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Chemoselective Chan-Lam Coupling Reactions between Benzimidazoline-2-Thiones and Arylboronic Acids

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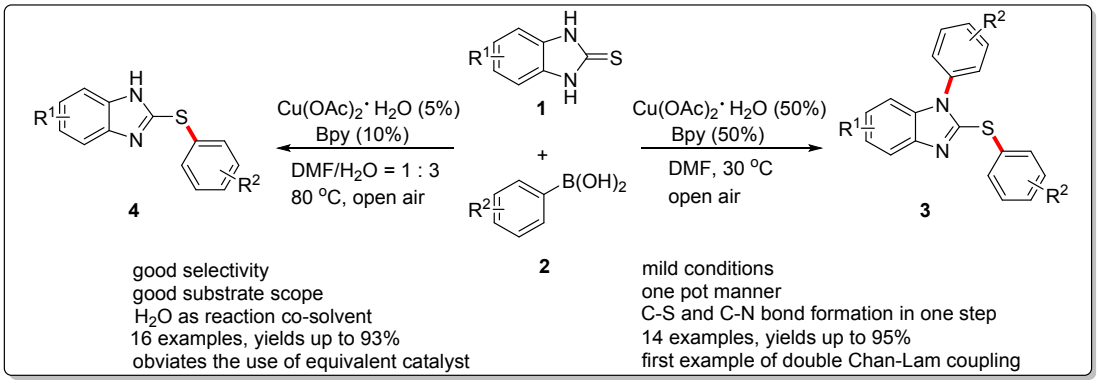


ABSTRACT

An efficient Chan-Lam-type methodology for the selective synthesis of *S*-arylbenzimidazoles and *N,S*-diarylbenzimidazoles was developed. The selectivity was controlled by varying the amount of the catalyst $Cu(OAc)_2 \cdot H_2O$, temperature and solvent switching. These transformations feature a simple protocol, broad functional group tolerance, high selectivity, and good to excellent yields. It is noteworthy that these reactions represent the first examples of the application of the selective Chan-Lam coupling.

INTRODUCTION

Benzimidazoline-2-thione derivatives represent a class of very important heterocyclic organosulfur compounds widely used in the fields of medicine, agriculture, dye industry, and functional materials.[1] The heteroatom-containing aryl sulfide is universal and serves as a critically important structural motif in certain biologically active natural products and drugs.[2] The tautomeric nature of benzimidazoline-2-thiones make them a unique structural class due to the presence of two adjacent nucleophilic nitrogen and sulfur atoms. According to the literature, benzimidazole sulfides have attracted much attention from synthetic chemists mainly for their wide range of biological activities (Figure 1).[3]

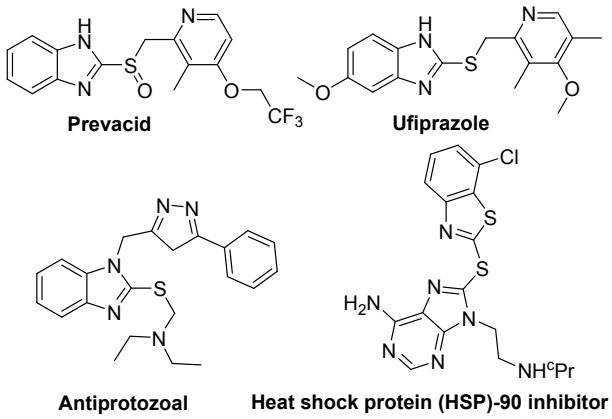
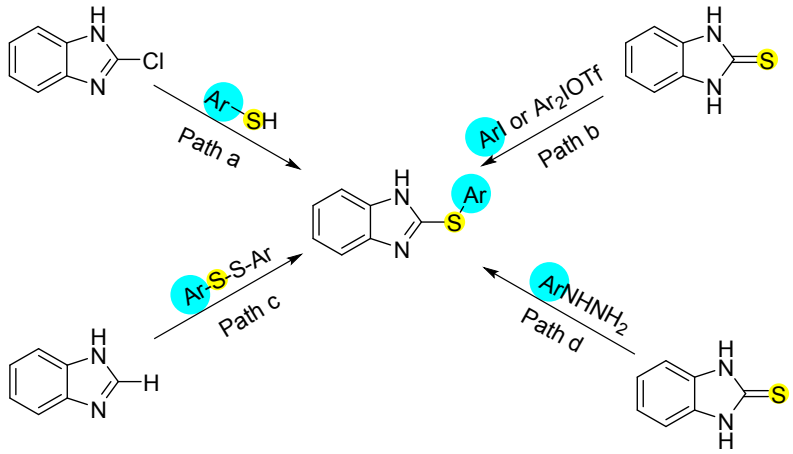


Figure 1. Some biologically active benzimidazole sulfides.

Given their importance, several synthetic strategies to access benzimidazole sulfides have been developed (Scheme 1). General methods for the synthesis of 2-thio-substituted benzimidazoles include: nucleophilic addition of arylthiols on pre-formed 2-halobenzimidazoles (path a),[4] cross-coupling reactions between benzimidazoline-2-thiones and aryl iodides or diaryliodonium triflates (path b),[5] and the *S*-arylation of benzimidazoles with diaryl disulfides (path c).[6,3d] Recently, Hajra and co-workers reported the visible-light-mediated synthesis of 2-thiobenzimidazoles

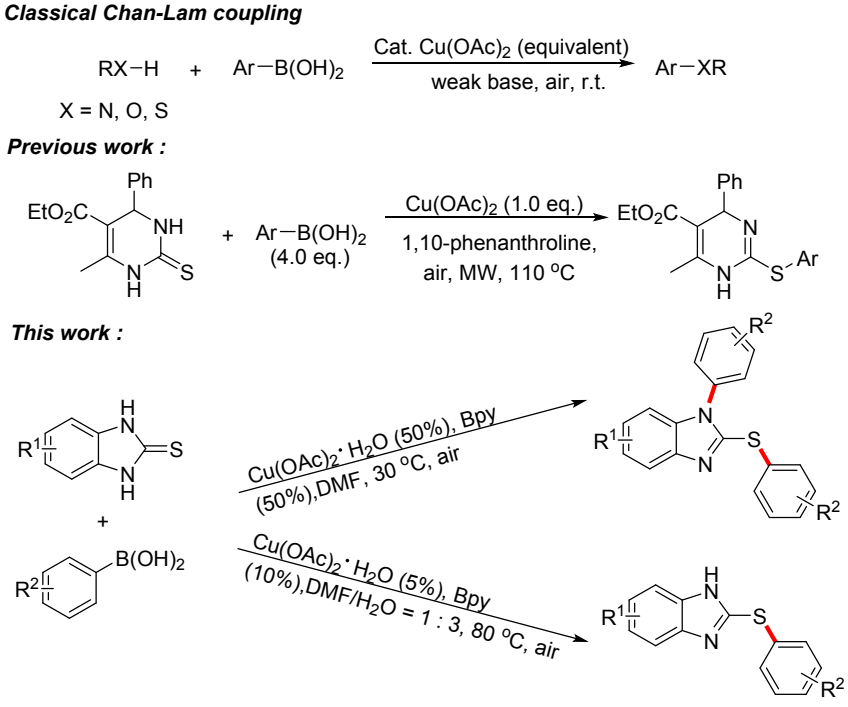
via oxidative coupling of benzimidazoline-2-thione with arylhydrazine (path d).[7] However, these synthetic processes involve the requirement of stoichiometric strong bases and/or high reaction temperatures, which somehow limit their synthetic applications. Though significant progress has been achieved, protocols that are environmentally benign, mild, and efficient are still highly valuable.



Scheme 1. Existing synthetic strategies towards 2-thiobenzimidazoles.

The Chan-Lam coupling is a generally known efficient tool for the construction of carbon-heteroatom bonds to proceed at ambient temperature as opposed to high temperature transformations.[8] Many efficient Chan-Lam-type coupling reactions of aromatic and heteroaromatic NH-derivatives have been reported,[9] while *S*-arylation has received less attention as compared to *N*- or *O*-arylations. Difficulties in C-S bond formation may be attributed to the sulfur species rapidly and irreversibly deactivating the catalyst.[10] Although several examples of Chan-Lam-type C-S coupling reactions have been developed,[11] the C-S bond formation between potentially ambiphilic thiocarbonyl compounds and phenylboronic acids is rare (Scheme 2, previous work).[12] Recently, we disclosed an efficient Chan-Lam *S*-arylation of arylthioureas with aryl boronic acids.[13] To the best of our knowledge, to date Chan-Lam-type mono- and bis-arylation of benzimidazoline-2-thiones with arylboronic acids was not

reported. As part of our longstanding interest in organosulfur chemistry[14] and our expertise in the development of Chan-Lam chemistry,[15] we anticipated that chemoselective C-S and C-N bond formations with benzimidazoline-2-thiones *via* Chan–Lam-type cross-coupling reactions could be feasible. Here, we disclose un-precedented one-pot double and single Chan–Lam coupling reactions to access diversely substituted bis- and mono-arylbenzimidazoles (Scheme 2, this work). Unlike the previously reported work, the protocol here features broad substrate scope, simple and mild reaction conditions, as well as good to excellent yields. Notably, the use of an inorganic base and the exclusion of air and water were not required. The selectivity was shown to be modulated by varying the amount of $Cu(OAc)_2 \cdot H_2O$, temperature and solvent switching, which could be an attractive alternative approach to accessing these important compounds.



Scheme 2. Chan-Lam-type coupling reactions: (i) previous work; (ii) this work: chemoselective C-S and C-N bond formations.

