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铜催化苯并噻唑与二芳基碘鎓盐的芳基化反应

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摘要 二芳基碘盐具有毒性低、反应条件温和及选择性高的优点, 在有机合成中一直受到关注, 已被广泛用作芳基化试剂, 可用于芳杂环化合物的交叉偶联反应和芳基化反应等. 发展了一种铜催化下苯并噻唑与二芳基碘鎓盐反应合成2-芳基苯并噻唑衍生物的方法. 该方法具有底物范围广泛、基团耐受性良好及产率高等优点.
关键词 苯并噻唑; 芳基化; 二芳基碘鎓盐; 交叉偶联反应; C—H 键的活化

Cu-Catalyzed Direct Arylation of Benzothiazoles with Diaryliodonium Salts

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Abstract Diaryliodonium salts have low toxicity and good stability, and their mediated reactions often have advantages of mild reaction conditions and high selectivity. They have received extensive attention and have been widely used as arylating agents in organic synthesis. A simple and efficient method for the synthesis of 2-arylbenzothiazole derivatives via copper-catalyzed C—H direct arylation of benzothiazoles with diaryliodonium salts as electrophilic arylating reagents was developed. This method shows wide range of substrates, good group tolerance, simple operation and high product yields.
Keywords benzothiazole; arylation; diaryliodonium salt; cross coupling; C—H activation

1 Introduction

Arylbenzothiazole is an important structural motif which can be seen in many organic compounds. 2-Arylbenzothiazole derivatives always show some bioactivities and are used as pharmaceuticals, such as antineoplastic agents,[1] neurological drugs,[2] hematology drugs[3] and cardiovascular drugs[4] (Figure 1). Scientists are highly concerned about the synthesis of 2-arylbenzothiazole derivatives,[5] and always try to develop some efficient synthetic methods. In the past years, scientists have reported many protocols for the synthesis of 2-arylbenzothiazoles, as seen in Scheme 1.[6-8] However, some of them have major drawbacks, such as poor tolerance of functional groups, high temperatures and strong oxidants. Therefore, it is urgent to find a suitable, convenient and safe method for the syntheses of 2-arylbenzothiazoles.

Diaryliodonium salts have low toxicity and good stability, their mediated reactions often have advantages of mild reaction conditions and high selectivity since diaryliodonium salts were prepared and used in organic synthesis for the first time.[9] In recent years, diaryliodonium salts have been widely used as arylating agents in organic synthesis.[10-13] They can also be successfully used for cross-coupling arylation reaction of hetero atom nucleophilic compounds.[14-18]

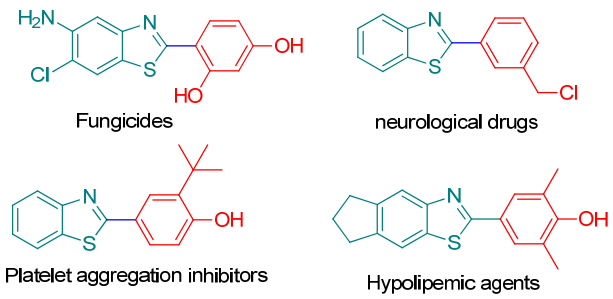

Figure 1 Representative bioactive 2-arylbenzothiazole compounds

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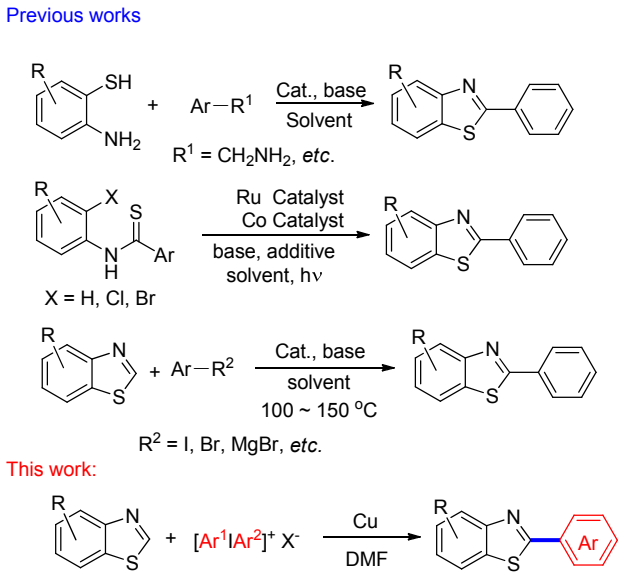


