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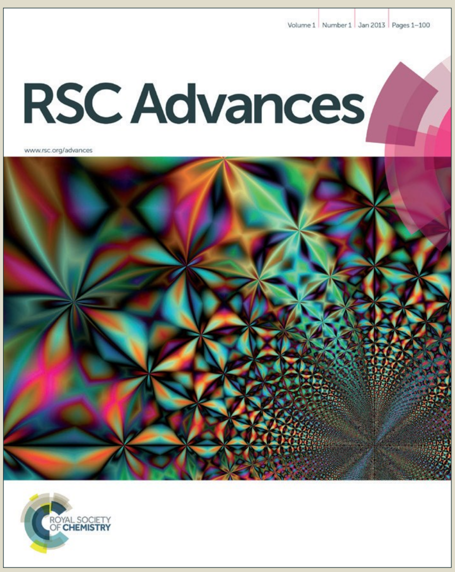

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Journal Name

ARTICLE

H_2O_2 in WERSA: An efficient Green Protocol for *Ipso*-hydroxylation of Aryl/Heteroarylboronic Acid

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A mild, green, economic and efficient protocol has been developed for *ipso*-hydroxylation of aryl/heteroarylboronic acids to phenols using 30% aqueous H_2O_2 as oxidant and WERSA (Water Extract of Rice Straw Ashes) as neat reaction media. All reactions were carried out without using metal, ligand, activator and hazardous organic solvent with excellent yield within a very short reaction time at room temperature. Therefore, this appears to be the cleanest and greenest alternative protocol for ipso-hydroxylation of aryl/heteroarylboronic acids.

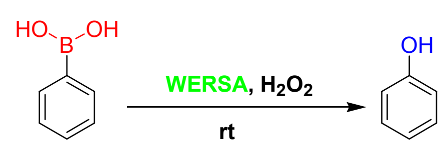
Introduction

Phenols are ubiquitous in nature as they are the key structural constituent of various pharmaceuticals,[1] agrochemicals,[2] polymers[3] and naturally occurring compounds mainly as polyphenols[4] (natural antioxidants). Traditional methods for the preparation of phenols involved nucleophilic substitution of activated aryl halides, Cu-catalysed conversion of diazoarenes[5] and Pd-catalysed conversion of aryl halides[6] to phenols. But these existing routes require harsh reaction conditions due to inactive nature of starting materials. However, as a result of continuous effort of many research groups, arylboronic acids have replaced the traditional inactive synthetic precursor for phenols. *Ipso*-hydroxylation, the generalized method for the conversion of arylboronic acids to phenols is gaining enormous importance due to higher availability, stability and greater functional group diversity of arylboronic acids. As a result various protocols for *ipso*-hydroxylation of arylboronic acids were put forward using different catalysts such as biosilica-H_2O_2,[7] I_2-H_2O_2,[8] Al_2O_3-H_2O_2,[9] PEG-H_2O_2,[10] NH_2OH,[11] KOH-TBHP,[12] $CuSO_4$-Phenantholine,[13] H_3BO_4-H_2O_2,[14] Amberlite IR- 120 resin,[15] supported silver nano particle,[16] organic hypervalent iodine (III)[17] etc.

Even with all the existing protocols, majority of which found to be effective for conversion of arylboronic acids to phenols via. *Ipso*-hydroxylation, there is a serious need for “Green” protocols with greater environmental and economical viability due to some unavoidable drawbacks of the reported protocols such as use of transition metal as catalyst, ligands, bases and harmful organic solvents. Recently Saikia *et.al.,* following the Green Chemistry tools have explored natural feedstock as green alternatives for carrying out two popular organic reactions Suzuki-Miyaura cross coupling[18] and Dakin reaction[19]. Inspired by their work and following the motion of “greening-up” here we wish to report a superb protocol for *ipso*-hydroxylation of arylboronic acids to phenols using WERSA (Water Extract of Rice Straw Ashes) a highly abundant, cheap natural feedstock as neat reaction media and 30% aqueous H_2O_2 as oxidant. To the best of our knowledge this is the first report on *ipso*-hydroxylation of arylboronic acids to phenols using WERSA and we therefore believe that this is an outstanding alternative protocol for synthesis of phenols from arylboronic acids, as reaction condition is mild, straightforward and without use of metal, ligand, bases and solvents. Additional beauty of the protocol is the use of H_2O_2 as oxygen source rather than other oxygen sources like $NaClO_2$,[20] N-Oxide,[21] HOF[22] as H_2O_2 is richer source of oxygen and forms water as byproduct.