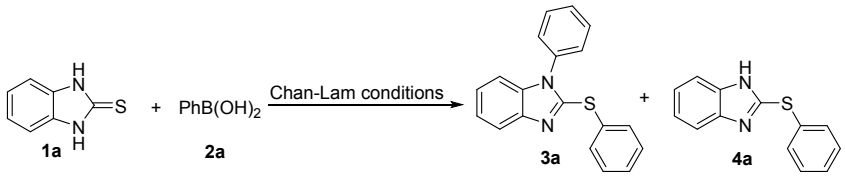
RESULTS AND DISCUSSION

Based on our earlier study,[13] benzimidazoline-2-thione (**1a**; 0.5 mmol) and phenylboronic acid (**2a**; 1.0 mmol) were used as substrates in the model reaction (Table 1). When $Cu(OAc)_2•H_2O$ (0.8 equiv) and 2,2'-bipyridine (Bpy; 0.8 equiv) were tested as catalyst system in THF, *N*,*S*-diarylation product **3a** and *S*-arylation product **4a** were obtained in a trace amount and 65% yield, respectively (entry 1). On the other hand, when dichloromethane was used as solvent, *S*-arylation product **4a** was obtained in 59% yield (entry 2). Interestingly, *N*,*S*-diarylation product **3a** was obtained as the sole product in 51% yield when DMF was used as a solvent (entry 3). Based on these results, we focused on improving the yield of **3a** by increasing the amounts of $Cu(OAc)_2•H_2O$ and **2a** but satisfactory results were not obtained (entries 4 and 5). Similarly, the use of different mediators such as $CuCl_2$, $Cu(OAc)_2•5H_2O$, and $Cu(OTf)_2$ did not facilitate this reaction (entries 6–8). In the same line, the use of different ligands such as 1,10-phenanthroline, pyridine, and NEt_3 proved that Bpy was most effective (entry 4 *vs* entries 9-11). The yield of product **3a** was improved to 76% when an increased ratio **1a**:**2a** was used (entry 4 *vs* entry 12). Replacement of DMF by other solvents such as DMSO or toluene proved to be ineffective (entries 13 and 14). Somehow surprisingly, screening the catalyst and ligand loading gave product **3a** in 91% yield (entries 15-17). The optimal reaction conditions for the selective formation of **3a** were as follows: **3a**:**2a** = 1:4, $Cu(OAc)_2•H_2O$ (50 mol%), Bpy (50 mol%), DMF (3 mL), 30 ^oC, 3.5 h (Table 1, entry 15).

Next, we examined the selective synthesis of mono-*S*-arylbenzimidazole **4a** (Table 1, entries 18-25). Nishiura and co-workers reported that the addition of a certain amount of water to a polar aprotic solvent (such as DMF) may improve the Chan-Lam

coupling reaction.[16] The adding of water makes the reaction proceed in heterogeneous way, which might slow down the reaction speed, thus allows the reaction to give the *S*-arylation selectivity, and decreasing the catalyst loading might also help the selective synthesis. We anticipated that a decreased amount of the mediator and the addition of water may favor the formation of **4a** over the production of **3a**. Hence, a tentative experiment was carried out under the following conditions: **1a**:**2a** = 1:1.5, $Cu(OAc)_2$•H_2O (0.1 equiv), Bpy (0.2 equiv), DMF:H_2O = 1:1 (Table 1, entry 18), and product **4a** was obtained in 80% yield. Further screening of the catalyst and ligand loadings as well as the phenylboronic acid ratio (entries 19-21) were conducted. Finally, the reaction temperature screening (80°C) and the modulation of solvent (DMF : H_2O = 1:3) gave the mono-*S*-arylbenzimidazole product **4a** in 95% yield (entry 23). The control experiments (entries 26-27) in THF with a low mediator loading (entry 1 *vs* entry 26) and addition of water showed the parameter modulation based on THF had no help for the yields (entry 23 *vs* entry 27).

Table 1. Optimizing of the selective formations of **3a** and **4a**[a]



Entry	Ratio (**1a:2a**)	Cat. [Cu]	Ligand	Solvent	Temp. (°C)	Yield **3a** (%)[b]	Yield **4a** (%)[b]
1	1:2	0.8 eq $Cu(OAc)_2$·H_2O	0.8 eq Bpy[c]	THF	30	trace	65
2	1:2	0.8 eq $Cu(OAc)_2$·H_2O	0.8 eq Bpy	CH_2Cl_2	30	trace	59
3	1:2	0.8 eq $Cu(OAc)_2$·H_2O	0.8 eq Bpy	DMF	30	51	0
4	1:3	0.8 eq $Cu(OAc)_2$·H_2O	0.8 eq Bpy	DMF	30	71	trace
5	1:3	1.0 eq $Cu(OAc)_2$·H_2O	1.0 eq Bpy	DMF	30	64	trace

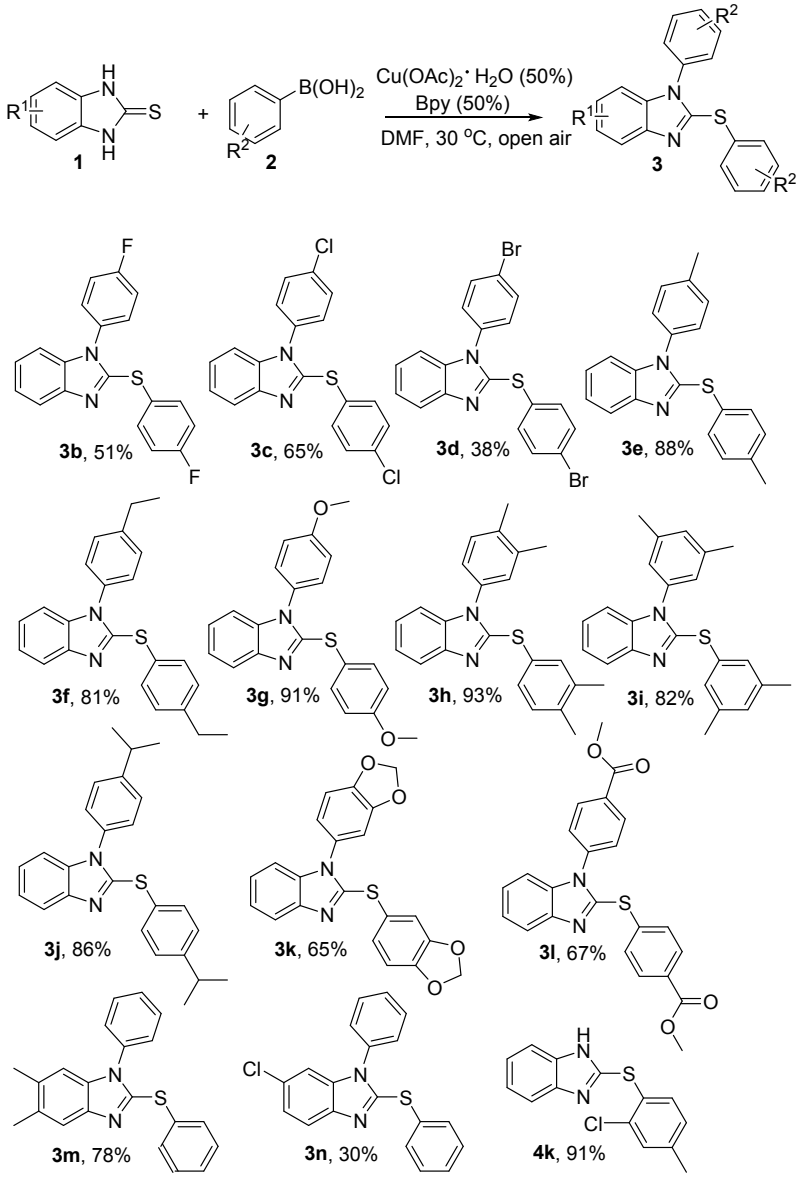
6	1:3	0.8 eq $CuCl_2$	0.8 eq Bpy	DMF	30	0	0
7	1:3	0.8 eq $Cu(OAc)_2{\cdot}5H_2O$	0.8 eq Bpy	DMF	30	0	0
8	1:3	0.8 eq $Cu(OTf)_2$	0.8 eq Bpy	DMF	30	0	0
9	1:3	0.8 eq $Cu(OAc)_2{\cdot}H_2O$	0.8 eq 1,10-Phen[d]	DMF	30	56	trace
10	1:3	0.8 eq $Cu(OAc)_2{\cdot}H_2O$	0.8 eq Py[e]	DMF	30	0	trace
11	1:3	0.8 eq $Cu(OAc)_2{\cdot}H_2O$	0.8 eq Et_3N	DMF	30	0	0
12	1:4	0.8 eq $Cu(OAc)_2{\cdot}H_2O$	0.8 eq Bpy	DMF	30	76	trace
13	1:4	0.8 eq $Cu(OAc)_2{\cdot}H_2O$	0.8 eq Bpy	DMSO	30	57	trace
14	1:4	0.8 eq $Cu(OAc)_2{\cdot}H_2O$	0.8 eq Bpy	Toluene	30	0	0
15	**1:4**	**0.5 eq $Cu(OAc)_2{\cdot}H_2O$**	**0.5 eq Bpy**	**DMF**	**30**	**91 (85)**	**0**
16	1:4	0.4 eq $Cu(OAc)_2{\cdot}H_2O$	0.4eq Bpy	DMF	30	87	0
17	1:4	0.1 eq $Cu(OAc)_2{\cdot}H_2O$	0.1 eq Bpy	DMF	30	0	0
18	1:1.5	0.1 eq $Cu(OAc)_2{\cdot}H_2O$	0.2 eq Bpy	DMF:H_2O= 1:1	80	trace	80
19	1:1.5	0.05 eq $Cu(OAc)_2{\cdot}H_2O$	0.1 eq Bpy	DMF:H_2O= 1:1	80	trace	87
20	1:1.5	0.05 eq $Cu(OAc)_2{\cdot}H_2O$	0.05 eq Bpy	DMF:H_2O= 1:1	80	--	47
21	1:1.2	0.05 eq $Cu(OAc)_2{\cdot}H_2O$	0.1 eq Bpy	DMF:H_2O= 1:1	80	--	61
22	1:1.5	0.05 eq $Cu(OAc)_2{\cdot}H_2O$	0.1 eq Bpy	DMF:H_2O= 1:2	80	0	93
23	**1:1.5**	**0.05 eq $Cu(OAc)_2{\cdot}H_2O$**	**0.1 eq Bpy**	**DMF:H_2O= 1:3**	**80**	**0**	**95 (90)**
24	1:1.5	0.05 eq $Cu(OAc)_2{\cdot}H_2O$	0.1 eq Bpy	DMF:H_2O= 1:4	80	0	79
25	1:1.5	0.05 eq $Cu(OAc)_2{\cdot}H_2O$	0.1 eq Bpy	DMF:H_2O= 1:3	60	0	61
26	1:2	0.1 eq $Cu(OAc)_2{\cdot}H_2O$	0.1 eq Bpy	THF	30	trace	45[f]
27	1:2	0.1 eq $Cu(OAc)_2{\cdot}H_2O$	0.2 eq Bpy	THF:H_2O= 1:3	60	trace	48[g]

