

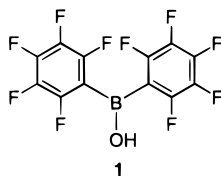
## Bis(pentafluorophenyl)borinic Acid as a Highly Effective Oppenauer Oxidation Catalyst for Allylic and Benzylic Alcohols

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Oppenauer (OPP) oxidation is one of the most useful methods for transforming secondary alcohols into ketones.<sup>1,2</sup> Functional groups such as carbon–carbon double and triple bonds, aldehydes, amino groups, halogens, or sulfur atom-containing groups are not affected by this reaction, which is a great advantage over many oxygen-transferring oxidation processes. In general, however, it is difficult to oxidize primary alcohols to the corresponding aldehydes by the OPP method. Although a variety of basic organo- and inorganometallic reagents have been reported as OPP catalysts, there are only a few examples of the oxidation of primary allylic alcohols.<sup>3,4</sup> For the selective oxidation of allylic alcohols in the presence of saturated alcohols, activated MnO<sub>2</sub> is still one of the most useful reagents, despite the large amount required.<sup>5</sup> We report here that bis(pentafluorophenyl)borinic acid (**1**) is a suitable OPP catalyst for primary and secondary allylic and benzylic alcohols.<sup>6</sup>



Borinic acid **1** was prepared from the known chloroborane (C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>BCl by hydrolysis with aqueous 2 N HCl.<sup>7</sup> Compound **1** is a white, microcrystalline solid which can be readily handled in air and is soluble in many organic solvents. Furthermore, **1** is a stronger Lewis acid than (pentafluorophenyl)borinic acid, but is weaker than tris(pentafluorophenyl)boron.<sup>6</sup>

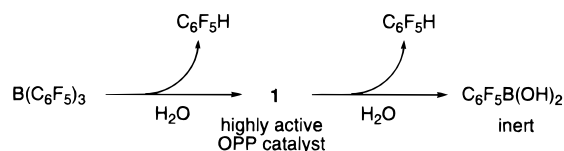
We first examined several arylboron compounds with electron-withdrawing substituents at their aryl groups as catalysts for the OPP oxidation of (*S*)-perillyl alcohol (**2**). Catalysis was carried out using 1–2 mol % of the catalysts in the presence of 6 equiv of pivalaldehyde<sup>8</sup> as

Table 1. Catalytic Activities of Arylboron Compounds in the Oppenauer Oxidation of **2**<sup>a</sup>

entry	catalyst (mol %)	conditions (°C, h)	yield (%)
1	C <sub>6</sub> F <sub>5</sub> B(OH) <sub>2</sub> ( <b>2</b> )	80, 3	0
2	<b>1</b> ( <b>1</b> )	40, 3 <sup>b</sup>	92
3	<b>1</b> ( <b>2</b> )	80, 3	>99
4	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> ( <b>1</b> )	40, 3 <sup>b</sup>	48
5	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> ( <b>2</b> )	80, 3	>99
6	(3,5-(CF <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> ) <sub>2</sub> BOH ( <b>1</b> )	40, 3 <sup>b</sup>	58
7	(3,4,5-F <sub>3</sub> C <sub>6</sub> H <sub>2</sub> ) <sub>2</sub> BOH ( <b>2</b> )	80, 3	47

<sup>a</sup> Unless otherwise noted, the oxidation of **2** (1 equiv, 0.25 M) was carried out in benzene in the presence of pivalaldehyde and a catalyst. <sup>b</sup> The oxidation of **2** (1 equiv, 0.5 M) in toluene.

Scheme 1



a hydride acceptor in toluene or benzene. Representative results are summarized in Table 1. As expected, the catalytic activity of borinic acid **1** was much higher than those of other diarylborinic acids (entries 2 and 3 versus entries 6 and 7). In contrast, (pentafluorophenyl)borinic acid was inert (entry 1). Their catalytic activities were in proportion to their Lewis acidities. Surprisingly, tris(pentafluorophenyl)boron,<sup>9</sup> a commercially available Lewis acid, was also active as a catalyst for the present oxidations (entries 4 and 5). These results can be understood by assuming that borinic acid **1**, generated from tris(pentafluorophenyl)boron in situ, acted as the actual catalyst (Scheme 1). In fact, we determined by <sup>19</sup>F NMR analyses that tris(pentafluorophenyl)boron gradually decomposed to **1** and pentafluorobenzene, and finally to (pentafluorophenyl)borinic acid, under these reaction conditions. In general, triarylborons and diarylborinic acids with electron-withdrawing substituents at their aryl groups are relatively stable in acidic aqueous solutions, but are unstable in neutral and basic aqueous solutions, to give arylboronic acids and arenes.

