# Articles

## Anomalous Rapid Reduction of Salicylaldehyde by Pyridine–Borane. Mechanism and Application to Selective Aldehyde Reduction

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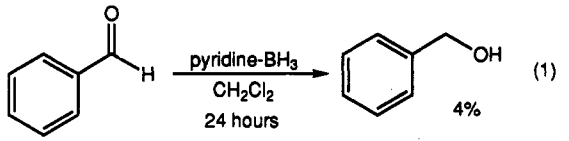
The reduction of salicylaldehyde by pyridine–borane complex (PB) is much faster than that of other substituted benzaldehydes and ketones (seconds vs hours). Experiments reveal that this acceleration is due to an autocatalytic process involving a pyridinium boronate salt, a component of the equilibrating product mixture from PB reduction of salicylaldehyde. This pyridinium salt behaves as a mild Brønsted acid and effectively accelerates aldehyde but not ketone reductions by PB. The observation that mild Brønsted acids are catalysts for PB reductions led to the development of a method using AcOH in $CH_2Cl_2$ to promote the selective reduction of aldehydes in the presence of ketones.

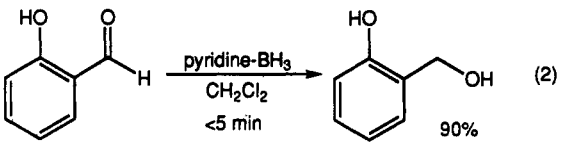
**Introduction.** Amine–borane complexes have gained a reputation for being mild reducing and hydroborating agents.[1] Of this large family, pyridine–borane complex (PB) is one of the mildest. For example, treatment of 4-*tert*-butylcyclohexanone with PB (1:1) in $CH_3OH/H_2O$ leads to only 29% reduction after 18 h at 20 °C.[2] It was then surprising to observe that the reduction of salicylaldehyde to salicyl alcohol by the same reagent required *less than 5 min* at 20 °C in various organic solvents. During the course of experiments to understand the origin of this acceleration, it became clear that the combination of mild Brønsted acids and PB could have useful applications. In this paper, we report experiments that illuminate a novel autocatalytic process and the development of a protocol to reduce selectively aldehydes in the presence of ketones.[3]

### Results and Discussion

**Anomalous Reduction of Salicylaldehyde.** In order to compare relative reduction rates, solutions of benzaldehyde and salicylaldehyde were prepared (0.23 M, $CDCl_3$), treated with equimolar amounts of PB, and monitored by $^1H$ NMR. In the case of salicylaldehyde, reduction was complete before a spectrum could be obtained, while for benzaldehyde only 23% conversion was observed after 7 h. This corresponds to a roughly 800-fold difference in the time required to achieve complete reduction (eqs 1 and 2). This level of acceleration relative to benzaldehyde appears unique to salicylaldehyde. Replacement of salicylaldehyde by *o*-anisaldehyde (blocking the hydroxyl group) or by *p*-hydroxybenzaldehyde (relocating the hydroxyl group) leads to rates of reduction similar to benzaldehyde. Replacement of salicylaldehyde by *o*-hydroxyacetophenone leads to an acceleration over the rate observed for acetophenone reduction under identical




(1)




(2)

conditions, but much smaller than the system of interest. When 4-hydroxy-4-methyl-2-butanone was used as a substrate, a similar slight acceleration was observed relative to 2-heptanone. The replacement of PB by trimethylamine–borane and *tert*-butylamine–borane complexes was examined with similar reduction rates observed for salicylaldehyde and benzaldehyde.

The acceleration with salicylaldehyde is the consequence of an autocatalytic process, as supported by the following. After combining salicylaldehyde and PB, there is an induction period of 1–2 min before reduction occurs. The onset of reduction is accompanied by gas evolution, presumably dihydrogen. The reaction is complete by the time gas evolution has finished, 1–2 min after its onset. The induction period, which varied with concentration, hinted at an autocatalytic process. This was confirmed by allowing a salicylaldehyde reduction to go to completion and then adding either additional salicylaldehyde, benzaldehyde, or acetophenone followed by PB. With salicylaldehyde, gas evolution was immediate and the reduction was complete within 1 min. With benzaldehyde, reduction was complete within 10 min without gas evolution. With acetophenone, a rate acceleration was observed but of a much smaller degree than that observed for benzaldehyde.