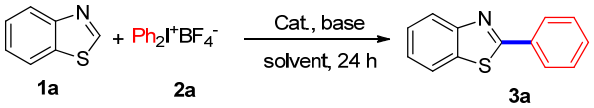
Scheme 1 Synthetic methods of 2-arylbenzothiazoles

With continuous research interests in C—H activation and functionalization, some transition metal-catalyzed C—H arylation protocols of aromatics and heteroaromatics by using diaryliodonium salts and aryl halides as coupling partners were developed and good results were obtained.[19-21] Herein, a copper-catalyzed direct C—H arylation of benzothiazoles with diaryliodonium salts as arylating reagents (Scheme 1) is reported. It is a simple, cheap and efficient method to synthesize 2-arylbenzothiazole derivatives.

2 Results and discussion

In order to explore the best conditions for the reaction, our study was initiated with the reaction of benzothiazole (**1a**) and diphenyliodonium tetrafluoroborate (**2a**). The results of the reaction condition optimization are listed in Table 1. The reaction was first conducted in acetonitrile at 80 ℃ with K_2CO_3 as a base, (*o*-tolyl)$_3$P as a ligand and copper powder as a catalyst. Unfortunately, there is no

Table 1 Optimization of the reaction conditions[a]



Entry	Base (equiv.)	Catalyst	Ligand	Solvent	Temp./℃	Yield of **3a**/%
1	K_2CO_3 (1.0)	Cu	(*o*-tolyl)$_3$P	CH_3CN	80	NR
2	K_2CO_3 (1.0)	CuI	(*o*-tolyl)$_3$P	CH_3CN	80	Trace
3	K_2CO_3 (2.0)	CuI	(*o*-tolyl)$_3$P	CH_3CN	80	22
4	Na_2CO_3 (2.0)	CuI	(*o*-tolyl)$_3$P	CH_3CN	80	10
5	$NaHCO_3$ (2.0)	CuI	(*o*-tolyl)$_3$P	CH_3CN	80	12
6	K_2PO_4 (2.0)	CuI	(*o*-tolyl)$_3$P	CH_3CN	80	25
7	Cs_2CO_3 (2.0)	CuI	(*o*-tolyl)$_3$P	CH_3CN	80	32
8	Cs_2CO_3 (3.0)	CuI	(*o*-tolyl)$_3$P	CH_3CN	80	43
9	Cs_2CO_3 (3.0)	CuBr	(*o*-tolyl)$_3$P	CH_3CN	80	trace
10	Cs_2CO_3 (3.0)	CuCl	(*o*-tolyl)$_3$P	CH_3CN	80	NR
11	Cs_2CO_3 (3.0)	Cu-MOF	(*o*-tolyl)$_3$P	CH_3CN	80	NR
12	Cs_2CO_3 (3.0)	Fe_2O_3	(*o*-tolyl)$_3$P	CH_3CN	80	NR
13	Cs_2CO_3 (3.0)	$NiCl_2(PPh_3)_2$	(*o*-tolyl)$_3$P	CH_3CN	80	trace
14	Cs_2CO_3 (3.0)	CuI	PPh_3	CH_3CN	80	28
15	Cs_2CO_3 (3.0)	CuI	1,10-Phenanthroline	CH_3CN	80	31
16	Cs_2CO_3 (3.0)	CuI	dppp	CH_3CN	80	52
17	Cs_2CO_3 (3.0)	CuI	TCHP	CH_3CN	80	45
18	Cs_2CO_3 (3.0)	CuI	dppe	CH_3CN	80	47
19	Cs_2CO_3 (3.0)	CuI	bpy	CH_3CN	80	65
20	Cs_2CO_3 (3.0)	CuI	bpy	DMSO	140	30
21	Cs_2CO_3 (3.0)	CuI	bpy	1,4-Dioxane	80	55
22	Cs_2CO_3 (3.0)	CuI	bpy	DMF	140	86
23	Cs_2CO_3 (3.0)	CuI	bpy	Toulene	80	72
24	Cs_2CO_3 (3.0)	CuI	bpy	THF	80	26
25	Cs_2CO_3 (3.0)	CuI	bpy	CH_2Cl_2	80	trace
26	Cs_2CO_3 (3.0)	CuI	bpy	DCE	80	58
27	Cs_2CO_3 (3.0)	CuI	bpy	Pyridine	115	trace