Experimental

At the beginning we tried our first reaction with phenylboronic acid (1 mmol) using 30% aqueous H_2O_2 (0.10 mL) as oxidant in WERSA (2 mL) (Scheme 1) which was prepared using the established procedure[23] to check the feasibility of the reaction. We monitored the reaction by TLC in every min and to our delight phenylboronic acid fully converted to the desired product phenol within 10 minutes at room temperature. After that we moved on for optimization of oxidant H_2O_2 needed for full conversion taking phenylboronic acid as model substrate. As a result of optimization as depicted in Table 1 we found that 0.20 mL of 30% aqueous H_2O_2 oxidant were sufficient to complete the reaction within 5 minutes. Along with mild reaction condition, excellent yield, lesser toxicity, operational plainness, cost effectiveness makes this hydroxylation protocol one of the cleanest and greenest alternative protocol ever.



Scheme 1: *Ipso*-hydroxylation of phenylboronic acid to phenol

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† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

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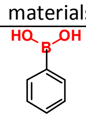
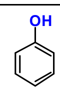
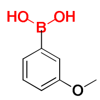
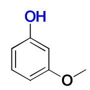
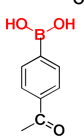
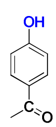
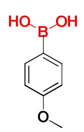
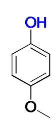
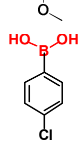
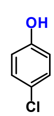
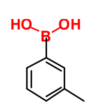
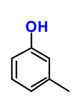
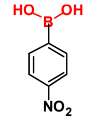
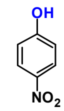
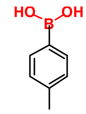
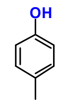
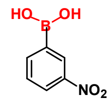
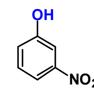
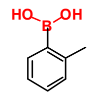
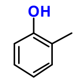
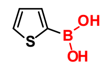
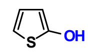
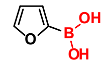
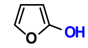
Table 1: Effects of the amount of 30% H_2O_2 and time in the *ipso*-hydroxylation of phenylboronic acid in WERSA at room temperature[a]

Entry	30% H_2O_2 (mL)	Time (min/h)	Yield[b] (%)
1[c]	0.10	24 h	trace
2	0.10	10 min	92
3	0.15	7 min	95
4	0.20	5 min	98

[a] Reaction conditions: phenylboronic acid (1 mmol), 30% H_2O_2 in WERSA (2 mL) at room temperature.
[b] Isolated yields.
[c] Reaction carried out without WERSA.

With the optimized condition, we then carried out numbers of reactions with different electron-rich and electron-poor arylboronic acid to study the substrate scope using this newly designed protocol. According to our expectation, reactions proceeded very smoothly converting various electron-donating and electron-withdrawing groups bearing arylboronic acids to phenols with very good to excellent yield within very short reaction time (Table 2). Results showed that substrate containing electron withdrawing groups were more efficient than electrons donating ones. Moreover, we readily carried out the reaction with some heteroarylboronic acids (Table 2). Till now, there is no earlier report on *ipso*-hydroxylation using such a mild, green and economic reaction condition. Therefore, this seems to be an evergreen protocol with a wide range of substrate scope for *ipso*-hydroxylation of arylboronic acids to phenols.

Table 2: Conversion of aryl/heteroarylboronic acid to phenols in H_2O_2-WERSA system at room temperature[a]

Entry	Starting materials	Products	Time (min)	Yield[b] (%)
1			5	98
2			10	92
3			7	95
4			10	94
5			15	90
6			10	92
7			6	95
8			8	94
9			8	97
10			10	92
11			15	90
12			15	91

[a] Reaction conditions: aryl/heteroarylboronic acid (1 mmol), 30% H_2O_2 (0.2 mL for each substrate) in WERSA (2 mL) at room temperature.
[b] Isolated yields.

