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The Competing Dehalogenation versus Borylation of Aryl Iodides and Bromides under Transition Metal-Free Basic Conditions

Yi-Jie Niu,[†#] Guo-Hui Sui,[†#] Hong-Xing Zheng,[‡] Xiang-Huan Shan,[§] Lin Tie,[§] Jia-Le Fu,[§] Jian-Ping Qu,[†*] and Yan-Biao Kang[§*]

† Institute of Advanced Synthesis, School of Chemistry and Molecular Engineering, Jiangsu National Synergetic Innovation Center for Advanced Materials, Nanjing Tech University, Nanjing 211816, China, ias_jpqu@njtech.edu.cn

‡ School of Chemistry and Chemical Engineering, Liaocheng University, Liaocheng, Shandong 252059, China

§ Department of Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, China, ybkang@ustc.edu.cn

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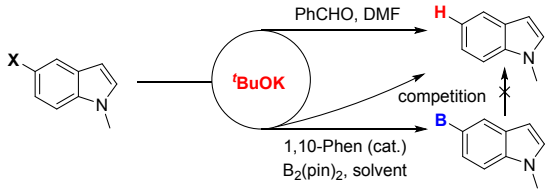


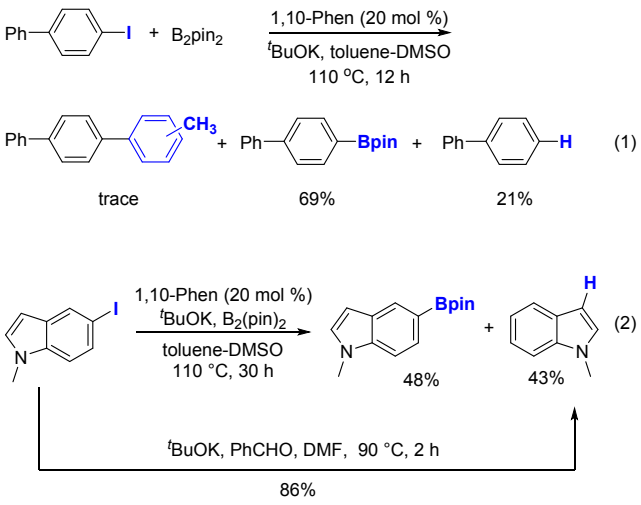
ABSTRACT: In this work, a selectivity-controllable base-promoted transition metal-free borylation and dehalogenation of aryl halides are described. Under the conditions of borylation, the dehalogenation which emerges as a competitive side-reaction has been well-controlled by carefully controlling the borylation conditions. On the other hand, the dehalogenation using benzaldehyde as hydrogen source has also been accomplished. The applications of direct radical borylation and dehalogenation of aryl halides demonstrate their synthetic practicability in pharmaceutical-oriented organic synthesis. Based on the experimental evidences, the ^{t}BuOK/1,10-Phen triggered radical nature of both competitive reactions has been revealed.

INTRODUCTION

Boronic esters and acids are both useful reagents for C-C bond formation reactions such as Suzuki coupling reaction and recently developed C-H boronation reactions.[1] The typical preparation of boronic esters involves the alkylation of trialkyl borates with Grignard or aryllithium reagents. A modification has been established by the metal-catalyzed cross coupling of diboronic esters with aryl halides.[2] Near recently, a novel zinc-catalyzed borylation has also been developed by Marder *et al.*,[3] and transition-metals have been generally involved as catalysts in such coupling reactions. However, for the pharmaceutical-oriented synthesis, the problem of heavy-metal residues or high costs often restricts their applications in the drug synthesis. Alternatively, the transition metal-free borylation reactions such as the Sandmeyer-type borylations by Wang *et al.*[4] and the borylation of aryl halides promoted by bases were reported.[5]

In recent years, we have devoted to explore the new organic reactions based on the transition metal-free hydride transferring strategy, especially under the promotion of bases.[6-8] In 2014, we noticed Marder's report on the Zn-promoted borylation under basic conditions,[3c] and we were interested in the effect of zinc catalyst in such reactions. We performed a control reaction in the absence of zinc salt using only base to promote boronation reaction of 4-biphenyl iodide under transition metal-free conditions (Scheme 1, eq 1). After 12 hours' reaction at 110 °C, boronic ester was obtained in 69% yield, and of the dehalogenation product was also obtained in 21% yield as the main side-product which consumes quite percentage of aryl halide starting materials. Trace amount of coupling product from the coupling of 4-biphenyl iodide with toluene was observed.

Scheme 1. Borylation versus Dehalogenation of Aryl Halides.

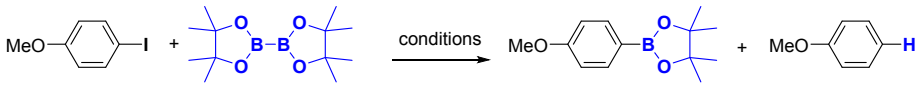


Another example attracted us is using 5-iodo-1-methyl-1H-indole as substrate, in which we observed relatively low yield in borylation (Scheme 1, eq 2). Only 48% yield of desired boryl ester was obtained under basic conditions in the presence of $B_2(pin)_2$, whereas the dehalogenation product dominated the half of the reaction. When the reaction was performed in the presence of benzaldehyde instead of diboronic ester in DMF, the deiodinated product was then obtained in 86% (Scheme 1, eq 2). [8c] This indicates benzaldehyde and DMF cooperatively work as a promoter and a hydrogen source to efficiently achieve the dehalogenation.