[a]Reaction conditions (for entries 1–17): [Cu], ligand, **1a** (0.5 mmol), solvent (0.16 M, total 3 mL), open air, 3.5 h; reaction conditions (for entries 18–25): [Cu], ligand, **1a** (0.5 mmol), solvent (0.16 M, total 3 mL), open air, 18 h. [b]Isolated yield; scaled-up (5mmol) yields are shown in brackets. [c]Bpy = 2,2'-bipyridine. [d]1,10-Phen = 1,10-phenanthroline. [e]Py = pyridine. [f]open air, 3.5 h. [g]open air, 18 h.

Under the optimized conditions we explored the substrate generality for the selective synthesis of *N*,*S*-diarylbenzimidazoles **3** (Table 2). A range of phenylboronic acids containing electron-donating and electron-withdrawing groups were tolerated. Halogen substituted arylboronic acids successfully coupled with benzimidazoline-2-thione to give the desired products in moderate to good yields (**3b-3d**). Arylboronic acids with electron-donating substituents such as methyl, ethyl, methoxy, and *iso*propyl at the *para*- position afforded the corresponding products (**3e**, **3f**, **3g**, **3j**) with good to excellent yields (81%-91%). Di-substituted 3,4-dimethylphenylboronic acid and 3,5-dimethylphenylboronic acid underwent the coupling reation smoothly to give the corresponding products **3h** and **3i** in 93% and 82% yields, respectively. To our delight, 3,4-methylenedioxyphenylboronic acid and

4-(methoxycabonyl)phenylboronic acid were also suitable for this transformation (**3k** and **3l**). It is a pity that 2-chloro-4-methylbenzeneboronic acid could not be converted to desired di-substituted arylbenzimidazole product under the optimal reaction conditions, and the mono-*S*-aryl benzimidazole **4k** was obtained in 91% yield. The effect of the substituent attached on the benzimidazoline-2-thione ring was examined, and it showed that the electron donating benzimidazoline-2-thione was more reactive than the electron withdrawing benzimidazoline-2-thione (**3m** *vs* **3n***)*.

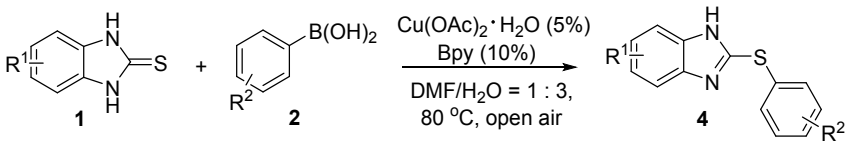
Table 2. Substrate scope for the selective synthesis of *N*,*S*-diarylbenzimidazoles **3**[a]

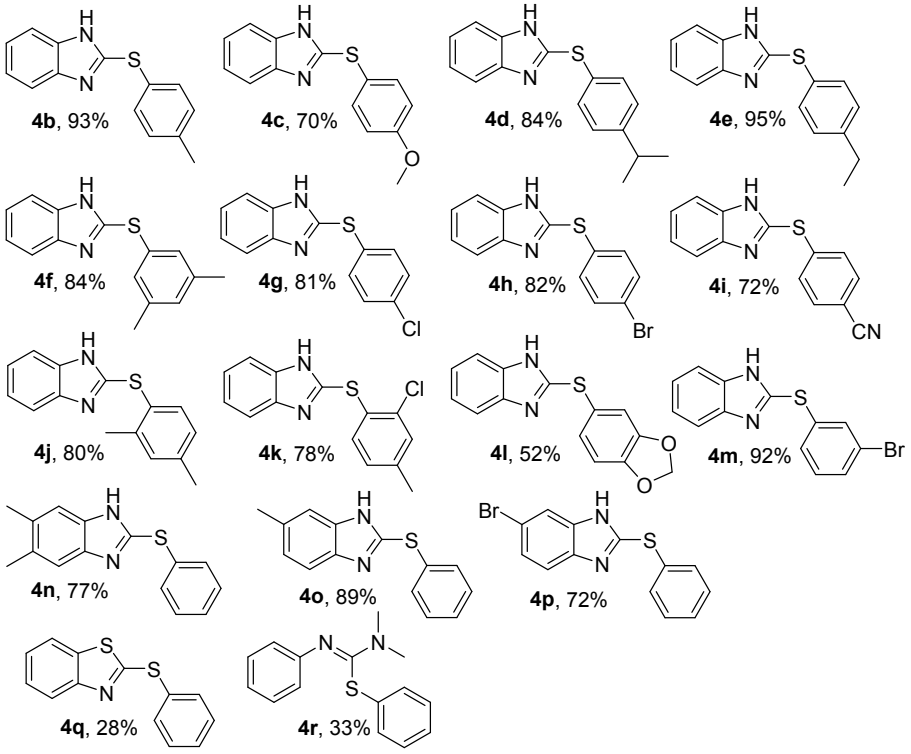


[a] Reaction conditions: **1** (0.5 mmol), **2** (2.0 mmol), $Cu(OAc)_2 \cdot H_2O$ (50 mol%), Bpy (50 mol%), DMF (3 mL), 30 °C, open air, 3.5-9 h; Isolated yield based on **1**.

Next, we explored the substrate generality for the selective synthesis of *N*-arylbenzimidazoles **4** (Table 3). Here again, a variety of phenylboronic acids containing electron-donating and electron-withdrawing groups were tolerated. Both electron-donating groups, such as methyl, methoxy, isopropyl, ethyl (**4b-4e**) and electron-withdrawing groups, such as chloro, bromo, cyano (**4g-4i**) on the aromatic ring gave the respective mono-*S*-arylation products in good to high yields (70-95%). Due to the possible steric hindrance reason, the *o*-methyl and *o*-chloro compound showed similar activity with good yields (**4j**, **4k**), while no significant effect of steric hindrance was observed when *m*-methyl and *m*-bromo groups were applied (**4f**, **4m**). It was noteworthy that both electron-rich and electron-deficient benzimidazoline-2-thiones were suitable for this transformation (**4n**-**4p**). The extension of this protocol was also applied to 2-mercaptobenzothiazole and 1,1-dimethyl-3-phenylthiourea, and the desired product **4q** and **4r** were obtained in poor yields (28% and 33%, respectively).

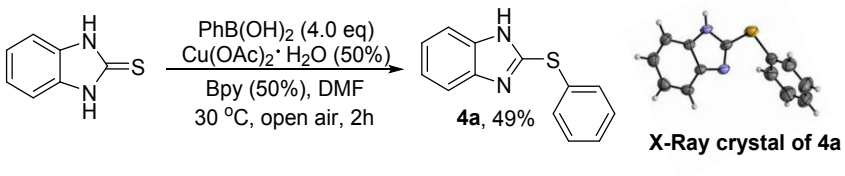
Table 3. Substrate scope for the selective synthesis of *S*-arylbenzimidazoles **4**[a]





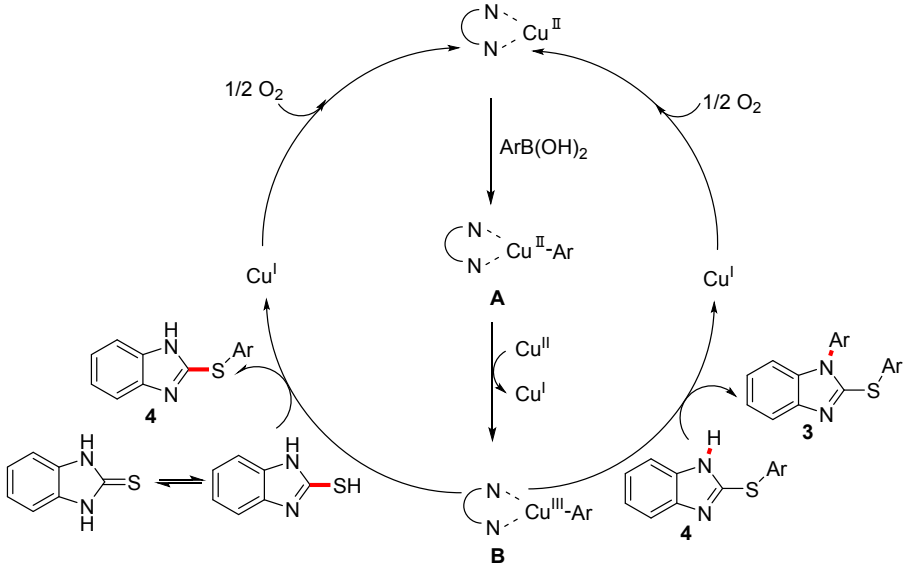
[a] Reaction conditions: **1** (0.5 mmol), **2** (0.75 mmol), $Cu(OAc)_2{\cdot}H_2O$ (5 mol%), Bpy (10 mol%), DMF : H_2O = 1 : 3 (total 3 mL), 80 °C, open air, 18-24 h; Isolated yield based on **1**.