The decomposition of borinic acid **1** in OPP oxidation may be caused by a nucleophilic attack on the boron atom of **1** by water, alcohols, or aldehydes. To prevent the decomposition of **1**, several additives were examined in the oxidation of **2** under milder conditions (1 mol % of **1**, ambient temperature). The results are summarized in Table 2. Fortunately, the addition of magnesium sulfate efficiently prevented the inactivation of **1** and obviously promoted the oxidation; **2** was completely oxidized to the

(8) Pivalaldehyde was a more suitable oxidant than other aliphatic aldehydes and ketones. Although benzaldehyde was also a good oxidant, it was not easy to remove excess benzaldehyde and benzyl alcohol produced after the oxidation.

(9) (a) Ishihara, K.; Hanaki, N.; Yamamoto, H. *Synlett* **1993**, 577. (b) Ishihara, K.; Funahashi, M.; Hanaki, N.; Miyata, M.; Yamamoto, H. *Synlett* **1994**, 963. (c) Ishihara, K.; Hanaki, N.; Funahashi, M.; Miyata, M.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1721. (d) Ishihara, K.; Hanaki, N.; Yamamoto, H. *Synlett* **1996**, 721. (e) Parks, D. J.; Piers, W. E. *J. Am. Chem. Soc.* **1996**, *118*, 9440.

<sup>†</sup> ResCWE, Nagoya University.

(1) Oppenauer, R. V. *Rec. Trav. Chim. Pays-Bas* **1937**, *56*, 137.

(2) Reviews, see: (a) Djerassi, C. *Org. React.* **1951**, *6*, 207. (b) de Grauw, C. F.; Peters, J. A.; van Bekkum, H.; Huskens, J. *Synthesis* **1994**, 1007.

(3) For Cp<sub>2</sub>ZrH<sub>2</sub> (2 mol %, 130 °C), see: Ishii, Y.; Nakano, T.; Inada, A.; Kishigami, Y.; Sakurai, K.; Ogawa, M. *J. Org. Chem.* **1986**, *51*, 240.

(4) For Zr(O<sup>*t*</sup>Bu)<sub>4</sub> (20 mol %, 20 °C), see: Krohn, K.; Knauer, B.; Küpke, J.; Seebach, D.; Beck, A. K.; Hayakawa, M. *Synthesis* **1996**, 1341.

(5) Fatiadi, A. J. *Organic Syntheses by Oxidation with Metal Compounds*; Mijs, W. J., de Jonge, C. R. H. I., Eds.; Plenum Press: New York, 1986; p 119.

(6) For the selective dehydration of *anti* aldols to  $\alpha,\beta$ -enones catalyzed by **1**, see: Ishihara, K.; Kurihara, H.; Yamamoto, H. *Synlett* **1997**, 597.

(7) (a) Chambers, R. D.; Chivers, T. *J. Chem. Soc.* **1964**, 4782. (b) Chambers, R. D.; Chivers, T. *J. Chem. Soc.* **1965**, 3933.

**Table 2. Additive Effect in the OPP Oxidation of 2 Catalyzed by 1**

entry	1 (1 mol%), <i>t</i> -BuCHO (3 equiv)	
	additive, toluene, rt, 3 h	yield (%) <sup>a</sup>
1	MgSO <sub>4</sub> (100)	>99
2	MS 4A <sup>b,c</sup>	<10
3	none	90
4	EtCO <sub>2</sub> H (5)	85
5	CHCl <sub>3</sub> <sup>d</sup>	85

<sup>a</sup> Isolated yield. <sup>b</sup> 250 mg of MS 4A per 1 mmol of **2** was used. <sup>c</sup> Stirred for 24 h. <sup>d</sup> Chloroform was used in place of toluene as a solvent.

desired perillaldehyde (**3**) within 3 h (entry 1).<sup>10</sup> Removal of water with magnesium sulfate may prevent the hydrolysis of **1** and shift the equilibrium between the mixture of **1** and **2**, and the mixture of the borinate and water toward the borinate. On the other hand, the addition of 4Å molecular sieves notably deactivated **1**. Although acidic additives such as propanoic acid and chloroform stabilized **1**, the oxidation was not accelerated.


