (m, 1H), 7.44-7.30 (m, 4H), 2.68 (s, 3H). ^{1}H NMR data were identical with those in literature.[23b] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{12}NS^+$: 226.0685; found: 226.0682.

6-fluoro-2-(o-tolyl)benzo[d]thiazole (**1c**), 196.8 mg (81% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04-8.01 (m, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.59-7.56 (m, 1H), 7.39-7.28 (m, 3H), 7.25-7.20 (m, 1H), 2.65 (s, 3H). ^{1}H NMR data were identical with those in literature.[23c] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{11}FNS^+$: 244.0591; found: 244.0587.

2-(2-chlorophenyl)benzo[d]thiazole (**1d**), 225.4 mg (92% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21-8.19 (m, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.53-7.50 (m, 2H), 7.43-7.39 (m, 3H). ^{1}H NMR data were identical with those in

literature.[23d] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_9ClNS^+$: 246.0139; found: 246.0142.

2-(2-chlorophenyl)-6-methylbenzo[d]thiazole (**1e**), 230.5 mg (89% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21-8.18 (m, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.73 (s, 1H), 7.54-7.51 (m, 1H), 7.42-7.37 (m, 2H), 7.35-7.32 (m, 1H), 2.52 (s, 3H). ^{1}H NMR data were identical with those in literature.[23a] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{11}ClNS^+$: 260.0295; found: 260.0295.

2-(2-fluorophenyl)benzo[d]thiazole (**1f**), 199.2 mg (87% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.43-8.38 (m, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.52-7.37 (m, 3H), 7.30-7.18 (m, 2H). ^{1}H NMR data were identical with those in literature.[23d] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_9FNS^+$: 230.0434; found: 230.0436.

6-methyl-2-(m-tolyl)benzo[d]thiazole (**1g**), 217.5 mg (91% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95-7.91 (m, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.66 (s, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.28-7.27 (m, 1H), 2.47 (s, 3H), 2.43 (s, 3H). ^{1}H NMR data were identical with those in literature.[23b] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{15}H_{14}NS^+$: 240.0841; found: 240.0838.

2-(m-tolyl)benzo[d]thiazole (**1h**), 191.3 mg (85% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.0 Hz, 1H), 7.93 (s, 1H), 7.87-7.84 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 6.8 Hz, 1H), 2.42 (s, 3H). ^{1}H NMR data were identical with those in literature.[23b] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{12}NS^+$: 226.0685; found: 226.0682.

6-fluoro-2-(m-tolyl)benzo[d]thiazole (**1i**), 213.8 mg (88% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 9.2, 4.8 Hz, 1H), 7.89 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.58-7.56 (m, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.24-7.18 (m, 1H), 2.45 (s, 3H). ^{1}H NMR data were identical with those in literature.[23b] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{11}FNS^+$: 244.0591; found: 244.0593.

2-(3-chlorophenyl)benzo[d]thiazole (**1j**), 222.9 mg (91% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09-8.05 (m, 2H), 7.92-7.86 (m, 2H), 7.51-7.47 (m, 1H), 7.44-7.36 (m, 3H).[23d] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_9ClNS^+$: 246.0139; found: 246.0142.

6-chloro-2-(p-tolyl)benzo[d]thiazole (**1k**), 220.1 mg (85% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 2.0 Hz, 1H), 7.43-7.40 (m, 1H), 7.27 (d, *J* = 8.0 Hz, 2H), 2.41 (s, 3H). ^{1}H NMR data were identical with those in literature.[23d] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{11}ClNS^+$: 260.0295; found: 260.0296.

2-(p-tolyl)benzo[d]thiazole (**1l**), 180.0 mg (80% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 2.43 (s, 4H). ^{1}H NMR data were identical with those in literature.[23d] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{12}NS^+$: 226.0685; found: 226.0682.

2-phenylbenzo[d]thiazole (**1m**), 183.5 mg (87% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.06 (m, 3H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.49-7.46 (m, 4H), 7.35 (t, *J* = 7.6 Hz, 1H). ^{1}H NMR data were identical with those in literature.[23b] **HRMS** (ESI): m/z [M +

H]$^+$ calcd for $C_{14}H_{12}NS^+$: 212.0528; found: 212.0526

6-methyl-2-phenylbenzo[d]thiazole (**1n**), 200.2 mg (89% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 3.6 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.68 (s, 1H), 7.47 (s, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 2.49 (s, 3H). ^{1}H NMR data were identical with those in literature.[23b] **HRMS** (ESI): m/z [M + H]$^+$ calcd for $C_{14}H_{12}NS^+$: 226.0685; found: 226.0684.