In an additional experiment, *S*-arylbenzimidazole product **4k** (cf. Table 2) was obtained under the optimal conditions for the synthesis of *N*,*S*-diarylbenzimidazoles **3**, and **4a** was isolated in 49 % yield in 2 h by using the double Chan-Lam reaction conditions (control experiment shown in Scheme 3 as well). These indicate that the *S*-arylbenzimidazole **4a** is an intermediate for the double Chan-Lam reaction, and the *S*-arylation is faster than the *N*-arylation. Product **4a** was characterized by X-ray crystallography (Scheme 3, CCDC 1905719), and this supports the fact that *S*-arylation is more favored than the *N*-arylation.



Scheme 3. Control experiment under the "double" Chan-Lam reaction conditions: *S*-aryl intermediate **4a** was obtained.

Base on the above experimental results and previous literature reports,[17,11a] a reaction mechanism for the mono- and bis-arylation of benzimidazoline-2-thiones with boronic acids was proposed (Scheme 4). As for the assumed Cu(I/II/Ⅲ) catalysis cycle, the intermediary Cu(I) complex would be oxidized under aerobic conditions. For the *S*-arylation, aryl boronic acid would reacted with Cu(II) to form complex **A**. The intermediate **A** was oxidized by Cu(II), forming an Cu(III) species **B** that would react with the tautomeric form of benzimidazoline-2-thione (2-mercaptobenzimidazole), the subsequent reductive elimination gave product **4** and Cu(I). Finally, rapid aerobic oxidation of Cu(I) regenerates Cu(II). For the bis-*S/N*-arylation, the *S*-arylation took place firstly to give mono-*S*-arylation product **4**, **4** further reacted with **B** to give product bis-*S/N*-arylated product **3** and Cu(I) *via* reductive elimination.



Scheme 4. Proposed mechanism for the formation of **3a** and **4a**.

CONCLUSION

In summary, we describe herein an easy and efficient method for the controllable synthesis of *S*-arylbenzimidazoles and *N*,*S*-diarylbenzimidazoles by using inexpensive and commercially available arylboronic acids as well as $Cu(OAc)_2•H_2O$ as catalyst. The products were selectively formed in good to excellent yields by varying the amount of $Cu(OAc)_2•H_2O$, temperature and solvent switching. The protocol features good selectivity, easy performance, broad functional group tolerance, and good to excellent yields. To the best of our knowledge, this is the first report of selective synthesis of mono- and bis-*S*/*N*-arylbenzimidazoles performed by Chan-Lam reaction, which might be useful and practical for the synthesis of some potentially biologically active compounds.

EXPERIMENTAL SECTION

The thione substrates **1** were prepared by using our previously reported method, see ref 14(e). All other starting materials were purchased from commercial suppliers and used without further purification unless otherwise stated. Yields refer to isolated compounds estimated to be >95% pure as determined by ^1H NMR and capillary GC analysis. NMR spectra were recorded on a Bruker AM400 NMR instrument in $CDCl_3$ and DMSO-d_6 using TMS as an internal standard. Chemical shifts are given in ppm and coupling constants (J) are given in Hz. All melting points were determined on a RY-1G melting point instrument without correction. High-resolution mass spectra (HRMS) were recorded on a Finnigan MAT 95Q or Finnigan 90 mass instrument (ESI). TLC was performed using aluminum plates coated with SiO_2 (Merck 60, F-254) and visualized with UV light at 254 nm. Column chromatography was performed on

silica gel (200-300 mesh) with petroleum ether-EtOAc as eluent.

Typical procedure for the synthesis of bis-arylbenzimidazoles 3 (TP1).

Benzimidazoline-2-thione **1a** (0.5 mmol) and phenylboronic acid **2a** (2.0 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.25 mmol), bipyridine (0.25 mmol) were added in a dried tube (open to air) equipped with a magnetic stirring bar, DMF (3.0 mL) was then added. The mixture was stirred at 30 ^oC and checked by TLC until the starting material was finished. The reaction was terminated with sat. NH_4Cl solution (3 mL) and then extracted with ethyl acetate. The crude solution was dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by flash column chromatography to afford the desired product **3a**.

Typical procedure for the synthesis of mono-arylbenzimidazoles 4 (TP2).

Benzimidazoline-2-thione **1a** (0.5 mmol) and phenylboronic acid **2a** (0.75 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol), bipyridine (0.05 mmol) were added in a dried tube (open to air) equipped with a magnetic stirring bar, DMF (0.75 mL) and H_2O (2.25 mL) was then added. The mixture was stirred at 80 ^oC and checked by TLC until the starting material was finished. The reaction was terminated with sat. NH_4Cl solution (3 mL) and then extracted with ethyl acetate. The crude solution was dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by flash column chromatography to afford the desired product **4a**

Analytical data of the products

1-phenyl-2-(phenylthio)-1H-benzo[*d*]imidazole (3a)

According to **TP1**, the residue was purified by flash chromatography on silica gel

(petroleum ether/ethyl acetate = 5:1) to give the target compound **3a** as a colorless oil (137 mg, yield = 91%; for 5mmol scale-up syntheses, 1283 mg, yield = 85%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 5.59 (d, 1H, *J* = 8.0 Hz), 5.54-5.45 (m, 3H), 5.41 (d, 2H, *J* = 8.0 Hz), 5.37-5.35 (m, 2H), 5.29-5.26 (m, 3H), 5.19-5.11 (m, 2H), 5.01 (d, 1H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 154.1, 148.0, 142.0, 139.9, 137.4, 135.3, 135.0, 134.6, 134.4, 133.7, 132.4, 128.5, 127.8, 123.9, 115.1. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{19}H_{15}N_2S$ (303.0951), found: 303.0955.

1-(4-fluorophenyl)-2-((4-fluorophenyl)thio)-1H-benzo[*d*]imidazole (3b)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3b** as a colorless oil (86 mg, yield = 51%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.64 (d, 1H, *J* = 8.0 Hz), 7.30-7.26 (m, 2H), 7.22-7.08 (m, 6H), 6.96 (d, 1H, *J* = 8.0 Hz), 6.87 (t, 2H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 161.9 (d, *J* = 248 Hz), 161.5 (d, *J* = 248 Hz), 148.8, 142.0, 136.3, 134.0 (d, *J* = 9.0 Hz), 130.2 (d, *J* = 4.0 Hz), 128.3 (d, *J* = 8.0 Hz), 124.1 (d, *J* = 3.0 Hz), 122.4, 121.8, 118.4, 115.7 (d, *J* = 23.0 Hz), 115.5 (d, *J* = 23.0 Hz), 108.6. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{19}H_{13}F_2N_2S$ (339.0762), found: 339.0765.

1-(4-chlorophenyl)-2-((4-chlorophenyl)thio)-1H-benzo[*d*]imidazole (3c)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3c** as a colorless oil (120 mg, yield = 65%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.65 (d, 1H, *J* = 8.0 Hz), 7.38 (d, 2H, *J* = 12.0 Hz), 7.24-7.10 (m, 8H), 6.99 (d, 1H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 147.8, 142.0, 136.0, 134.1, 133.8, 132.7, 132.7, 128.9, 128.5, 128.1, 127.7, 127.6, 122.7, 122.0, 118.5, 115.9, 108.7. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{19}H_{13}Cl_2N_2S$ (371.0171), found: 371.0169.

1-(4-bromophenyl)-2-((4-bromophenyl)thio)-1H-benzo[*d*]imidazole (3d)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3d** as a colorless oil (87 mg, yield = 38%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.66 (d, 1H, *J* = 8.0 Hz), 7.56 (d, 2H, *J* = 8.0 Hz), 7.30 (d, 2H, *J* = 8.0 Hz), 7.21-7.11 (m, 6H), 7.01 (d, 1H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 155.6, 147.5, 142.0, 135.9, 133.2, 132.8, 131.9, 131.4, 131.0, 128.4, 127.9, 122.7, 122.1, 122.1, 121.9, 118.5, 116.5, 108.8. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{19}H_{13}Br_2N_2S$ (458.9161), found: 458.9165.

1-(*p*-tolyl)-2-(*p*-tolylthio)-1H-benzo[*d*]imidazole (3e)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3e** as a colorless oil (145 mg, yield = 88%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.60 (d, 1H, *J* = 8.0 Hz), 7.19 (d, 2H, *J* = 8.0 Hz), 7.13 (d, 2H, *J* = 8.0 Hz), 7.08-7.04 (m, 3H), 7.00 (t, 1H, *J* = 8.0 Hz), 6.93 (t, 3H, *J* = 8.0 Hz), 2.27 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 154.2, 149.5, 142.0, 137.9, 137.6, 136.2, 132.0, 131.5, 129.1, 128.9, 128.4, 126.0, 125.3, 121.8, 121.3, 118.0, 114.4, 108.7, 20.1, 20.1. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{21}H_{19}N_2S$ (331.1264), found: 331.1269.