[a] Reagents and conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), catalyst (10 mol%), ligand (10 mol%), solvent (3 mL) at reflux temperature (140 ℃ for *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO)) for 24 h. NR means no reaction. Yield is isolated yield. TCHP=tricyclohexylphosphine, dppe=bis(diphenylphosphino)ethane, bpy=2,2'-bipyridine.

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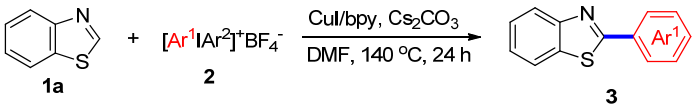
target product generation (Entry 1). Then the catalyst was replaced with CuI, only trace of target product was formed (Entry 2). To our delight, when the amount of K_2CO_3 was doubled, the desired 2-phenylbenzothiazole (**3a**) was obtained in 22% yield (Entry 3). Next, different bases and the dosage of bases were examined in the reaction (Entries 4～8). When 3 equiv. of Cs_2CO_3 were used, the yield of the product was up to 43% (Entry 8). Then we continued to screen catalysts (Entries 9～13) and ligands (Entries 14～19). The results showed that the yield could reach 65% when using CuI as a catalyst and 2,2'-bipyridine as a ligand (Entry 19). The screening result of organic solvents showed *N*,*N*-dimethylformamide (DMF) was the best choice in terms of product yield and reaction time (Entries 20～27). Finally, we found that the optimal conditions for this reaction were: benzothiazole (**1a**) (1.0 equiv.), diphenyliodonium tetrafluoroborate (**2a**) (1.0 equiv.), Cs_2CO_3 (3.0 equiv.), CuI (10 mol%), 10 mol% of bipyridine and 3 mL of DMF at 140 ℃ for 24 h and the best product yield was 86% (Entry 22).

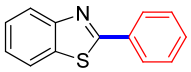
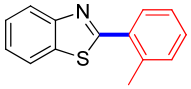
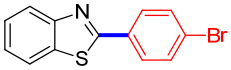
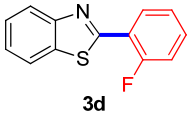
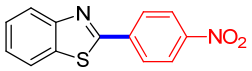
With the optimized reaction conditions in hand, the effect of different substituents of diaryliodonium salts on 2-arylation of benzothiazoles was investigated. Three symmetric diaryliodonium tetrafluoroborates bearing a variety of functional groups, such as 2-methyl, 4-bromo and 2-fluoro, on the aromatic ring worked well in the protocol to get the corresponding products in the yield of 72%, 81% and 78%, respectively (Table 2, Entries 2～4). When phenyl(2,6-dimethylphenyl)iodonium salt was used in this reaction, **3a** was formed exclusively in 63% yield. It may be due to the large steric hindrance of 2,6-dimethylphenyl (Entry 5). Using (4-nitrophenyl)phenyliodonium salt as an arylating coupling partner, 2-(4-nitrophenyl)benzothiazole (**3e**) was formed in 69% yield and **3a** was not observed in this reaction (Entry 6). However, when benzothiazole was treated with unsymmetrical (2-methylphenyl)phenyliodonium tetrafluoroborate and (2-fluorophenyl)phenyliodonium tetrafluoroborate respectively, two arylation products were obtained in total yield of about 80% (Entries 7 and 8). It is obvious that mixed arylation products will be obtained when electron and hindrance effect of substituents of unsymmetrical diaryliodonium salts are not manifest.

