Boric Acid as Highly Efficient Catalyst for the Synthesis of Phenols from Arylboronic Acids

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ABSTRACT: A simple, efficient, and environmentally benign boric acid catalyzed methodology for the ipsohydroxylation of arylboronic acid to phenol has been developed using aqueous hydrogen peroxide as an oxidizing agent and ethanol as the solvent. The versatility of this protocol is that the reactions were performed at room temperature in short reaction time under metal-, ligand-, and base-free conditions. © 2014 Wiley Periodicals, Inc. Heteroatom Chem. 25:127–130, 2014; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21138

INTRODUCTION

Phenols and their derivatives are ubiquitous in numerous natural products in monomeric or polymeric forms. They have vast application potential as a key synthetic precursor for the construction of pharmaceuticals, polymers, and naturally occurring compounds [1]. Over the years, various modifications have been made to the reaction conditions leading to novel synthetic methods for their synthesis. Phenols are commonly prepared by nucleophilic aromatic substitution of aryl halides, and Cu-catalyzed

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transformation of diazoarenes and benzyne protocols [2]. However, these methods suffer from major drawbacks such as harsh reaction conditions and diazotization of amino groups to diazoarenes, which is often not compatible with many other functional groups. In addition to it, some literature reported the conversion of aryl halides such as aryl bromides and chlorides into phenols in the presence of Pdbased catalysts, phosphine ligands [3], and aryl iodides into the corresponding phenols in the presence of a Cu-catalyst using non-phosphine ligands [4] at high temperature. Over the last decade, arylboronic acids and their derivatives have emerged as an important moiety in a wide range of organic reactions [5]. Although phenols have been reported as byproducts in many metal-catalyzed reactions of arylboronic acids [6], a detailed literature search revealed only a handful of recent reports available on the direct and efficient conversion of arylboronic acids into phenols. Arylboronic acids are considered as a suitable and potent precursor of phenols because they are safe, stable to heat, moisture, and air, and are commercially available in many forms substituted by functional groups. Accordingly, hydroxylation of arylboronic acids to phenols is reported to be feasible in the presence of MCPBA-H₂O-EtOH [7], acidic Al₂O₃-H₂O₂ $[8], I_2-H_2O_2[9], CuSO_4$ -phenanthroline $[10], H_2O_2$ poly(N-vinylpyrollidone) [11], NH₂OH.HCl:NaOH [12], potassium peroxymonosulfate [13], or aqueous H₂O₂ [14], clay-entrapped Cu(OH)x [15], aqueous ammonia [16], sodium chlorite [17], and tert-butyl

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	$ \begin{array}{c} & OH \\ & & H_{3}BO_{3}/H_{2}O_{2} (30\% \text{ aq}) \\ & & \\ OH \end{array} \xrightarrow{H_{3}BO_{3}/H_{2}O_{2} (30\% \text{ aq})} \\ & & \\$					
Entry	Oxidant	Solvent	Catalyst	Time (min)	Yield (%) ^b	
1.	H_2O_2	_	_	60	05	
2.	$H_2 O_2$	EtOH	_	60	08	
3.	$H_2 O_2$	-	H ₃ BO ₃ (10 mol%)	40	74	
4.	$H_2 O_2$	_	H_3BO_3 (5 mol%)	40	70	
5.	$H_2 O_2$	EtOH	$H_{3}BO_{3}$ (10 mol%)	35	88	
6.	$H_2 O_2$	MeCN	H_3BO_3 (10 mol%)	40	79	
7.	$H_2 O_2$	MeOH	H_3BO_3 (10 mol%)	40	80	
8.	$H_2 O_2$	THF	H_3BO_3 (10 mol%)	40	78	
9.	$H_2 O_2$	CH ₂ Cl ₂	$H_{3}BO_{3}$ (10 mol%)	50	73	
10.	$H_2 O_2$	EtOH-H ₂ O (1:1)	H_3BO_3 (10 mol%)	40	81	
11.	$H_2 O_2$	MeCN-H ₂ O (1:1)	H_3BO_3 (10 mol%)	40	78	
12.	$H_2 O_2$	$MeOH-H_2O(1:1)$	$H_{3}BO_{3}$ (10 mol%)	40	80	
13.	$H_2 O_2$	THF_H ₂ O (1:1)	H_3BO_3 (10 mol%)	40	81	
14.	_	H ₂ O	H_3BO_3 (10 mol%)	60	Trace	
15.	H_2O_2			36 h	80 ^c	