1-(4-ethylphenyl)-2-((4-ethylphenyl)thio)-1H-benzo[*d*]imidazole (3f)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3f** as a colorless oil (145 mg, yield = 81%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.62 (d, 1H, *J* = 8.0 Hz), 7.22-7.17 (m, 4H), 7.10 (t, 3H, *J* = 8.0 Hz), 7.03 (t, 1H, *J* = 8.0 Hz), 6.96 (t, 3H, *J* = 8.0 Hz), 2.63-2.57 (m, 2H), 2.48-2.42 (m, 2H), 1.18 (t, 3H, *J* = 8.0 Hz), 1.05 (t, 3H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 155.5, 150.7, 145.3,

145.0, 143.1, 137.4, 134.6, 133.3, 132.9, 129.0, 128.9, 128.5, 127.3, 126.8, 123.1, 122.6, 119.2, 115.6, 110.0, 28.7, 28.6, 15.5, 15.4. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{23}H_{23}N_2S$ (359.1577), found: 359.1574.

1-(4-methoxyphenyl)-2-((4-methoxyphenyl)thio)-1H-benzo[*d*]imidazole (3g)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3g** as a colorless oil (165 mg, yield = 91%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.60 (d, 1H, *J* = 8.0 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 7.15-7.01 (m, 4H), 6.94 (d, 1H, *J* = 8.0 Hz), 6.89 (d, 2H, *J* = 8.0 Hz), 6.71 (d, 2H, *J* = 8.0 Hz), 3.73 (s, 3H), 3.64 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 159.2, 158.8, 150.6, 142.1, 136.7, 134.5, 127.7, 126.9, 121.8, 121.3, 119.1, 118.1, 113.9, 113.7, 108.6, 54.6, 54.3. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{21}H_{19}N_2O_2S$ (363.1162), found: 363.1166.

1-(3,4-dimethylphenyl)-2-((3,4-dimethylphenyl)thio)-1H-benzo[*d*]imidazole (3h)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3h** as a yellow oil (166 mg, yield = 93%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.61 (d, 1H, *J* = 8.0 Hz), 7.13-7.07 (m, 4H), 7.02 (t, 1H, *J* = 8.0 Hz), 6.97-6.90 (m, 4H), 2.20 (s, 3H), 2.15 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 154.4, 149.6, 142.0, 136.9, 136.4, 136.3, 136.3, 133.3, 131.8, 129.8, 129.4, 129.3, 127.1, 125.4, 123.5, 121.6, 121.1, 117.9, 108.7, 18.6, 18.5, 18.4. 18.3. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{23}H_{23}N_2S$ (359.1577), found: 359.1580.

1-(3,5-dimethylphenyl)-2-((3,5-dimethylphenyl)thio)-1H-benzo[*d*]imidazole (3i)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3i** as a white soild (147 mg, yield = 82%). mp: 112-114 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm)

7.65 (d, 1H, *J* = 8.0 Hz), 7.11 (t, 1H, *J* = 8.0 Hz), 7.04 (t, 1H, *J* = 8.0 Hz), 6.97 (t, 2H, *J* = 8.0 Hz), 6.89 (s, 2H), 6.75 (s, 3H), 2.21 (s, 6H), 2.09 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 148.7, 142.0, 138.0, 137.5, 136.2, 134.1, 129.3, 129.3, 129.0, 128.8, 123.9, 121.8, 121.2, 118.1, 108.8, 20.0. 19.9. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{23}H_{23}N_2S$ (359.1577), found: 359.1582.

1-(4-isopropylphenyl)-2-((4-isopropylphenyl)thio)-1H-benzo[*d*]imidazole (3j)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3j** as a colorless oil (166 mg, yield = 86%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.64 (d, 1H, *J* = 8.0 Hz), 7.19 (d, 4H, *J* = 8.0 Hz), 7.11 (t, 3H, *J* = 8.0 Hz), 7.04 (t, 1H, *J* = 8.0 Hz), 6.98 (t, 3H, *J* = 8.0 Hz), 2.90-2.83 (m, 1H), 2.75-2.68 (m, 1H), 1.19 (d, 6H, *J* = 8.0 Hz), 1.08 (d, 6H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 154.5, 149.4, 148.7, 148.3, 142.1, 138.1, 136.4, 132.0, 132.0, 126.5, 126.4, 126.2, 126.1, 125.9, 122.0, 121.5, 118.2, 114.4, 108.9, 32.9, 32.8, 23.0, 22.8. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{25}H_{27}N_2S$ (387.1890), found: 387.1894.

1-(benzo[*d*][1,3]dioxol-5-yl)-2-(benzo[*d*][1,3]dioxol-5-ylthio)-1H-benzo[*d*]imidazole (3k)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3k** as a white soild (127 mg, yield = 65%). mp: 137-139 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.61 (d, 1H, *J* = 8.0 Hz), 7.13-7.05 (m, 2H), 6.99 (d, 1H, *J* = 8.0 Hz), 6.87 (d, 2H, *J* = 8.0 Hz), 6.81 (d, 1H, *J* = 8.0 Hz), 6.71 (t, 2H, *J* = 8.0 Hz), 6.61 (d, 1H, *J* = 8.0 Hz), 5.96 (s, 2H), 5.83 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 150.1, 147.6, 147.3, 147.1, 147.1, 142.0, 136.5, 127.7, 127.0, 121.9, 121.4, 120.2, 118.1, 113.1, 108.6, 107.8, 107.5, 107.3, 101.0, 100.5. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for

$C_{21}H_{15}N_2O_4S$ (391.0747), found: 391.0744.

methyl 4-((1-(4-(methoxycarbonyl)phenyl)-1H-benzo[*d*]imidazol-2-yl)thio)benzoate (3l)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3l** as a colorless oil (140 mg, yield = 67%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 8.09 (d, 2H, *J* = 8.0 Hz), 7.79 (d, 2H, *J* = 8.0 Hz), 7.72 (d, 1H, *J* = 8.0 Hz), 7.35 (d, 2H, *J* = 8.0 Hz), 7.27-7.18 (m, 4H), 7.09 (d, 1H, *J* = 8.0 Hz), 3.88 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 166.1, 165.2, 164.9, 160.6, 145.9, 141.9, 138.0, 136.2, 135.6, 130.6, 130.0, 129.6, 129.3, 128.4, 126.1, 123.3, 122.5, 120.2, 118.7, 114.3, 109.1, 51.5, 51.2. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{23}H_{19}N_2O_4S$ (419.1060), found: 419.1064.

5,6-dimethyl-1-phenyl-2-(phenylthio)-1H-benzo[*d*]imidazole (3m)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3m** as a white soild (129 mg, yield = 78%). mp: 102-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.45 (s, 1H), 7.30 (d, 3H, *J* = 8.0 Hz), 7.15-7.12 (m, 4H), 7.04 (t, 3H, *J* = 4.0 Hz), 6.77 (s, 1H), 2.22 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 146.2, 140.6, 134.7, 134.6, 131.8, 130.7, 130.6, 130.3, 128.3, 128.0, 127.6, 126.6, 126.3, 118.5, 109.2, 19.3, 19.1. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{21}H_{19}N_2S$ (331.1264), found: 331.1268.

6-chloro-1-phenyl-2-(phenylthio)-1H-benzo[*d*]imidazole (3n)

According to **TP1**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the target compound **3n** as a yellow oil (50 mg, yield = 30%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.64 (s, 1H),

7.46-7.42 (m, 3H), 7.32 (t, 2H, J = 4.0 Hz), 7.25-7.18 (m, 5H), 7.07 (d, 1H, J = 8.0 Hz), 6.93 (d, 1H, J = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 150.3, 142.8, 134.8, 133.9, 131.7, 128.9, 128.6, 128.2, 128.2, 127.5, 127.2, 126.2, 122.5, 118.0, 109.5. HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{19}H_{14}ClN_2S$ (337.0561), found: 337.0558.

2-(phenylthio)-1H-benzo[*d*]imidazole (4a)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4a** as a white soild (107 mg, yield = 95%; for 5mmol scale-up syntheses, 1017 mg, yield = 90%). mp: 202-204 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.78 (s, 1H), 7.58-7.41 (m, 7H), 7.19 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 151.8, 148.9, 140.5, 136.4, 136.4, 134.8, 133.4, 127.8, 126.8, 123.5, 116.2. HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{13}H_{11}N_2S$ (227.0638), found: 227.0642.

2-(*p*-tolylthio)-1H-benzo[*d*]imidazole (4b)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4b** as a white soild (112 mg, yield = 93%). mp: 174-176 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.65 (s, 1H), 8.00-7.14 (m, 8H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 148.2, 139.8, 138.8, 134.7, 134.0, 132.8, 130.7, 128.6, 128.5, 127.3, 122.4, 21.1. HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{14}H_{13}N_2S$ (241.0794), found: 241.0790.

2-((4-methoxyphenyl)thio)-1H-benzo[*d*]imidazole (4c)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4c** as a white soild (90 mg, yield = 70%). mp: 206-208 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ

(ppm) 12.43 (s, 1H), 7.57-7.36 (m, 4H), 7.13 (d, 2H, J = 8.0 Hz), 7.03 (d, 2H, J = 8.0 Hz), 3.80 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 160.5, 149.4, 144.2, 135.8, 122.5, 121.8, 120.2, 118.3, 115.7, 111.2, 55.8. HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{14}H_{13}N_2OS$ (257.0743), found: 257.0747.