Next, the scope and group tolerance of benzothiazoles were investigated. As seen from the results in Table 3, the different substituents attached to benzothiazole produced corresponding 2-arylation products **3f**～**3l** in moderate to good yields (42%～83%). These substituents include alkyl, alkyloxy, halo atom and nitro group. Among of them, 6-ethoxybenzothiazole delivered the product **3l** yield of 83% and 6-nitrobenzothiazole delivered 42% of 2-phenyl-

Table 2 Scope of diaryliodonium salts in arylation of **1a**[a]



1a **2** **3**

Entry	Ar^1	Ar^2	**3**	Yield/%
1	C_6H_5	C_6H_5	 **3a**	86
2	2-MeC_6H_4	2-MeC_6H_4	 **3b**	72
3	4-BrC_6H_4	4-BrC_6H_4	 **3c**	81
4	2-FC_6H_4	2-FC_6H_4	 **3d**	78
5	C_6H_5	2,6-$Me_2C_6H_3$	**3a**	63
6	4-$O_2NC_6H_4$	C_6H_5	 **3e**	59
7	2-MeC_6H_4	C_6H_5	**3a**, **3b**	55 (**3a**), 23 (**3b**)
8	2-FC_6H_4	C_6H_5	**3d**, **3a**	57 (**3d**), 21 (**3a**)

[a] Reagents and conditions: **1a** (0.2 mmol), **2** (0.2 mmol), CuI (0.02 mmol), Cs_2CO_3 (0.6 mmol), bpy (0.02 mmol) in DMF (3 mL) at 140 ℃ for 24 h.

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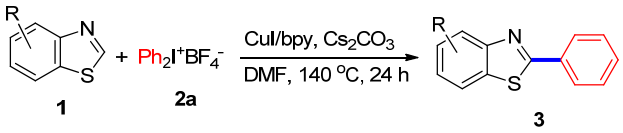
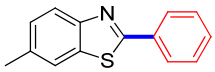
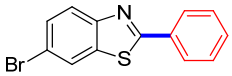
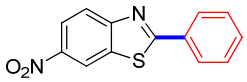
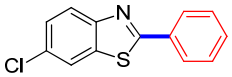
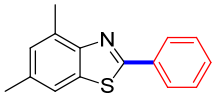
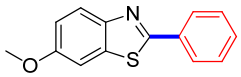
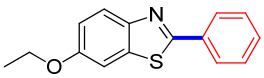
ation product **3h**. Manifestly, both electron-deficient and electron-rich benzothiazoles can participate in the reaction, affording 2-arylbenzothiazole compounds in satisfactory yields, whereas electron-donating groups on benzothiazole ring are more beneficial for the reaction. The reason may be that electron-donating groups increase the electron cloud density of aromatic ring to improve the nucleophilicity of C(2) of benzothiazoles.

Table 3 2-Arylation of substituted benzothiazoles with **2a**[a]

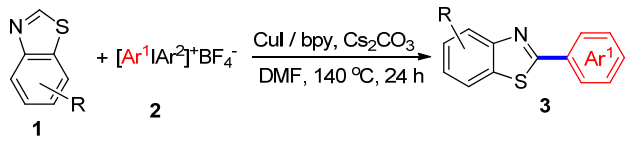


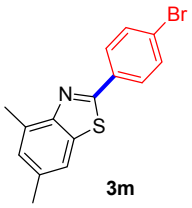
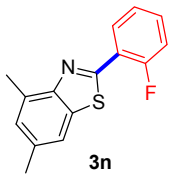
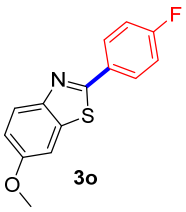
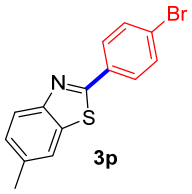
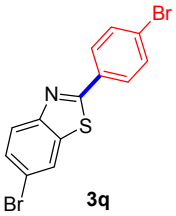
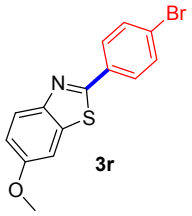
Entry	R	3	Yield/%
1	6-Me	 **3f**	71
2	6-Br	 **3g**	70
3	6-NO_2	 **3h**	42
4	6-Cl	 **3i**	68
5	4,6-Me_2	 **3j**	58
6	6-MeO	 **3k**	76
7	6-EtO	 **3l**	83