Dehalogenation is also an important organic transformation in synthesis,[9a] and various methods have been developed, including metal-halogen exchange, reduction using transition-metal catalyst, and radical dehalogenation reactions.[9b-f] In radical processes, Bu_3SnH and SmI_2[11-12] have been widely applied as an efficient dehalogenation reagents albeit with the potential health risks. Alcohols have also been utilized in the dehalogenation reactions. However, large excess amounts of alcohols and strong bases are normally needed.[9e-f] The fact that aldehydes have been barely reported as a reductant for such reactions together with the results summarized above inspired us to dig out the nature of the direct borylation as well as the competing dehalogenation of aryl halides.

Unfortunately, during our systematically exploration of the nature the competing hydride transferring dehalogenation and borylation since 2015, several reports concerning the transition-metal free radical borylation reactions emerged sequentially (Table 1).[10] In some of these reports, the dehalogenation was mentioned but no systematically investigation has been presented.

Table 1. Borylation of Aryl Halides



entry	reference	conditions	reported results		repeated results	
			R-B (%)[a]	**R-H** (%)	**R-B** (%)[a]	**R-H** (%)
1	ref. 3d	KOMe, $ZnBr_2$ (10 mol %), IMes (20 mol %), MTBE, rt, 12 h	68	8[b]	62 (GC: 69)[b]	(GC: 5)[b]
2	ref. 10e	KOMe, 4-PhPy (cat.), MTBE, 85 °C, 12 h	85 (GC: 90)[b]	–	73 (GC: 79)[b]	(GC: trace)[b]
3	ref. 10f	CsF, Py, DMSO, 105 °C, 2 h	75 (NMR: 94)[c]	–	75 (GC: 80)[b]	(GC: 7)[b]
4	this work	KO^{t}Bu, 1,10-Phen (cat.), toluene-DMSO, 110 °C, 12 h	–	–	65 (GC: 70)[b]	(GC: 16)[b]

[a] Isolated yield. [b] Yield was determined by GC analysis. [c] Yield was determined by NMR analysis.

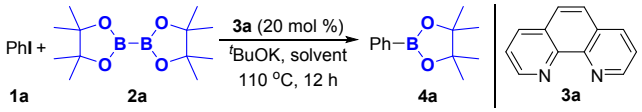
Later, after partially report the results on the dehalogenation reaction,[8c] in this article, we report the development and controlling of both the direct borylation of aryl halides promoted by 1,10-phentharoline and bases, and its competing dehalogenation of aryl halides using aldehydes as a powerful hydrogen source.

There are several questions involving in this base-promoted borylation versus dehalogenation of aryl halides: 1) Are these two transformations radical processes? 2) What is the pathway of the dehalogenation? 3) Are the borylation and dehalogenation controllable? 4) How to inhibit the diborylation[3e] products in the borylation reaction? We now present our research by trying to understand above questions.

RESULTS AND DISCUSSION

Investigations of direct borylation of aryl halides versus dehalogenation of aryl halides. On the basis of aforementioned results in Scheme 1, the reaction conditions of direct borylation of aryl halides has been investigated. First, various solvents were investigated using 1,10-phenathroline **3a** as an initiator. In all cases, the starting material **1a** disappeared. The only side-product was deiodination product. The reaction between **1a** and **2a** in DMSO and DMA gave much better yield of **4a** than the other solvents screened (Table 2, entries 2, 7 vs 1, 3-6). Then the mixed solvent was studied (entries 8-13), and among them the mixture of toluene and DMSO further increased the yield of **4a** to 68% (entry 3), whereas the others gave no improvement of yields.

Table 2. Screening of Solvents for the Direct Borylation of Aryl Halides



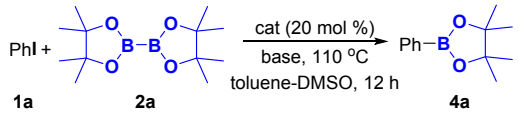
entry[a]	solvent	**4a**(%)[b]
1	toluene	22
2	DMSO	56
3	DMF	46
4	dioxane	20
5	DME	5
6	DMP	23
7	DMA	59
8	toluene-DMA[c]	52
9	toluene-dioxane[c]	27

10	toluene-DMF[c]	23
11	toluene-DMP[c]	42
12	toluene-DME[c]	6
13	toluene-DMSO[c]	68

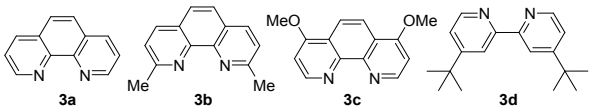
[a] Conditions: **1a** (0.5 mmol), **2a** (1.5 mmol), **3a** (20 mol %), ^{t}BuOK (1 mmol), solvent (1 mL), 110 °C, argon, 12 h. [b] Conversions determined by GC using mesitylene as internal standard. [c] The volume ratio for the mixed solvent is 1:1.

Next, initiator , base, and reaction temperature were studied using the mixture of toluene and DMSO (1:1) as solvent (Table 3). Except metal butoxides (entries 1-3), other bases such as MeOK and KOH afforded much lower yields (entries 4 and 5). What should be pointed out is MeOK and KOH have been used as bases in previous work as the optimized bases in zinc-catalyzed or base-promoted borylation reactions.[2d,5a-c] Moreover, the initiator herein, 1,10-pehnthroline **3a**, has been normally used as a ligand in previous work.[13] Several other substituted phenanthronlines **3b-d** were also investigated, while phenanthronlines **3b** and **3c** gave only 6% to 8% yields (entries 6 and 7). Bipyridine **3d** could work as a promoter despite the yield was much lower than that of 1,10-phenanthroline (entry 8). The blank reaction without 1,10-phenanthroline afforded only trace of **4a** (entry 9), indicating 1,10-phenanthroline may play a role of a catalyst. When the reaction was performed at lower temperature, the yield of **4a** decreased too (entries 10-11). Finally, we chose the conditions listed in entry 1 as the standard reaction conditions for further study.