6-chloro-2-phenylbenzo[d]thiazole (**1o**), 210.7 mg (86% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96-9.94 (m, 3H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.35-7.31 (m, 4H), 7.21 (t, *J* = 7.6 Hz, 1H). ^{1}H NMR data were identical with those in literature.[23b] **HRMS** (ESI): m/z [M + H]$^+$ calcd for $C_{13}H_9ClNS^+$: 246.0139; found: 246.0142.

2-phenylthiazole (**3a**), 122.3 mg (76% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.85 (s, 1H), 7.50-7.42 (m, 3H). ^{1}H NMR data were identical with those in literature.[24a] **HRMS** (ESI): m/z [M + H]$^+$ calcd for $C_9H_8NS^+$: 162.0372; found: 162.0370.

2-(m-tolyl)thiazole (**3b**), 141.7 mg (81% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 3.2 Hz, 1H), 7.80 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.33-7.27 (m, 2H), 7.21 (d, *J* = 7.6 Hz, 1H), 2.40 (s, 3H). ^{1}H NMR data were identical with those in literature. [24b] **HRMS** (ESI): m/z [M + H]$^+$ calcd for $C_{10}H_{10}NS^+$: 176.0528; found: 176.0530.

2-(3-fluorophenyl)thiazole (**3c**), 153.9 mg (86% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.2 Hz, 2H), 7.78 (s, 1H), 7.35 (d, *J* = 6.8 Hz, 3H), 7.23 (s, 1H). ^{1}H NMR data were identical with those in literature. [24b] **HRMS** (ESI): m/z [M + H]$^+$ calcd for $C_9H_7FNS^+$: 180.0278; found: 180.0276.

2-(naphthalen-2-yl)thiazole (**3d**), 166.7 mg (79% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.07-8.04 (m, 1H), 7.89-7.78 (m, 4H), 7.50-7.46 (m, 2H), 7.30 (d, J = 3.6 Hz, 1H). ^{1}H NMR data were identical with those in literature. [24b] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_{10}NS^+$: 212.0528; found: 212.0530.

2-(o-tolyl)thiazole (**3e**), 143.5 mg (82% yield), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, J = 3.6 Hz, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 3.6 Hz, 1H), 7.24-7.17 (m, 3H), 2.50 (s, 3H). ^{1}H NMR data were identical with those in literature. [24b] **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{10}H_{10}NS^+$: 176.0528; found: 176.0531.

General procedure for Ru-catalyzed meta-selective C–H nitration of 2-arylbenzothiazoles **1** *and 2-arylthiazoles* **3***:*

1 or **3** (0.2 mmol), $Cu(NO_3)_2{\cdot}3H_2O$ (96.6 mg, 0.4 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 5 mol%), $K_2S_2O_8$ (81.1 mg, 1.5 equiv), CF_3COOAg (66.6 mg, 1.5 equiv), DCE (2 mL) under air was stirred at 80 °C for 20 h in a sealed pipe using heating mantle. After the completion of the reaction (monitored by TLC), the solvent was concentrated in vacuum, and the residue was purified by flash column chromatography on silica gel with petroleum ether/EtOAc (20:1–10:1) as the eluent to give the desired products **2** or **4**.

6-methyl-2-(2-methyl-3-nitrophenyl)benzo[d]thiazole ***(2a)***, white solid, 50.0 mg (88%), R_f = 0.5 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.4 Hz, 1H), 7.79-7.74 (m, 2H), 7.64 (s, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 2.56 (s, 3H), 2.43 (s, 3H).; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.2, 151.7, 145.0, 136.3, 136.1, 136.0, 134.3, 131.7, 128.2, 126.6, 125.2, 123.3,

121.2, 21.6, 16.7; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{15}H_{13}N_2O_2S^+$: 285.0692; found: 285.0690.