Spectroscopic techniques were then applied to the $CDCl_3$ solutions that resulted from combining salicylaldehyde and PB to help elucidate the structure of the reduction product/catalyst. $^1H$ and $^{13}C$ NMR spectra showed complete consumption of salicylaldehyde and the formation of a new material. The signals expected for a salicyl

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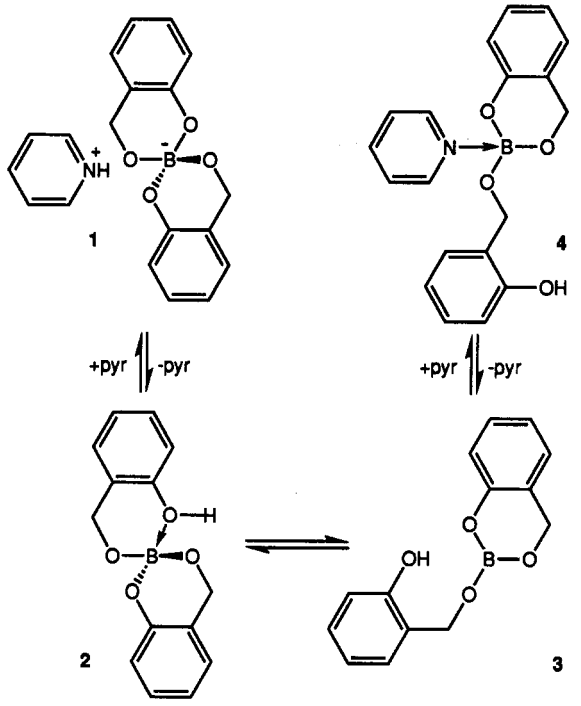
(1) For reviews, see: Lane, C. F. *Aldrichim. Acta* **1973**, *6*, 51–58. Hutchins, R. O.; Learn, K.; Nazer, B.; Pytlewski, D.; Pelter, A. *Org. Prep. Proc. Int.* **1984**, *16*, 335–372.

(2) Concentration was not specified, see: Andrews, G. C.; Crawford, T. C. *Tetrahedron Lett.* **1980**, *21*, 693–696.

(3) For an overview of aldehyde vs ketone selective reduction, see: Greeves, N. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 8, pp 16–17.

0022-3263/94/1959-0523$04.50/0 

**Scheme 1. Possible Products and Their Equilibria from Pyridine–Borane Reduction of Salicylaldehyde**




alcohol derivative and pyridine were found, but were shifted slightly downfield from their normal locations. Addition of pyridine showed that the reduction product/catalyst pyridine was freely exchanging with the added pyridine (one set of upfield shifted pyridine resonances in $^1$H NMR). These spectra also revealed the presence of unreacted PB using a 1:1 ratio of reactants. When salicylaldehyde and PB were combined in a 2:1 ratio, no reactants could be observed. As only signals for one type of salicyl unit were observed, a symmetrical species or a rapid exchange process of two different salicyl units is indicated. The application of $^{11}$B NMR revealed a single broad peak ($\delta$ 6.90, width = 253 Hz). The location and width of this peak did not change upon $^1$H decoupling.

While the information presented is consistent with the formation of symmetrical pyridinium boronate 1, a rapid equilibrium among compounds 1–4 is probably the best description of the reduction product/catalyst with compounds 1 and 4 predominating (Scheme 1). This is suggested by the $^{11}$B chemical shifts of amine–B(OEt)$_3$ complexes (9.3–13.7 ppm[4]) and LiB(OMe)$_4$ (2.9 ppm[5]), which are roughly an average of the observed 6.90 ppm value. Compounds 2 and 3 are proposed to allow the interconversion of 1 and 4 and are probably minor components of the mixture. For example, large amounts of borate ester 3 would significantly perturb the observed average $^{11}$B chemical shift given B(OMe)$_3$ appears at 18.1 ppm.[4] No $^{11}$B chemical shift information regarding compounds similar to 2 could be found. Attempts to slow the suggested equilibria and resolve the individual components failed.[6]

Additional support for the assignments made comes from independent synthesis.[7] When salicyl alcohol (2.0 equiv) was combined with boric acid (1.0 equiv) in refluxing benzene, the mixture soon became homogeneous, and the water formed was removed by distillation. Concentration of the resulting benzene solution, followed by dissolution in $CDCl_3$ and addition of pyridine (1.0 equiv), gives material possessing $^1$H and $^{13}$C NMR spectra indistinguishable from those resulting from the reduction of salicylaldehyde by PB.

