



## Ligand- and base-free synthesis of phenols by rapid oxidation of arylboronic acids using iron(III) oxide



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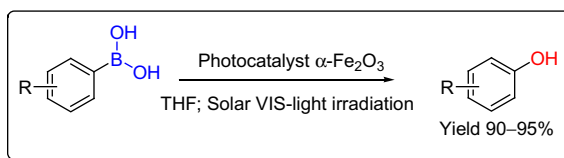
Arylboronic acid

Phenol

Oxidation

Solar VIS-light irradiation

### ABSTRACT



Fe<sub>2</sub>O<sub>3</sub> catalyzed rapid oxidation of arylboronic acids to obtain phenols in excellent yields (90–95%) in the presence of atmospheric oxygen under solar VIS-light irradiation using  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> as a catalyst in ligand- and base-free conditions is presented.

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The oxidation of arylboronic acids gives access to phenols that might be difficult to obtain by other means.<sup>1,2</sup> Phenols serve as synthetic building blocks for the construction of compounds ranging from polymers to pharmaceuticals and agrochemicals.<sup>3a</sup> The synthesis of phenols continues to attract the attention of organic chemists and many methods are available. Among the approaches, nucleophilic aromatic substitution of aryl halides, copper-catalyzed transformation of diazoarenes, and benzyne protocols are dominant.<sup>3b–f</sup>

In continuation of our interest in designing and developing new organometallic reactions we aim to develop new methods based on metal catalyzed transformations.<sup>4</sup> Metal oxides are the largest family of catalysts in heterogeneous catalysis due to the acid–base and redox properties. These metal oxides have been proved as efficient catalysts for several coupling and other reactions. We carried out the reactions of arylboronic acid using iron catalyst which successfully ended in phenol. After observing phenol formation, optimization of reaction was started with screening of various available iron catalysts. At first instance, different commercially available iron catalysts viz FeO, Fe<sub>2</sub>O<sub>3</sub>, Fe<sub>3</sub>O<sub>4</sub>, FeCl<sub>3</sub>, Fe(OH)<sub>3</sub>, and

Fe(acac)<sub>3</sub> were taken for screening. The results for conversion of arylboronic acids to phenol are summarized in Table 1. Amongst all the catalysts, Fe<sub>2</sub>O<sub>3</sub> gives only the desired phenol in 50% yield (Table 1, entry 6a) and we moved our attention for optimization of yields. In this direction, we envisioned the possibility of nanoparticle size and photocatalytic properties of  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> could play a vital role and may help to improve the yields. The photocatalytic activity of  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> particularly is found to depend on its particle size and it is known that amorphous Fe<sub>2</sub>O<sub>3</sub> may also be photocatalytically active. In recent years, there has been an increase in the applications of heterogeneous photocatalysis for example, there are applications in air or water purification and also in some other reactions.<sup>5</sup> However, a few other examples have also been reported on amorphous photocatalysts such as TiO<sub>2</sub>, Ta<sub>2</sub>O<sub>5</sub>, and others which are presently used widely for various applications.<sup>6</sup> We conducted the reaction with commercially available  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> (particle size <5  $\mu$ m, Sigma–Aldrich; Lot# 10012LEV) for confirmation of our findings and the reaction culminated into the expected product formation. It is established that the photocatalytic reactions proceed usually with oxygen molecules (O<sub>2</sub>) in air (Table 2, Scheme 1).

Next, we planned the reaction under solar VIS-light irradiation, since  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> is reported to have the photocatalytic properties as discussed earlier. In this case, the improved yields were observed

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**Table 1**  
Catalyst screening for optimization of phenol formation from phenylboronic acid

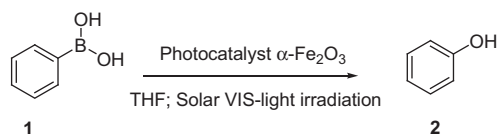
Entry	Catalyst (10 mol %)	Solvent	Temp (°C)/time (h)	Phenol <sup>a</sup> (% yield)
1	Fe <sub>3</sub> O <sub>4</sub>	THF	rt, >5	NR
2	FeO	THF	rt, >5	NR
3	FeCl <sub>3</sub>	THF	rt, >5	NR
4	Fe(OH) <sub>3</sub>	THF	rt, >5	NR
5	Fe(acac) <sub>3</sub>	THF	rt, >5	NR
6	α-Fe <sub>2</sub> O <sub>3</sub>	(a) THF (b) THF:ACN (1:1) (c) DCM (d) ACN (e) H <sub>2</sub> O	rt, >5 rt, >5 rt, >5 rt, >5 rt, >5	05 30 20 25 10
7	α-Fe <sub>2</sub> O <sub>3</sub>	THF	Ambient (solar VIS-light irradiation), 3.5 h	>95
8	α-Fe <sub>2</sub> O <sub>3</sub>	THF	rt (dark), >5 h	Trace

<sup>a</sup> Yields are based on GC–MS results; rt—room temperature; NR—no reaction.