*2-(2-methyl-3-nitrophenyl)benzo[d]thiazole (**2b**)*, white solid, 47.6 mg (88%), R_f= 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.90-7.86 (m, 2H), 7.56 (dt, *J* = 1.2, 7.2 Hz, 1H), 7.50-7.44 (m, 2H), 2.67 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.3, 153.5, 151.9, 137.5, 136.2, 135.8, 134.3, 131.7, 126.6, 125.8, 125.3, 123.8, 121.5, 16.7; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{11}N_2O_2S^+$: 271.0536; found: 271.0530.

*6-fluoro-2-(2-methyl-3-nitrophenyl)benzo[d]thiazole (**2c**)*, white solid, 49.1 mg (85%), R_f= 0.5 (petroleum ether/EtOAc = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 9.2, 4.8 Hz, 1H), 7.90-7.84 (m, 2H), 7.63 (dd, *J* = 8.0, 2.8 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.32-7.26 (m, 1H), 2.66 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.0, 161.3 (d, $^1J_{CF}$ = 245.7 Hz), 151.9, 150.2, 141.2, 136.8 (d, $^3J_{CF}$ = 11.2 Hz), 134.2, 126.7, 125.4, 124.8 (d, $^3J_{CF}$ = 9.4 Hz), 120.0, 115.4 (d, $^2J_{CF}$ = 24.7 Hz), 107.7 (d, $^2J_{CF}$ = 26.7 Hz), 16.6; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{10}FN_2O_2S^+$: 289.0442; found: 289.0466.

*2-(2-chloro-3-nitrophenyl)benzo[d]thiazole (**2d**)*, pale yellow solid, 33.7 mg (58%), R_f=0.5 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 1H), 7.85 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.61-7.53 (m, 2H), 7.49 (dt, *J* = 1.2, 8.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.9, 152.4, 150.2, 136.2, 135.1, 134.7, 127.5, 126.7, 126.2, 126.0, 125.0, 123.9, 121.5; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_8ClN_2O_2S^+$: 290.9990;

found: 290.9984.

*2-(2-chloro-3-nitrophenyl)-6-methylbenzo[d]thiazole (**2e**)*, white solid, 31.1 mg (51%), R_f = 0.4 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.83 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.76 (s, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 2.54 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.8, 150.5, 150.2, 136.5, 136.4, 135.2, 134.6, 128.4, 127.4, 125.8, 124.8, 123.3, 121.1, 21.6; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{10}ClN_2O_2S^+$: 305.0146; found: 305.0152.

*2-(2-fluoro-3-nitrophenyl)benzo[d]thiazole (**2f**)*, yellow solid, 29.6 mg (54%), R_f = 0.4 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.38 (dd, *J* = 6.0, 2.8 Hz, 1H), 8.37-8.33 (m, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.60–7.56 (m, 1H), 7.50–7.46 (m, 1H), 7.41 (t, *J* = 9.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.3 (d, $^1J_{CF}$ = 261.7 Hz), 158.1, 152.4, 144.8, 135.9, 135.8, 126.8 (d, $^3J_{CF}$ = 8.9 Hz), 126.1, 125. 9 (d, $^3J_{CF}$ = 4.8 Hz), 123.9, 122.9 (d, $^2J_{CF}$ = 13.4 Hz), 121.6, 117.7 (d, $^2J_{CF}$ = 24.6 Hz); **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_8FN_2O_2S^+$: 275.0285; found: 275.0281.

*6-methyl-2-(3-methyl-5-nitrophenyl)benzo[d]thiazole (**2g**)*, white solid, 52.3 mg (92%), R_f = 0.5 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.23 (s, 1H), 8.13 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.73 (s, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 2.57 (s, 3H), 2.52 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.2, 152.1, 148.7, 140.8, 136.3, 135.3, 135.1, 133.4, 128.4, 125.5, 123.1, 121.5, 119.6, 21.6, 21.3; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{15}H_{13}N_2O_2S^+$: 285.0692; found:

285.0691.