Two experiments reveal the mode of catalysis. If diisopropylamine (0.1 equiv) is added to a solution of salicylaldehyde (0.23 M, $CDCl_3$) and then PB (0.5 equiv), no reduction is observed by $^1$H NMR after 1 h. If a solution of benzaldehyde (0.53 M, $CDCl_3$) is treated with pyridinium *p*-toluenesulfonate (PPTS, 0.2 equiv) and PB (1.0 equiv), $^1$H NMR reveals 94% reduction after 2.5 h. Apparently, Brønsted acid catalysis is taking place. This has been recognized as a way of accelerating amine–borane reductions for some time, but stronger or larger amounts of acid were generally used.[8] While the reaction time for PPTS-catalyzed PB reduction of benzaldehyde is much longer than that of PB reduction of salicylaldehyde, PPTS and the reduction product/catalyst from PB reduction of salicylaldehyde are comparable catalysts. When a solution of benzaldehyde (0.53 M, $CDCl_3$) is treated with reduction product/catalyst (0.1 equiv) and PB (1.0 equiv), $^1$H NMR reveals 51% reduction after 2.5 h.

While it may seem unlikely that 2 is capable of protonating pyridine to any degree, a large body of work supports this.[9] Boric acid achieves its acidity ($pK_a$ ($H_2O$) = 9.82) not by proton donation, but by hydroxyl-ion acceptance.[10] When diols or polyols and their corresponding borate esters are involved instead, acidities can increase dramatically. For example, combining mannitol with boric acid gives a material possessing a $pK_a$ of 5.15. An estimate of the $pK_a$ of 2 can be derived from the $^1$H NMR spectra of the reduction product/catalyst, PPTS, and pyridine.[11] With PPTS, the pyridine is completely protonated, and the three $^1$H NMR signals of the pyridine are downfield relative to those of pyridine. If the pyridine of the reduction product/catalyst were completely protonated, it would display the chemical shifts of PPTS. If the converse were true, chemical shifts would be similar to pyridine. The following chemical shifts (*ortho*/*para*/*meta*; 0.23 M, $CDCl_3$) are observed for PPTS, reduction product/catalyst, and pyridine, respectively: 9.03/8.42/7.97; 8.62/7.94/7.50; 8.62/7.68/7.30. With the signals for the reduction product/catalyst more like those of pyridine than pyridinium, these data indicate that 2 is a somewhat weaker acid than pyridinium, consistent with the obser-

(4) Landesman, H.; Williams, R. E. *J. Am. Chem. Soc.* **1961**, *83*, 2663–2666.

(5) Onak, T. P.; Landesman, H.; Williams, R. E.; Shapiro, I. *J. Phys. Chem.* **1959**, *63*, 1533–1535.

(6) The $^1$H NMR spectrum of a reduction solution at −45 °C showed no loss of symmetry or line broadening. This is consistent with the weak association of amine bases to borates and the facile nature of proton exchange between oxygen and nitrogen acids and bases.

(7) For a survey of borate ester synthesis methods, see: Nesmeyanov, A. N.; Sokolik, R. A. In *Methods of Elemento-Organic Chemistry*; Nesmeyanov, A. N., Kocheshkov, K. A., Eds.; World Publishing: New York, 1967; Vol. 1, Chapter 15.

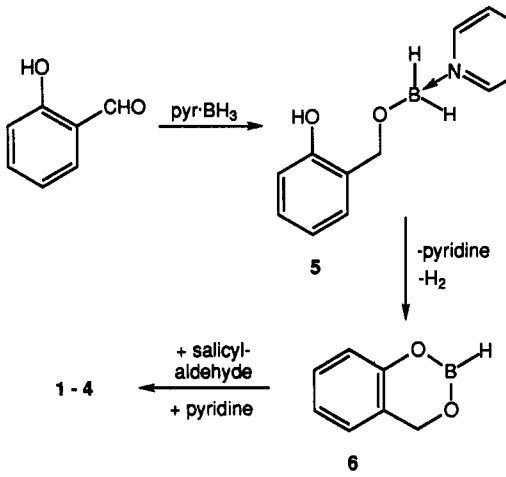
(8) Kelly, H. C.; Giusto, M. B.; Marchelli, F. R. *J. Am. Chem. Soc.* **1964**, *86*, 3882–3884. White, S. S., Jr.; Kelly, H. C. *J. Am. Chem. Soc.* **1968**, *90*, 2009–2011. White, S. S., Jr.; Kelly, H. C. *J. Am. Chem. Soc.* **1970**, *92*, 4203–4209.