[a] Reagents and conditions: **1** (0.2 mmol), **2a** (0.2 mmol), CuI (0.02 mmol), Cs_2CO_3 (0.6 mmol), and bpy (0.02 mmol) in DMF (3 mL) at 140 ℃ for 24 h. Yield is isolated yield.

Finally, substituted benzothiazoles were encountered with various symmetric and unsymmetric diaryliodonium tetrafluoroborates under optimized reaction conditions and the results are summarized in Table 4. It can be seen that most of substrates can be smoothly converted into corresponding 2-arylation products in good yields. The reaction results of substituted benzothiazoles with phenyl(2,6-dimethylphenyl)iodonium salt further confirmed that steric hindrances severely affected the reactivity and chemoselectivity of unsymmetrical diaryliodonium salts.

Table 4 Reaction of substituted benzothiazoles with various diaryliodonium salts[a]



Entry	R	Ar^1	Ar^2	3	Yield/%
1	4,6-Me_2	4-BrC_6H_4	4-BrC_6H_4	 **3m**	65
2	4,6-Me_2	C_6H_5	2-FC_6H_4	 **3n**	78
3	6-MeO	2-FC_6H_4	2-FC_6H_4	 **3o**	72
4	6-Me	4-BrC_6H_4	4-BrC_6H_4	 **3p**	80
5	6-Br	4-BrC_6H_4	4-BrC_6H_4	 **3q**	58
6	6-MeO	4-BrC_6H_4	4-BrC_6H_4	 **3r**	70

[a] Reagents and conditions: **1** (0.2 mmol), **2** (0.2 mmol), CuI (0.02 mmol), Cs_2CO_3 (0.6 mmol), bpy (0.02 mmol) in DMF (3 mL) at 140 ℃ for 24 h.

Finally, a possible reaction mechanism for Cu-catalyzed

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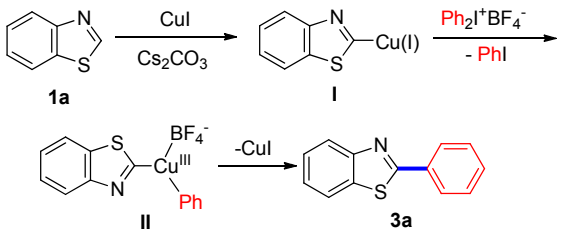
direct arylation of benzothiazoles with diaryliodonium salts was proposed based on our experimental observations and previous literatures (Scheme 2).[19,21-22] An initial cupration of benzothiazole (**1a**) with CuI in the presence of Cs_2CO_3 affords thiazolyl-copper species **I**. Subsequent oxidative addition of **I** to diphenyliodonium tetrafluoroborate delivers to an electrophilic Cu(III)-aryl species **II** with the removal of iodobenzene. Then product **3a** is obtained upon reductive elimination of **II**, and the Cu(I) catalyst is released simutaneously.



Scheme 2 Proposed reaction mechanism for the arylation of benzothiazoles

3 Conclusions

In summary, a simple and low-cost copper-catalyzed C—H direct arylation of benzothiazoles with diaryliodonium salts as arylation reagents to synthesize 2-arylbenzothiazoles was developed. This method shows wide scope of substrates and good group tolerance as well as high product yields.

4 Experimental section

4.1 General information

All of ^{1}H NMR and ^{13}C NMR spectra were performed in 600 MHz and 150 MHz Bruker spectrometers (unless special instructions are used for 400 MHz and 100 MHz) and $CDCl_3$ was used as solvent and TMS as internal standard. All chemicals were used as received without further purification. All solvents were dried and degassed by standard methods before use. Reactions were monitored by thin-layer chromatography (TLC) and high performance liquid chromatography (HPLC).