2-((4-isopropylphenyl)thio)-1H-benzo[*d*]imidazole (4d)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4d** as a white soild (113 mg, yield = 84%). m.p: 207-209 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.69 (s, 1H), 7.56-7.15 (m, 8H), 2.94-2.87 (m, 1H), 1.21 (s, 3H), 1.19 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 149.4, 147.9, 144.1, 135.8, 132.5, 128.1, 128.0, 122.8, 122.0, 118.6, 111.4, 33.6, 24.1. HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{16}H_{17}N_2S$ (269.1107), found: 269.1104.

2-((4-ethylphenyl)thio)-1H-benzo[*d*]imidazole (4e)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4e** as a white soild (121 mg, yield = 95%). mp: 189-191 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.67 (s, 1H), 7.46 (d, 4H, J = 8.0 Hz), 7.27 (d, 2H, J = 8.0 Hz), 7.17 (s, 2H), 2.64-2.58 (m, 2H), 1.18 (t, 3H, J = 8.0 Hz). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 148.0, 144.9, 134.7, 132.6, 129.5, 127.8, 127.3, 122.7, 122.0, 118.6, 111.3, 28.2, 15.8. HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{15}H_{15}N_2S$ (255.0951), found: 255.0954.

2-((3,5-dimethylphenyl)thio)-1H-benzo[*d*]imidazole (4f)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4f** as a white soild (107 mg, yield = 84%). mp: 178-180 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ

(ppm) 12.71 (s, 1H), 7.57 (s, 1H), 7.43 (s, 1H), 7.15 (d, 4H, *J* = 12.0 Hz), 6.99 (s, 1H), 7.17 (s, 2H), 2.25 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 147.6, 144.2, 139.3, 135.8, 130.7, 130.4, 129.7, 122.9, 122.0, 118.7, 111.4, 21.1. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{15}H_{15}N_2S$ (255.0951), found: 255.0957.

2-((4-chlorophenyl)thio)-1H-benzo[*d*]imidazole (4g)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4g** as a white soild (105 mg, yield = 81%). mp: 220-222 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.82 (s, 1H), 7.60-7.50 (m, 5H), 7.44 (d, 1H, *J* = 8.0 Hz), 7.23-7.16 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 146.7, 144.1, 135.8, 133.6, 133.5, 130.5, 130.0, 123.1, 122.1, 118.8, 111.5. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{13}H_{10}ClN_2S$ (261.0248), found: 261.0253.

2-((4-bromophenyl)thio)-1H-benzo[*d*]imidazole (4h)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4h** as a white soild (125 mg, yield = 82%). mp: 213-215 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.84 (s, 1H), 7.63 (d, 3H, *J* = 8.0 Hz), 7.46 (d, 3H, *J* = 8.0 Hz), 7.21 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 146.5, 144.1, 135.8, 133.7, 132.9, 131.2, 123.1, 122.1, 122.0, 118.8, 111.5. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{13}H_{10}BrN_2S$ (304.9743), found: 304.9745.

4-((1H-benzo[*d*]imidazol-2-yl)thio)benzonitrile (4i)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4i** as a white soild (90 mg, yield = 72%). mp: 178-180 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 13.17 (s, 1H), 7.84 (d, 2H, *J* = 8.0 Hz), 7.67 (s, 1H), 7.55 (d, 3H, *J* = 8.0 Hz),

7.26 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 144.2, 143.8, 140.4, 135.8, 133.5, 129.6, 123.7, 122.5, 119.3, 118.9, 111.9, 110.0. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{14}H_{10}N_3S$ (252.0590), found: 252.0593.

2-((2,4-dimethylphenyl)thio)-1H-benzo[*d*]imidazole (4j)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4j** as a white soild (102 mg, yield = 80%). mp: 177-179 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.51 (s, 1H), 7.51 (s, 1H), 7.41 (d, 2H, *J* = 8.0 Hz), 7.18 (s, 1H), 7.14 (d, 2H, *J* = 8.0 Hz), 7.06 (d, 1H, *J* = 8.0 Hz), 2.34 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 148.6, 144.3, 140.9, 139.6, 135.8, 134.8, 132.1, 128.2, 126.0, 122.5, 121.8, 118.3, 111.2, 21.1, 20.8. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{15}H_{15}N_2S$ (255.0951), found: 255.0954.

2-((2-chloro-4-methylphenyl)thio)-1H-benzo[*d*]imidazole (4k)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4k** as a white soild (107 mg, yield = 78%). mp: 161-163 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.82 (s, 1H), 7.57 (s, 1H), 7.44 (s, 2H), 7.34 (d, 1H, *J* = 8.0 Hz), 7.18 (t, 3H, *J* = 8.0 Hz), 2.31 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 146.2, 144.2, 140.8, 135.8, 134.7, 133.7, 131.0, 129.4, 127.1, 123.0, 122.1, 118.7, 111.5, 20.7. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{14}H_{12}ClN_2S$ (275.0404), found: 275.0408.

2-(benzo[*d*][1,3]dioxol-5-ylthio)-1H-benzo[*d*]imidazole (4l)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4l** as a white soild (70 mg, yield = 52%). mp: 185-187 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.49 (s, 1H), 7.53 (s, 1H), 7.40 (s, 1H), 7.19-7.13 (m, 4H), 7.00 (d, 1H, *J* = 8.0

Hz), 6.11 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 149.2, 148.9, 148.5, 144.2, 135.8, 128.3, 122.6, 121.9, 121.6, 118.4, 114.1, 111.3, 109.6, 102.2. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{14}H_{11}N_2O_2S$ (271.0536), found: 271.0533.

2-((3-bromophenyl)thio)-1H-benzo[*d*]imidazole (4m)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4m** as a white soild (140 mg, yield = 92%). mp: 144-146 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.93 (s, 1H), 7.70 (s, 1H), 7.57 (d, 2H, *J* = 8.0 Hz), 7.48 (d, 2H, *J* = 8.0 Hz), 7.37 (t, 1H, *J* = 8.0 Hz), 7.21 (d, 2H, *J* = 4.0 Hz). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 146.0, 144.1, 135.8, 134.4, 133.2, 131.9, 131.4, 130.3, 123.3, 122.7, 122.2, 118.9, 111.6. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{13}H_{10}BrN_2S$ (304.9743), found: 304.9746.

5,6-dimethyl-2-(phenylthio)-1H-benzo[*d*]imidazole (4n)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4n** as a white soild (98 mg, yield = 77%). mp: 167-169 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.64 (s, 1H), 7.43-7.31 (m, 7H), 2.29 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 144.8, 143.0, 132.8, 130.7, 129.9, 128.1, 118.9, 111.5, 20.4. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{15}H_{15}N_2S$ (255.0951), found: 255.0956.

6-methyl-2-(phenylthio)-1H-benzo[*d*]imidazole (4o)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4o** as a white soild (107 mg, yield = 89%). mp: 135-137 °C. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ (ppm) 12.71 (s, 1H), 7.47-7.24 (m, 7H), 7.01 (d, 1H, *J* = 8.0 Hz), 2.40 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6, TMS): δ (ppm) 145.8, 144.6, 136.0, 132.2, 131.2, 130.0,

128.4, 124.5, 123.6, 118.5, 111.2, 21.7. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{14}H_{13}N_2S$ (241.0794), found: 241.0791.

6-bromo-2-(phenylthio)-1H-benzo[*d*]imidazole (4p)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4p** as a yellow oil (109 mg, yield = 72%). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.46 (t, 3H, *J* = 8.0 Hz), 7.22 (s, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 149.4, 139.2, 136.9, 132.4, 128.8, 128.4, 128.0, 124.7, 116.4, 114.6, 114.5. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{13}H_{10}BrN_2S$ (304.9743), found: 304.9740.

2-(phenylthio)benzo[d]thiazole (4q)

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give the target compound **4q** as a colorless oil (34 mg, yield = 28%). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.80 (d, 1H, *J* = 8.0 Hz), 7.66 (d, 2H, *J* = 4.0 Hz), 7.56 (d, 1H, *J* = 8.0 Hz), 7.44-7.37 (m, 3H), 7.32 (t, 1H, *J* = 8.0 Hz), 7.18 (d, 1H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 168.7, 152.8, 134.5, 134.3, 129.5, 128.9, 128.9, 125.1, 123.3, 120.9, 119.7. HRMS (ESI) *m*/*z* $[M+H]^+$ Calcd for $C_{13}H_{10}NS_2$ (244.0249), found: 244.0245.

phenyl-*N*,*N*-dimethyl-*N′*-phenylcarbamimidothioate (4r):

According to **TP2**, the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give the target compound **4r** as a yellow oil (42 mg, yield = 33%). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 7.13-7.04 (m, 7H), 6.85 (t, 1H, *J* = 8.0 Hz), 6.66 (d, 2H, *J* = 4.0 Hz), 3.01 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 152.3, 150.3, 133.1, 129.9, 128.6, 128.0, 126.3, 121.9, 121.8, 39.4. HRMS (ESI) *m*/*z* [M+H]+ Calcd for $C_{15}H_{17}N_2S$ (257.1107), found: 257.1111.