**Table 2**  
Optimization of catalyst quantity

Entry	Substrate	Catalyst	Mol % of catalyst	Isolated yields <sup>a</sup> (%)
1	Phenyl boronic acid	α-Fe <sub>2</sub> O <sub>3</sub>	0.1	Trace
2			1	5
3			10	95
4			25	>95

<sup>a</sup> All yields mentioned are isolated yields after column purification.

**Scheme 1.** α-Fe<sub>2</sub>O<sub>3</sub> catalyzed formation of phenol from arylboronic acid.

in less time and this was found to be the best condition offering highest yields amongst all experiments conducted (Table 1, entry 7). Under dark conditions, the reaction gave very poor yields (Table 1, entry 8), suggesting that the reaction is accelerated by light. Further we moved our attention to ascertain the participation of air oxygen, thus we conducted an experiment using isotope labeled <sup>18</sup>O<sub>2</sub> as oxygen source. The products observed had given desired <sup>18</sup>O<sub>2</sub> labeled phenols (Supplementary Fig. 1), which could be confirmed by GC–MS analysis. H<sub>2</sub><sup>18</sup>O experiment does not give the desired product. The experiments with <sup>18</sup>O<sub>2</sub> and H<sub>2</sub><sup>18</sup>O suggested that the reaction uses air oxygen for the oxidation process. Moreover, additional oxygen supply in the reaction has given the products in very less time, which also supports the involvement of oxygen in the reaction.

We used different solvents as depicted in Table 1 (entry 6a–e), to see the best conversion. While tetrahydrofuran has given best results, reaction in other solvents like dichloromethane, acetonitrile, water, or in a mixture of water/tetrahydrofuran (1:1) has not given good results. The quantity of catalyst was optimized by conducting reactions using various mol % of catalysts; the best results were obtained with 10 mol % catalyst. Therefore, after optimization, all reactions were performed using this condition (Table 1, entry 7) in tetrahydrofuran. To explore the applicability of the present method on various substrates, different electron withdrawing and donating groups containing arylboronic acid substrates were converted to respective phenols at optimized conditions.<sup>7</sup> The experiment for the used Fe<sub>2</sub>O<sub>3</sub> catalyst was carried out which has given the product with excellent yields (90%), confirmed by GC–MS (Table 3).

The present protocol described herein for the synthesis of phenol offers excellent yields under mild conditions and therefore this protocol can be widely applied. Various substituted arylboronic

acid substrates undergo this transformation smoothly. Based on the literature reports, we hypothesize here that α-Fe<sub>2</sub>O<sub>3</sub> may play a similar role like TiO<sub>2</sub>, a widely used photocatalyst for oxidation reactions, which is reported for experiencing an electron-hole pair process.<sup>8</sup>

As reported by Brown et al., organoboranes are readily oxidized by a wide variety of agents including molecular oxygen. Based on these reports we propose here that the combination of Fe<sub>2</sub>O<sub>3</sub>–O<sub>2</sub> also works in a similar manner. First the molecular oxygen will be adsorbed on Fe<sub>2</sub>O<sub>3</sub> and then reacted with boron and forms the expected product.<sup>9</sup> Based on the literature evidences, we assume that α-Fe<sub>2</sub>O<sub>3</sub> behaves as an active photocatalyst as previously reported in various studies.<sup>8,9</sup> Adsorption of a photon with energy greater than the band gap of the iron oxide leads to the formation of an electron hole pair (h<sub>vb</sub><sup>+</sup>/e<sub>cb</sub><sup>-</sup>). The valence band hole of α-Fe<sub>2</sub>O<sub>3</sub> (h<sub>vb</sub><sup>+</sup>) [E<sub>H</sub> = 2.1 V] acts as a powerful oxidant and the conduction band electron (e<sub>cb</sub><sup>-</sup>) is a relatively poor reductant. The conduction band electron, e<sub>cb</sub><sup>-</sup>, does not react with oxygen, but it may lead to the dissolution of α-Fe<sub>2</sub>O<sub>3</sub>.

Quantitative oxidation of the organoborane to the corresponding alcohol would presumably involve the uptake of oxygen of organoborane, followed by hydrolysis of the intermediate boron derivative. The oxygen adsorbed on iron oxide will attack on phenylboronic acid generating phenyl radical. The first carbon–boron bond is oxidized very rapidly by a radical-chain process. This initial oxidation produces peroxide, which may either react with a second mole of oxygen or may undergo an intermolecular redox reaction. This ultimately produces phenol and boric acid as side product. However, in the absence of oxygen or under inert conditions the reaction does not proceed, indicating the reaction requires air oxygen for oxidation. Moreover, as supporting evidence the reaction without catalyst has not given the product, this indicates that the catalyst plays an important role in this oxidation reaction, the plausible mechanism is given as shown in Scheme 2.

Even though there are many methods described in the literature for the conversion of arylboronic acids into phenols,<sup>10</sup> these methods involve ligand or base mediated transformations. Our method offers several advantages over present methods. The established procedure is very simple and the reactions can be conducted in an ordinary flask under sunlight using α-Fe<sub>2</sub>O<sub>3</sub> as a catalyst and

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