

WEPBA as an Efficient Natural Feedstock for *Ips*-hydroxylation Arylboronic Acids

Balaji P. Kotkar

Adarsh Education Society's Arts, Commerce and Science College, Akola Road, Hingoli – 431513.

Abstract

A green and efficient protocol for ipso-hydroxylation of arylboronic acids has been developed using WEPBA (water extract of papaya bark ash) as neat reaction media. The present WEPBA as neat reaction media provides a clean and green strategy to get phenols in excellent yields.

Keywords: Arylboronic acid, Phenol, WEPBA, *ipso*-Hydroxylation

Introduction

Phenol and its derivatives are important functionalities in natural products,¹ pharmaceuticals²⁻⁴ and agrochemicals. Traditional methods for the synthesis of phenols are cumene-phenol process (Hock's process),⁵ hydrolysis of diazonium salts⁶ and Dow's process. Unfortunately, these processes suffer from drawbacks like long reaction time, hazardous reagents and drastic reaction conditions. In order to avoid these drawbacks, the development of mild and time efficient protocols is still of critical importance. Nowadays, ipsohydroxylation have received much attention for the synthesis of phenols. Because arylboronic acids are inexpensive, non toxic and easily available.

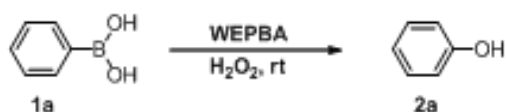
Different *ipso*hydroxylation reactions have been used for the synthesis of phenols in presence of various catalysts such as Oxone,⁷ N-Oxide,⁹ TBHP,¹⁰ CuSO₄-phenanthroline,¹¹ H₂O₂-I₂,¹² H₃BO₃-H₂O₂,¹³ potassiumperoxymonosulphate,¹⁴ MCPBA,¹⁵ lactic acid-H₂O₂,¹⁶ AgNPs-H₂O₂,¹⁷ quinone,¹⁸ biosilica-H₂O₂¹⁹ etc. But, these reported methods suffer from many drawbacks like, use of excess oxidizing agent, higher temperature, expensive metal catalysts, long reaction time etc.

Herein, we wish to report a process for ipso-hydroxylation of arylboronic acid using WEPBA as novel green media.

Results and discussion

Table 1

Optimization of the reaction conditions



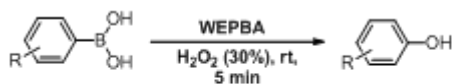
Entry	H ₂ O ₂ (ml)	Time (min)	Yield (%) ^b
1	0.20	120	10
2	0.20	20	80
3	0.30	10	94
4	0.40	5	98

^aReaction condition: Phenylboronic acid (1 mmol), H₂O₂ (30% aq), WEPBA (2 ml) at room temperature.

^bIsolated yields.

^cReaction carried out without WEPBA.

Table 2 Substrate scope



Entry	R	Yield ^b (%)
1	H	95
2	<i>p</i> -Me	93
3	<i>p</i> -OMe	91
4	<i>p</i> -NO ₂	91
5	<i>p</i> -NH ₂	92
6	<i>p</i> -Cl	89
7	α -Naphthol	93
8	<i>p</i> -OH	92
9	<i>p</i> -CHO	90
10	<i>p</i> -COCH ₃	94
11	<i>m</i> -CN	93

^a Reaction conditions: Arylboronic acid (1 mmol), 30% H₂O₂ (0.4 mL), WEPBA (2 ml) at room temperature.

^b Isolated yield.

In preliminary studies, we used, phenylboronic acid (1a) for *ipso* hydroxylation in water extract of papaya bark ash (WEPBA) which was prepared using the established procedure²⁰ and the results are presented in Table 1. When phenylboronic acid was reacted with stoichiometric amount of aq 30% H₂O₂ the corresponding phenol (2a) was obtained in 10% yield (Table 1, entry 1). Interestingly, the combination of 30% H₂O₂ and WEPBA gave 90% conversions within short reaction time of 20 min (entry 2). The amount of H₂O₂ used in the present protocol was also investigated. By increasing the amount of oxidant to 0.40 ml increase in the yield of phenol was observed within 5 minutes (entry 4, Table 1).

The oxidative hydroxylation of aryl boronic acids carrying either electron-donating or electron withdrawing substituents provided the desired phenols in high to excellent yields. Results are summarized in the table 2.

Conclusion

We have developed a a green and sustainable protocol for the *ipso* hydroxylation of arylboronic acids under base and ligand-free conditions. The *ipso* hydroxylation reactions proceeded efficiently employing WEPBA as a green solvent and H₂O₂ as oxidant, affording phenols as products in a short reaction time. Electronically diverse arylboronic acids undergo the hydroxylation reaction and furnished phenols in good yields.

General procedure for the synthesis of phenols

Aryl boronic acids (1 mmol), 30% H₂O₂ (0.2 ml) and WEPBA (2 ml) were added to a 25 mL pressure tube under oxygen atmosphere. The mixture was then stirred until the starting material had been consumed after 5 min. When the reaction was finished, the crude product was purified by flash chromatography on silica gel (PE/EA).

Spectral data of some selected phenols

Phenol: ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.27 (d, *J* = 8 Hz, 2H), 6.85 (d, *J* = 8 Hz, 3H), 4.22 (s, br, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 155.5, 129.4, 120.9, 115.2

4-methoxyphenol: ¹H NMR (400 MHz, CDCl₃, ppm): δ 6.72-6.77 (m, 4H), 4.46 (s, br, 1H), 3.74 (s, 3H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 153.7, 149.4, 116.2, 114.9, 55.5

4-chlorophenol: ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.19 (d, *J* = 8 Hz, 2H), 6.74 (d, *J* = 8 Hz, 2H), 5.21 (s, br, 1H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 154.7, 129.1, 125.9, 116.9

4-hydroxybenzaldehyde ¹H NMR (DMSO, 400 MHz) δ 10.54 (s, 1H), 9.79 (s, 1H), 7.84 – 7.69 (m, 2H), 7.01 – 6.80 (m, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 190.97, 163.32, 132.15, 128.45, 115.91.

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