CHAPTER 2

IPSO-HYDROXYLATION OF ARYLBORONIC ACIDS UNDER CATALYST-FREE CONDITION

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2.1INTRODUCTION

Solvents play an important role in organic synthesis while in some cases solvents themselves drive the reaction in the absence of catalysts [1]. Such kind of catalyst-free organic reactions offers several advantages like reduced environmental pollutions, uncomplicated experimental and workup procedures, simple purification steps, etc., [2, 3]. Therefore, the catalyst-free organic transformations have received more attention in recent years. On the other hand, "green solvents" have been focused in the past few decades in order to minimize the environmental pollution resulting from the use of hazardous solvents in chemical production [4-7].

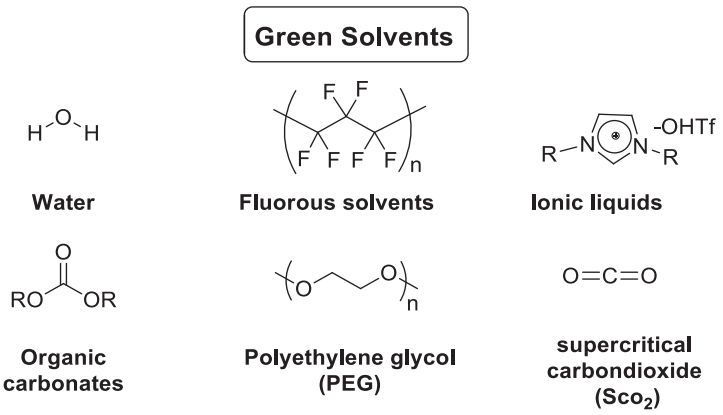


Figure2.1 Various green solvents used in organic synthesis.

Green solvents have been majorly characterized by their level of toxicity, volatility, reusability, stability, flammability, bio-degradability and renewability [8, 9]. In the past decade, water, supercritical CO_2, ionic liquids, organic carbonates, fluorous

compounds and polyethylene glycol (PEG) were identified as green solvents and efficiently used in organic synthesis (Figure**2.1**) [4-9].

Recently, bio-based solvents which are produced from renewable sources have received much attention due to their sustainability and eco-compatibility (Figure**2.2**) [10]. From environmental point of view, bio-based solvents are also considered as green solvents which could be an alternative not only to the conventional petroleum based solvents, but also to the expensive non-bio based green solvents in organic synthesis [10-12].

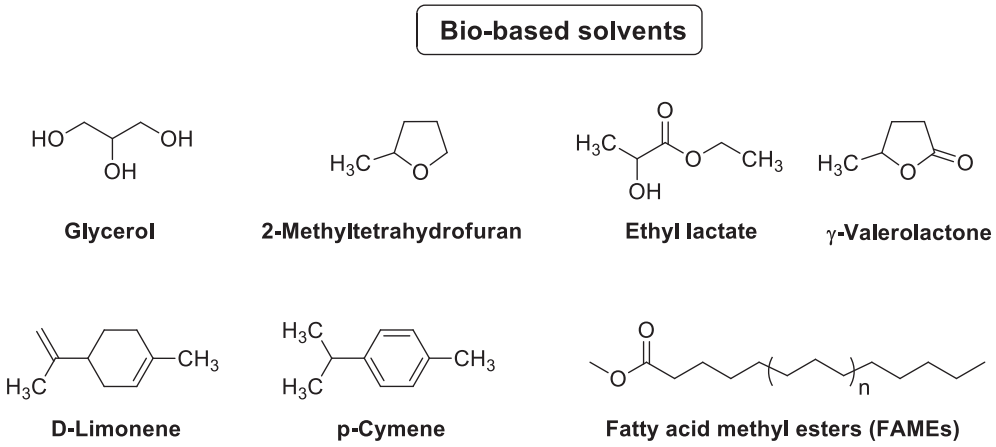


Figure 2.2 Structure of various bio-based solvents used in organic synthesis.

Glycerol, a by-product obtained from triglycerides during the bio-diesel production, was already explored as a green solvent in many organic reactions [13,14]. Other bio-based solvents such as 2-methyltetrahydrofuran, ethyl lactate, ɤ-valerolactone, D-limonene, *p*-cymene and fatty acid methyl esters (FAMEs) are now significantly replacing the hazardous petroleum solvents in many organic transformations [4-12]. In addition, eutectic mixture of various biomass derived

chemicals or solvents (example: eutectic mixture of glycerol, levulinic acid, carbohydrates, gluconic acid, etc.,) have found selective applications in organic synthesis as well as in pharmaceutics [15-18].

Phenolic compounds have found wide applications in various fields like medicines, cosmetics, food industry, materials and polymers, etc., (Figure**2.3**) [19-25]. Natural phenolic compounds isolated from herbs and dietary plants (e.g. phenolic acids, flavonoids, tannins, curcuminoids, coumarins, lignans, etc.,) exhibit a wide range of biological activities including antimicrobial, anti-inflammatory, anticancer, antithrombotic, anti-allergenic and antioxidant activities [20, 22, 26].

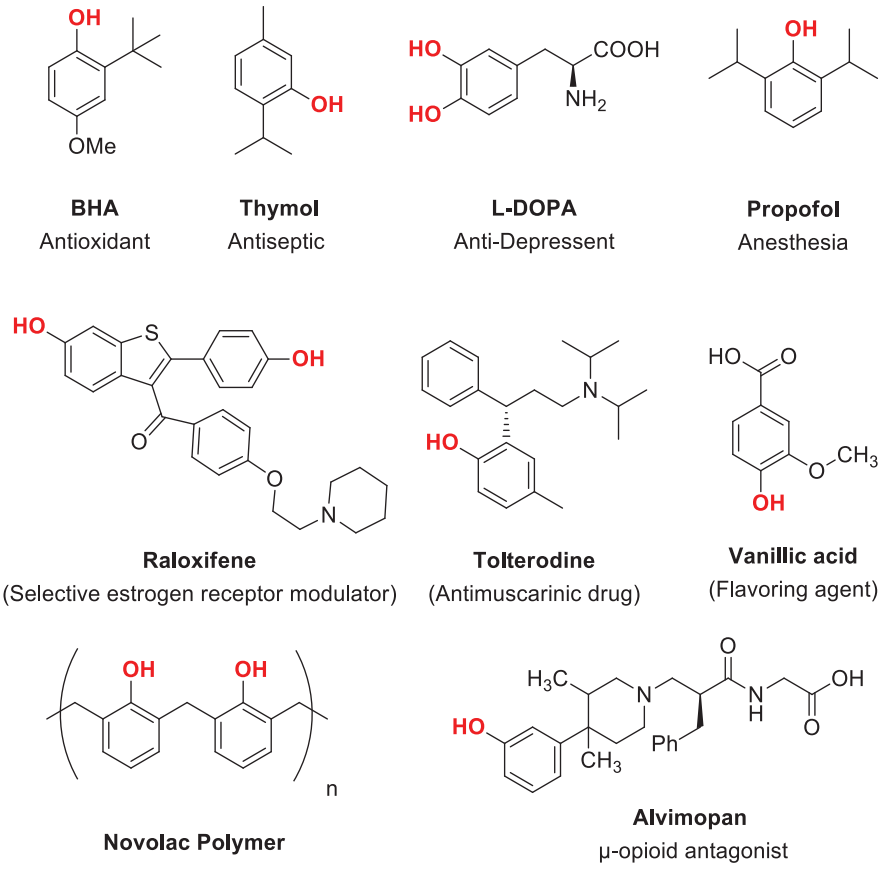
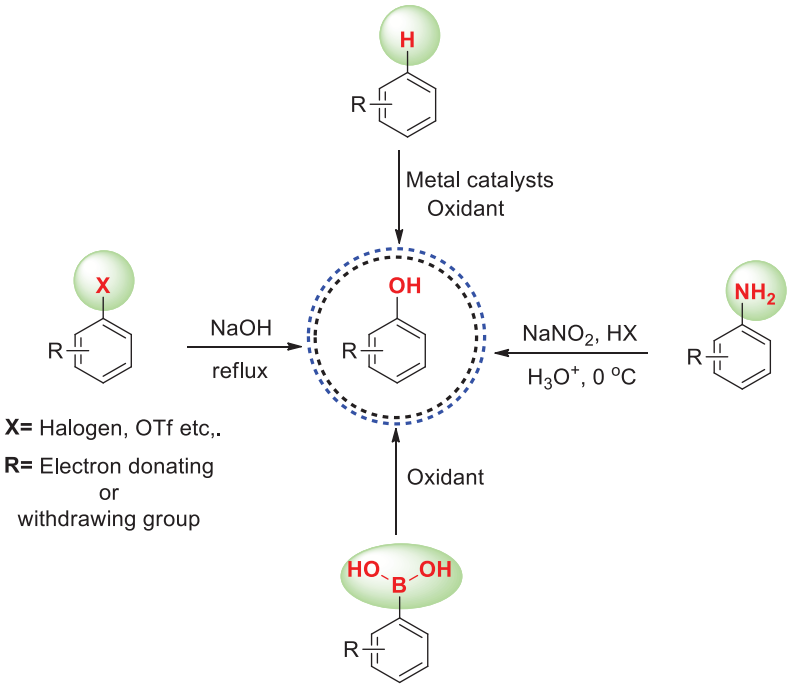


Figure2.3 Applications of phenolic compounds in different fields.

Besides the biological importance, phenols serve as key intermediates for the preparation of various natural products, pharmaceuticals, agrochemicals, materials, polymers, etc., [21, 24, 27].

2.2 DIFFERENT APPROACHES FOR THE SYNTHESIS OF PHENOLS

There are four different approaches have been developed for the preparation of phenolic compounds (**Scheme 2.1**) [27] which includes, nucleophilic substitution reaction of aryl halides with hydroxyl nucleophile, diazotization of aromatic amines followed by aqueous hydrolysis, *C*-H oxidation of aryl rings and oxidative hydrolysis of arylboronic acids.

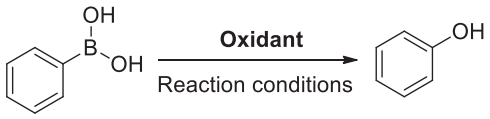


Scheme 2.1. Different approaches for the preparation of phenolic compounds.

Synthesis of phenols from arylboronic acids is becoming more preferable as compared to other methods due to ready availability, low toxicity and high stability

(toward heat, air and moisture) of arylboronic acids [28]. Therefore, recently numerous methods have been developed for the oxidative conversion of arylboronic acids into phenols using transition metals, hydrogen peroxide with different catalysts, hypervalent iodine reagents, *N*-oxides, photocatalysts and electrochemical techniques (**Table 2.1**) [29-40].

Table 2.1. Synthesis of phenols from arylboronic acids.



S. No.	Reaction Conditions	Limitations	References
1	$CuSO_4$ 1,10-Phenanthroline KOH, O_2, H_2O, 1-10 h	* Harsh reaction condition * Use of metal and ligand * Longer reaction time * Sensitive functional group incompatibility	*Org. Letts*., **2010**, *12*, 1964
2	H_2O_2 Amberlite IR 120 H_2O, 5-15 min	Use of catalyst	*Tetrahedron Lett*., **2012**, *53*, 6004
3	m-CPBA, H_2O EtOH, 6 h	*Longer reaction time	*Synlett*, **2013**, 499
4	PhI/$NaIO_4$ CH_3CN:H_2O, 80 ^oC, 8 h	*Higher reaction temperature *Longer reaction time	*Tetrahedron Lett*. **2015**, *56*, 1524
5	Benzoquinone, KOH, H_2O, 15-45 h, Reflux	*Higher reaction temperature *Longer reaction time	*Synthesis,* **2014**, 46, 263

2.3 LIMITATIONS OF PREVIOUS REPORTS

The common problems associated with majority of these reports are the use of harsh reaction conditions [38], non-ecofriendly solvents [36], high reaction temperature [38], longer reaction time [35], excess oxidants [29, 30, 37], non-commercially available catalysts or oxidants [31, 32, 36], etc. Therefore, the development of simple, efficient and greener method is still in demand and we have directed our studies towards finding a suitable catalyst-free system for the oxidative conversion of arylboronic acids into phenols using green oxidant aqueous hydrogen peroxide.