*2-(3-methyl-5-nitrophenyl)benzo[d]thiazole (**2h**)*, white solid, 52.8 mg (83%), R_f= 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.21 (s, 1H), 8.12-8.07(m, 2H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.54-7.50 (m, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 2.55 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.2, 153.9, 148.8, 140.8, 135.1, 135.0, 133.5, 126.8, 125.9, 125.7, 123.6, 121.8, 119.7, 21.3; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{11}N_2O_2S^+$: 271.0536; found: 271.0537.

*6-fluoro-2-(3-methyl-5-nitrophenyl)benzo[d]thiazole (**2i**)*, white solid, 46.0 mg (85%), R_f= 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.19 (s, 1H), 8.14 (s, 1H), 8.04 (dd, *J* = 8.8, 4.8 Hz, 1H), 7.61 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.27 (dd, *J* = 8.8, 2.4 Hz, 1H), 2.57 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.9, 160.9 (d, $^1J_{CF}$ = 245.9 Hz), 150.6, 148.8, 141.0, 136.2 (d, $^3J_{CF}$ = 11.2 Hz), 134.7, 133.4, 125.8, 124.7 (d, $^3J_{CF}$ = 9.4 Hz), 119.6, 115.6 (d, $^2J_{CF}$ = 24.6 Hz), 108.0 (d, $^2J_{CF}$ = 26.8 Hz), 21.3; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{10}FN_2O_2S^+$: 289.0442; found: 289.0443.

*2-(3-chloro-5-nitrophenyl)benzo[d]thiazole (**2j**)*, pale yellow solid, 47.1 mg (81%), R_f = 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.35 (m, 2H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.90 (s, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.3, 152.5, 148.8, 136.3, 134.9, 132.9, 132.1, 130.2, 127.7, 125.4, 124.5, 122.3, 121.4; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_8ClN_2O_2S^+$: 290.9990; found: 290.9988.

*6-chloro-2-(4-methyl-3-nitrophenyl)benzo[d]thiazole (**2k**)*,[25] pale yellow solid, 43.9

mg (72%), R_f = 0.5 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.8 Hz, 1H), 7.89 (s, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 2.68 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.4, 152.5, 149.7, 136.3, 136.2, 133.6, 132.5, 131.8, 131.1, 127.6, 124.3, 123.4, 121.4, 20.5.

*2-(4-methyl-3-nitrophenyl)benzo[d]thiazole (**2l**)*,[26] white solid, 42.1 mg (78%), R_f = 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47-7.40 (m, 2H), 2.66 (s, 3H); $^{13}C\{^1H\}$ NMR (100MHz, $CDCl_3$) δ 165.0, 154.0, 149.7, 136.0, 135.1, 133.5, 132.9, 131.2, 126.7, 125.8, 123.6, 123.4, 121.8, 20.4.

*2-(3-nitrophenyl)benzo[d]thiazole (**2m**)*,[27] white solid, 36.4 mg (71%), R_f = 0.5 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.93 (t, *J* = 1.2 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 8.3 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.69 (t, *J* = 8.0 Hz, 1H), 7.57-7.53 (m, 1H), 7.47-7.43 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.9, 154.0, 148.8, 135.3, 135.2, 133.0, 130.1, 126.8, 126.0, 125.2, 123.8, 122.4, 121.8.

*6-methyl-2-(3-nitrophenyl)benzo[d]thiazole (**2n**)*,[28] yellow solid, 47.2 mg (87%), R_f = 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.37 (d, *J* = 7.6 Hz, 1H), 8.29 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.71 (s, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 2.51 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.8, 152.1, 148.8, 136.4, 135.4, 135.4, 132.8, 130.0, 128.5, 124.9, 123.2, 122.2, 121.5, 21.6.

*2-(3-chloro-5-nitrophenyl)benzo[d]thiazole (**2o**)*, white solid, 47.1 mg (81%), R_f= 0.7 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.76 (t, *J* = 2.0 Hz, 1H), 8.41 (t, *J* = 2.0 Hz, 1H), 8.29 (t, *J* = 2.0 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.58-7.54 (m, 1H), 7.49-7.45 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.4, 153.8, 149.2, 136.5, 136.3, 135.2, 132.7, 127.1, 126.4, 125.2, 124.0, 121.9, 120.4; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_8ClN_2O_2S^+$: 290.9990; found: 290.9990.