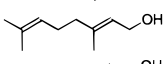
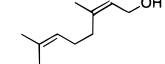
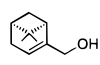
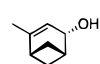
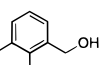
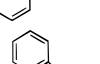
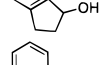

The generality and scope of the borinic acid **1**-catalyzed OPP oxidation were explored using several different primary and secondary alcohols.<sup>9</sup> The results are summarized in Table 3. All of the allylic alcohols used were oxidized to  $\alpha,\beta$ -enals and  $\alpha,\beta$ -enones in high yields (entries 1–5). Unfortunately, however, *E*–*Z* isomerization occurred between geraniol and neral (entries 2 and 3). Primary and sterically less-hindered secondary benzylic alcohols were oxidized fairly well in good yields (entries 6 and 7). The oxidation of 1-phenylpropanol gave propiophenone in a somewhat low yield (entry 8). Saturated alcohols were slowly oxidized to the corresponding carbonyl compounds (entries 9 and 10).

We used these results to demonstrate the synthetic usefulness of this method. In the oxidation of a diastereomeric mixture of carveol (*syn:anti* = 42:58), the *syn* alcohol was stereoselectively oxidized and the *anti* alcohol was recovered in 98% diastereomeric purity; this showed that **1** was a very sensitive catalyst for the steric hindrance of alcohols. In the oxidations of equimolar mixtures of geraniol and  $\beta$ -citronellol, geraniol was obtained in 96% yield and most of  $\beta$ -citronellol was recovered. The selective conversion of allylic alcohols in the presence of saturated alcohols is particularly noteworthy.<sup>5</sup>

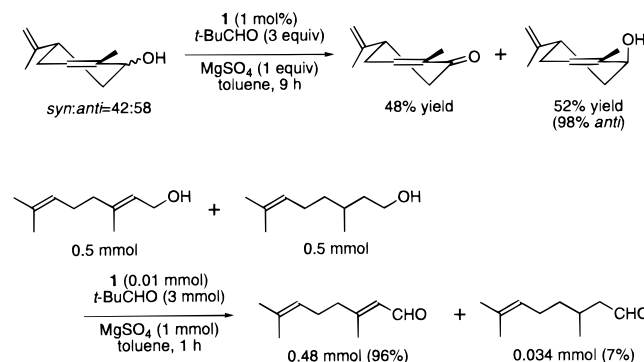
In summary, we have found that **1** is a highly effective catalyst for the OPP oxidation of allylic and benzylic alcohols. Mechanistically, the present reaction is similar to ordinary OPP oxidations catalyzed by metal alkoxides

(10) The following representative procedure was used: To a white suspension of **1** (3.6 mg, 0.01 mmol), magnesium sulfate (120 mg, 1.0 mmol), and **2** (159  $\mu$ L, 1.0 mmol) in dry toluene (2 mL) was added pivalaldehyde (326  $\mu$ L, 3.0 mmol) at ambient temperature under Ar. After being stirred for 3 h, the reaction mixture was diluted with aqueous sodium hydrogen carbonate (5 mL) and extracted twice with ether (5 mL each time). The combined organic phase was dried over magnesium sulfate, filtered, and evaporated. The product was purified by column chromatography on silica gel using pentane–ether (7:1) as the eluant (149 mg of **3**, 99% yield).

**Table 3. The OPP Oxidation of Various Alcohols Catalyzed by 1<sup>a</sup>**

entry	alcohol	<b>1</b> (mol%)	time (h)	yield (%) <sup>b</sup>
1 <sup>c</sup>		2	27	85
2		1	3	95 <sup>d</sup>
3		1	3	98 <sup>e</sup>
4		1	3	>99
5		1	2	>99
6 <sup>c</sup>		2	42	85
7 <sup>f</sup>		2	5	90
8 <sup>f</sup>		2	5	20
9 <sup>f</sup>	<i>n</i> -C <sub>13</sub> H <sub>27</sub> OH	2	6	<26 <sup>g</sup>
10 <sup>f</sup>	<i>t</i> -Bu- 	2	8.5	49 <sup>i</sup>

<sup>a</sup> For a typical experimental procedure, see reference 9. <sup>b</sup> Isolated yield. <sup>c</sup> 4 equiv of pivalaldehyde was used. <sup>d</sup> *E:Z* = 99:1. <sup>e</sup> *E:Z* = 72:28. <sup>f</sup> 2 equiv of MgSO<sub>4</sub> was used. <sup>g</sup> Other products were included. <sup>h</sup> *cis:trans* = 65.5:34.5. <sup>i</sup> 51% of the recovered alcohols (*cis:trans* = 65.5:34.5).



which have a basic character, but the strong Lewis acidity of **1** remarkably enhances the coordination of the carbonyl acceptor with the metal, the driving force in OPP oxidations. Other applications of strongly Lewis acidic diarylborinic acids are under investigation.

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**Supporting Information Available:** Experimental procedures and characterization data for all new compounds (3 pages).

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