2.4 RESULTS AND DISCUSSION

2.4.1 Optimization of reaction condition

At the outset, 4-chlorophenylboronic acid was chosen as a model substrate and oxidized with 1.0 equivalent of 30% aqueous hydrogen peroxide in various solvents such as methanol, ethanol, *t*-butanol, water, tetrahydrofuran (THF), acetonitrile, toluene, glycerol and acetic acid (**Table 2.2**). Among the polar protic solvents, methanol provides the maximum yield of 4-chlorophenol, *i.e.* 41% after 60 minutes (**Table 2.2, entry 1**) while other protic solvents such as ethanol, *t*-BuOH, glycerol and water gave relatively lower yields (**Table 2.2, entries 2-5**).

It is also important to note that even after prolonged reaction time (12 h) full conversion of boronic acid into phenol was not observed in methanol (**Table 2.2, entry 6**). Further, the oxidation reaction was carried out in polar aprotic solvents such as THF, acetonitrile and toluene (**Table 2.2, entries 7-9**). The maximum yield of 42% was

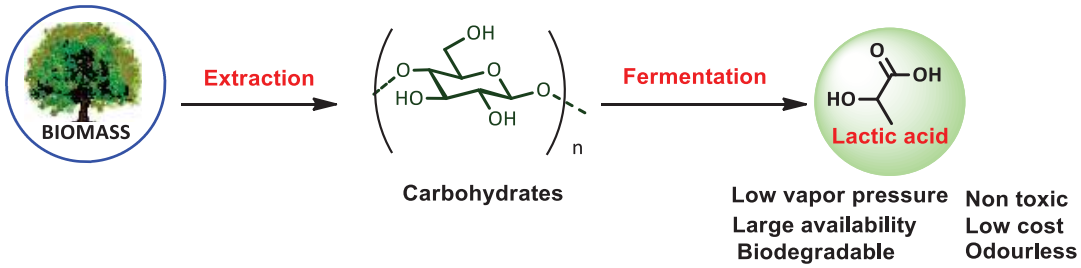
observed in acetonitrile while THF and toluene provide less than 40% of the desired product. Finally, we have tested the reaction in acetic acid and fortunately the reaction went to completion in 15 minutes to yield 95% of 4-chlorophenol (**Table 2.2, entry 10**). Despite the efficiency, acetic acid (glacial) is corrosive, and its vapor irritates the eyes, produces a burning sensation in the nose, and can lead to a sore throat and lung congestion [41]. Moreover, about 75% of the acetic acid used in the industry is currently produced through chemical methods [42, 43].

Table 2.2. Oxidation of 4-chlorophenylboronic acid in various solvents with hydrogen peroxide.[a]

Entry	Solvent	H_2O_2 (equiv.)	Time (min)	Yield (%)[b]
1	CH_3OH	1.0	60	41
2	C_2H_5OH	1.0	60	37
3	*t*-BuOH	1.0	60	33
4	Glycerol	1.0	60	18
5	H_2O	1.0	60	31
6	CH_3OH	1.0	12 h	84
7	THF	1.0	60	38
8	CH_3CN	1.0	60	42
9	Toluene	1.0	60	35
10	CH_3COOH	1.0	15	95
11	Lactic Acid	1.0	05	95

[a]**Reaction conditions:** Substrate (0.5 mmol), Solvent (1 mL), H_2O_2 (1.0 equiv.), stirred at RT. [b] Isolated yield

Lactic acid is a biomass derived weak acid widely used in the food, agricultural, textile, pharmaceutical and cosmetic industries [44, 45]. However, lactic acid is less explored as a solvent in organic synthesis while acetic acid has found wide applications. In contrast with acetic acid, lactic acid is a non-toxic and odorless liquid produced through the safer fermentation method from carbohydrates (**Scheme 2.2**) [46].

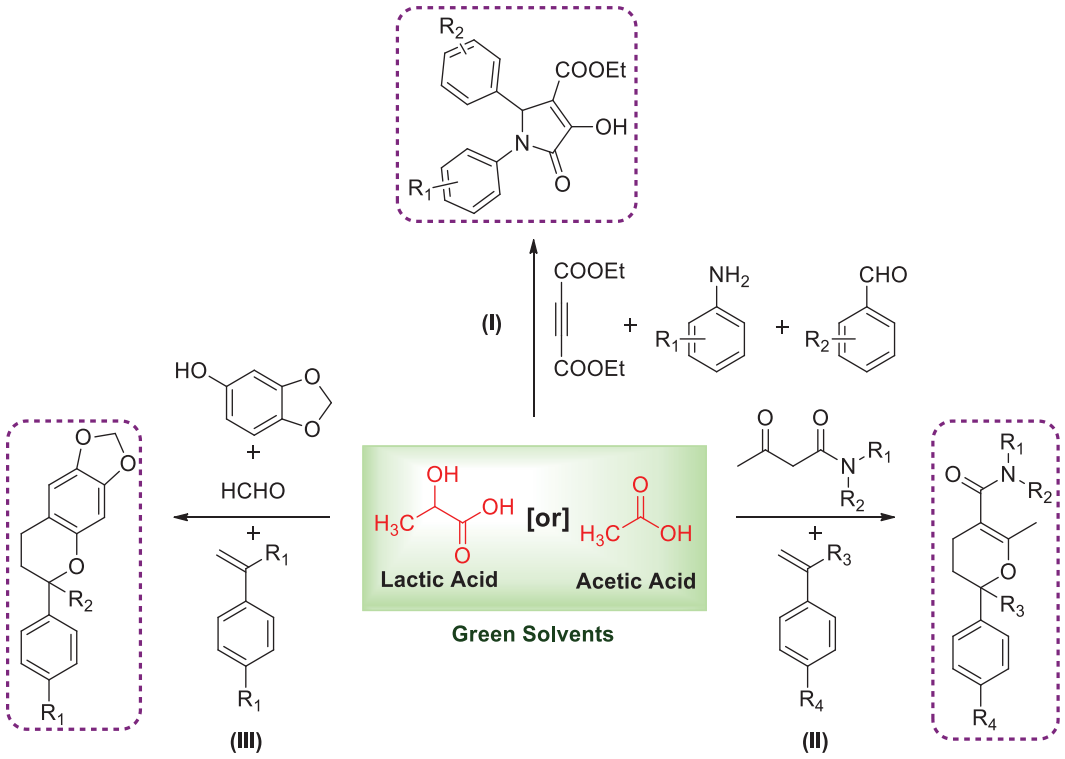


Scheme 2.2. Production of lactic acid from biomass.

The pKa, density and boiling point of lactic acid is 3.7, 1.20 g/cm^3 and 120 $^\circ$C, respectively, which is comparable with acetic acid (pKa. 4.7, d: 1.05g/cm^3 and bp.117 $^\circ$C) and therefore we anticipate that lactic acid can be a suitable alternative to the acetic acid [47]. Recently, Yanlong Gu group has demonstrated the first application of lactic acid as a green solvent for multi-component reactions (MCR) (**Scheme 2.3**) with several advantages like reusability of the reaction medium, high efficiency, easy isolation of products etc., [47].

Impressed by the above work, we have carried out the oxidation reaction in lactic acid and pleased to observe a quick and clean conversion of 4-chlorophenylboronic acid into 4-chlorophenol (**Table 2.2, entry 11**). Encouraged, we

have further studied the oxidation of various functionalized arylboronic acids not only in lactic acid, but also in acetic acid in order to compare the efficiency of the reaction mediums. The results obtained were summarized in **Table 2.3**.



Scheme 2.3. Lactic acid as a green solvent for multi-component reactions (MCR).

2.4.2 Substrates scope

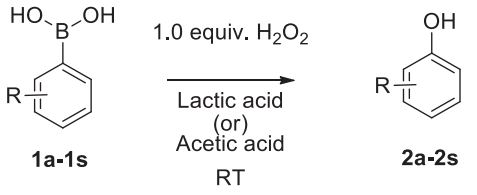
The unsubstituted arylboronic acids such as phenylboronic acid and α, β-naphthylboronic acids were converted into corresponding phenol and naphthols (**Table 2.3, 2a-2c**) within 5 minutes in lactic acid, while acetic acid required about 15 minutes. Nevertheless, both solvents gave the desired products in excellent yields. Subsequently, the oxidation of methoxy, methyl, ethyl, *tertiary* butyl, phenyl, nitro, fluoro, chloro and

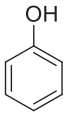
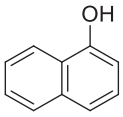
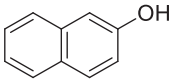
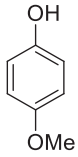
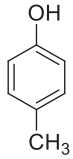
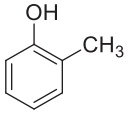
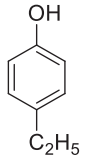
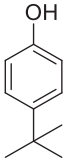
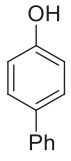
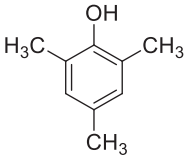
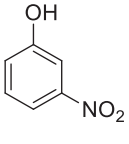
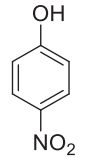
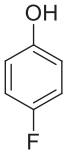
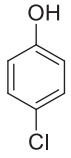
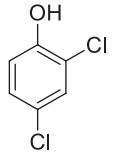
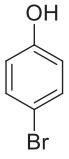
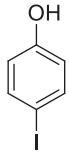
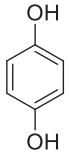
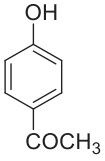
iodo- substituted phenylboronic acids were tested in order to establish a general applicability of this methodology in complex synthesis (**Table 2.3, 1d-1q**). All these substrates underwent *ipso*-hydroxylation smoothly irrespective of electronic properties of the arylboronic acids and desired products were obtained up to 97% yield (**Table 2.3, 2d-2q**). Similarly, 1,4-phenylenediboronic acid was oxidized to hydroquinone in quantitative yield with 2.5 equivalent of hydrogen peroxide (**Table 2.3, 2r**).

Further to extend the scope of this methodology, oxidation of 4-acetyl phenylboronic acid (a substrate which can undergo *Baeyer-Villiger* oxidation) was examined in both lactic acid and acetic acid medium. Remarkably, ketone functional group was found to be very stable during the oxidation and gave 4-acetylphenol in 95% yield in both solvents (**Table 2.3, 2s**). Over all, lactic acid was found to be very efficient solvent medium for the oxidative *ipso*-hydroxylation reaction when compared with acetic acid.