Table 3. Screening of Other Conditions for the Direct Borylation of Aryl Halides

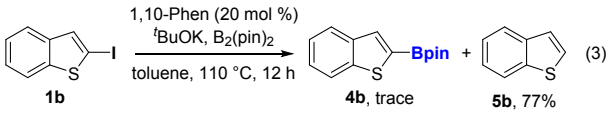


entry[a]	cat	base	temperature(°C)	**4a**(%)[b]
1	**3a**	^{t}BuOK	110	68
2	**3a**	^{t}BuONa	110	54
3	**3a**	^{t}BuOLi	110	63
4	**3a**	MeOK	110	30
5	**3a**	KOH	110	17
6	**3b**	^{t}BuOK	110	8
7	**3c**	^{t}BuOK	110	6
8	**3d**	^{t}BuOK	110	30
9	–	^{t}BuOK	110	trace
10	**3a**	^{t}BuOK	100	53
11	**3a**	^{t}BuOK	90	32



[a] Conditions: **1a** (0.5 mmol), **2a** (1.5 mmol), **3a** (20 mol %), ^{t}BuOK (1 mmol), solvent (1 mL, a mixture of toluene/DMSO with the volume ratio 1:1), 110 °C, argon, 12 h. [b] Conversions determined by GC using mesitylene as internal standard.

In the further investigations, we found **1b** could not give the desired boronic ester **4b** under standard borylation conditions, but only dehalogenation product **5b** was obtained in 77% yield (eq 3). Although the competing dehalogenation reaction wastes starting material in the borylation reaction, exhibiting a serious practical problem, the investigation of the dehalogenation could help to understand and might open a window for understanding the borylation and the related reactions. In addition, the dehalogenation reaction is a side reaction here but very useful in organic synthesis. Thus the dehalogenation was then investigated.



Hypothesizing the borylation reaction passes through a radical process, the dehalogenation reaction might involve a transfer hydrogenation process, in which the hydrogen source seems crucial. Thus, some compounds might work as more efficient hydrogen sources. In our investigations of direct alkylations of amines and the direct Julia-olefination, we found that alcohols could react through a aldehyde intermediate via a self-hydrogen transferring process.[7] Therefore, we assume that alcohols and aldehydes could be used as the possible hydrogen source. After screening several alcohols and aldehydes, we found that 1 equiv of benzaldehyde could serve as an efficient hydrogen source as 0.5 equiv of benzyl alcohol (Table 4). The solvent effects were also investigated, and we found that using DMF as the solvent without the involvement of **3a** turned to be the best condition for the production of **5b**.[8c]

Table 4. Conditions for Dehalogenation of 1b[a]

entry	[H]	x	**5b**(%)[b]
1	BnOH	0.5	77
2	PhCHO	1	70

[a] Conditions: **1b** (0.5 mmol), ^{t}BuOK (1.0 mmol), [H], DMF (1 mL), 90 °C, argon. [b] By ^{1}H NMR.

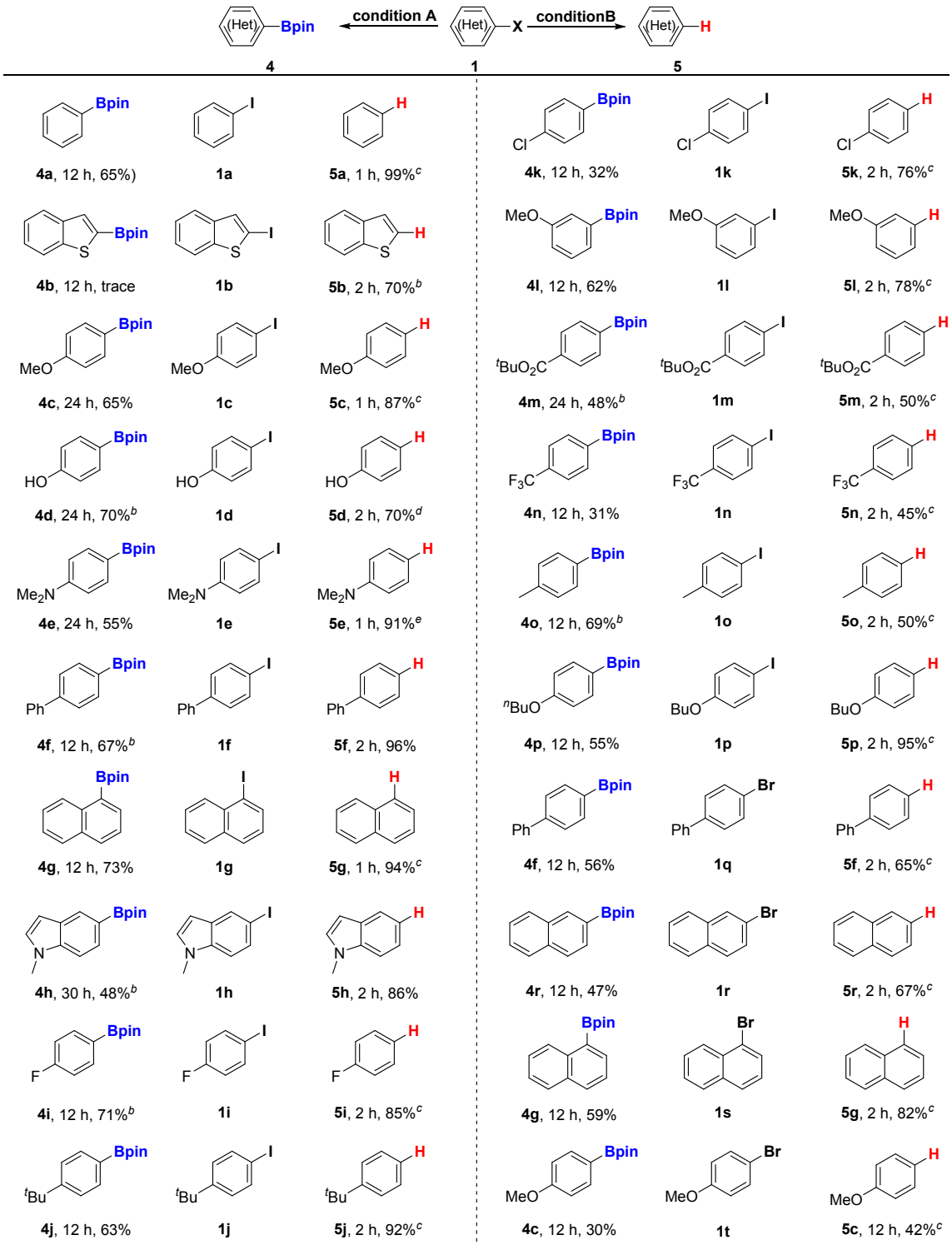
The scope of substrate for both borylation and dehalogenation was then investigated under the standard reaction conditions (Scheme 2).