4.2 Experimental procedure for Cu-catalyzed direct arylation of benzothiazoles

Catalyst (0.02 mmol, 10 mol%), ligand (0.02 mmol, 10 mol% for mono-P ligand; 0.01 mmol, 5 mol% for di-P ligand), benzothiazoles (0.2 mmol), diaryliodonium salts (0.2 mmol) and solvent (3.0 mL) were sequentially added into a 10 mL reaction tube, and the resulting mixture was stirred in a preheated oil bath at 140 ℃ for 24 h. Reaction mixture was cooled to room temperature and the solvent was removed in vacuum. The crude product was purified by column chromatography on silica gel (ethyl acetate/dichloromethane/petroleum ether, V∶V∶V=1∶1∶20) to give the desired 2-arylbenzothiazoles. The byproduct iodobenzene was recovered to prepare diaryliodonium salts.

Phenylbenzothiazole (**3a**): White solid. m.p. 113～115 ℃ (lit.[23] 110.5～111 ℃); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.10 (dd, J=2.4, 3.6 Hz, 3H), 7.90 (d, J=7.6 Hz, 1H), 7.50～7.45 (m, 4H), 7.38 (t, J=7.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 168.0, 154.2, 135.1, 133.6, 131.0, 130.9, 129.0, 128.8, 127.6, 126.3, 125.2, 123.2, 121.6.

2-(2-Methylphenyl)benzothiazole (**3b**):[24] Colorless solid. m.p. 56～58 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.11～8.04 (m, 2H), 7.98 (d, J=7.6 Hz, 1H), 7.92～7.88 (m, 1H), 7.49 (d, J=4.2 Hz, 2H), 7.40～7.35 (m, 1H), 7.30 (d, J=7.8 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 168.2, 154.2, 141.4, 134.9, 133.6, 129.7, 129.0, 127.5, 126.2, 125.0, 123.0, 121.6, 121.6, 21.5.

2-(4-Bromophenyl)benzothiazole (**3c**): Colorless solid. m.p. 130～132 ℃ (lit.[25] 129～131 ℃); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.07 (d, J=8.4 Hz, 1H), 7.96 (d, J=8.4 Hz, 2H), 7.90 (d, J=8.4 Hz, 1H), 7.63 (d, J=8.4 Hz, 2H), 7.52～7.48 (m, 1H), 7.42～7.38 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 166.7, 154.1, 135.0, 133.8, 132.6, 132.2, 129.9, 128.9, 126.5, 125.4, 123.4, 123.3, 121.6.

2-(2-Fluorophenyl)benzothiazole (**3d**): Light yellow solid. m.p. 67～68 ℃ (lit.[26] 67～68 ℃); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.42 (t, J=7.8 Hz, 1H), 8.13 (d, J=8.4 Hz, 1H), 7.95 (d, J=7.8 Hz, 1H), 7.52 (t, J=7.6 Hz, 1H), 7.48 (q, J=13.8, 6.5 Hz, 1H), 7.42 (t, J=7.6 Hz, 1H), 7.32 (t, J=7.6 Hz, 1H), 7.25～7.21 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 161.4, 159.7 (d, J=5.7 Hz), 152.6, 135.8 (d, J=8.2 Hz), 132.1 (d, J=8.7 Hz), 129.8 (d, J=2.4 Hz), 126.3, 125.3, 124.7, 123.3, 121.5, 121.4, 116.3 (d, J=22.0 Hz).

2-(4-Nitrophenyl)benzothiazole (**3e**):[27] Yellow solid. m.p. 229～230 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.36 (d, J=8.4 Hz, 2H), 8.30 (d, J=9.0 Hz, 2H), 7.80 (d, J=8.4 Hz, 2H), 7.18 (d, J=9.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 160.7, 148.0, 145.0, 144.2, 130.9, 128.8, 128.3, 126.2, 124.4, 124.4, 119.3.