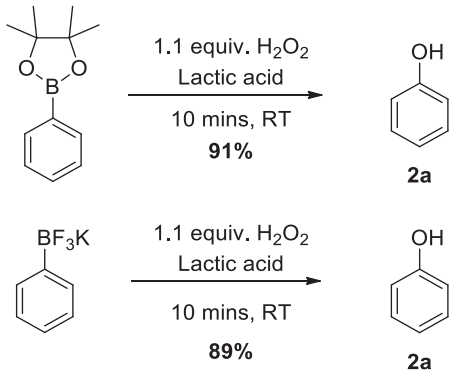
Similar to arylboronic acids, other surrogates such as phenylboronic acid pinacol ester and potassium phenyltrifluoroborate were successfully converted to phenol in a short time (**Scheme 2.4**). In addition, alkylboronic acids such as 2-phenylethylboronic acid (**1t**) and cyclohexylboronic acid (**1u**) were oxidized to corresponding alcohols in good yields with equal efficiency (**Scheme 2.5**).

Table 2.3. Oxidation of various functionalized arylboronic acids in lactic acid and acetic acid.[a]

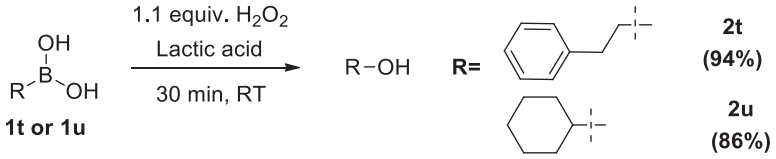


				
2a	**2b**	**2c**	**2d**	**2e**
(5 min, **95%**)[b] (15 min, **95%**)[c]	(5 min, **93%**)[b] (15 min, **95%**)[c]	(5 min, **94%**)[b] (15 min, **96%**)[c]	(5 min, **90%**)[b] (15 min, **95%**)[c]	(5 min, **95%**)[b] (15 min, **93%**)[c]
				
2f	**2g**	**2h**	**2i**	**2j**
(10 min, **95%**)[b] (30 min, **95%**)[c]	(5 min, **93%**)[b] (15 min, **95 %**)[c]	(5 min, **96%**)[b] (20 min, **93%**)[c]	(5 min, **93%**)[b] (20 min, **97%**)[c]	(30 min, **94%**)[b] (60 min, **94%**)[c]
				
2k	**2l**	**2m**	**2n**	**2o**
(10 min, **91%**)[b] (30 min, **95%**)[c]	(5 min, **92%**)[b] (30 min, **94%**)[c]	(5 min, **92%**)[b] (30 min, **92%**)[c]	(5 min, **95%**)[b] (15 min, **95%**)[c]	(15 min, **93%**)[b] (30 min, **90%**)[c]
				
2p	**2q**	**2r**	**2s**	
(10 min, **94%**)[b] (30 min, **96%**)[c]	(15 min, **94%**)[b] (30 min, **91%**)[c]	(10 min, **95%**)[b,d] (30 min, **95%**)[c,d]	(10 min, **95%**)[b] (30 min, **95%**)[c]	

[a]**Reaction conditions:** Substrate (0.5 mmol), Solvent (1 mL), H_2O_2 (1.0 equiv.), stirred at RT; Isolated yield is shown in the table. [b]Lactic acid is used as solvent. Acetic acid is used as solvent. [d]1,4-phenylenediboronic acid is used as a substrate with 2.5 equiv. H_2O_2.



Scheme 2.4. Oxidation of phenylboronic acid pinacol ester and potassium phenyltrifluoroborate in lactic acid.

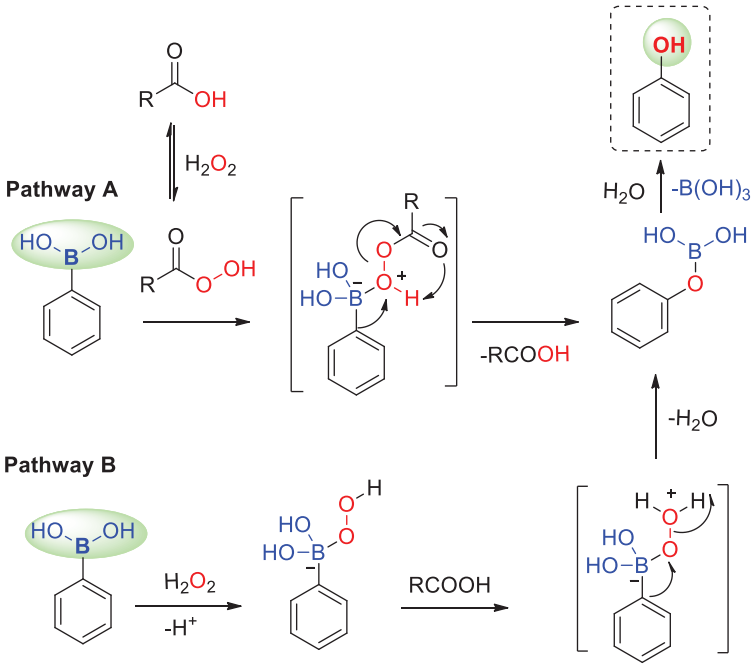


Scheme 2.5. Oxidation of alkylboronic acids with hydrogen peroxide in lactic acid.

2.5 PLAUSIBLE REACTION MECHANISM

Although the exact mechanism of the reaction is unclear, two possible mechanistic pathways (**A** and **B**) are shown in **Scheme 2.6**. According to pathway **A**, the first step would be the formation of peracid (peracetic/perlactic acid) which is generally known as more reactive species than simple hydrogen peroxide [48]. The resulted peracid reacts with arylboronic acid to provide boronate ester which is further hydrolyzed to phenol and boric acid in the presence of water (**Scheme 2.6, A**) [39]. On the other hand, the oxidation may involve the electrophilic attack of the hydrogen peroxide on boron followed by protonation of the peroxide by the acetic acid or lactic acid [30]. Subsequent migration of the aryl group from boron to oxygen generates boronate ester which is further hydrolyzed to phenol by water (**Scheme 2.6,B**). However, we believe that the acidity of the reaction medium would play an important

role in the oxidation reaction. Because, lactic acid (pKa: 3.7) is relatively more acidic than acetic acid (pKa: 4.7) and it could be a reason for the enhanced activity of lactic acid over acetic acid.



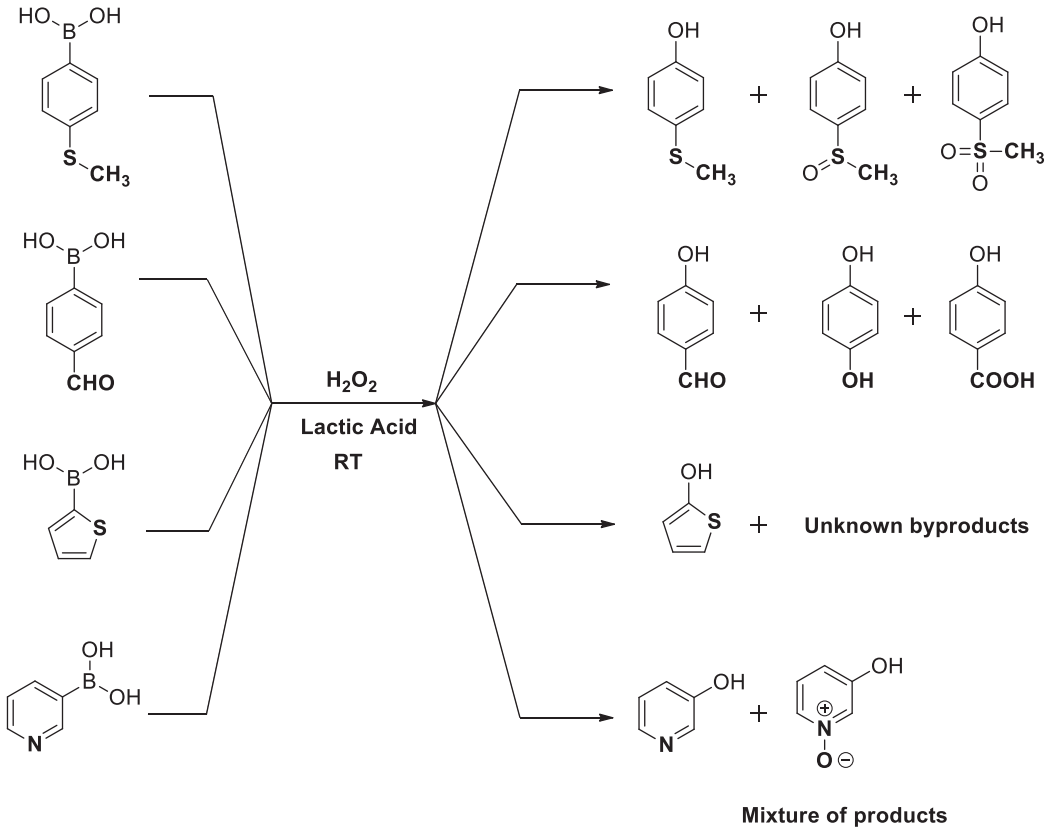
Scheme 2.6. Two different mechanistic pathways (**A** and **B**) for the oxidation reaction.

2.6 SUMMARY OF THE WORK

We have successfully demonstrated the catalyst-free *ipso*-hydroxylation of arylboronic acids into phenols with green oxidant aqueous hydrogen peroxide. This study reveals that lactic acid can be used not only for acid catalyzed reactions [47], but also to the oxidation reactions. The efficiency of lactic acid was found to be equal or even slightly better than acetic acid and therefore acetic acid can be efficiently replaced by lactic acid in organic synthesis.

2.7 REQUIREMENT OF CERTAIN MODIFICATIONS

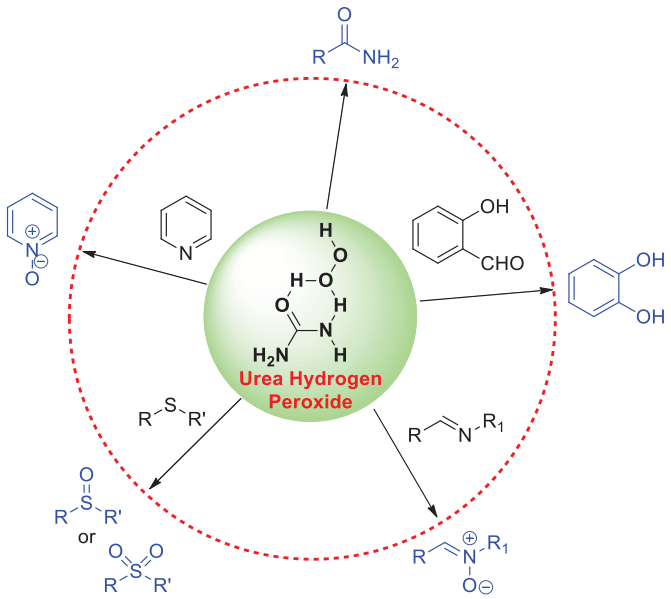
Despite having many credentials, the current method also suffers from some disadvantages. During the course of our investigation on *ipso*-hydroxylation of arylboronic acids with H_2O_2/lactic acid or acetic acid system, we have observed the incompatibility of some oxidation sensitive functional groups. For example, oxidation of sulfide and aldehyde functionalized boronic acids as well as heteroaromatic boronic acid was unsuccessful (**Scheme 2.7**).



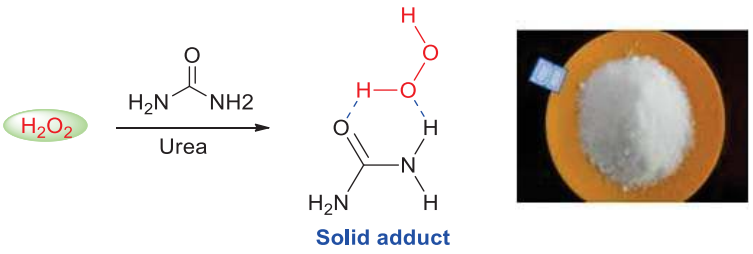
Scheme 2.7. Limitations of *ipso*-hydroxylation using lactic acid for other functional groups.