First, various aryl and heteroaryl iodides have been subjected to the direct borylation conditions using 20 mol% **3a** as an additive in the presence of a mixture of toluene and DMSO; the desired boronic esters were obtained generally in moderate yields (Scheme 2). With respect to the substituted phenyl boronic esters, the products bearing para-substituents such as methoxyl (**4c**), hydroxyl (**4d**), dimethyaminyl (**4e**), phenyl (**4f**), flouro (**4i**), *tert*-butyl (**4j**), chloro (**4k**), methyl (**4o**), and tert-butoxyl (**4p**) were obtained in up to 71% yields. What should be noted is that the hydroxyl group did not need the protections in the reaction. When the para-substituents are electron deficient bearing such as ester (**4m**), trifluoromethyl (**4n**) groups, the borylation yield decreased. 1-Iodonaphthalene (**1g**), 5-iodo-1-methyl-1*H*-indole (**1h**), 1-iodo-3-methoxybenzene (**1l**) gave the corresponding boronic esters **4g**, **4h**, and **4l** in an acceptable yield as well. Aryl and heteroaryl bromides such as 4-bromo-1,1'-biphenyl (**1q**), 2-bromonaphthalene (**1r**),1-bromonaphthalene (**1s**), and 1-bromo-4-methoxybenzene (**1t**) have also been subjected to the direct borylation conditions affording the corresponding boronic esters in moderated yields.

Whereas the treatment of the same starting materials with ^{t}BuOK with 1.0 equiv of benzaldehydes afforded the desired

dehalogenation products **5** in high yields (Scheme 2). When substituted phenyl ioides bearing para-substituents such as methoxyl (**1c**), hydroxyl (**1d**), dimethyaminyl (**1e**), phenyl (**1f**), flouro (**1i**), *tert*-butyl (**1j**), chloro (**1k**), methyl (**1o**), and tert-butoxyl (**1p**) were subjected to the dehalogenation conditions, up to 99% yields were obtained. Hydroxyl group in aryl iodides (**1d**) does not need the protections in the reaction, yielding the corresponding phenol in 70% yield. When the para-substituents are electron deficient bearing such as ester (**1m**), trifluoromethyl (**1n**) groups, the dehalogenation yields were moderate. 1-Iodonaphthalene (**1g**), 5-iodo-1-methyl-1*H*-indole (**1h**), 1-iodo-3-methoxybenzene (**1l**) gave the corresponding **5g**, **5h**, and **5l** in good yields as well. Aryl and heteroaryl bromides such as 4-bromo-1,1'-biphenyl (**1q**), 2-bromonaphthalene (**1r**),1-bromonaphthalene (**1s**), and 1-bromo-4-methoxybenzene (**1t**) have also been subjected to the dehalogenation conditions affording the corresponding in good yields.

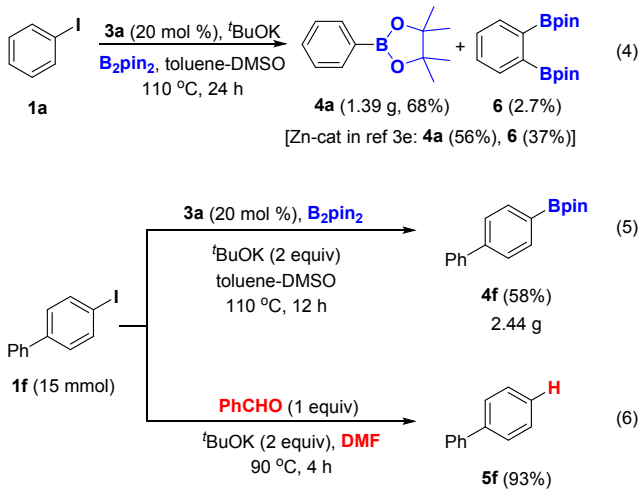
Scheme 2. Control of the Competing Dehalogenation versus Borylation of Aryl Hadides under Transition Metal-Free Conditions [a]



[a] **Condition A: 1** (0.5 mmol), **2a** (1.5 mmol), **3a** (20 mol %), ^{t}BuOK (1 mmol), toluene (0.5 mL), DMSO (0.5 mL), 110 °C, argon. **Condition B: 1** (0.5 mmol), ^{t}BuOK (1.0 mmol), PhCHO (0.5 mmol), DMF (1 mL), 90 °C, argon. [b] 4 equiv of B_2pin_2. [c] Determined by GC. [d] Determined by ^{1}H NMR. [e] 3 equiv of ^{t}BuOK.