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*Supporting Information: concise list of ^{1}H and ^{13}C NMR of products, X-ray crystallography data and CIF file of **4a** found in the SI.*

REFERENCES

(1) (a) Beard, R. L.; Colon, D. F.; Song, T. K.; Davies, P. J.; Kochhar, D. M.; Chandraratna, R. A. Synthesis and Structure-Activity Relationships of Retinoid X Receptor Selective Diaryl Sulfide Analogs of Retinoic Acid. *J. Med. Chem*. **1996**, *39*, 3556-3563. (b) Liu, G.; Link, J.; Pei, Z.; Reilly, E. B.; Leitza, S.; Nguyen, B.; Marsh, K. C.; Okasinski, G. F.; von Geldern, T. W.; Ormes, M. Discovery of Novel *p*-Arylthio Cinnamides as Antagonists of Leukocyte Function-Associated Antigen-1/Intracellular Adhesion Molecule-1 Interaction. 1. Identification of an Additional Binding Pocket Based on an Anilino Diaryl Sulfide Lead. *J. Med. Chem*. **2000**, *43*, 4025-4040. (c) Liu, G.; Huth, J. R.; Olejniczak, E. T.; Mendoza, R.; DeVries, P.; Leitza, S.; Reilly, E. B.; Okasinski, G. F.; Fesik, S. W.; von Geldern, T. W. Novel *p*-Arylthio Cinnamides as Antagonists of Leukocyte

Function-Associated Antigen-1/Intracellular Adhesion Molecule-1 Interaction. 2. Mechanism of Inhibition and Structure-Based Improvement of Pharmaceutical Properties. *J. Med. Chem*. **2001**, *44*, 1202-1210. (d) De Martino, G.; Edler, M. C.; La Regina, G.; Coluccia, A.; Barbera, M. C.; Barrow, D.; Nicholson, R. I.; Chiosis, G.; Brancale, A.; Hamel, E. New Arylthioindoles: Potent Inhibitors of Tubulin Polymerization. 2. Structure-Activity Relationships and Molecular Modeling Studies. *J. Med. Chem*. **2006**, *49*, 947-954. (e) Chen, H.-Y.; Peng, W.-T.; Lee, Y.-H.; Chang, Y.-L.; Chen, Y.-J.; Lai, Y.-C.; Jheng, N.-Y.; Chen, H.-Y. Use of Base Control to Provide High Selectivity between Diaryl Thioether and Diaryl Disulfide for C-S Coupling Reactions of Aryl Halides and Sulfur and a Mechanistic Study. *Organometallics* **2013**, *32*, 5514-5522.

(2) (a) Carcanague, D.; Shue, Y.-K.; Wuonola, M. A.; Uria-Nickelsen, M.; Joubran, C.; Abedi, J. K.; Jones, J.; Kühler, T. C. Novel Structures Derived from 2-[[(2-Pyridyl)methyl]thio]-1H-benzimidazole as Anti-Helicobacter pylori Agents, Part 2. *J. Med. Chem*. **2002**, *45*, 4300-4309. (b) Huang, W.; Yang, G.-F. Microwave-Assisted, One-Pot Syntheses and Fungicidal Activity of Polyfluorinated 2-Benzylthiobenzothiazoles. *Bioorgan. Med. Chem*. **2006**, *14*, 8280-8285. (c) Huang, W.; Zhao, P.-L.; Liu, C.-L.; Chen, Q.; Liu, Z.-M.; Yang, G.-F. Design, Synthesis, and Fungicidal Activities of New Strobilurin Derivatives. *J. Agr. Food. Chem*. **2007**, *55*, 3004-3010. (d) Bennamane, N.; Zaïoua, K.; Akacem, Y.; Kaoua, R.; Bentarzi, Y.; Bakhta, S.; Nedjar-Kolli, B.; Ouhab, L. Synthesis of Benzimidazol-2-Thiones from Dimedone : An Unexpected

Cyclisation into a Five-Membered Ring. *Org. Commun.* **2009**, *2*, 49-59. (e) Shin, J. M.; Sachs, G.; Cho, Y.-m.; Garst, M. 1-Arylsulfonyl-2-(Pyridylmethylsulfinyl) Benzimidazoles as New Proton Pump Inhibitor Prodrugs. *Molecules* **2009**, *14*, 5247-5280.

(3) (a) Oksuzoglu, E.; Tekiner-Gulbas, B.; Alper, S.; Temiz-Arpaci, O.; Ertan, T.; Yildiz, I.; Diril, N.; Sener-Aki, E.; Yalcin, I. Some Benzoxazoles and Benzimidazoles as DNA Topoisomerase I and II Inhibitors. *J. Enzym. Inhib. Med. Ch*. **2008**, *23*, 37-42. (b) Maske, P.; Lokapure, S.; Nimbalkar, D.; Disouza, J. Synthesis and Antiprotozoal Activity of Nitro and Halogeno Substituted Some Novel Mercaptobenzimidazole Derivatives. *Der Pharma Chemica* **2012**, *4*, 1283-1287. (c) Liu, H.; Jiang, X. Transfer of Sulfur: From Simple to Diverse. *Chem-Asian. J.* **2013**, *8*, 2546-2563. (d) Bianxiang, Z.; Kai, C.; Lihua, Y.; Ruijie, Z.; Lina, Z.; Ruixue, S. C-S Coupling Reaction of Heteroaromatic Compounds via Copper Catalyst. *Chin. J. Org. Chem*. **2015**, *35*, 905-909. (e) Vessally, E.; Mohammadi, R.; Hosseinian, A.; Didehban, K.; Edjlali, L. *S*-Arylation of 2-Mercaptobenzazoles: A Comprehensive Review. *J. Sulfur Chem*. **2018**, *39*, 443-463. (f) Maske, P.; Lokapure, S.; Nimbalkar, D.; Disouza, J. Synthesis and Antiprotozoal Activity of Nitro and Halogeno Substituted Some Novel Mercaptobenzimidazole Derivatives. *Der Pharma Chemica* **2012**, *4*, 1283-1287. (g) Zhang, L.; Fan, J.; Vu, K.; Hong, K.; Le Brazidec, J.-Y.; Shi, J.; Biamonte, M.; Busch, D. J.; Lough, R. E.; Grecko, R. 7'-Substituted Benzothiazolothio- and

Pyridinothiazolothio-Purines as Potent Heat Shock Protein 90 Inhibitors. *J. Med. Chem*. **2006**, *49*, 5352-5362.

(4) Allin, S. M.; Bowman, W. R.; Karim, R.; Rahman, S. S. Aromatic Homolytic Substitution using Solid Phase Synthesis. *Tetrahedron* **2006**, *62*, 4306-4316.

(5) (a) Schwab, R. S.; Singh, D.; Alberto, E. E.; Piquini, P.; Rodrigues, O. E.; Braga, A. L. C-S Cross-Coupling of Thiols with Aryl Iodides under Ligand-Free Conditions using Nano Copper Oxide as a Recyclable Catalyst in Ionic Liquid. *Catal. Sci. Technol*. **2011**, *1*, 569-573. (b) Sekar, R.; Srinivasan, M.; Marcelis, A. T.; Sambandam, A. *S*-Arylation of Mercaptobenzimidazoles using Cu (I) Catalysts-Experimental and Theoretical Observations. *Tetrahedron Lett*. **2011**, *52*, 3347-3352. (c) Panda, N.; Jena, A. K.; Mohapatra, S. Heterogeneous Magnetic Catalyst for *S*-Arylation Reactions. *Appl. Catal. A-Gen.* **2012**, *433*, 258-264. (d) Bianxiang, Z.; Lihua, Y.; Ruixue, S.; Yongqiang, K. Synthesis of Heterocyclic Aromatic Sulfides under Microwave Irradiation. *Chin. J. Org. Chem*. **2016**, *36*, 352-357. (e) Zhang, B.; Kang, Y.; Yang, L.; Chen, X. A *S*-Arylation of 2-Mercaptoazoles with Diaryliodonium Triflates under Metal-Free and Base-Free Conditions. *ChemistrySelect* **2016**, *1*, 1529-1532. (f) Tan, B. Y.-H.; Teo, Y.-C. Ligand-Free CuI-Catalyzed Chemoselective *S*-Arylation of 2-Mercaptobenzimidazole with Aryl Iodides. *Synlett* **2018**, *29*, 2056-2060.

(6) Katritzky, A. R.; Akutagawa, K. A New Synthetic Method for the 2-Substitution of *N*-Unsubstituted Benzimidazoles: Formaldehyde as a Versatile Protecting Agent for Heterocyclic NH^1. *J. Org. Chem.* **1989**, *54*, 2949-2952.

(7) Kibriya, G.; Mondal, S.; Hajra, A. Visible-Light-Mediated Synthesis of Unsymmetrical Diaryl Sulfides via Oxidative Coupling of Arylhydrazine with Thiol. *Org. Lett*. **2018**, *20*, 7740-7743.

(8) (a) Lam, P. Y.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M.; Combs, A. New Aryl/Heteroaryl C-N Bond Cross-Coupling Reactions Via Arylboronic Acid/Cupric Acetate Arylation. *Tetrahedron Lett*. **1998**, *39*, 2941-2944. (b) Combs, A. P.; Saubern, S.; Rafalski, M.; Lam, P. Y. Solid Supported Arylheteroaryl C-N Cross-Coupling Reactions. *Tetrahedron Lett*. **1999**, *40*, 1623-1626. (c) Lam, P. Y.; Vincent, G.; Clark, C. G.; Deudon, S.; Jadhav, P. K. Copper-Catalyzed General C-N and C-O Bond Cross-Coupling with Arylboronic Acid. *Tetrahedron Lett.* **2001**, *42*, 3415-3418. (d) Lam, P. Y.; Vincent, G.; Bonne, D.; Clark, C. G. Copper-Promoted/Catalyzed C-N and C-O Bond Cross-Coupling with Vinylboronic Acid and Its Utilities. *Tetrahedron lett*. **2003**, *44*, 4927-4931. (e) Qiao, J. X.; Lam, P. Y. Copper-Promoted Carbon-Heteroatom Bond Cross-Coupling with Boronic Acids and Derivatives. *Synthesis* **2011**, *2011*, 829-856.

