

# Boric Acid: A Mild and Efficient Green Catalyst for Organic Transformations

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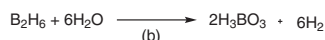
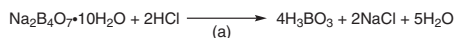
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Boric acid is a simple, inexpensive (500 g, Rs-620, Loba Chemie CAS No. 10043-35-3), commercially available, water-soluble, eco-friendly colorless crystalline inorganic solid. It is also employed as a preservative, pesticide, pH buffer, antiseptic agent, acne treatment, swimming pool chemical, and a precursor to other valuable compounds. Boric acid is a weak acid with  $pK_a$  of 9.15 in pure water at 25 °C.<sup>1</sup> It combines with water to form  $H^+$  ions. Boric acid was synthesized by the reaction of borax (sodium tetraborate decahydrate) and mineral acid such as hydrochloric acid<sup>2</sup> (Scheme 1a). Boric acid was also produced as a byproduct of the hydrolysis of diborane and boron trihalides<sup>3</sup> (Scheme 1b).



**Scheme 1** Synthesis of boric acid



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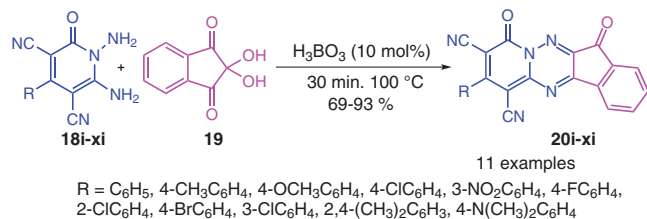
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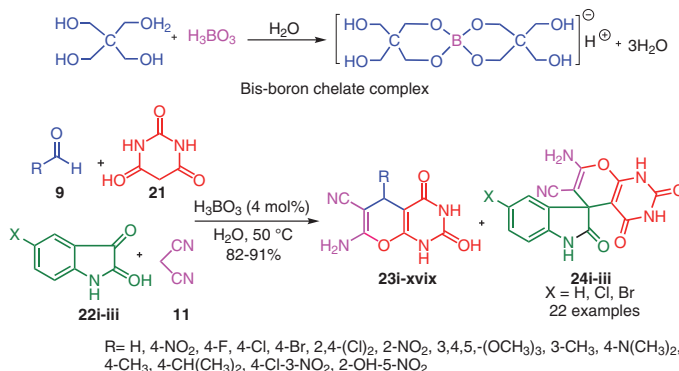
**Table 1** Recent Applications of Boric Acid in Organic Transformations<sup>4</sup>