Results and discussion

Nucleophilic activation of H_2O_2 is a general fact to use H_2O_2 as oxidant; as a result numbers of bases have already been used to activate H_2O_2 by abstracting a proton so far. Here in this protocol we used only WERSA with H_2O_2 as a neat reaction media for *ipso*-hydroxylation of arylboronic acids to phenols. Perhaps the exact role of WERSA for the reaction is not clearly understood yet. However, literature[24] reveals that rice straw ashes contains oxides of SiO_2 (74.31%), Al_2O_3 (1.40%), Fe_2O_3 (0.73%), TiO_2 (0.02%), CaO (1.61%), MgO (1.89%), K_2O (11.30%), Na_2O (1.85%), P_2O_5 (2.65%) as primary ingredients. Thus water extract of rice straw ashes may contain KOH, NaOH which may be responsible for making WERSA basic enough for nucleophilic activation of H_2O_2 by abstracting its proton. Therefore we proposed a plausible mechanism for *ipso*-hydroxylation of arylboronic acid to phenol using H_2O_2 in WERSA (Figure 1).

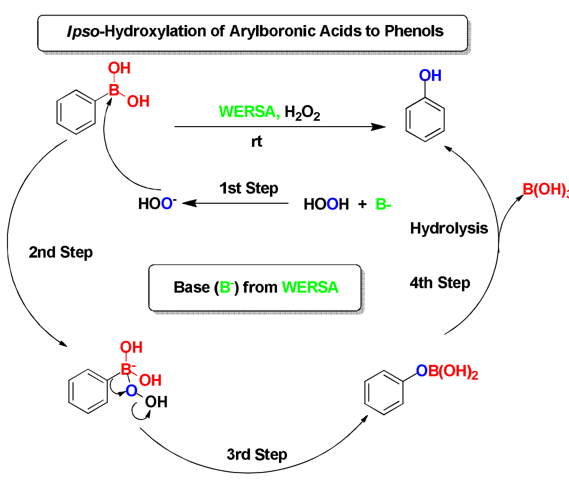


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Figure 1: A plausible mechanism for *ipso*-hydroxylation of arylboronic acids to phenols

Recyclability of WERSA is another attractive feature of this protocol. We reused WERSA upto 5th cycle without significant lose of efficiency (Table 3). Taking phenylboronic acid as model substrate we carried out the WERSA recyclability test. After completion of the reactions, products were extracted with diethylether and WERSA separated from product was washed with more diethylether and reused. Thus we can consider WERSA as a reusable homogeneous catalyst.

Table 3: Recyclability of the catalytic system[a]

Entry	Run	Time (min)	Yield[b](%)
1	1st	5	98
2	2nd	5	98
3	3rd	5	96
4	4th	7	94
5	5th	10	90

[a] Reaction conditions: phenylboronic acid (1 mmol), 30% H_2O_2 (0.2 mL) in WERSA (2 mL) at room temperature.
[b] Isolated yields.

Conclusions

In conclusion, we have developed a green, mild, efficient and aerobic protocol for *ipso*-hydroxylation of arylboronic acids to phenols using H_2O_2 as oxidant in WERSA at room temperature. With these mild reaction conditions, our method is very compatible with various electron-donating and electron-withdrawing groups at *ortho*, *meta* and *para* positions on the aromatic ring. In addition, all reactions occur in shortest reaction time without using any activating agent, metal, ligand and organic solvent. From the environmental and economical point of view, we believe that this is the most greener and efficient protocol for *ipso*-hydroxylation of arylboronic acids to phenols. All these advantages make H_2O_2-WERSA a very adaptable and competitive catalyst system, consequently can be used as clean and safer alternative for various other reactions in laboratory as well as in industry in near future.