(9) Steinberg, H. *Organoboron Chemistry*; Wiley: New York, 1964; Vol. 1, Chapter 15. Sandersen, B. R. In *Mellor's Comprehensive Treatise on Inorganic and Theoretical Chemistry*; Thompson, R., Welch, A. J. E., Eds.; Longman: London, 1980; Vol. 5, Suppl. 1, Part A: Boron, pp 721–737. Indeed, the conductance of aqueous solutions of 2 were studied more than 50 years ago by Böeseken, see: Böeseken, J. H.; Gonggrijp, J. H.; van Rhijn, A. E. A. *Rec. Trav. Chim.* **1938**, *57*, 1356–1358.

(10) Greenwood, N. N.; Earnshaw, A. *Chemistry of the Elements*; Pergamon: New York, 1984; pp 229–230.

(11) This analysis assumes that any shifting of pyridine resonances due to the association present in 4 is small and that proton transfer processes are rapid.

**Scheme 2. Proposed Mechanism for Formation of Reduction Product Mixture**




vation that PPTS is a more effective catalyst on a per mole basis than the reduction product/catalyst.

Experiments were also performed to determine the sequence of events leading to reduction product/catalyst formation (Scheme 2). A solution of β-naphthol was treated with PB and the reduction product/catalyst obtained from salicylaldehyde and PB. No evolution of hydrogen was observed, and $^1$H NMR spectra showed the hydroxyl hydrogen of β-naphthol to be still present.[12] This indicates that aldehyde reduction is the first step and hence the intermediacy of **5**. As hydrogens are replaced by oxygens in amine–borane complexes, the strength of the boron–nitrogen bond decreases,[13] suggesting two possible paths for releasing $H_2$ and formation of another B–O bond to give dialkoxyborane **6**:[14] (1) nucleophilic displacement of pyridine from **5** by the hydroxyl group followed by loss of $H_2$, or (2) dissociation of pyridine from **5** to give a monoalkoxyborane, association of the hydroxyl oxygen, and loss of hydrogen. Since pyridine is still present, **6** is presumably in equilibrium with its corresponding pyridine adduct.

The final event of Scheme 2 is conversion of **6** to the **1–4** mixture.[15] To achieve this, dialkoxyborane **6** must act as a reducing agent; however, dialkoxyboranes are mild reducing agents. For example, ketone reductions by borane become quite slow at the $(RO)_2BH$ stage,[16] and catecholborane requires 5.5 h to reduce heptanal to heptanol (0.5 M).[17] As **6** proved inaccessible,[18] catecholborane was used in its stead to evaluate the kinetic competence of dialkoxyboranes in this scheme.[19] A solution of catecholborane and acetophenone ($CDCl_3$, 0.28 M) was monitored by $^1$H NMR with and without added PPTS. After 30 min, only 2% reduction was observed without PPTS while 18% reduction was observed with PPTS (0.15 equiv). A parallel experiment with benzaldehyde showed 46% reduction after 17 min without PPTS and 91% reduction with PPTS (0.1 equiv). From these data, mild acid catalysis for the reduction of salicylaldehyde by **6** is again necessary to rationalize the reaction rates observed.

The anomalous rapidity with which salicylaldehyde is reduced by PB apparently demands an interesting confluence of events: the presence of an *o*-hydroxy group, leading to the formation of dialkoxyborane **6** and eventually acidic **1/2**; the acceleration of PB reduction of aldehydes by mild acids; the acceleration of dialkoxyborane reduction of aldehydes by mild acids as well, which to our knowledge has not been noted elsewhere. These suggested the exploration of several avenues of which the following is one.