Methyl-2-phenylbenzothiazole (**3f**): White solid. m.p. 124～125 ℃ (lit.[28] 126～128 ℃); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.14～8.04 (m, 2H), 7.78 (d, J=32.4 Hz, 1H), 7.68 (s, 1H), 7.63～7.60 (m, 1H), 7.57 (s, 1H), 7.51 (s, 1H), 7.48 (s, 1H), 2.47 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 167.0, 152.3, 135.3, 135.2, 133.7, 130.7, 128.9, 128.8, 127.9, 127.6, 127.4, 122.7, 121.3, 21.5.

6-Bromo-2-phenylbenzothiazole (**3g**):[24] Pale brown solid. m.p. 151～152 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.11～8.01 (m, 3H), 7.95～7.89 (m, 1H), 7.59 (dd, J=1.8, 2.4 Hz, 1H), 7.54～7.47 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 167.2, 152.9, 139.2, 136.6, 132.3, 131.9, 130.0, 128.9, 128.6, 125.8, 124.4, 124.2, 119.0.

6-Nitro-2-phenylbenzothiazole (**3h**):[29] Pale orange solid. m.p. 190～192 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.84 (d, J=2.4 Hz, 1H), 8.37 (dd, J=9.0, 2.4 Hz, 1H), 8.14 (t, J=7.6 Hz, 3H), 7.56 (dd, J=12.8, 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 173.7, 157.8, 135.3, 132.7, 132.2, 129.3, 127.9, 123.3, 121.9, 118.2.

6-Chloro-2-phenylbenzothiazole (**3i**): Light yellow sol-

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id. m.p. 157～158 ℃ (lit.[24] 156～157 ℃); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.06 (dd, J=1.8, 3.6 Hz, 1H), 7.96 (d, J=9.0 Hz, 1H), 7.87 (d, J=1.8 Hz, 1H), 7.52～7.47 (m, 3H), 7.44 (dd, J=1.8, 2.4 Hz, 1H), 7.33 (t, J=7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 168.5, 152.7, 136.2, 133.2, 131.2, 131.1, 129.7, 129.1, 127.5, 127.1, 123.9, 121.2, 118.9.

4,6-Dimethyl-2-phenylbenzothiazole (**3j**):[30] Yellow solid. m.p. 188～191 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, J=6.0 Hz, 2H), 7.51 (s, 1H), 7.47 (d, J=5.2 Hz, 3H), 7.10 (s, 1H), 2.76 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5, 151.7, 135.2, 135.1, 134.1, 132.7, 130.4, 129.7, 128.9, 128.8, 128.4, 127.4, 118.7, 21.5, 18.3.

6-Methoxy-2-phenylbenzothiazole (**3k**): White solid. m.p. 113～114 ℃ (lit.[31] 112～114 ℃); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.07～8.02 (m, 2H), 7.97～7.93 (m, 1H), 7.50～7.44 (m, 3H), 7.35 (d, J=3.0 Hz, 1H), 7.12～7.07 (m, 1H), 3.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 165.5, 157.8, 148.7, 136.4, 133.8, 130.9, 130.5, 128.9, 128.8, 127.2, 123.7, 115.6, 104.2, 55.8.

6-Ethyoxyl-2-phenylbenzothiazole (**3l**): White solid. m.p. 113～115 ℃ (lit.[32] 113～115 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.87 (d, J=8.4 Hz, 1H), 7.58 (d, J=2.0 Hz, 1H), 7.44～7.38 (m, 2H), 7.35 (dd, J=2.4, 2.4 Hz, 2H), 7.17 (q, J=2.8 Hz, 1H), 6.59 (d, J=2.0 Hz, 1H), 4.09 (q, J=6.8 Hz, 2H), 1.46 (t, J=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.6, 151.8, 146.2, 145.0, 135.5, 134.3, 134.2, 131.9, 129.6, 128.6, 119.5, 114.6, 104.3, 64.5, 14.7.