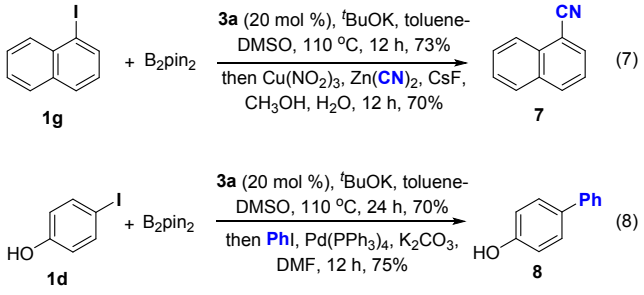
Synthetic applications of direct borylation and dehalogenation. To demonstrate the potential utilities of current methods, the gram-scale synthesis of phenyl boronic ester **4a** was performed under the standard reaction condition A in 68% yield (Scheme 3, eq 4). The diborylation side-product **6** was obtained in 37% along with the target borylation product **4a** in 1/1.5 ratio.[3d] In current work, the diborylation side-product **6** has been inhibited and only less than 3% of **6** was isolated in the gram-scale reaction. The mechanism for the formation of diborylation products is not clear. We believe it might be related to a benzyne pathway. 4-Iodo-1,1'-biphenyl **1f** was then subjected to both borylation and dehalogenation conditions. **4f** and **5f** were obtained in more than 2 grams, respectively (Scheme 3, eq 5 and eq 6).

Scheme 3. The Competition Control[a]



This method was also applied in the synthesis of nitrile **7** and hydroxyl benzene **8** under protecting group-free conditions (Scheme 4, eq 7 and eq 8). The results mentioned above demonstrated the synthetic ability of this work.

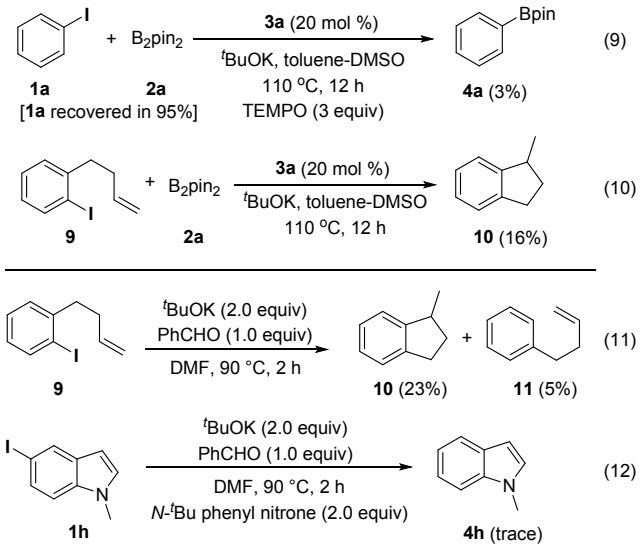
Scheme 4. The Competition Control



The radical nature of borylation and dehalogenation. The competing borylation and dehalogenation reactions of aryl halides are both suspected as radical reactions, passing through the same aryl radical intermediates. To probe the mechanism of both reactions, the radical trapping experiments were carried out (Scheme 5). In the standard borylation conditions, the addition of three equivalents of radical trapping reagent TEMPO could efficiently inhibit the reaction of **1a** and **2a** (Scheme 5, eq 9). This indicates that radical intermediates could be involved in the borylation. The radical nature of borylation reaction was further confirmed by the radical clock experiment, in which the cyclization compound **10** was obtained in 16% yield (eq 10).

On the other hand, in the dehalogenation reaction, trapping experiments were also investigated. The radical clock experiment of **9** gave corresponding cyclization product **10** in 23% yield (eq 11). And *N-tert* butyl phenyl nitrone, a typical radical scavenger, could inhibit the dehalogenation reaction of **1h** (eq 12). All these experimental results indicate that the dehalogenation reaction also undergo a radical pathway. The near recent report also supports the conclusions.[9f]