On the other hand, the use of acidic medium *i.e.* lactic acid or acetic acid as a solvent, also limits the method from the extensive uses in organic synthesis. In this context, it is important to develop an alternative protocol for the chemoselective *ipso*-hydroxylation of arylboronic acids under catalyst and metal-free conditions.

Aqueous hydrogen peroxide is a green oxidant widely used for the oxidation of various functional groups in organic synthesis. However, basically it is a weak oxidant which requires a catalyst or different additives for the activation. For example, from our previous observation it is apparent that in the absence of lactic acid or acetic acid *ipso*-hydroxylation does not reach to the completion. In this respect, hydrogen peroxide-solid adducts (e.g. sodium percarbonate and urea-hydrogen peroxide) also get considerable attention in organic synthesis due to many advantages including stability, easy handling and storing, high safety, etc. [46a].



Scheme 2.8. Urea-hydrogen peroxide used for oxidation of various functional groups in organic synthesis.



Scheme 2.9. Synthesis of urea-hydrogen peroxide solid adduct.

One of such solid adducts is urea-hydrogen peroxide (UHP) which has been explored in a several solution as well as solid phase oxidation reactions (**Schemes 2.8**) [49]. Urea-hydrogen peroxide is crystalline solid which can be easily synthesized from urea and aqueous hydrogen peroxide under mild condition (**Scheme 2.9**).

Being an anhydrous neutral complex, UHP adduct is considered to be a safer alternative to the high concentrated liquid hydrogen peroxide [49a]. Commercial availability, inexpensiveness, odorless, and non-toxic nature are the additional advantages of urea-hydrogen peroxide. Therefore, UHP has been used not only in organic synthesis but also in cosmetics and pharmaceuticals as a disinfectant and bleaching agent [50].

In light of these aspects, we were interested to explore the *ipso*-hydroxylarion of arylboronic acids into corresponding phenols using urea-hydrogen peroxide in the absence of catalysts under neutral conditions.

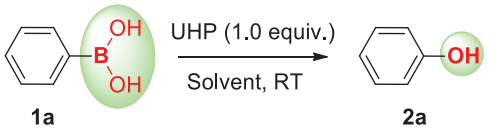
2.7.1 Optimization of reaction condition with urea-hydrogen peroxide

At the outset, commercially available phenylboronic acid (**1a**) was chosen as a model substrate and subjected for *ipso*-hydroxylation with UHP in various solvents and

solvent free condition (**Table 2.3**). All the reactions were performed at room temperature with 1.0 equiv. of urea-hydrogen peroxide under catalyst-free condition. Among the aprotic solvents, only acetonitrile provided the desired product in a quantitative yield (97%) within 15 minutes (**Table 2.4, entry 5**) while tetrahydrofuran (THF), toluene, diethyl ether and chloroform did not lead to completion even after prolonged reaction time (**Table 2.4, entries 1-4**). It is also important to note that by replacing UHP with 30% aqueous hydrogen peroxide in acetonitrile the reaction did not lead to completion even after 60 minutes (**Table 2.4, entry 6**) [31]. The low yield in this reaction may be attributed to the formation of peroxyimidic acid. In the case of protic solvents, methanol was found to be very efficient to provide 97% of the desired product within 5 minutes while ethanol, *t*-butanol and water took slightly longer reaction time (**Table 2.4, entries 7-10**). It is interesting to note that the reactivity of 30% aqueous hydrogen peroxide in methanol was found to be relatively efficient when compared with acetonitrile which provides 69% of the desired product after 60 minutes at room temperature (**Table 2.4, entry 11**).

Nevertheless, the oxidative *ipso*-hydroxylation of phenylboronic acid was also achieved in a high yield under solid-state condition (*i.e.* solvent-free) with UHP, however at 45 °C (**Table 2.4, entry 12**). Based on the optimization study, acetonitrile as well as methanol was found to be an efficient medium for the *ipso*-hydroxylation reaction with UHP at room temperature under catalyst-free condition (**Table 2.4, entries 5 & 7**). Considering the slight variation in time requirement, we have decided to perform the reaction in methanol.

Table 2.4. Oxidation of phenylboronic acid using urea-hydrogen peroxide (UHP).[a]



1a 2a

Entry	Solvent	Time (min)	Yield (%)[b]
1	THF	120	40
2	Toluene	120	30
3	Diethyl ether	120	68
4	$CHCl_3$	120	20
5	CH_3CN	15	97
6	CH_3CN	60	07[c]
7	CH_3OH	5	97
8	C_2H_5OH	35	90
9	*t*-BuOH	40	80
10	H_2O	90	65
11	CH_3OH	60	69[c]
12	Solvent free	30	95[d]

[a]**Reaction conditions:** Substrate (1.0 mmol) and UHP (1.0 equiv.) was stirred in 3 mL of solvent at room temperature. [b]Isolated yield. [c]Instead of UHP, 30% aqueous hydrogen peroxide was used. [d] Reaction was carried out at 45 °C.

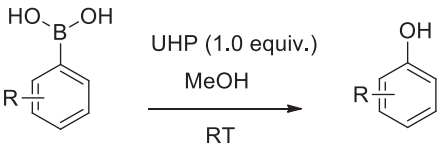
2.7.2 Substrate scope with urea-hydrogen peroxide

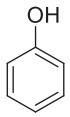
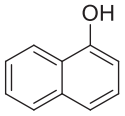
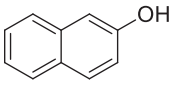
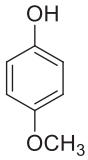
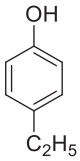
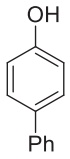
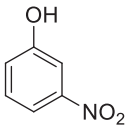
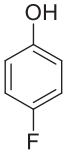
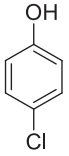
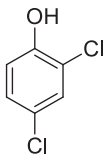
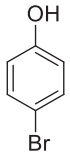
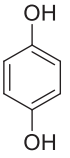
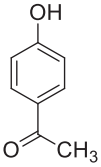
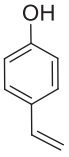
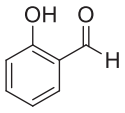
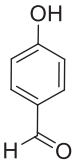
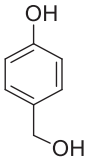
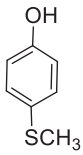
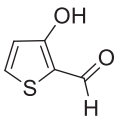
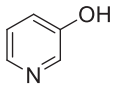
As optimized condition in hand, a general applicability of the method was further explored by subjecting various substituted arylboronic acids for the *ipso*-hydroxylation and the results were summarized in **Table 2.5**. Similar to phenylboronic acid, α-and β-naphthylboronic acids were converted into corresponding naphthols in 96% yields (**Table 2.5, 2b&2c**). In addition, the electron rich, *i.e.* methoxy, ethyl and phenyl substituted arylboronic acids underwent *ipso*-hydroxylation in excellent yields (>95%) within the period of 15 minutes at room temperature (**Table 2.4, 2d, 2g &2i**).

On the other hand, deactivated arylboronic acids such as nitro, fluoro, chloro, and bromo substituted arylboronic acids have also undergone *ipso*-hydroxylation smoothly to provide the desired products in a comparable yield (> 95%) to those of activated arylboronic acids (**Table 2.4, 2k, 2m-2p**). Also, aryl diboronic compound such as 1,4-phenylenediboronic acid was successfully converted to hydroquinone in a quantitative yield with 2.0 equiv. of urea-hydrogen peroxide at room temperature (**Table 2.5, 2r**). It has been widely observed that urea-hydrogen peroxide (UHP) cannot oxidize the organic functional groups (e.g. sulfides, thiols, amines, olefins, alcohols, aldehydes etc.,) efficiently in the absence of catalyst [49a-c].

However, the current study reveals that *ipso*-hydroxylation of arylboronic acids can be achieved very efficiently under catalyst-free condition at room temperature. By considering these facts, we have anticipated that UHP can be used as a chemoselective oxidant for the *ipso*-hydroxylation of arylboronic acids which contain oxidation susceptible functional groups. To test the hypothesis, olefin, aldehyde, alcohol and sulfide functionalized arylboronic acids (**3a-3e)** as well as heteroarylboronic acids (**3f** and **3g)** were subjected for the *ipso*-hydroxylation reactions under optimized condition. However, during the course of *ipso*-hydroxylation in methanol, we have observed the formation of minor amount of undesired products (~10-15%), particularly in the case of substrates with aldehyde (**3b** &**3c**) and sulfide (**3e**) functional groups [52]. Therefore, the reactions of sensitive group functionalized arylboronic acids were performed in acetonitrile which took slightly longer time for completion, however with high chemoselectivity (**Table 2.5, 4a-4g**).

Table 2.5. Oxidation of substituted arylboronic acids to corresponding phenols using UHP.[a,b]



				
2a	**2b**	**2c**	**2d**	**2g**
(5 mins, **97%**)	(10 mins, **96%**)	(5 mins, **96%**)	(15 mins, **96%**)	(2 mins, **97%**)
				
2i	**2k**	**2m**	**2n**	**2o**
(15 mins, **96%**)	(5 mins, **95%**)	(5 mins, **95%**)	(15 mins, **96%**)	(5 mins, **95%**)
				
2p	**2r**	**2s**	**4a**	**4b**
(10 mins, **96%**)	(5 mins, **96%**)[c]	(30 mins, **96%**)[d]	(45 mins, **95%**)[d]	(45 mins,**92%**)[d]
				
4c	**4d**	**4e**	**4f**	**4g**
(45 mins, **92%**)[d]	(30 mins, **95%**)[d]	(5 mins, **92%**)[d]	(2 h, **87%**)[d]	(6 h, **91%**)[c]

[a]**Reaction condition:** Substrate (1.0 mmol) and UHP (1.0 equiv.) was stirred in 3 mL of methanol at room temperature. [b]Isolated yield. [c]2.0 equiv. of UHP was used. [d]Acetonitrile was used as the solvent.

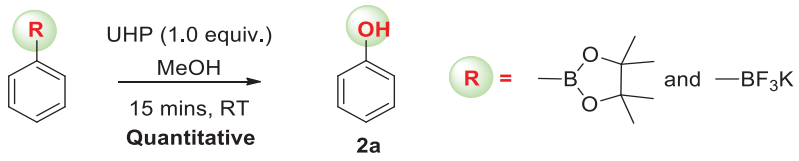
In general, olefins are prone to epoxidation or dihydroxylation in the presence of oxidizing agents (e.g. *m*-CPBA, *t*-BuOOH, Oxone etc.,) [12]. Interestingly, olefin was found to be remained intact during the *ipso*-hydroxylation with UHP and gave the desired product in 95% yield (**Table 2.5, 4a**). Similarly, aryl aldehydes and ketones were known to undergo different oxidation reactions including *Dakin* oxidation, *Baeyer-Villiger* oxidation etc., [53]. In addition, aryl alcohols can get easily oxidized to corresponding aldehydes or carboxylic acids in the presence of oxidizing agents. Interestingly, all these functionalities were well tolerated during the *ipso*-hydroxylation and gave the desired phenols in >92% yields (**Table 2.5,2s** and**4b**-**4d**). It is well known that sulfides are highly oxophilic in nature which readily undergo oxidation to sulfoxide or sulfone with most of the oxidizing agents (e.g. *m*-CPBA, H_2O_2 with different catalysts, oxone etc.,) [53,54]. Therefore a sulfide containing arylboronic acid (*i.e.* 4-(methylthio)phenylboronic acid, **3e**) was tested for *ipso*-hydroxylation reaction with UHP in acetonitrile. Remarkably, sulfide group was found to be stable while chemoselective oxidation of boronic acid was observed in 92% yield (**Table 2.5,4e**). In contrast, other reagents which were reported for *ipso*-hydroxylation such as *m*-CPBA [34], I_2/H_2O_2 [31], and Amberlite/H_2O_2 [30] gave only a minor amount of desired product (<15%) along with a mixture of undesired products (**Scheme 2.10**).