2-(4-Bromophenyl)-4,6-dimethylbenzothiazole (**3m**): White solid. m.p. 110～113 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.95 (dd, J=1.2, 1.2 Hz, 2H), 7.63～7.58 (m, 2H), 7.51 (s, 1H), 7.11 (s, 1H), 2.75 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 164.1, 151.6, 147.2, 135.5, 135.2, 133.0, 132.8, 132.1, 128.7, 128.6,126.0, 124.8, 118.7, 21.5, 18.3; HRMS (ESI) calcd. for $C_{15}H_{13}BrNS$ $(M+H)^+$ 317.9947, found 317.9944.

4,6-Dimethyl-2-(2-fluorophenyl)benzothiazole (**3n**): White solid. m.p. 122～124 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.45 (t, J=7.2 Hz, 1H), 7.55 (s, 1H), 7.43 (q, J=6.0 Hz, 1H), 7.30 (t, J=7.6 Hz, 1H), 7.21 (dd, J=8.4, 8.4 Hz, 1H), 7.13 (s, 1H), 2.78 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 161.3, 158.5 (d, J=5.7 Hz), 150.1, 135.3 (d, J=7.6 Hz), 132.7, 131.5 (d, J=8.6 Hz), 129.7 (d, J=2.6 Hz), 128.4, 124.6 (d, J=3.4 Hz), 121.9 (d, J=11.1 Hz), 121.8, 118.4, 116.2 (d, J=21.9 Hz), 21.5, 18.2; HRMS (ESI) calcd for $C_{15}H_{13}FNS$ $(M+H)^+$ 258.0747, found 258.0744.

2-(2-Flurophenyl)-6-methoxybenzothiazole (**3o**):[33] Light yellow solid. m.p. 104～107 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.36 (t, J=7.8 Hz, 1H), 7.99 (d, J=9.0 Hz, 1H), 7.43 (dd, J=6.6, 6.6 Hz, 1H), 7.37 (s, 1H), 7.28 (t, J=7.6 Hz, 1H), 7.24～7.17 (m, 1H), 7.14～7.09 (m, 1H), 3.90 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 161.1, 159.5 (d, J=5.8 Hz) , 157.8, 147.2, 137.2 (d, J=7.8 Hz), 131.6 (d, J=8.7 Hz), 129.4 (d, J=2.5 Hz), 124.6, 124.6, 123.8, 116.2, 116.0 (d, J=21.9 Hz), 103.6, 55.8.

2-(4-Bromophenyl)-6-methylbenzothiazole (**3p**):[34] White solid. m.p. 156～159 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.87 (d, J=8.4 Hz, 2H), 7.61 (d, J=10.8 Hz, 2H), 7.55 (d, J=3.0 Hz, 2H), 7.24 (d, J=7.8 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 135.7, 132.7, 132.2, 132.0, 131.9, 128.8, 128.1, 127.3, 125.1, 122.8, 121.4, 21.6.

6-Bromo-2-(4-bromophenyl)benzothiazole (**3q**):[33] Light yellow solid. m.p. 168～171 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.02 (s, 1H), 7.91 (dd, J=7.8, 9.6 Hz, 2H), 7.64～7.57 (m, 3H), 7.52～7.46 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 167.2, 152.9, 139.2, 136.6, 132.3, 131.9, 130.0, 128.9, 128.6, 125.8, 124.4, 124.2, 119.0.

2-(4-Bromophenyl)-6-methoxybenzothiazole (**3r**): White solid. m.p. 137～140 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.92 (dd, J=9.0, 8.4 Hz, 2H), 7.61 (d, J=7.8 Hz, 2H), 7.47 (dd, J=7.8, 7.8 Hz, 1H), 7.35 (s, 1H), 7.10 (d, J=8.4 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 164.1, 157.9, 148.6, 136.4, 132.7, 132.3, 132.1, 128.7, 128.6, 124.8, 123.8, 115.9, 104.1, 55.8; HRMS (ESI) calcd for $C_{14}H_{11}BrOSN$ $(M+H)^+$ 319.9739, found 319.9735.

Supporting Information ^{1}H NMR and ^{13}C NMR spectra of products **3a**～**3r**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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