Scheme 5. Radical Trapping Experiments

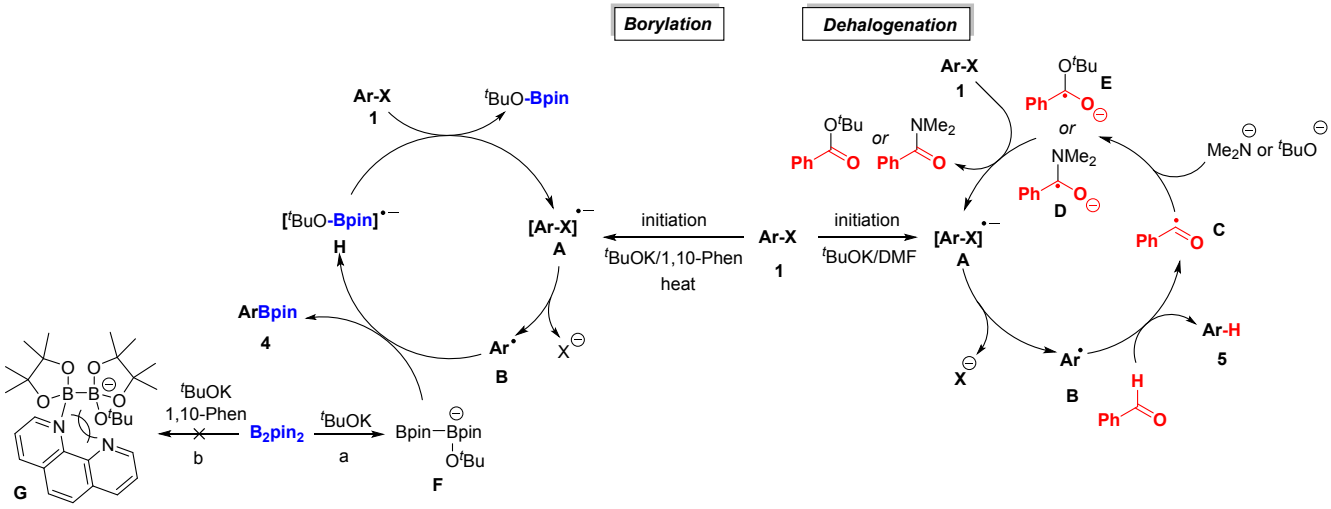


Discussion of the plausible reaction mechanism. A plausible reaction mechanism for the competing borylation and dehalogenation reactions has been proposed in Scheme 6. First, radical anion **A** is generated from aryl halides **1** by trapping electrons from 1,10-Phen and ^{t}BuOK under heating conditions.[6,13] 1,10-Phen plays same role as reported in our previous work.[6] Radical anion **A** quickly converts to aryl radical **B**, which is trapped by ^{t}BuO-(B_2pin_2) anion **F** to borylation products **4** or by hydrogen source (PhCHO or DMF) to form the dehalogenation products **5**. Both 1,10-Phen and ^{t}BuOK are bulky ligands for B_2pin_2, therefore the formation of complex **G**, which is similar to previous proposed key intermediate as an electron donor, is not possible under our conditions. This is why such reaction pathway via intermediate **G** is not suitable in this work. In other hand, under the borylation conditions, the aryl radical can trap the active hydrogen on the solvent to produce the dehalogenation product, which is a remarkable completing side-reaction. Thus by the control of hydrogen source, the dehalogenation reaction can be either inhibited or realized. This mechanism is different from previous proposals in which unbulky pyridine rings were bonding to B_2pin_2 to trigger the radical process.

The detailed pathway for the dehalogenation via a benzoyl radical has been well established based on the studies including

kinetic study, KIE and trapping reactions, deuterium labelling experiments, and control reactions.[8c] In Scheme 6, radical anions **E** or **D** is in situ generated by the reaction of benzoyl radical **C** and Me_2N- from DMF. **D** or **E** then reacts with Ar-X via a SET process to afford radical anion **A**, followed by the formation of aryl radical **B**. Benzoyl radical **C** was regenerated during the hydrogen transferring reduction of **B**. The kinetic study showed that the initial rate of PhCHO is 35.6 mM/min, and this is faster than that of $PhCH_2OH$ (9.3 mM/min), suggesting $PhCH_2OH$ is not the indirect hydrogen source in the presence of PhCHO via a Cannizzaro reaction.

Scheme 6. Proposed Mechanism.



CONCLUSION

In conclusion, a selectivity-controllable transition metal-free borylation and dehalogenation of aryl halides promoted by 1,10-phentharoline and bases has been developed. The competing dehalogenation side-products have been controlled by carefully controlling the borylation conditions under borylation conditions. The dehalogenation of aryl halides using benzyl aldehyde as hydrogen source under basic conditions has also been developed. Based on the experimental evidence, the radical nature of these transformations have been revealed. As a complement of Grignard reagent-based borylation and hydrogenation of aryl halides, this work demonstrates the synthetic practicability in pharmaceutical-oriented organic synthesis.

EXPERIMENTAL SECTION

General information. Solvents were pre-dried over activated 4 Å molecular sieves and heated to reflux over sodium (toluene, THF) or calcium hydride (CH_3CN, DMF, DMA, DMP DME, 1,4-dioxane, DMSO) under an argon atmosphere and collected by distillation. ^1H, $^{13}C\{^1H\}$ NMR spectra were recorded on a Bruker 400 spectrometer; Chemical shifts are reported in δ units relative to $CDCl_3$ [^1H, δ = 7.26; ^{13}C, δ = 77.36]. **1a-1d**, **1f-1g**, **1i-t** were purchased from commercial sources.

*4-Iodo-N,N-dimethylaniline (**1e**).* 4-Iodoaniline (10 mmol) was dissolved in acetic acid (50 mL). Paraformaldehyde (100 mmol) was added and slowly added sodium cyanoborohydride (50 mmol). The reaction mixture was stirred at room temperature for 12 h. Then the solution of NaOH (1 M) was slowly added until it was strongly basic. The mixture was extracted with ethyl acetate and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, concentrated and purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 20:1:1) to give the **1e**, green solid, 704 mg, 9%, mp 78−79 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (dt, *J* = 9.6, 2.6 Hz, 2H), 6.48 (dt, *J* = 9.6, 2.6 Hz, 2H), 2.91 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 137.6, 114.7, 77.5, 40.4.[14]

*5-Iodo-1-methyl-1H-indole (**1h**).* 5-Iodo-1*H*-indole was weighed directly into a Schlenk tube and dried under high vacuum for 15 min. THF was added and stirred. NaH (1.5 equiv.) was slowly added at 0 °C. After stirring for 30 min at 0 °C, methyl iodide (1.5 equiv.) was added. The mixture was then warmed up to r.t. and the resulting reaction mixture was monitored by TLC. The reaction was quenched by H_2O and extracted with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, concentrated and purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford **1h** as a yellow solid, 1.3 g, 85%, mp 74−75 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 131.0, 129.8, 129.7, 129.6, 111.3, 100.3, 83.0, 33.0.[15]

General procedure for Borylation of Aryl Halides (General Procedure 1). 2 (1.5 mmol, 389 mg), **3a** (0.1 mmol, 18 mg) and ^{t}BuOK (1.0 mml, 112 mg) were weighed directly into a Schlenk tube and dried under high vacuum for 15 min. Solvent (1 mL) was added. **1** (0.5 mmol) was added at 110 °C under stirring. The reaction was monitored by TLC. The reaction was quenched by H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, concentrated and purified on silica gel chromatography to give the product.