It is also worthy to note that heterocyclic boronic acids such as 2-formyl-3-thienylboronic acid and 3-pyridylboronic acid were successfully converted to corresponding alcohols (**Table 2.5,4f** and **4g**) in good yield at room temperature, which showed the broad synthetic utility of this method.

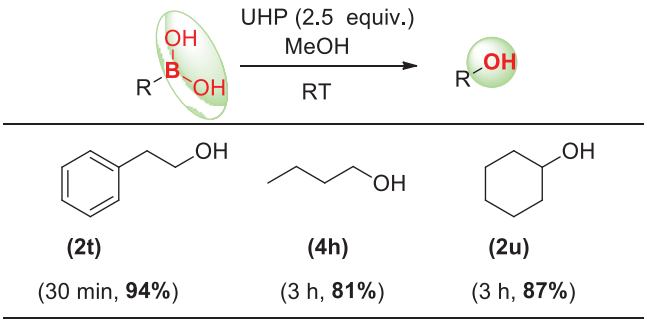
Methods	Time	Yield
UHP/AcCN (This work)	5 min	92%
I_2/H_2O_2	30 min	<10%
m-CPBA/EtOH	30 min	<15%
Amberlite/H_2O_2	30 min	< 10%

Scheme 2.10. Oxidation of 4-(methylthio)phenylboronic acid in different conditions.

Similar to arylboronic acids, other surrogates such as phenylboronic acid pinacol ester and potassium phenyltrifluoroborate were hydroxylated in quantitative yields (**Scheme 2.11**). In addition, alkylboronic acids such as 2-phenylethyl-, *n*-butyl- and cyclohexylboronic acids were also efficiently converted to corresponding alcohols in high yields (**Scheme 2.12**). It is interesting to note that a large number of reactions can occur very efficiently under solid state condition (*i.e.* solvent-free) when compared to the reactions carried out in solvents [55].

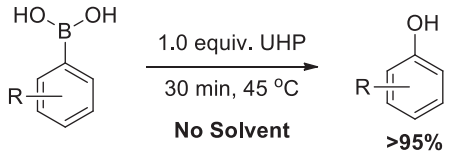


Scheme 2.11. Oxidation of phenylboronic acid pinacol ester and potassium phenyltrifluoroborate.



Scheme 2.12. Oxidation of alkylboronic acids with urea-hydrogen peroxide.

During the optimization, we have observed that phenylboronic acid undergoes *ipso*-hydroxylation efficiently under solvent-free condition with 1.0 equiv. of UHP at 45 °C (**Table 2.4, entry 12**). To understand the scope and limitation of this protocol, other substituted arylboronic acids were subjected for *ipso*-hydroxylation under solid state condition [56]. The substrates without sensitive functional groups gave the desired products (**2a-2d, 2g, 2i, 2k, 2m-2p & 4a**) in high yield (>95%) within 30 minutes (**Scheme 2.13**) while a mixture of undesired products were observed in the case of substrates with oxidation sensitive functional groups (**2s**, **4b-4g**) except **4a** [57]. We presume that high reaction temperature as well as uneven mixing of substrates with oxidant (while melting), perhaps the reason for this poor selectivity. Therefore, we believe that solvent would be essential for performing a chemoselective oxidation of functionalized arylboronic acids with UHP at room temperature.

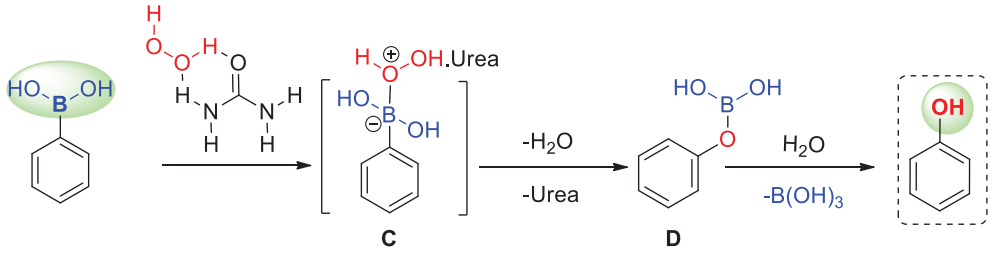


R = H, Naphthyl, 4-C_2H_5, 4-OCH_3, 4-Ph, 4-F, 4-Cl, 4-Br, 2,4-Dichloro, 3-NO_2, 4-(C_2H_3)

Scheme 2.13. Oxidation of arylboronic acids under solvent-free condition.

2.8 PLAUSIBLE REACTION MECHANISM

A proposed mechanism for the oxidative *ipso*-hydroxylation reaction was shown in **Scheme 2.14**. An electrophilic attack of urea-hydrogen peroxide on the boron (**C**) followed by migration of the aryl group from boron to oxygen generates the boronate ester (**D**) [34]. This unstable ester was further hydrolyzed into phenol and boric acid in the presence of water. The strong hydrogen bonding between the urea and hydrogen peroxide probably enhances the stability of UHP and releases the hydrogen peroxide in a controlled manner which results in high selectivity and reactivity [49c]. On the other hand, high peroxide concentration (~97%) present in the urea-hydrogen peroxide may be another reason for the better reactivity over simple 30% aqueous hydrogen peroxide.



Scheme 2.14. Proposed mechanism for the *ipso*-hydroxylation of arylboronic acids.

2.9 CONCLUSION

In conclusion, we have demonstrated an efficient and practical method for the oxidative *ipso*-hydroxylation of arylboronic acids with urea hydrogen peroxide under catalyst and metal-free condition at room temperature. The electron donating and withdrawing functional group substituted arylboronic acids as well as alkylboronic acids underwent *ipso*-hydroxylation smoothly at room temperature. Remarkably, oxidation susceptible functional groups such as olefin, aldehyde, alcohol, ketone and

sulfide were tolerated under the standard reaction condition which showed the broad scope of this methodology. In addition, heterocyclic moieties such as pyridine and thiophene were found to be very stable during the *ipso*-hydroxylation to give the desired alcohols in good yields. A solid state *ipso*-hydroxylation of arylboronic acids with urea hydrogen peroxide has been investigated and observed that substrates having no sensitive functional groups underwent *ipso*-hydroxylation smoothly while a poor chemoselectivity was observed in the case of substrates containing oxidation sensitive groups.

2.10 EXPERIMENTAL SECTION

All reactions were performed under open air atmosphere using round bottom flasks. The ^{1}H NMR and ^{13}C NMRs of the phenols and alcohols were compared with literature reports.

2.10.1 Experimental procedure for the oxidation of boronic acids using aqueous hydrogen peroxide

To a stirred solution of arylboronic acid (or) aliphatic boronic acid (0.5 mmol) in lactic acid (or) acetic acid (1.0 mL) was added 1.0 equivalent of 30% aqueous hydrogen peroxide at room temperature and the progress of the reaction was monitored by TLC. *In case of acetic acid,* after completion of the reaction (as seen by TLC), solvent was evaporated to dryness and the residue was subjected to column chromatography to obtain pure phenols. *In case of lactic acid,* after completion, the reaction mixture was diluted with water and extracted with petroleum ether-ethyl acetate mixture (2:1, 5 × 5mL) [47]. The combined organic layer was dried over sodium

sulphate (Na_2SO_4), evaporated and subjected to chromatography to obtain pure products.

2.10.2 Experimental procedure for oxidation of boronic acids with urea-hydrogen peroxide (UHP)

(a) Solution Phase Protocol

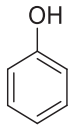
To a stirred solution of aryl/alkyl boronic acid (1 mmol) in methanol or acetonitrile (1 mL) was added 1 equiv. of urea-hydrogen peroxide (UHP) (2.5 equiv. for alkyl boronic acids) at room temperature and the progress of the reaction was monitored by TLC. After completion, the reaction mixture was diluted with water and extracted with dichloromethane (DCM). The combined organic layer was dried over anhydrous sodium sulfate (Na_2SO_4), evaporated and subjected to silica-gel column chromatography for further purification.

(b) Solid Phase Protocol

In a Round bottom flask, aryl/alkyl boronic acid (1mmol) was taken with finely powdered urea hydrogen peroxide adduct (1.0 equiv.) in open air and heated on oil bath at 45°C. After completion (~ 30 min), the reaction mixture was diluted with water and extracted with dichloromethane (DCM). The combined organic layer was dried over anhydrous sodium sulfate (Na_2SO_4), evaporated and subjected to silica-gel column chromatography for further purification.

2.11 ANALYTICAL DATA FOR THE PRODUCTS

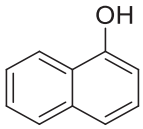
2.11.1 Phenol (2a)



2a

The titled compound was obtained as white solid (Yield: 45 mg (95%) in both lactic acid and acetic acid). The crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 85:15); R_f= 0.32. Melting point: 41-43 °C. **IR** (neat, cm^{-1}): 3328, 2353, 1941, 1588, 1471, 1369, 1249, 1062, 817, 691. **^{1}H NMR** (400 MHz, $CDCl_3$) [35]: δ 7.27 (m, 2H), 6.97 (m, 1H), 6.87 (m, 2H), 6.16 (br, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.6, 129.8, 121.0, 115.5. **HRMS:** Calc. for C_6H_7O $[M+H]^+$: 95.0491, Obser. 95.0495.

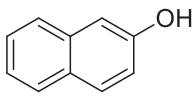
2.11.2 1-Naphthol (2b)



2b

The titled compound was obtained as a white solid (Yield: 67 mg (93%) in lactic acid; 68 mg (95%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 90:10); R_f = 0.36. Melting point: 95-97 °C. **IR** (neat, cm^{-1}): 3301, 3059, 1604, 1084. **^{1}H NMR** (400 MHz, $CDCl_3$) [35]: δ 8.20 (m, 1H), 7.80 (m, 1H), 7.57-7.42 (m, 3H), 7.32 (t, *J* = 7.8 Hz, 1H), 6.82 (d, *J* = 7.3 Hz, 1H), 5.40 (br, OH). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 151.5, 134.9, 127.8, 126.6, 126.0, 125.4, 124.5, 121.7, 120.9, 108.8. **HRMS:** Calc. for $C_{10}H_9O$ $[M+H]^+$: 145.0648, Obser. 145.0649.

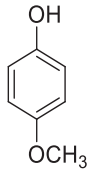
2.11.3 2-Naphthol (2c)



2c

The titled compound was obtained as a white solid (Yield: 68 mg (94%) in lactic acid; 69 mg (96%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 90:10); R_f = 0.35. Melting point: 120-121 °C. **IR** (neat, cm^{-1}): 3312, 3068, 2945, 1624, 1455, 1055. **^{1}H NMR** (400 MHz, $CDCl_3$) [35]: δ 7.77 (t, *J* = 9.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.44 (t, *J* = 7.3 Hz, 1H), 7.35 (t, *J* = 8.2 Hz, 1H), 7.17-7.08 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.2, 135.6, 130.3, 129.3, 128.4, 127.0, 123.9, 118.9, 110. **HRMS:** Calc. for $C_{10}H_9O$ $[M+H]^+$: 145.0648, Obser. 145.0649.