TABLE 1 Optimization of Reaction Conditions for Boric Acid Mediated *ipso*-Hydroxylation^a

^aReaction conditions: phenylboronic acid (0.5 mmol), H₂O₂ (30% aq. 2 mL), and solvent (2 mL); room temperature.

^bIsolated yields.

^cThe reaction did not reach completion.

hydroperoxide [18] etc. Aqueous hydrogen peroxide is an environmentally benign oxidant that shows a high efficiency per weight of oxidant and it is relatively easy to handle [19]. Moreover, in recent years, from the viewpoint of green chemistry, boric acid has achieved special attention as a catalyst in organic synthesis because of its excellent solubility in water, commercial availability, stability, ease to handle, inexpensiveness, and ecofriendly nature. Boric acid is a useful catalyst that has been successfully utilized in numerous organic transformations such as esterification reaction [20], transesterification reaction [21], aza-Michael addition [22], thia-Michael addition [23], Biginelli reaction [24], and decarboxylation of cyclic β -enaminoketoesters [25]. Thus, in this respect, boric acid-H₂O₂ system and use of innocuous ethanol as the solvent offers a perfect combination for the chosen oxidation reaction. In this communication, we wish to report the use of easily available, cheap and environment friendly boric acid as an excellent promoter to convert arylboronic acids to phenols at room temperature under metal-, ligand-, and base-free conditions.

To prove the catalytic activity of boric acid and study the efficacy of hydrogen peroxide in the hydroxylation reactions, we have chosen arylboronic acid (1a; 0.5 mmol) as a model substrate and the reactions were performed under aerobic condition at room temperature. The results are summarized in Table 1. Initially, we conducted a blank reaction in which a mixture of **1a** (0.5 mmol) and aqueous hydrogen peroxide (2 mL) was stirred at room temperature for 1 h. The result was not encouraging and only a small amount of phenol was obtained at the end of the reaction (Table 1, entry 1). When the reaction was performed using ethanol as the solvent, the yield of phenol 2a was slightly enhanced (Table 1, entry 2). We interestingly observed that the reaction furnished the desired product 2a in 74% vield on introducing boric acid (10 mol%) as catalyst (Table 1, entry 3). It was observed that the reaction showed comparatively reduced yield in the presence of 5 mol% catalyst. Encouraged by the good result (Table 1, entry 3), we started to screen the effect of various solvents on the reaction using arylboronic acid, aqueous hydrogen peroxide, and 10 mol% boric acid as reaction promoter (Table 1, entries 5-13). We were pleased to find that the reaction using ethanol as the solvent gave the desired phenol in 88% yield. The reaction was found to proceed smoothly in other solvents as well although showing variation in yields (Table 1, entries 6–13). Likewise, under the same reaction condition, 1:1 aqueous solvents such as ethanol, acetonitrile, methanol, and tetrahydrofuran (THF), respectively, gave comparable results (Table 1, entries 10–13). Interestingly, the use of dichloromethane as the solvent resulted in a relatively reduced yield (Table 1, entry 9). The reaction did not progress in the absence of hydrogen peroxide in aqueous medium (Table 1, entry 14). The catalytic activity of boric acid could further be established by the observation that phenol (2a) was