*4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4a**).* This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford an orange oil, 67 mg, 62%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82-7.80 (m, 2H), 7.46 (tt, *J* = 7.4, 1.6 Hz, 1H), 7.38-7.34 (m, 2H), 1.34 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.8, 131.3, 127.7, 83.8, 24.9.[5a]

*2-(4-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4c**).* This compound was prepared according to General Procedure 1 for 24 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a yellow oil, 72.1 mg, 62%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz,

2H), 6.89 (d, J = 8.4 Hz, 2H), 3.82 (s, 3H), 1.33 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 136.5, 113.3, 83.6, 55.1, 24.9.[16]

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenol ***(4d)***. This compound was prepared according to General Procedure 1 for 24 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 20:1:1) to afford a yellow solid, 77.5 mg, 70%, mp 110−111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 5.68 (brs, 1H), 1.33 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 136.7, 114.9, 83.7, 24.6.[5a]

N,N-Dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline ***(4e)***. This compound was prepared according to General Procedure 1 for 24 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a white solid, 67.5 mg, 55%, mp 119−120 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.4 Hz, 2H), 6.69 (d, J = 8.4 Hz, 2H), 2.98 (s, 6H), 1.32 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 136.2, 111.3, 83.2, 40.1, 24.8.[5a]

2-([1,1'-Biphenyl]-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane ***(4f)***. This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a yellow solid, 93.1 mg, 67%, mp 111−112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.0 Hz, 2H), 7.61 (dd, J = 8.0, 1.6 Hz, 4H), 7.45-7.42 (m, 2H), 7.37-7.33(m, 1H), 1.36 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 141.1, 135.3, 128.8, 127.6, 127.3, 126.5, 83.8, 24.9.[16]

4,4,5,5-Tetramethyl-2-(naphthalen-1-yl)-1,3,2-dioxaborolane ***(4g)***. This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a yellow solid, 92.5 mg, 73%, mp 52−53 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 8.0 Hz, 1H), 8.08 (dd, J = 6.8, 1.2 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.55-7.51 (m, 1H), 7.47 (dd, J = 15.8, 7.0 Hz, 2H), 1.42 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.0, 135.7, 133.2, 131.6, 128.4 (two peak), 126.3, 125.5, 125.0, 83.7, 25.0.[17]

(1-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole ***(4h)***. This compound was prepared according to General Procedure 1 for 30 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a yellow solid, 62 mg, 48%, mp 98−99 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.03 (d, J = 3.0 Hz, 1H), 6.50 (d, J = 3.0 Hz, 1H). 3.79 (s, 3H), 1.37 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 128.9, 128.8, 128.2, 127.6, 108.6, 101.7, 83.4, 32.8, 25.0.[5a]

2-(4-Fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane ***(4i)***. This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a yellow oil, 78.6 mg, 71%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 8.4, 6.4 Hz, 2H), 7.05 (t, J = 9.0 Hz, 2H), 1.34 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 163.8, 137.0 (d, J = 7.8 Hz), 114.8 (d, J = 20 Hz), 83.9, 24.7.[5a]

2-(4-(tert-Butyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4j**). This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a colorless oil, 81.7 mg, 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 1.35 (s, 12H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 134.9, 124.8, 83.7, 35.0, 31.3, 25.0. [18]

2-(4-Chlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4k**). This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a white solid, 38.3 mg, 32%, mp 50−51 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 1.34 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 136.3, 128.2, 84.2, 25.0. [5a]

2-(3-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4l**). This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a colorless oil, 72.3 mg, 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.6 Hz, 1H), 7.33–7.25 (m, 2H), 7.00 (dd, J = 8.4, 2.4 Hz, 1H), 3.83 (s, 3H), 1.34 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 129.1, 127.3, 118.9, 118.0, 84.0, 55.4, 25.0. [18]

Tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate ***(4m)***. This compound was prepared according to General Procedure 1 for 24 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a yellow oil, 73.7 mg, 48%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 2H), 7.83(d, J = 7.6 Hz, 2H), 1.59 (s, 9H), 1.35 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 134.5, 134.2, 128.4, 84.1, 81.1, 28.2, 24.9.[5a]

4,4,5,5-Tetramethyl-2-(4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane ***(4n)***. This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a yellow solid, 42.5 mg, 31%, mp 72−73 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz. 2H), 7.61 (d, J = 7.6 Hz, 2H), 1.36 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.0, 133.0, 132.7, 129.4, 126.1, 124.3 (q, J = 3.8 Hz), 122.8, 84.3, 24.8.[16]

(4,4,5,5-tetramethyl-2-(p-tolyl)-1,3,2-dioxaborolane ***(4o)***. This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a yellow oil, 75.3 mg, 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0, 2H), 7.18 (d, J = 8.0, 2H), 2.36 (s, 3H), 1.33 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 134.8, 128.6, 83.6, 24.9, 21.7.[5a]

2-(4-Butoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4p**). This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a colorless oil, 75.7 mg, 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.0 Hz, 2H), 3.99 (t, J = 6.8 Hz, 2H), 1.80-1.73 (m, 2H), 1.54-1.44 (m, 2H), 1.33 (s, 12H), 0.97 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 136.6, 114.0, 83.6, 67.6, 31.4, 25.0, 19.4, 14.0.[16]

4,4,5,5-Tetramethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborolane (**4r**). This compound was prepared according to General Procedure 1 for 12 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a white solid, 59.5 mg, 47%, mp 55−56 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.86–7.83 (m, 3H), 7.53-7.46 (m, 2H), 1. 40 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 135.2, 133.0, 130.6, 128.8, 127.9, 127.1 (two peaks), 125.9, 84.1, 25.1. [18]

General procedure for dehalogenation of Aryl Halides (General Procedure 2). ^{t}BuOK (1.0 moml, 112 mg) was weighed directly into a Schlenk tube and dried under high vacuum for 15 min. Then DMF (1 mL), **1**, and PhCHO(52 μL) were added and stirred at 90 °C and the reaction was monitored by TLC. The reaction mixture was purified on silica gel chromatography (EtOAc/petroleum ether as eluent) to give the product.