<p>(A) Bowen Luo et al. reported hydrodeoxygenation (HDO) of phenolic compounds <b>1</b> and raw lignin oil (<b>2</b>) by using a novel homogeneous catalyst called boric acid in combination with Ru/C. The raw lignin oil also gave good (HDO) results with bifunctional catalyst (H<sub>3</sub>BO<sub>3</sub>, Ru/C). The results were improved when reaction was carried out at high temperature. When boric acid was used as a homogeneous catalyst, the rate of conversion of raw lignin oil to biofuel <b>4</b> increased.<sup>5</sup></p>	<p>R = H, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub></p> <p>10 examples</p>
<p>(B) Bhattacharyya et al. reported boric acid assisted hydrogenation of substituted quinolines <b>5</b> to 1,2,3,4-tetrahydroquinolines <b>6</b> was demonstrated under mild reaction conditions using Hantzsch ester (HE) as an organic hydrogen source. The majority of hydrogenation reactions have been carried out with high pressure of hydrogen gas and a metal catalyst, even though the current method is said to be a metal-free synthesis of 1,2,3,4-tetrahydroquinolines <b>6</b> from quinolines <b>5</b> without hydrogen gas.<sup>6</sup></p>	<p>40 examples</p> <p>R = H, 4-CH<sub>3</sub>, 6-OH, 6-F, 3-Br, 3-CN, 3-CH<sub>3</sub>, 6-OCH<sub>3</sub>, 8-OH, 8-CH<sub>3</sub>, 4,7-Cl, 6-CH<sub>3</sub>, 2-CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, 2-CH<sub>2</sub>OH, 2-CH<sub>3</sub>-8-OH, 8-NH<sub>2</sub>, 5-NH<sub>2</sub>, 2-CH<sub>3</sub>, 6-CHO, 2-COOCH<sub>3</sub>, 6-Cl, 6-NO<sub>2</sub>, 6-F, 7-Cl, 8-Br, 8-F-2-CH<sub>3</sub></p>
<p>(C) The reduction of ketone and aldehyde is necessary for the synthesis of primary and secondary alcohols, whereas the reduction of esters is a more challenging transformation to carry out. In fact, the reduction of the former substrates can be accomplished with ease by mild reductants like NaBH<sub>4</sub>, but the reduction of esters typically calls for aggressive reagents like LiAlH<sub>4</sub> or BH<sub>3</sub>. These reagents, despite being extremely active, are pyrophoric and carry significant handling risks. To make this operation safer, Lavergne et al. reported ester hydroboration by benzyl benzoate and pinacolborane reactions with and without a boric acid catalyst. The ester–pinacolborane reaction was carried out at high temperature in methyl tetrahydrofuran, but the product yield was low. Furthermore, the same reaction was carried out with 10 mol% H<sub>3</sub>BO<sub>3</sub>, and quantitative ester hydroboration yield was observed.<sup>7</sup></p>	<p>12 examples</p>
<p>(D) The role of boric acid in the synthesis of 2-amino-4,6-diarylnicotinonitriles <b>13</b> was evaluated. The reaction required the boric acid catalyst in order to proceed, and the highest yield of the product was obtained when 1 equivalent of boric acid was used. Hosseinzadeh et al. prepared a library of substituted 2-amino-4,6-diarylnicotinonitriles <b>13</b> by one-pot multiple components reaction using substituted benzaldehyde <b>9</b>, acetophenone (<b>10</b>), malononitrile (<b>11</b>), and ammonium acetate (<b>12</b>) catalyzed by boric acid. All reactions were carried out in microwave irradiation without solvent in short reaction time with good yield.<sup>8</sup></p>	<p>13 examples</p> <p>R = H, 4-Cl, 3-Cl, 2-Cl, 4-F, 3-F, 2-F, 4-NO<sub>2</sub>, 3-NO<sub>2</sub>, 4-Br, 4-CN, 2,6-(Cl)<sub>2</sub>, 2,4-(Cl)<sub>2</sub></p>
<p>(E) Dipyrromethanes are prime precursors of various biomolecules. Dipyrromethanes have been produced by a variety of methods, but the majority of them required the presence of strong acids and prolonged reaction time. It is not a good practice for strong acids to directly impact the environment and human health. In order to solve the problem Singhal et al. reported one-pot green synthesis of 5-<i>meso</i>-substituted dipyrromethanes <b>15</b> by the reaction of aldehyde <b>9</b> and pyrrole (<b>14</b>) in water catalyzed by boric acid at ambient temperature.<sup>9</sup></p>	<p>11 examples</p> <p>R = H, Ph, 4-ClC<sub>6</sub>H<sub>4</sub>, 4-FC<sub>6</sub>H<sub>4</sub>, 4-BrC<sub>6</sub>H<sub>4</sub>, 4-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>, 4-OCH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, CH<sub>3</sub>CO, 4-pyridyl, 2,4,6-(CH<sub>3</sub>)<sub>3</sub>C<sub>6</sub>H<sub>2</sub></p>
<p>(F) Quinazolinone derivatives are a group of chemicals that are found in many bioactive natural products as well as pharmaceutical substances. The biological, pharmacological, and therapeutic properties of 2,3-dihydroquinazolinone derivatives<sup>10</sup> include but are not limited to antibiotic, anticancer, antidepressant, antihistamine, antihypertonic, antipyretic, antitumor, antituberculosis. The 2,3-dihydroquinazolin-4(1<i>H</i>)-ones <b>17</b> are produced by the reaction of anthranilamide (<b>16</b>) and benzaldehydes <b>9</b> catalyzed by H<sub>3</sub>BO<sub>3</sub>/montmorillonite K10 (H<sub>3</sub>BO<sub>3</sub>/mont K10).<sup>11</sup></p>	<p>9 examples</p> <p>R = C<sub>6</sub>H<sub>5</sub>, 2-Cl-C<sub>6</sub>H<sub>4</sub>, 3-Cl-C<sub>6</sub>H<sub>4</sub>, 4-Cl-C<sub>6</sub>H<sub>4</sub>, 2-OH-C<sub>6</sub>H<sub>4</sub>, 4-OH-C<sub>6</sub>H<sub>4</sub>, 4-OCH<sub>3</sub>-C<sub>6</sub>H<sub>4</sub>, 2-NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>, 3-NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub></p>

(G) 1,2,4-Triazine derivatives **20** have a wide range of biological properties, such as anticancer, muscle relaxant, hypnotic, anti-inflammatory, diuretic, and antihypertensive activities.<sup>12</sup> Darehkordi et al. synthesized dihydroindeno[1,2-*e*]pyrido[1,2-*b*][1,2,4]triazine-1,3- dicarbonitriles. The starting material 4-(aryl)-1,6-diamino-2-oxo-1,2- dihydropyridine-3,5-dicarbonitrile derivatives **18** were obtained by cyclocondensation reaction of cyanoacetohydrazide with *p*-benzidene malononitriles in absolute ethanol while refluxing in piperidine. The reaction of 1,6-diamino-2-oxo-4-phenyl-1,2-dihydropyridine-3,5-dicarbonitrile **18** with ninhydrin (**19**) in acetic acid catalyzed by boric acid produced dihydroindeno[1,2-*e*]pyrido[1,2-*b*][1,2,4]triazine-1,3- dicarbonitriles **20** in moderate to excellent yield.<sup>13</sup>



(H) Dehkordi and coworkers published the green, reusable boric acid/pentaerythritol catalyst catalyzed synthesis of mono- and bispyrano[2,3-*d*]pyrimidinone derivatives **23** in water at 50 °C. Although boric acid is thought to be a very weak acid, when polyhydroxy alcohols are present in an aqueous medium, it behaves as a strong acid. The formation of a bisboron chelate complex when pentaerythritol was added to a boric acid solution had been confirmed by Orthner and Freyss.<sup>14</sup> The complex accumulates in the water and turns more acidic, accelerating the reaction.<sup>15</sup>



A number of organic transformations have been completed successfully using the effective and environment friendly catalyst known as boric acid (Table 1). Almost all organic reactions that are catalyzed by boric acid are safe for the environment, don't require any hazardous solvents, and are uncomplicated to set up and have simple product separation in shorter reaction time. Boric acid was used to create a catalytic system that could be used repeatedly without significant loss of its catalytic activity. Because of all the benefits listed above, the scientific community may choose to use boric acid as an alternative acid catalyst in the future.

## Conflict of Interest

The authors declare no conflict of interest.

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