**Selective Aldehyde Reductions.** The area of selective carbonyl reduction has been an active one[3] with approximately 30 reported methods of selectively reducing aldehydes in the presence of ketones.[20] While almost all of these methods are effective, few are also convenient as measured by reagent accessibility, reaction conditions, expense, etc. Given the accessibility and properties of PB, it seemed appropriate to investigate further our observation that pyridinium was an effective catalyst for carbonyl reductions. It should be noted that PB has already been exploited in this manner by Babler and Sarussi by using activated alumina as a support.[21]

PB is itself not discriminating as a reducing agent, reducing acetophenone only twice as fast as benzaldehyde.[22] Experiments outlined earlier, however, suggested a different situation under conditions of acid catalysis. For example, the **1–4** mixture significantly accelerated the reduction rate of benzaldehyde but not that of acetophenone, and the reduction rate of *o*-hydroxyacetophenone was not signficantly enhanced even though species similar to **1** and **2** could form. This prompted a competition experiment in which a benzaldehyde and acetophenone mixture (each 0.54 M, $CDCl_3$) was treated with first PPTS (0.1 equiv) and then PB (1 equiv). $^1$H NMR spectra showed that benzaldehyde was consumed *25 times faster* than acetophenone.

While the selectivity supplied by PPTS was satisfactory, it was deficient as a catalyst. Reactions were sluggish and difficult to drive to completion (0.1 equiv PPTS, 33 h, 66% conversion), leading to a search for other mild Brønsted acids. Acetic acid proved an excellent replacement, given that acids are slowly consumed under the reaction condition (vide infra).[23] Standard conditions are to treat a 0.25 to 0.5 M $CH_2Cl_2$ solution of substrate and acetic acid (1.0 equiv) with PB (0.5 equiv). It should be

(12) Aqueous and alcoholic media are used for PB reductions without difficulty, highlighting the stability of the complex to hydroxyl groups.

(13) Woods, W. G.; Strong, P. *J. Am. Chem. Soc.* **1966**, *88*, 4667–4671. Young, D. E.; McAchran, G. E.; Shore, S. G. *J. Am. Chem. Soc.* **1966**, *88*, 4390–4396. McAchran, G. E.; Shore, S. G. *Inorg. Chem.* **1966**, *5*, 2044–2046.

(14) The intramolecular reaction to produce **6** is assumed to be much faster than intermolecular ones. Alkoxyboranes are known to undergo disproportionation reactions, potentially leading to complex mixtures in this system, but these are recognized as being slow, see: Uchida, H. S.; Kreider, H. B.; Murchison, A.; Masi, J. F. *J. Chem. Phys.* **1963**, *75*, 1414–1424. Pasto, D. J.; Balasubramaniyan, V.; Wojtkowski, P. W. *Inorg. Chem.* **1969**, *8*, 594–598.

(15) That **6** and not its pyridine adduct is the active reductant is suggested from experiments with catecholborane. The rate of reduction of acetophenone with catecholborane is roughly halved in the presence of pyridine (1 equiv). As catecholborane is a weak Lewis acid, it is only partially associated with pyridine. Presumably, that fraction associated is no longer an active reductant with a consequent depression of the reduction rate.

(16) Brown, H. C.; Schlesinger, H. I.; Burg, A. B. *J. Am. Chem. Soc.* **1939**, *61*, 673.

(17) Lane, C. F.; Kabalka, G. W. *Tetrahedron* **1976**, *32*, 981–990.

(18) Combining $BH_3$·THF solutions with salicyl alcohol followed by pyridine gave complex mixtures.

(19) Catecholborane is presumably a better reducing agent than **6**, see: Fish, R. H. *J. Org. Chem.* **1973**, *38*, 158.

(20) Ward, D. E.; Rhee, C. K. *Synth. Commun.* **1988**, *18*, 1927–1933.

(21) Babler, J. H.; Sarussi, S. J. *J. Org. Chem.* **1983**, *48*, 4416–4419.

(22) Andrews, G. C. *Tetrahedron Lett.* **1980**, *21*, 697–700.

(23) Acetic acid was also found to be an effective solvent for PB reduction of ketones, see: Yorka, K. V.; Truett, M. L.; Johnson, W. S. *J. Org. Chem.* **1962**, *27*, 4580–4587.

