



D-glucose: An efficient catalyst for oxidative hydroxylation of arylboronic acids to phenols

Balaji P. Kotkar

Research Student,

Department of chemistry, Savitribai Phule Pune University, Ganeshkhind Road,
Ganeshkhind, Pune, Maharashtra 411007.

Email: balajikotkar@gmail.com

Abstract: This article unveils mild and a highly efficient phenol synthesis procedure via aerobic hydroxylation of organoboronic acid using D-glucose as a organocatalyst and aqueous H₂O₂ as an oxidant. The synthesis of phenols was accomplished in the absence of metal, base, ligand and organic solvent in short reaction time.

Key Words: Arylboronic acids, Phenol, ipso-hydroxylation, Hydrogen peroxide, Water.

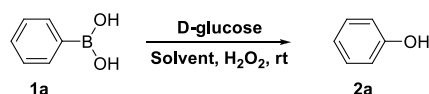
1. INTRODUCTION:

Phenol scaffolds are found in many natural products, agrochemicals and pharmaceuticals¹⁻³. Several methods have been made including Hock's Process⁴, Dow's process and hydrolysis of diazonium salts⁵ for the preparation of phenols. But most of these methods associated with harsher conditions and inferior yield. In recent years, oxidative hydroxylation of arylboronic acid to phenol got much attention due to versatile nature, greater stability and low toxicity of arylboronic acid. Reported literature methods for ipso-hydroxylation use reagents such as N-Oxide,⁶ Oxone,⁷ MCPBA,⁸ CuSO₄-phenanthroline,⁹ CuFe₂O₄,¹⁰ H₂O₂-Cu₂O NP,¹¹ CuNP,¹² H₂O₂-Amberlite IR-120,¹³ H₂O₂-H₃BO₃,¹⁴ H₂O₂-biosilica,¹⁵ HOF,¹⁶ H₂O₂-WERSA (Water Extract of Rice Straw Ashes),¹⁷ dimethyl carbonate¹⁸ etc. Most of these protocols suffer from disadvantages such as metal catalysts, excess oxidizing agent, harsh reaction condition and expensive reagent etc.

In an effort to develop mild, green and efficient method, herein we report the catalytic applicability of D-glucose in ipso-hydroxylation for synthesis of phenols. To the best of our knowledge, this is the first route of direct usage of D-glucose as a catalyst in ipso-hydroxylation reactions.

2. RESULTS AND DISCUSSION

Table 1 Catalyst Screening for ipso-hydroxylation



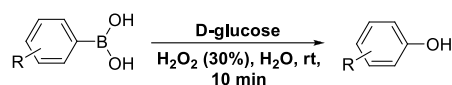
Entry	D-glucose (mol%)	H ₂ O ₂ (ml)	Solvent (2ml)	Time (min)	yields (%) ^b
1	10	-	H ₂ O	120	-
2	-	0.50	H ₂ O	120	45
3	10	0.50	H ₂ O	10	95
4	20	0.50	H ₂ O	10	95
5	10	0.50	EtOH	10	85
6	10	0.50	CH ₃ CN	10	76
7	10	0.50	DMSO	10	81
8	10	0.50	THF	10	66
9	5	0.50	H ₂ O	10	85
10	10	0.25	H ₂ O	10	81

^a Reaction conditions: Phenylboronic acid (1 mmol), 30% H₂O₂, D-glucose catalyst.



^b Isolated yield.

Table 2 Substrate scope^a



Entry	R	Isolated yield (%)
1	H	95
2	<i>p</i> -Me	94
3	<i>p</i> -OMe	90
4	<i>o</i> -Me	91
5	<i>p</i> -NO ₂	94
6	<i>p</i> -NH ₂	93
7	<i>p</i> -Cl	89
8	α -Naphthol	93
9	β -Naphthol	91
10	<i>p</i> -OH	92
11	<i>p</i> -CHO	90
12	<i>p</i> -COCH ₃	95
13	<i>m</i> -CN	93
14	<i>p</i> -I	92

^a Reactions were performed with 1 mmol Arylboronic acid, 0.5 mL 30% H₂O₂ and 10 mol% of D-glucose in 2 ml of water at room temperature.

The initial reaction of phenylboronic acid (1a) with H₂O₂ (0.5 mL) in the presence of 40 mol% of D-glucose in H₂O provided quantitative yield of the phenol (Table 1). The oxidative hydroxylation reaction did not go to completion in the absence of D-glucose (entry 1), which shows the oxidant H₂O₂ alone without D-glucose is not a catalyst for the phenol synthesis. Further optimization showed that only 10 mol% of D-glucose sufficient for the quantitative yield of the product phenol. Different solvents were tested. Water was identified as the best solvent for this reaction. With standard reaction condition, a variety of arylboronic acids were examined to generate the hydroxylation products and the results are summarized in Table 2. Arylboronic acids containing both electron-donating and electron-withdrawing substituents provided good to excellent yields.

3. GENERAL METHOD:

The phenylboronic acid (1 mmol), 30% H₂O₂ (0.50 ml) and D-glucose (10 mol%) were taken in a two-neck round bottomed flask. Then 2 mL of water was added to it and the reaction mixture was stirred at room temperature for 10 min. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was diluted with water, and the filtrate was extracted with ethylacetate (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na₂SO₄, purified by column chromatography on silica-gel (100-200) using hexane/ethyl acetate (9:1) as eluent. Phenol: ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.28 (d, *J* = 8Hz, 2H), 6.84 (d, *J* = 8Hz, 3H), 4.21 (s, br, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 155.4, 129.5, 120.7, 115.1.

4. CONCLUSION:

In summary, we have developed inexpensive and efficient catalyst for the conversion of arylboronic acids to corresponding phenols. A variety of electronically diverse phenols were accessed by operationally simple and safe protocol. The present protocol revamps the phenol synthesis with easy and eco-friendly strategy and offers a clean and environmentally benign alternate to metal chemistry with an excellent scope.

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