*2-(3-nitrophenyl)thiazole (**4a**)*,[29] white solid, 29.6 mg (71%), R_f = 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.30-8.25 (m, 2H), 7.94 (d, *J* = 3.2 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 3.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.4, 148.8, 144.3, 135.2, 132.1, 130.0, 124.3, 121.4, 120.2.

*2-(3-methyl-5-nitrophenyl)thiazole (**4b**)*, white solid, 42.3 mg (95%), R_f = 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 1.6 Hz, 1H), 8.08 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.90 (d, *J* = 3.2 Hz, 1H), 7.43-7.40 (m, 2H), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.5, 149.6, 144.1, 134.9, 133.5, 132.8, 130.3, 122.5, 119.8, 20.3; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{10}H_9N_2O_2S^+$: 221.0379; found: 221.0373.

*2-(3-fluoro-5-nitrophenyl)thiazole (**4c**)*, white solid, 32.1 mg (71%), R_f = 0.5 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.07-8.04 (m, 1H), 7.98-7.95 (m, 2H), 7.49 (d, *J* = 3.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.9, 162.7 (d, $^1J_{CF}$ = 272.1 Hz), 149.6, 144.5, 136.8 (d, $^2J_{CF}$ = 8.4

Hz), 120.9, 119.2 (d, $^{3}J_{CF}$ = 23.7 Hz), 117.3 (d, $^{2}J_{CF}$ = 3.3 Hz), 112.0 (d, $^{3}J_{CF}$ = 26.6 Hz); **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_9H_6FN_2O_2S^+$: 225.0129; found: 225.0127;

*2-(4-nitronaphthalen-2-yl)thiazole (**4d**)*, white solid, 34.1 mg (66%), R_f = 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 1.6 Hz, 1H), 8.66 (s, 1H), 8.54 (d, *J* = 8.8 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 3.2 Hz, 1H), 7.75 (dt, *J* = 1.2, 6.8 Hz, 1H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.46 (d, *J* = 3.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.6, 147.3, 144.3, 134.5, 131.3, 130.2, 130.0, 129.2, 128.2, 125.4, 123.4, 122.0, 120.1; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_9N_2O_2S$+: 257.0379; found: 257.0371.

*2-(2-methyl-3-nitrophenyl)thiazole (**4e**)*, yellow solid, 32.6 mg (74%), R_f = 0.6 (petroleum ether/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 3.2 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 3.2 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 2.60 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.4, 151.9, 143.5, 136.0, 134.1, 131.3, 126.5, 124.8, 120.7, 16.6; **HRMS** (ESI): m/z $[M + H]^+$ calcd for $C_{10}H_9N_2O_2S^+$: 221.0379; found: 221.0378.

*Gram-scale experiment for the synthesis of nitrated product **2l**.*

Substrate **1l** (1.125 g, 5.0 mmol), $Cu(NO_3)_2{\cdot}3H_2O$ (2.415 g, 10 mmol), $Ru_3(CO)_{12}$ (120 mg, 5 mol%), $K_2S_2O_8$ (2.027 g, 37.5 mmol), CF_3COOAg (1.665 g, 37.5 mmol), DCE (50 mL) under air was stirred at 80 °C for 20 h in a sealed flask using heating mantle. After the completion of the reaction (monitored by TLC), the mixture was filtrated, and the solvent was concentrated in vacuum. Then the residue was purified

by flash column chromatography on silica gel with petroleum ether/EtOAc (20:1–10:1) as the eluent to give the desired product **2l** in 75% yield (1.014 g).

5-(benzo[d]thiazol-2-yl)-2-methylaniline **5**.[21] **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.12 (d, *J* = 7.6 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.56-7.52 (m, 1H), 7.47-7.43 (m, 2H), 7.22 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 5.28 (s, 2H), 2.17 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO) δ 168.8, 154.1, 147.8, 134.7, 131.7, 131.2, 126.9, 125.6, 125.5, 123.0, 122.6, 115.5, 112.4, 18.0.

Notes

The authors declare no competing financial interest.

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Supporting Information

Copies of ^{1}H NMR spectra for compounds **1** and **3**, and ^{1}H, ^{13}C NMR spectra for compounds **2**, **4**, and **5**, X-ray for compound **2k** (CCDC 1818469). This material is available free of charge via the Internet at http://pubs.acs.org.

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