$R \xrightarrow{OH} H_{3}BO_{3}/H_{2}O_{2} (30\% \text{ aq}) \xrightarrow{OH} OH$						
Entry	R	Time (min)	Yield (%) ^{b,c}			
1.	Н	35	88			
2.	4-C(CH ₃) ₃	25	95			
3.	3-Me	50	89			
4.	4-Me	50	85			
5.	2-OMe	45	88			
6.	4-OMe	45	92			
7.	4-CN	60	91			
8.	4-Cl	65	93			
9.	4-NO ₂	70	88			
10.	4-F	70	80			
11.		60	82			
12.		70	83			
13.	B(OH) ₂	60	88			

 TABLE 2
 Boric Acid Catalyzed Synthesis of Phenols^a

^aReaction conditions: ArB(OH)₂ (0.5 mmol), H₃BO₃ (10 mol%), H₂O₂ (30% aq, 2 mL), and ethanol (2 mL); room temperature.

^bYields of isolated products.

 $^{c}\mathrm{All}$ compounds were characterized by $^{1}\mathrm{H}$ NMR, $^{13}\mathrm{C}$ NMR, FT-IR, and MS.

obtained in good yield in the absence of boric acid only in extended reaction time (Table 1, entry 15).

To understand the scope and limitation of the current methodology, a variety of electronically diverse arylboronic acids were investigated to obtain the hydroxylation product, using boric acid as catalyst and ethanol as the solvent, and the results are summarized in Table 2. With various electron-donating and electron-withdrawing substituents, the *ipso*-hydroxylation products were isolated in good yield (80%–95%). It was observed that different sub-

stituents were tolerated on the aromatic substrate. Electron-rich phenols (Table 2, entries 1–6) were obtained in good yield whereas electron-deficient phenols (Table 2, entries 7–10) were also isolated in satisfactory yields, but comparatively long reaction time was required. The current catalyst system is also effective for aryl boronate esters (Table 2, entries 11 and 12) and heteroaryl boronic acid (Table 2, entry 13).

A probable mechanistic pathway has been proposed for the *ipso*-hydroxylation of arylboronic acids (Scheme 1) following the literature report [12, 26, 27]. Hydrogen peroxide in presence of boric acid is a known system for oxidation reactions [23]. It has been reported that the reaction between H_2O_2 and H_3BO_3 forms adduct **A** [27], which then reacts with phenylboronic acid to form the adduct **B**. Removal of the adduct **D** and subsequent phenyl migration to oxygen atom in the adduct **B** generates adduct **C**. Elimination of water regenerates boronic acid along with the formation of adduct **E**. Finally, hydrolysis of the adduct **E** leads to the formation of phenol.

In summary, we have developed a simple and facile one-pot synthetic method of *ipso*hydroxylation of arylboronic acids to the corresponding phenol using aqueous hydrogen peroxide as an oxidizing agent, ethanol as the solvent, and boric acid as a green catalyst. The characteristic of this protocol is that it is mild, facile, and feasible at room temperature under metal-, ligand-, and basefree conditions.

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SCHEME 1 A plausible mechanistic pathway.

EXPERIMENTAL

General Procedure for Hydroxylation of Arylboronic Acids

A 50-mL round-bottomed flask was charged with arylboronic acid (0.5 mmol), 30% aqueous H₂O₂ (2 mL), ethanol (2 mL), and H_3BO_3 (10 mol%), and the reaction mixture was stirred at room temperature. The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction, the reaction mixture was diluted with water (5 mL), brine (5 mL), and extracted with diethyl ether $(3 \times 15 \text{ mL})$. The separated organic layer was dried over anhydrous sodium sulphate, filtered, and evaporated in a rotary evaporator under reduced pressure. The crude was purified by column chromatography on silica gel (hexane-ethyl acetate) or by crystallization to obtain the desired product. All compounds were characterized by ¹H nuclear magnetic resonance spectroscopy (NMR), ¹³C NMR, Fourier transform infrared spectroscopy (FT-IR), and mass spectroscopy (MS).

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