5a, ***5c***, ***5d***, ***5g***, ***5i-5r*** were prepared according to General Procedure 2. Yields were determined by GC using mesitylene (69 μL) as internal standard. The structure was confirmed by standard benzene sample by GC.

N,N-Dimethylaniline ***(5e)***. This compound was prepared according to General Procedure 2 for 2 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 20:1:1) to afford a yellow oil, 55 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.22 (m, 2H), 6.26-6.70 (m, 3H), 2,93 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 129.1, 116.7, 112.7, 40.7. [8c]

*Biphenyl (**5f**)*. This compound was prepared according to General Procedure 2 for 2 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 150:1:1) to afford a white solid, 75.1 mg, 96%, mp 68−69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.57 (m, 4H), 7.44-7.40 (m, 4H), 7.32 (tt, *J* = 7.4, 1.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 128.8, 127.3(two peaks).[8c]

*1-Methyl-1H-indole (**5h**)*. This compound was prepared according to General Procedure 2 for 2 h and was purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to afford a colorless oil, 56.6 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.30 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.12-7.08 (m, 1H), 7,01 (d, *J* = 3.2 Hz, 1H), 6.47 (dd, *J* = 3.2, 0.8 Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 128.9, 128.5, 121.5, 120.9, 119.3, 109.3, 101.1, 32.7.[8c]

Gram scale preparation of 4a. B_2Pin_2 (30 mmol, 7.62 g), **3a** (2 mmol, 0.36 g) and ^{t}BuOK (20 mmol, 2.24 g) were weighed directly into a Schlenk tube and dried under high vacuum for 15 min. Then solvent (20 mL) was added and stirred. The **1a** (10 mmol) was then added and stirred at 110 °C and the reaction was monitored by TLC. Then the reaction was quenched by H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, concentrated and purified on silica gel chromatography using petroleum ether/CH_2Cl_2/EtOAc (50:1:1) to afford **4a** as a colorless oil, 1.39 g, 68%.

Gram scale preparation of 4f. B_2Pin_2 (45 mmol, 11.4 g), **3a** (3 mmol, 0.54 g) and ^{t}BuOK (30 mmol, 3.37 g) were weighed directly into a Schlenk tube and dried under high vacuum for 15 min. Then solvent (30 mL) was added and stirred. The **1f** (15 mmol) was then added and stirred at 110 °C and the reaction was monitored by TLC. Then the reaction was quenched by H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, concentrated and purified on silica gel chromatography using petroleum ether/CH_2Cl_2/EtOAc (50:1:1) to afford **4f** as a solid, 2.44 g, 58%.

Gram scale preparation of 5f. The ^{t}BuOK (30 moml, 3.37 g) was weighed directly into a Schlenk tube and dried under high vacuum for 15 min. Then solvent (30 mL) was added and stirred. The **1f** (15 mmol) and PhCHO (15 mmol, 1.52 mL) were added and stirred at 90 °C and the reaction was monitored by TLC. Then the reaction was quenched by H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, concentrated and purified on silica gel chromatography using petroleum ether/CH_2Cl_2/EtOAc (100:1:1) to afford **5f** as a white solid, 2.15 g, 93%.

*1-Naphthonitrile (**7**)*. To the solution of **4g** (0.29 mol, 74 mg) in 2.5 mL MeOH was added $Cu(NO_3)_2$•$3H_2O$ (242 mg, 1.00 mmol), $Zn(CN)_2$ (176 mg, 1.50 mmol), CsF (76.0 mg, 0.500 mmol), and H_2O (1.0 mL). The reaction vessel was sealed tube and stirred vigorously at 100 °C for 12 h. The reaction was quenched by saturated NH_4Cl aq. and extracted with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, concentrated and purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 100:1:1) to give the **7**, yellow solid, 31.2 mg, 70%, mp 34−35 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.93-7.90 (m, 2H), 7.71-7.67 (m, 1H), 7.64-7.60 (m, 1H), 7.52 (dd, *J* = 8.4, 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.3, 132.9, 132.7, 132.4, 128.7, 128.6, 127.6, 125.2, 125.0, 117.9, 110.2.[19]

*4-Phenylphenol (**8**)*. **4d** (0.3 mmol, 66 mg), $Pd(PPh_3)_4$ (18 mg, 1.5 mmol %) and K_2CO_3 (83 mg, 0.6 mmol) were weighed directly into a Schlenk tube and dried under vacuum for 15 min. DMF (1 mL) and PhI (41 μL, 0.36 mmol) were added, and the solution was stirred at 100 °C for 12 h. The solution was concentrated and purified on silica gel chromatography (petroleum ether/CH_2Cl_2/EtOAc = 20:1:1) to give the **8**, white solid, 38 mg, 75%, mp 161−162 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.58 (s, 1H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.48 (d, *J* = 8.8 Hz, 2 H), 7.40 (t, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.2, 140.3, 131.0, 128.8, 127.8, 126.4, 126.0, 115.8.[20]

ASSOCIATED CONTENT

Supporting Information

NMR spectra for all products. This material is available free of charge *via* the Internet at http://pubs.acs.org.

NMR spectra (PDF)

AUTHOR INFORMATION

ybkang@ustc.edu.cn
ias_jpqu@njtech.edu.cn
# These authors contributed equally to this work.

Notes

The authors declare no competing financial interest.

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