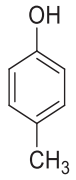
2.11.4 4-Methoxyphenol (2d)



2d

The titled compound was obtained as colorless oil. (Yield: 56 mg (90%) in lactic acid; 59 mg (95%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 80:20); R_f = 0.31. **IR** (neat, cm^{-1}): 3371, 2945, 2853, 1611, 1432, 1231, 1173, 1034, 821, 729. **^{1}H NMR** (400 MHz, $CDCl_3$) [35]: δ 6.82-6.75 (m, 4H), 3.77 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.9, 149.7, 116.3, 115.1, 56.0. **HRMS:** Calc. for $C_7H_9O_2$ $[M+H]^+$: 125.0597, Obser. 125.0600.

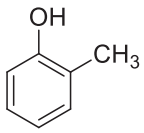
2.11.5 4-Methylphenol (2e)



2e

The titled compound was obtained as colorless oil (Yield: 51 mg (95%) in lactic acid; 50 mg (93%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 80:20); R_f = 0.32. **IR**(neat, cm^{-1}): 3349, 2921, 2853, 1701, 1617, 1443, 1256, 1237, 922, 734. **^{1}H NMR** (400 MHz, $CDCl_3$) [35]: δ 7.05 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.2 Hz, 2H), 2.31 (s, 3H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.2, 130.05, 129.97, 115.1, 20.4. **HRMS:** Calc. for C_7H_9O $[M+H]^+$: 109.0648, Obser. 109.0652.

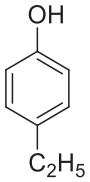
2.11.6 2-Methylphenol (2f)



2f

The titled compound was obtained as colorless oil (Yield: 51 mg (95%) in lactic acid; 51 mg (95%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 75:25); R_f = 0.28. **IR**(neat, cm^{-1}): 3498, 3287, 2956, 2938, 1411, 1359, 1148, 1015, 928, 742. **^{1}H NMR** (400 MHz, $CDCl_3$) [36]: δ 7.27 (m, 2H), 7.10-6.85 (m, 2H), 5.80 (br, OH), 2.42 (3H, s). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.7, 131.0, 123.7, 127.1, 120.7, 114.9, 15.7. **HRMS:** Calc. for C_7H_9O $[M+H]^+$: 109.0648, Obser. 109.0651.

2.11.7 4-Ethylphenol (2g)

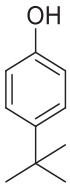


2g

The titled compound was obtained as a white solid (Yield: 57 mg (93%) in lactic acid; 58 mg (95%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 80:20); R_f = 0.34. Melting point: 44-46 °C. **IR**(neat, cm^{-1}):

3633, 2941, 1607, 1474, 1236. **^{1}H NMR** (400 MHz, $CDCl_3$) [40]: δ 7.03 (d, J = 8.4, 2H), 6.73 (d, J = 8.8 Hz, 2H), 4.89 (br, OH), 2.58 (q, J= 7.59 Hz, 2H), 1.22 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.6, 136.7, 129.1, 115.3, 28.1, 16.0. **HRMS:** Calc. for $C_8H_{11}O$ $[M+H]^+$: 123.0804, Obser. 123.0809.

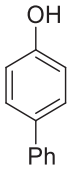
2.11.8 4-*tert.*-Butylphenol (2h)



2h

The titled compound was obtained as a colourless solid (Yield: 72 mg (96%) in lactic acid; 70 mg (93%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 70:30); R_f = 0.40.Melting point: 96-97 °C. **IR** (neat, cm^{-1}): 3336, 2981, 1596, 1487, 1217. **^{1}H NMR** (400 MHz, $CDCl_3$) [35]: δ 7.27-7.23 (m, 2 H), 6.79-6.74 (m, 2 H), 4.84 (br, OH), 1.29 (s, 9 H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.1, 143.6, 126.4, 114.7, 34.1, 31.5. **HRMS:** Calc. for $C_{10}H_{15}O$ $[M+H]^+$: 151.1117, Obser. 151.1118.

2.11.9 4-Phenylphenol (2i)

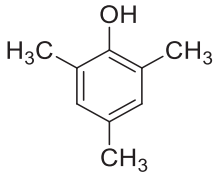


2i

The titled compound was obtained as a white solid (Yield: 79 mg (93%) in lactic acid; 83 mg (97%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 60:40); R_f = 0.41. Melting point 167-168 °C. **IR** (neat, cm^{-1}): 3618, 3069, 3028, 1581, 1484, 1429, 1348, 1226, 1184. **^{1}H NMR** (400 MHz, $CDCl_3$) [36]: δ 7.56-7.53 (m, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.32 (t, J = 7.4 Hz, 1H), 6.90 (d, J = 8.8 Hz, 2H), 5.00 (br, OH). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.3, 141.1, 133.0,

128.7, 128.3, 126.7, 126.5, 115.7. **HRMS:** Calc. for $C_{12}H_{11}O$ $[M+H]^+$: 171.0804, Obser. 171.0806.

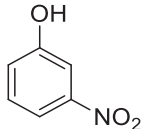
2.11.10 2,4,6-Trimethylphenol (2j)



2j

The titled compound was obtained as a white solid (Yield: 64 mg (94%) in both lactic acid and acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 80:20); R_f = 0.38. Melting point: 106-107 °C. **IR** ((neat, cm^{-1}): 3381, 1484, 1211, 1153. **^{1}HNMR** (400 MHz, $CDCl_3$) [58]: δ 6.79 (s, 2H), 4.47 (s, 1H), 2.22 (m, 9H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.7, 129.3, 129.1, 122.8, 20.4, 15.8. **HRMS:** Calc. for $C_9H_{13}O$ $[M+H]^+$: 137.0961, Obser. 139.0965.

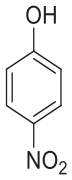
2.11.11 3-Nitrophenol (2k)



2k

The titled compound was obtained as a pale yellow solid (Yield: 63 mg (91%) in lactic acid; 66 mg (95%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 80:20); R_f = 0.42.Melting point: 98 °C. **IR** ((neat, cm^{-1}): 3351, 2933, 2846, 1710, 1617, 1551, 1357, 1236, 923, 731. **^{1}H NMR** (400 MHz, $CDCl_3$) [36]: δ 7.81-7.78 (m, 1H), 7.72 (t, J = 2.3 Hz, 1H), 7.41 (t, J = 8.2 Hz, 1H), 7.21–7.17 (m, 1H), 5.96 (br, OH). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.5, 149.4, 130.5, 122.1, 116.1, 110.7. **HRMS:** Calc. for $C_6H_6NO_3$ $[M+H]^+$: 140.0342, Obser. 140.0343.

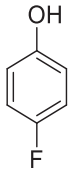
2.11.12 4-Nitrophenol (2l)



2l

The titled compound was obtained as a yellow solid (Yield: 64 mg (92%) in lactic acid; 65 mg (94%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 70:30); R_f = 0.41. Melting point: 112-113 °C. **IR** (neat, cm^{-1}): 3341, 2911, 2839, 1714, 1626, 1539, 1388, 1231, 977, 726. **^{1}HNMR** (400 MHz, $CDCl_3$) [35]: δ8.19-8.15 (m, 2H), 6.96-6.91 (m, 2H), 6.57 (s, OH). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 163.8, 134.5, 126.0, 115.6. **HRMS:** Calc. for $C_6H_6NO_3$ $[M+H]^+$: 140.0342, Obser. 140.0344.

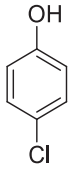
2.11.13 4-Fluorophenol (2m)



2m

The titled compound was obtained as a white solid (Yield: 52 mg (92 %) in both lactic acid and acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 90:10); R_f = 0.30. Melting point: 44-46 °C. **IR**(neat, cm^{-1}): 3334, 3228, 2921, 2836, 1483, 1349, 1220, 1061, 807, 716. **^{1}H NMR** (400MHz, $CDCl_3$) [35]: δ 6.95-6.88 (m, 2H), 6.80-6.75 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.4, 156.5, 151.7, 116.1. **HRMS:** Calc. for C_6H_6FO $[M+H]^+$: 113.0397, Obser. 113.0401.

2.11.14 4-Chlorophenol (2n)

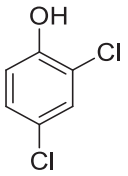


2n

The titled compound was obtained as a white solid (Yield: 61 mg (95%) in both lactic acid and acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 85:15); R_f = 0.31. Melting point: 43-44 °C. **IR** (neat, cm^{-1}): 3331, 3209,

2901, 2863, 1479, 1361, 1217, 1083, 823, 715. **^{1}H NMR** (400MHz, $CDCl_3$) [36]: δ 7.21-7.17 (m, 2H), 6.79-6.74 (m, 2H), 5.58 (br, OH). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.1, 129.7, 126.0, 116.8. **HRMS:** Calc. for C_6H_6ClO $[M+H]^+$: 129.0102, Obser. 129.0105.

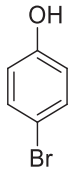
2.11.15 2,4-Dichlorophenol (2o)



2o

The titled compound was obtained as a white solid (Yield: 76 mg (93%) in lactic acid; 73 mg (90%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 80:20); R_f = 0.29. Melting point: 43-44 °C. **IR** (neat, cm^{-1}): 3512, 2979, 2282, 1419, 1263, 1077, 891. **^{1}H NMR** ($CDCl_3$, 400 MHz) [40]: δ 7.33 (s, 1H), 7.18 (d, J=8.0 Hz, 1H), 6.95 (d, 1H, J=8.0 Hz), 5.57 (br, OH). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.4, 128.8, 128.7, 125.8, 120.6, 117.3. **HRMS:** Calc. for $C_6H_5Cl_2O$ $[M+H]^+$: 162.9712, Obser. 162.9715.

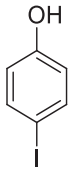
2.11.16 4-Bromophenol (2p)



2p

The titled compound was obtained as a semi-solid (Yield: 81 mg (94%) in lactic acid; 83 mg (96%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 80:20); R_f = 0.28. Melting point: 64-66 °C. **IR** (neat, cm^{-1}): 3033, 2976, 2323,1434, 1255, 894, 744. **^{1}H NMR** (400 MHz, $CDCl_3$) [35]: δ 7.32 (m, 2H), 6.72 (m, 2H), 5.36 (br, OH). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.9, 132.6, 117.4, 113.0. **HRMS:** Calc. for C_6H_6BrO $[M+H]^+$: 172.9597, Obser. 172.9597.

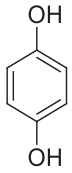
2.11.17 4-Iodophenol (2q)



2q

The titled compound was obtained as a semi-solid (Yield: 103 mg (94%) in lactic acid; 100 mg (91%) in acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 80:20); R_f = 0.30. Melting point: 90-93 °C. **IR** (neat, cm^{-1}): 3461, 1421, 1304, 1137, 743, 686. **^{1}H NMR** (400 MHz, $CDCl_3$) [35]: δ 7.51 (m, 2H), 6.62 (m, 2H), 5.15 (br, OH). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.2, 138.4, 117.8, 82.8. **HRMS:** Calc. for C_6H_6IO $[M+H]^+$: 220.9458, Obser.220.9461

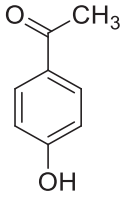
2.11.18 4-Hydroxyphenol (2r)



2r

The titled compound was obtained as a white solid (Yield: 52 mg (95%) in both lactic acid and acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 60:40); R_f = 0.36. Melting point: 120-122 °C. **IR** (neat, cm^{-1}): 3251, 3029, 1509, 1481, 1248, 1236, 1212, 1183, 1086, 826, 754. **^{1}HNMR** (400 MHz, $CDCl_3$) [40]: δ 6.72 (4H, s), 3.47 (2H, s). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.7, 115.9. **HRMS:** Calc. for $C_6H_7O_2$ $[M+H]^+$: 111.0441, Obser. 111.0444.