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Notes and references

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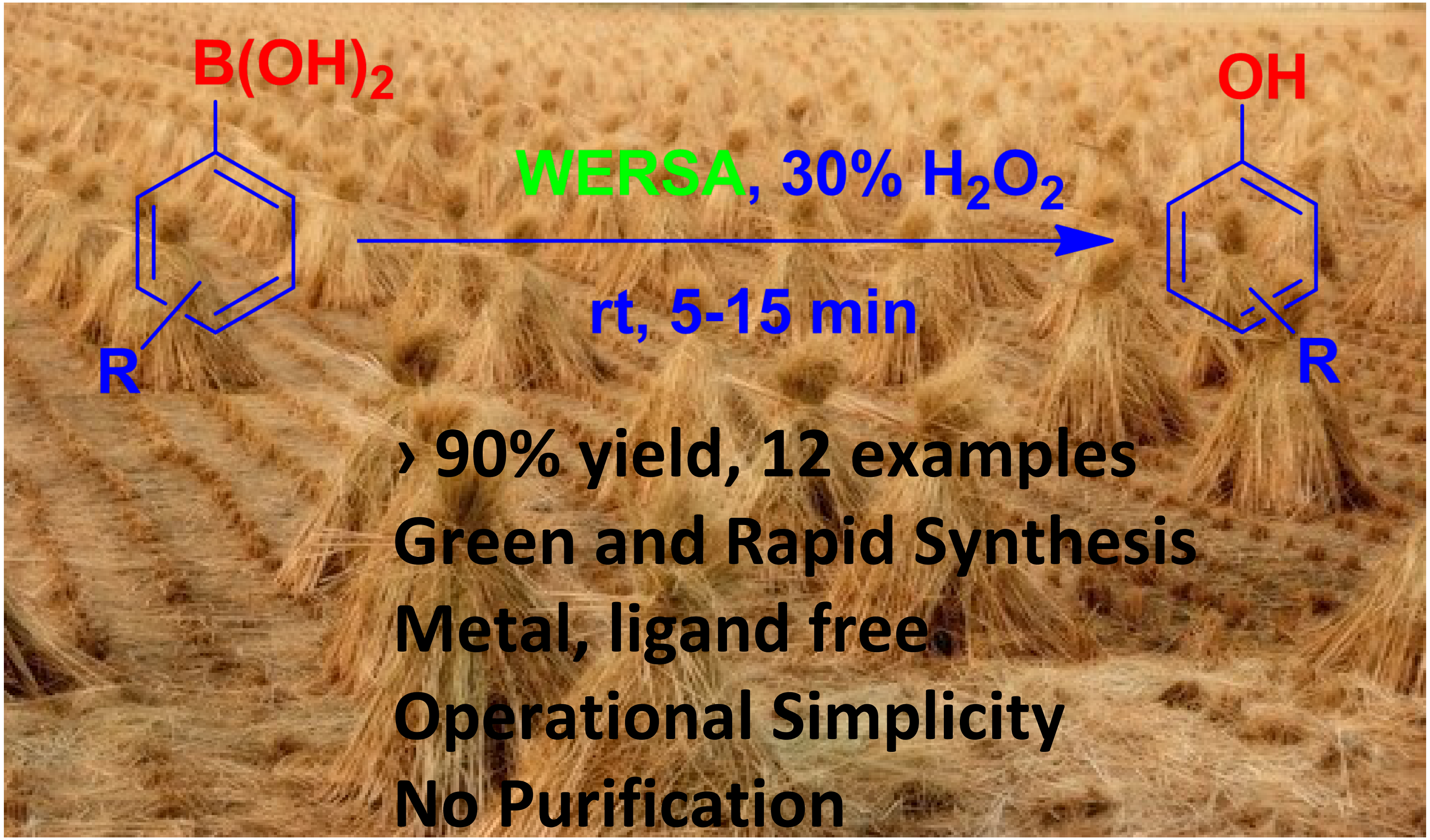
B(OH)2
OH
WERSA, 30% H2O2
rt, 5-15 min
R
R
› 90% yield, 12 examples
Green and Rapid Synthesis
Metal, ligand free
Operational Simplicity
No Purification