**Table 1. Relative Reactivities of Aldehydes with Respect to Ketones toward Pyridine–Borane Complex and Catalytic AcOH[a]**

| carbonyl compounds[b] | % reduction[c] |
|---|---|
| benzaldehyde | 99 |
| acetophenone | 6 |
| heptanal | 95 |
| 2-heptanone | 0 |
| benzaldehyde | 95 |
| cyclohexanone | 22 |

[a] Reactions were performed at 20 °C in $CDCl_3$. [b] Competition experiments between equimolar quantities of grouped carbonyl compounds and pyridine–borane complex. Use of 0.5 mol equiv of pyridine–borane led to similar ratios. [c] Reduction amounts determined by $^1H$ NMR.

noted that two hydride equivalents are used from PB and that the reaction takes place under mildly acidic conditions. Reaction times range from 1.5 to 24 h depending on substrate and concentration. Using these conditions, benzaldehyde, heptanal, and cyclohexanecarboxaldehyde were reduced to their corresponding alcohols in 84, 94, and 74% yield, respectively. Other organic solvents such as $Et_2O$, THF, and $CHCl_3$ have been used with similar results.

Regarding selective aldehyde reduction, acetic acid was again useful (see Table 1). No difficulties were encountered differentiating aromatic aldehyde and ketone or aliphatic aldehyde and acyclic ketone. The final example shows the worst possible pairing, that of a highly reactive cyclic ketone and an aromatic aldehyde.[24] As a cautionary note, it bears mentioning that the only meaningful way to record relative reactivities of aldehydes and ketones in these studies is by some type of internal competition. Quite often, the primary reduction products are themselves reducing agents with their own typically different powers of discrimination.

During a reduction, gas, presumably hydrogen, evolves steadily. This raised the possibility that pyridine–acetoxyborane complexes, proposed as intermediates in PB reductions in AcOH of heterocycles,[25] are the actual reductants (eq 3). Two experiments were performed to address this possibility. A $CDCl_3$ solution of PB (0.36 M) and AcOH (1.5 M) was monitored by $^{11}B$ NMR for 3 h.[26] Very slow gas evolution was observed, but no new species were observed spectroscopically, indicating that the first equivalent of hydride for reduction comes from PB itself. In addition, the volume of hydrogen evolved during a reaction was monitored (heptanal vs 2-heptanone). Gas evolution was fairly steady and totaled 0.71 mol equiv. Therefore, first-formed alkoxyborane–pyridine complexes combine with AcOH to give mixed alkoxyacetoxyborane–pyridine complexes (eqs 4 and 5), which explains the need for relatively large amounts of catalyst. Whether or not these complexes are behaving as reducing agents is unclear.

## Conclusion

The anomalous rapidity with which salicylaldehyde is reduced by PB relative to other carbonyl compounds has been determined to be the result of an autocatalytic process. The reduction product/catalyst is composed of a rapid equilibrium of several species, two of which are mild Brønsted acids that effectively catalyze PB reduction. The observation that mild acids can catalyze aldehyde reductions by PB has been exploited by the development of an aldehyde selective reduction protocol based on acetic acid catalysis.

$$\text{pyridine}\cdot BH_3 \xrightarrow{\text{AcOH}} \text{pyridine}\cdot BH_n(OAc)_{3-n} + H_2 \quad (3)$$

$$\text{pyridine}\cdot BH_2(OR) \xrightarrow{\text{AcOH}} \text{pyridine}\cdot BH(OAc)(OR) + H_2 \quad (4)$$

$$\text{pyridine}\cdot BH(OR)_2 \xrightarrow{\text{AcOH}} \text{pyridine}\cdot B(OAc)(OR)_2 + H_2 \quad (5)$$

## Experimental Section

**General.** All reactions were performed under a dry nitrogen atmosphere. $CH_2Cl_2$ and $CHCl_3$ were distilled from $CaH_2$ prior to use. $CDCl_3$ was distilled from $CaH_2$ and then filtered through basic, activated, Brockmann I alumina immediately prior to use. Pyridine–borane complex (PB) was used as received from Aldrich Chemical Co. or Boulder Scientific Co. and typically contained 10 mol % pyridine. The excess pyridine could be removed *in vacuo* from PB but did not change the chemistry observed. Catecholborane was used as received from Aldrich Chemical Co. $^1H$, $^{13}C$, and $^{11}B$ NMR spectra were recorded at 200.05, 50.30, and 96.42 MHz, respectively. All NMR spectra were acquired in $CDCl_3$.