2.11.19 4-Hydroxyacetophenone (2s)

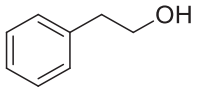


2s

The titled compound was obtained as white solid. (Yield: 65mg (95%) in both lactic acid and acetic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 60:40); R_f = 0.39. Melting point: 108-110 °C. **IR** (neat, cm^{-1}): 3304, 2988,

2370,1658, 1579, 1368, 1283, 1113, 959, 661. **^{1}H NMR** (400 MHz, $CDCl_3$) [35]: δ 7.91 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 2.57 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 198.3, 161.2, 131.3, 130.0, 115.7, 26.5. **HRMS:** Calc. for $C_8H_9O_2$ $[M+H]^+$: 137.0597, Obser. 137.0592.

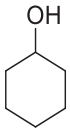
2.11.20 2-Phenylethanol (2t)



2t

The titled compound was obtained as colorless oil (Yield: 57 mg (94%) in lactic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 70:30); R_f = 0.42. **IR** (neat, cm^{-1}): 3340, 2938, 1488, 1462, 1051, 853, 754, 689. **^{1}H NMR** (300 MHz, $CDCl_3$) [59]: δ 7.30-7.34 (m, 3H), 7.24 (t, J = 7.4 Hz, 2H), 3.85 (t, J = 6.4 Hz, 2H), 2.87 (t, J = 6.4 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 138.7, 129.2, 128.7, 126.6, 63.8, 39.3. **HRMS:** Calc. for $C_8H_{11}O$ $[M+H]^+$: 123.0804, Obser. 123.0805.

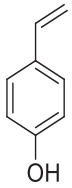
2.11.21 Cyclohexanol (2u)



2u

The titled compound was obtained as colorless oil (Yield: 43 mg (86%) in lactic acid). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 60:40); R_f = 0.39. **IR** (neat, cm^{-1}): 3405, 2379, 1109, 754. **^{1}H NMR** (400 MHz, $CDCl_3$) [59]: δ 3.61 (m, 1H), 2.00-1.50 (m, 6H), 1.35-1.10 (m, 4H). **^{13}C NMR** (125 MHz, CDCl3) δ 77.48, 35.7, 25.6, 24.3. **HRMS:** Calc. for $C_6H_{13}O$ $[M+H]^+$: 101.0961, Obser. 101.0960.

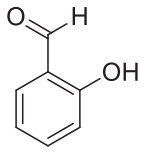
2.11.22 4-Hydroxystyrene (4a)



4a

The titled compound was obtained as white to pale yellow solid (yield = 114 mg, 95%). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 70:30); R_f = 0.40. Melting point: 62 °C. **IR** (neat, cm^{-1}): 3311, 3038, 2962, 2953, 2377, 1618, 1523, 1462, 1357, 1244, 1183, 1119, 1090, 1033, 922, 841, 733, 668. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.3 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.64 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.59 (d, *J* = 17.6 Hz, 1H), 5.22 (s, 1H), 5.12 (d, *J* = 10.9 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.4, 136.3, 130.8, 127.8, 115.6, 111.8. **HRMS:** Calc. for C_8H_9O $[M+H]^+$: 121.0653, Obser. 121.0651.

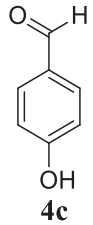
2.11.23 2-Hydroxybenzaldehyde (4b)



4b

The titled compound was obtained as clear oily liquid (yield = 112 mg, 92%). The crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 60:40); R_f = 0.42. **IR** (neat, cm^{-1}): 3144, 2954, 2859, 1649, 1577, 1469, 1378, 1281, 1209, 1118. 924. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 10.99 (s, 1H), 9.87 (s, 1H), 7.51 (dd, *J* = 18.7, 7.9 Hz, 2H), 7.11–6.87 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 196.7, 161.8, 137.1, 133.9, 120.8, 120.0, 117.8. **HRMS:** Calc. for $C_7H_7O_2$ $[M+H]^+$: 123.0441, Obser. 123.0443.

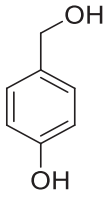
2.11.24 4-Hydroxybenzaldehyde (4c)



4c

The titled compound was obtained solid as yellow to tan powder (yield = 112 mg, 92%). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 75:25); R_f = 0.40. Melting point: 113-115 °C. **IR** (neat, cm^{-1}): 3149, 2948, 2847, 1670, 1588, 1484, 1351, 1279, 1204, 1135, 871, 611. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.79 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 2H), 6.94 (d, *J* = 8.1 Hz, 2H), 3.80 (s, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.6, 163.4, 132.5, 128.9, 116.0. **HRMS:** Calc. for $C_7H_7O_2$ $[M+H]^+$: 123.0441, Obser. 123.0443.

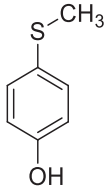
2.11.25 4-Hydroxybenzylalcohol (4d)



4d

The titled compound was obtained as off white powder (yield = 118 mg, 95%). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 60:40). R_f = 0.36. Melting point: 118-119 °C. **IR** (neat, cm^{-1}): 3310, 3016, 2909, 2368, 1643, 1537, 1429, 1380, 1236, 1181, 1087, 1051, 988, 912, 823, 709, 671. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.33 (s, 1H), 7.20 (d, *J* = 7.5 Hz, 2H), 6.80 (d, *J* = 7.5 Hz, 2H), 4.54 (s, 1H), 3.31 (s, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.3, 132.2, 128.9, 115.3, 64.6. **HRMS:** Calc. for $C_7H_9O_2$ $[M+H]^+$: 125.0603, Obser. 125.0601.

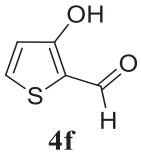
2.11.26 4-(Methylthio)phenol (4e)



4e

The titled compound was obtained as a white solid (yield = 129 mg, 92%).The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 90:10); R_f = 0.44. Melting point: 83-85°C. **IR** (neat, cm^{-1}): 3643, 3158, 2969, 1654, 1543, 1297, 1214, 861. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.22 (d, *J* = 7.2 Hz, 2H), 6.78 (d, *J* = 7.3 Hz, 2H), 5.04 (s, 1H), 2.43 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.2, 130.6, 129.1, 116.2, 18.2. **HRMS:** Calc. for C_7H_9OS $[M+H]^+$: 141.0369, Obser. 141.0371.

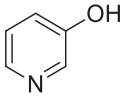
2.11.27 2-Formyl-3-hydroxythiophene (4f)



4f

The titled compound was obtained as a colourless crystal (yield = 111 mg, 87%). The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 80:20); R_f = 0.42. Melting point: 85-87 °C. **IR** (neat, cm^{-1}): 3304, 3290, 2958, 2850, 2762, 1741, 1623, 1504, 1349, 1186, 1018, 929, 753. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 10.70 (s, 1H), 9.97–9.20 (m, 1H), 7.58 (dd, *J* = 15.1, 4.8 Hz, 1H), 6.97–6.56 (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 185.9, 166.5, 136.5, 119.9, 115.8. **HRMS:** Calc. for $C_5H_5O_2S$ $[M+H]^+$: 129.0005, Obser. 129.0008.

2.11.28 3-Hydroxypyridine (4g)

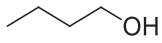


4g

The titled compound was obtained as white to off white crystal (yield= 86 mg, 91%) The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 10:1); R_f = 0.28. Melting point:

127-128 ºC. **IR** (neat, cm^{-1}): 2911, 2831, 2561, 2463, 1817, 1569, 1491, 1261. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.24 (s, 1H), 8.07 (s, 1H), 7.26–7.10 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.8, 139.9, 137.9, 123.8, 122.5. **HRMS:** Calc. for C_5H_6NO $[M+H]^+$: 96.0444, Obser. 96.0441.

2.11.29 *n*-Butanol (4h)



4h

The titled compound was obtained as colourless liquid (yield = 60 mg, 81%) The crude product was purified by silica-gel column chromatography (hexane: ethyl acetate = 70:30). R_f = 0.39. **IR** (neat, cm^{-1}): 3349, 2977, 1564, 1121, 979. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.65 (t, J = 6.6 Hz, 2H), 1.56 (dt, J = 14.6, 6.8 Hz, 2H), 1.47 (s, 1H), 1.43-1.34 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H)**^{13}C NMR** (125 MHz, $CDCl_3$) δ 77.4, 77.2, 76.9, 62.9, 35.0, 19.0, 14.0. **HRMS:** Calc. for $C_4H_{11}O$ $[M+H]^+$: 75.0804, Obser. 75.0807.

2.12 SPECTRAL DATA FOR FEW PRODUCTS

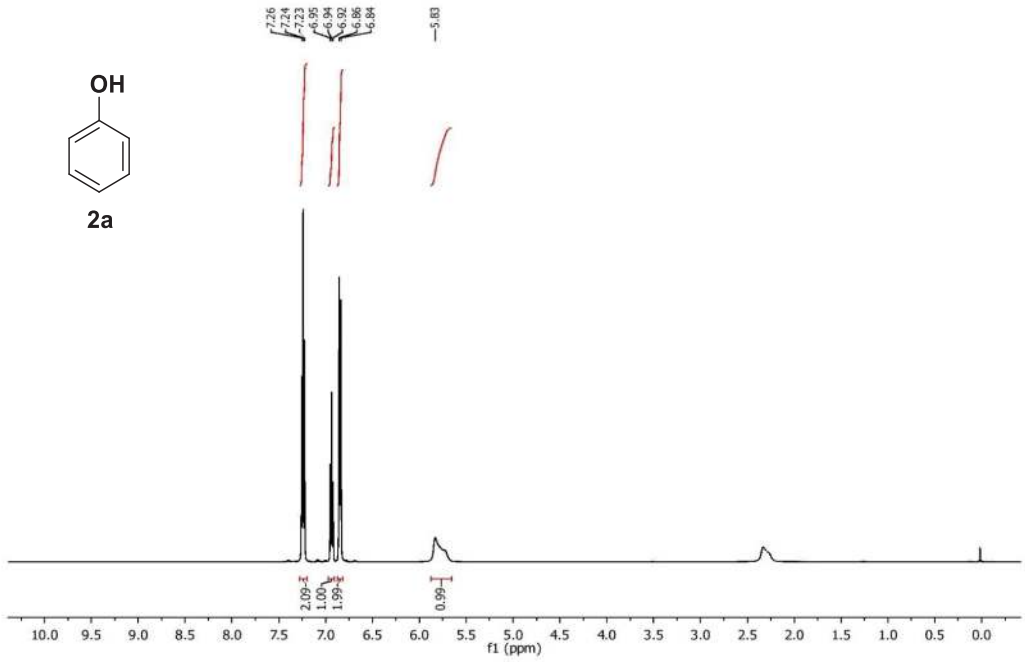


Figure 2.4 ^{1}H NMR of Phenol (**2a**)