(9) (a) Chen, S.; Huang, H.; Liu, X.; Shen, J.; Jiang, H.; Liu, H. Microwave-Assisted Efficient Copper-Promoted *N*-Arylation of Amines with Arylboronic Acids. *J. Comb. Chem*. **2008**, *10*, 358-360. (b) Rasheed, S.; Rao, D. N.; Das, P. Copper-Catalyzed Inter- and Intramolecular C-N Bond Formation: Synthesis of Benzimidazole-Fused Heterocycles. *J. Org. Chem.* **2015**, *80*, 9321-9327. (c) Dar'in, D.; Krasavin, M. The Chan-Evans-Lam *N*-Arylation of 2-Imidazolines. *J.*

Org. Chem. **2016**, *81*, 12514-12519. (d) Kumar, K. A.; Kannaboina, P.; Rao, D. N.; Das, P. Nickel-Catalyzed Chan-Lam Cross-Coupling: Chemoselective *N*-Arylation of 2-Aminobenzimidazoles. *Org. Biomol. Chem*. **2016**, *14*, 8989-8997. (e) Rao, D. N.; Rasheed, S.; Kumar, K. A.; Reddy, A. S.; Das, P. Copper-Catalyzed C-NH_2 Arylation of 2-Aminobenzimidazoles and Related C-Amino-NH-azoles. *Adv. Synth. Catal*. **2016**, *358*, 2126-2133.

(10) (a) Kondo, T.; Mitsudo, T.-a. Metal-Catalyzed Carbon-Sulfur Bond Formation. *Chem. Rev*. **2000**, *100*, 3205-3220. (b) Gangjee, A.; Zeng, Y.; Talreja, T.; McGuire, J. J.; Kisliuk, R. L.; Queener, S. F. Design and Synthesis of Classical and Nonclassical 6-Arylthio-2,4-diamino-5-ethylpyrrolo[2,3-d]pyrimidines as Antifolates. *J. Med. Chem*. **2007**, *50*, 3046-3053. (c) Correa, A.; Carril, M.; Bolm, C. Iron-Catalyzed *S*-Arylation of Thiols with Aryl Iodides. *Angewandte Chemie* **2008**, *120*, 2922-2925.

(11) (a) Herradura, P. S.; Pendola, K. A.; Guy, R. K. Copper-Mediated Cross-Coupling of Aryl Boronic Acids and Alkyl Thiols. *Org. Lett*. **2000**, *2*, 2019-2022. (b) Savarin, C.; Srogl, J.; Liebeskind, L. S. A Mild, Nonbasic Synthesis of Thioethers. The Copper-Catalyzed Coupling of Boronic Acids with *N*-Thio(alkyl, aryl, heteroaryl)imides. *Org. Lett*. **2002**, *4*, 4309-4312. (c) Taniguchi, N. Aryl-or Alkylation of Diaryl Disulfides using Organoboronic Acids and a Copper Catalyst. *Synlett* **2006**, *2006*, 1351-1354.

(12) (a) Dlin, E. A.; Averochkin, G. M.; Finko, A. V.; Vorobyeva, N. S.; Beloglazkina, E. K.; Zyk, N. V.; Ivanenkov, Y. A.; Skvortsov, D. A.; Koteliansky, V. E.;

Majouga, A. G. Reaction of Arylboronic Acids with 5-Aryl-3-Substituted-2-Thioxoimidazolin-4-Ones. *Tetrahedron Lett*. **2016**, *57*, 5501-5504. (b) Mugnaini, C.; Manetti, F.; Esté, J. A.; Clotet-Codina, I.; Maga, G.; Cancio, R.; Botta, M.; Corelli, F. Synthesis and Biological Investigation of *S*-Aryl-*S*-DABO Derivatives as HIV-1 Inhibitors. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3541-3544. (c) Prokopcova, H.; Kappe, C. O. Palladium(0)-Catalyzed, Copper(I)-Mediated Coupling of Boronic Acids with Cyclic Thioamides. Selective Carbon-Carbon Bond Formation for the Functionalization of Heterocycles. *J. Org. Chem.* **2007**, *72*, 4440-4448. (d) Pulakhandam, S. K.; Katari, N. K.; Manda, R. P. R. *J. Chem. Sci.* **2017**, *129*, 203-210.

(13) Liu, X.; Zhang, S. B.; Zhu, H.; Cheng, Y.; Peng, H. Y.; Dong, Z. B. Transition Metal-Promoted Synthesis of 2-Aryl/Heteroaryl-Thioquinazoline: C-S Bond Formation by "Chan-Lam Cross-Coupling" Reaction. *Eur. J. Org. Chem*. **2018**, 4483-4489.

(14)(a) Dong, Z.-B.; Liu, X.; Bolm, C. Copper-Catalyzed C(sp^2)-S Coupling Reactions for the Synthesis of Aryl Dithiocarbamates with Thiuram Disulfide Reagents. *Org. Lett*. **2017**, *19*, 5916-5919. (b) Liu, X.; Cao, Q.; Xu, W.; Zeng, M. T.; Dong, Z. B. Nickel-Catalyzed C-S Coupling: Synthesis of Diaryl Sulfides Starting from Phenyldithiocarbamates and Iodobenzenes. *Eur. J. Org. Chem*. **2017**, *2017*, 5795-5799. (c) Liu, X.; Liu, M.; Xu, W.; Zeng, M.-T.; Zhu, H.; Chang, C.-Z.; Dong, Z.-B. An Environmentally Benign and Efficient Synthesis of Substituted Benzothiazole-2-Thiols, Benzoxazole-2-Thiols, and

Benzimidazoline-2-Thiones in Water. *Green Chem*. **2017**, *19*, 5591-5598. (d) Chang, C.-Z.; Liu, X.; Zhu, H.; Wu, L.; Dong, Z.-B. Copper-Catalyzed and Air-Mediated Mild Cross-Dehydrogenative Coupling of Aryl Thioureas and Dialkyl H-Phosphonates: The Synthesis of Thiophosphonates. *J. Org. Chem*. **2018**, *83*, 13530-13535. (e) Liu, X.; Zhang, S.-B.; Zhu, H.; Dong, Z.-B. Copper (I)-Catalyzed Tandem One-Pot Synthesis of 2-Arylthiobenzothiazoles and 2-Arylthiobenzoxazoles in Water. *J. Org. Chem*. **2018**, *83*, 11703-11711. (f) Zhang, S.-B.; Liu, X.; Gao, M.-Y.; Dong, Z.-B. One-Pot Synthesis of 2-Benzyl/2-Allyl-Substituted Thiobenzoazoles using Transition-Metal-Free Conditions in Water. *J. Org. Chem*. **2018**, *83*, 14933-14941.

(15) (a) Cheng, Y.; Liu, X.; Dong, Z. B. Phenyldithiocarbamates: Efficient Sulfuration Reagents in the Chan-Lam Coupling Reaction. *Eur. J. Org. Chem*. **2018**, *2018*, 815-820. (b) Gao, M. Y.; Xu, W.; Zhang, S. B.; Li, Y. S.; Dong, Z. B. Synthesis of Phenyl Dithiocarbamates Starting from Sodium Dialkyldithiocarbamates and Aryl Boronic Acids: a Copper Catalyzed *S*-Arylation. *Eur. J. Org. Chem*. **2018**, *2018*, 6693-6698.

(16) Nishiura, K.; Urawa, Y.; Soda, S. *N*-Arylation of Benzimidazole with Arylboronate, Boroxine and Boronic Acids. Acceleration with an Optimal Amount of Water. *Adv. Synth. Catal*. **2004**, *346*, 1679-1684.

(17) (a) Taniguchi, N. Convenient Synthesis of Unsymmetrical Organochalcogenides Using Organoboronic Acids with Dichalcogenides via Cleavage of the S-S, Se-Se, or Te-Te Bond by a Copper Catalyst. *J. Org. Chem.* **2007**, *72*, 1241-1245. (b) Xu,

H.-J.; Zhao, Y.-Q.; Feng, T.; Feng, Y.-S. Chan-Lam-Type *S*-Arylation of Thiols with Boronic Acids at Room Temperature. *J. Org. Chem.* **2012**, *77*, 2878-2884. (c) King, A. E.; Brunold, T. C.; Stahl, S. S. Mechanistic Study of Copper-Catalyzed Aerobic Oxidative Coupling of Arylboronic Esters and Methanol: Insights into an Organometallic Oxidase Reaction. *J. Am. Chem. Soc.* **2009**, *131*, 5044-5045. (d) Vantourout, J. C.; Miras, H. N.; Isidro-Llobet, A.; Sproules, S.; Watson, A. J. Spectroscopic Studies of the Chan-Lam Amination: A Mechanism-Inspired Solution to Boronic Ester Reactivity. *J. Am. Chem. Soc.* **2017**, *139*, 4769-4779. (e) King, A. E.; Ryland, B. L.; Brunold, T. C.; Stahl, S. S. Kinetic and Spectroscopic Studies of Aerobic Copper (II)-Catalyzed Methoxylation of Arylboronic Esters and Insights into Aryl Transmetalation to Copper (II). *Organometallics* **2012**, *31*, 7948-7957.