**Reduction Product/Catalyst.** Under a nitrogen atmosphere, salicylaldehyde (17.5 μL, 0.164 mmol) and PB (8.3 μL, 0.082 mmol) were added to an NMR tube containing 600 μL of $CDCl_3$. After 1.5 min, large amounts of gas evolved for ca. 1 min. The tube was capped afterwards and NMR spectra acquired. Concentration *in vacuo* afforded an oil that was dissolved in $CH_2Cl_2$ to obtain IR data: IR ($CH_2Cl_2$) 3040, 2480, 2230, 1625, 1585, 1420, 1390, 1340, 1275, 1205, 1070, 1030, 1000 $cm^{-1}$; $^1H$ NMR δ 12.0–9.5 (s, br, 1H), 8.64 (dt, $J$ = 1.7, 4.8, 2H), 7.94 (t of t, $J$ = 1.7, 7.3, 1H), 7.50 (m, 2H), 7.09 (br t, $J$ = 7.2, 1H), 7.00 (br d, $J$ = 6.7, 1H), 6.90–6.80 (m, 2H), 5.02 (s, 2H); $^{13}C$ NMR δ 154.7, 143.6, 142.2, 127.8, 125.7, 125.1, 124.5, 118.7, 117.2, 62.2; $^{11}B$ NMR δ 6.90 (s, peak width = 253 Hz). Treatment of solutions containing 1 with 1 N HCl for 15 min, followed by extractive isolation, drying ($Na_2SO_4$), and concentration, afforded material that was indistinguishable by $^1H$ and $^{13}C$ NMR from salicyl alcohol.

**Independent Synthesis of Reduction Product/Catalyst.** A 25-mL round-bottom flask was charged with salicyl alcohol (100 mg, 0.806 mmol), boric acid (25 mg, 0.404 mmol), and 10 mL of benzene. The flask was fitted with a short path distillation head and heated until distillation commenced. The first 3–4 mL of distillate was cloudy. After the dropwise distillation of 8 mL total, the apparatus was allowed to cool and the remaining solvent removed under high vacuum. The residue was dissolved in 4 mL of dry $CDCl_3$ and treated with pyridine (32.6 μL, 0.404 mmol). A portion of the solution was removed and analyzed by $^1H$ and $^{13}C$ NMR. It proved to be identical to the material generated by PB reduction of salicylaldehyde.

**NMR Competition Experiment.** Heptanal (69.6 μL, 0.50 mmol) and 2-heptanone (69.8 μL, 0.50 mmol) were added consecutively to an NMR tube and dissolved in 1.00 mL of $CDCl_3$. After the liquids were mixed, glacial acetic acid (26.6 mL, 0.50 mmol) and PB (25.3 μL, 0.25 mmol) were added and again thoroughly mixed. $^1H$ NMR spectra were recorded periodically using a relaxation delay of 6 s. The extent of reaction was based on the suitably scaled areas associated with the carbinol methylene of heptanol and the aldehydic hydrogen of heptanal.

**General Pyridine–Borane Complex Selective Reduction.** Heptanal (0.252 g, 2.20 mmol) was dissolved in 4.4 mL of $CH_2Cl_2$

(24) Cyclohexanones are well documented to be more reactive than acyclic ketones, and in our hands, benzaldehyde is roughly 3 times less reactive than heptanal.

(25) Kikugawa, Y.; Saito, K, Yamada, S. *Synthesis* 1978, 447–448.

(26) This is a higher acetic acid concentration than that used in selective reductions.

under an inert atmosphere. To this were sequentially added glacial acetic acid (126 mL, 2.2 mmol) and PB (112 mL, 1.10 mmol), and the reaction was stirred for 3 h. Concentration of the reaction mixture and flash chromatography (25% EtOAc/hexanes) gave heptanol (0.227 g) as a colorless liquid (89%).

**Gas Volume Determination for Selective Reduction.** To a solution of heptanal (0.500 g, 4.38 mmol) and 2-pentanone (0.388 g, 4.38 mmol) in 8.75 mL of $CH_2Cl_2$ was added glacial acetic acid (0.250 mL, 0.438 mmol). This gently stirring mixture was attached to a gas buret equipped with leveling bulb. After 30 min of equilibration, PB (0.222 mL, 2.19 mmol) was added in one portion. After 2.5 h (enough time for complete reduction of heptanal), 35 mL (1.56 mmol) of gas had been evolved. Normal workup (see above) and $^1H$ NMR revealed essentially complete consumption of heptanal and trace amounts of 2-heptanol.

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