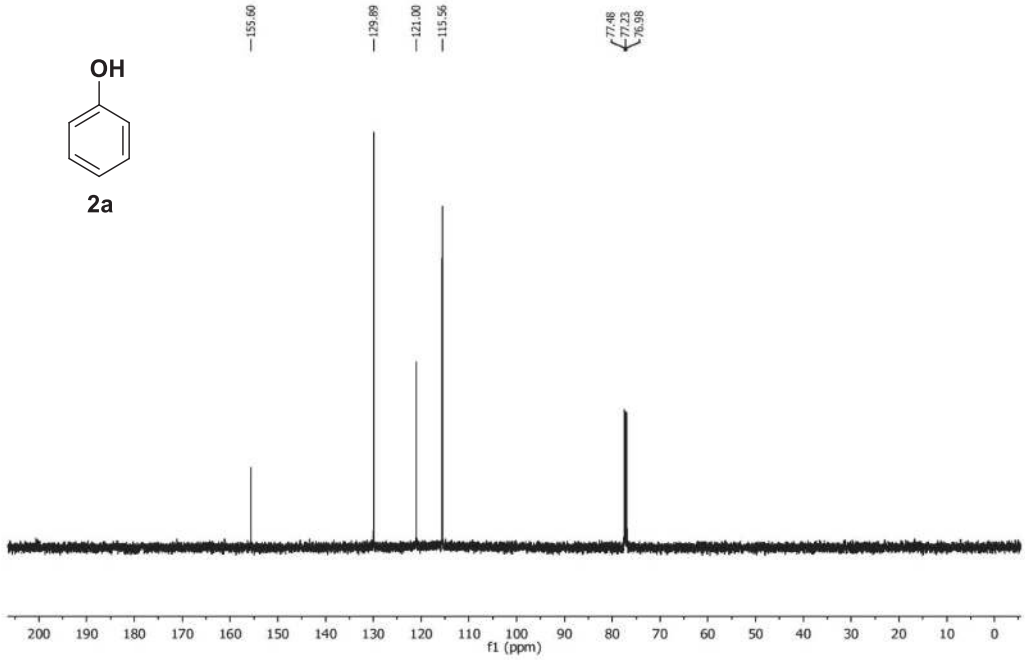


Figure 2.5 ^{13}C NMR of Phenol (**2a**)

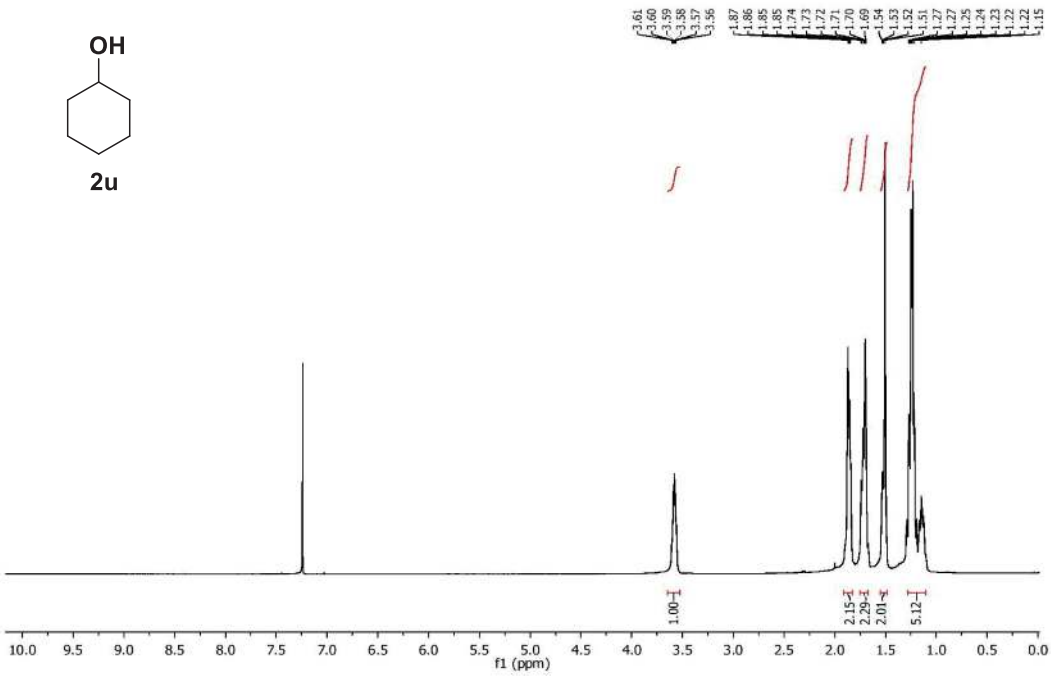


Figure 2.6 ^{1}H NMR of cyclohexanol (**2u**)

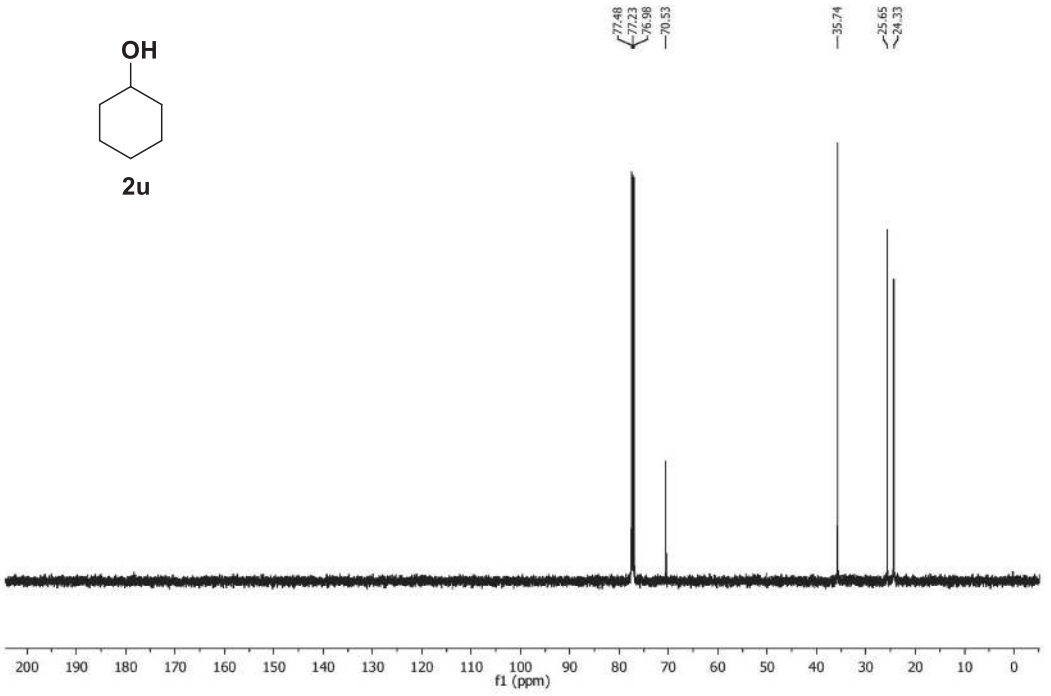


Figure 2.7 ^{13}C NMR of cyclohexanol (**2u**)

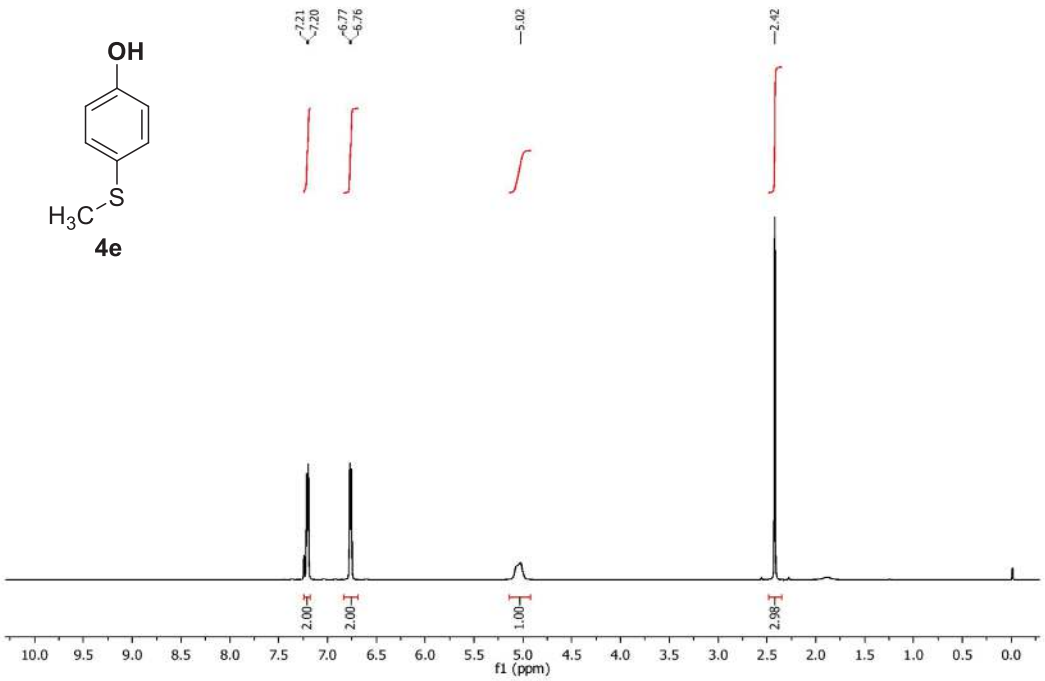


Figure 2.8 ^{1}H NMR of 4-(methylthio)phenol (**4e**)

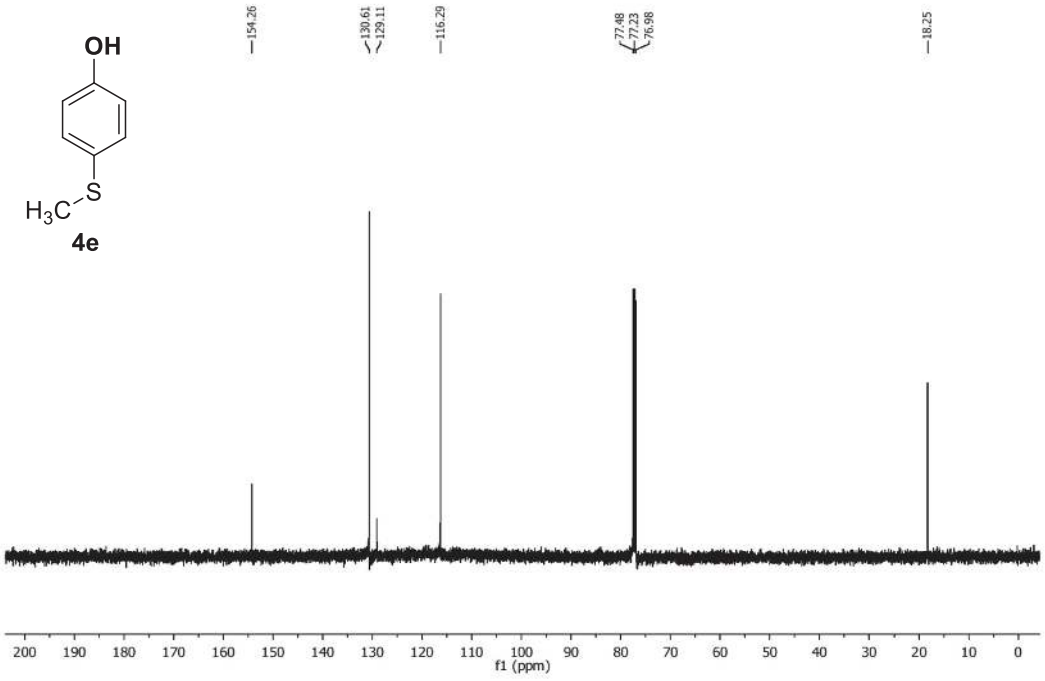


Figure 2.9 ^{13}C NMR of 4-(methylthio)phenol (**4e**)

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