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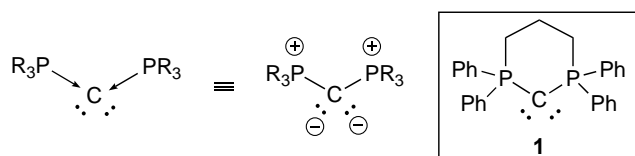
## Carbodiphosphorane-Catalyzed Hydroboration of Ketones and Imines

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**We report the use of a cyclic carbodiphosphorane catalyst for ketone and imine hydroboration reactions. To our knowledge, this represents the first use of a carbodiphosphorane as an organocatalyst. The carbodiphosphorane shows superior catalytic activity compared to other neutral carbon nucleophiles tested.**

Lewis bases have emerged as a powerful class of catalysts for sustainable organic transformations.<sup>1</sup> Within the context of Lewis base catalysis, there has been significant recent interest in the use of neutral carbon nucleophiles as organocatalysts. Most prominently, *N*-heterocyclic carbenes (NHCs) are established catalysts for a range of organic transformations.<sup>2</sup> Other carbon nucleophiles have more recently appeared as organocatalysts, including *N*-heterocyclic olefins,<sup>3</sup> carbodicarbenes,<sup>4</sup> and carbonyl-stabilized phosphorus ylides.<sup>5</sup>

Carbodiphosphoranes (CDPs) constitute an unusual class of molecules featuring a two-coordinate carbon center that is formally zerovalent and possesses two lone pairs (Figure 1).<sup>6</sup> As a result, the central carbon of a CDP is exceptionally electron rich. CDPs are of interest as ligands for transition metal and main group complexes,<sup>7</sup> as they are more strongly donating than NHC ligands based on Tolman electronic parameters.<sup>8</sup> Despite their rich coordination chemistry, to our knowledge, there are no previous reports using carbodiphosphoranes as organocatalysts. Herein, we disclose the use of the cyclic CDP **1**<sup>9</sup> as a catalyst for the efficient hydroboration of ketones and imines.



**Figure 1.** Two carbodiphosphorane (CDP) representations and the structure of cyclic CDP catalyst **1**.

Ketone reduction is a widely used route to prepare alcohols.<sup>10</sup> To complement hydrogenation methods, ketone hydroboration takes advantage of borane reagents, which can be used under mild reaction conditions and without the need for high-pressure apparatus. There have been significant advances developing main group and first-row transition metal catalysts for ketone hydroboration,<sup>11</sup> with nucleophilic motifs appearing often as activators or catalysts.<sup>12</sup>

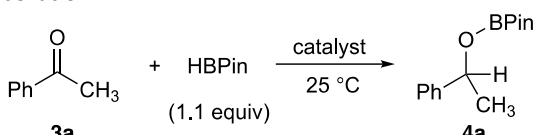
We have compared acetophenone hydroboration catalyzed by a range of neutral carbon nucleophiles as an initial proof-of-concept for carbodiphosphorane catalytic activity. Reactions were performed using 1.1 equiv of pinacolborane (HBPin) and 5 mol% catalyst loading in benzene-*d*<sub>6</sub> solvent for 1 h at 25 °C (Table 1). The *N*-heterocyclic carbene IPr (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) and its *N*-heterocyclic olefin analog IPrCH<sub>2</sub> have been previously reported by Rivard and coworkers to catalyze ketone and aldehyde hydroboration reactions.<sup>3c</sup> Under the reaction conditions tested, both IPr and IPrCH<sub>2</sub> showed low conversion of acetophenone (**3a**) to its corresponding boronate ester (**4a**) after 1 h (Table 1, entries 1 and 2; 17% and 33%, respectively). The cumulated ylide Ph<sub>3</sub>PCCO showed limited catalytic activity (entry 3; 8% conversion), while the nitrile- and carbonyl-stabilized phosphorus ylides Ph<sub>3</sub>PCHCN (entry 4) and Ph<sub>3</sub>PCHC(O)CH<sub>3</sub> (entry 5) were catalytically inactive.

High catalytic activity was observed using cyclic CDP **1** (entries 6 and 7), with 95% acetophenone conversion achieved after 15 min using 1 mol% catalyst loading. Interestingly, the unstabilized phosphorus ylide Ph<sub>3</sub>PCH<sub>2</sub> **2** was also highly active for acetophenone hydroboration (entries 8 and 9). The catalytic activity of **2** was unexpected, given the stoichiometric reactivity of phosphorus ylides with ketones in Wittig olefination reactions.<sup>13</sup>

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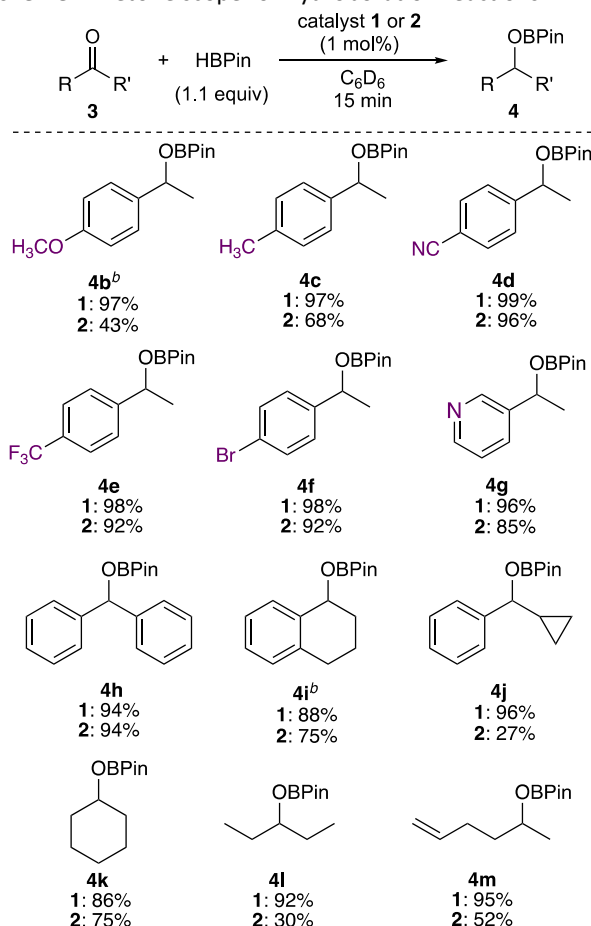
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**Table 1.** Lewis basic catalyst comparison for acetophenone hydroboration.<sup>a</sup>


Entry	Catalyst	Catalyst Loading (mol%)	Time (min)	Conversion (%) <sup>b</sup>
1	IPr	5	60	17%
2	IPrCH <sub>2</sub>	5	60	33%
3	Ph <sub>3</sub> PCCO	5	60	8%
4	Ph <sub>3</sub> PCHCN	5	60	0%
5	Ph <sub>3</sub> PCHC(O)CH <sub>3</sub>	5	60	0%
6	cyclic CDP ( <b>1</b> )	5	60	99%
7	cyclic CDP ( <b>1</b> )	1	15	95%
8	Ph <sub>3</sub> PCH <sub>2</sub> ( <b>2</b> )	5	60	99%
9	Ph <sub>3</sub> PCH <sub>2</sub> ( <b>2</b> )	1	15	90%

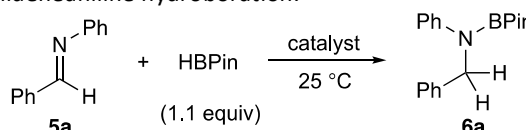
<sup>a</sup> Reaction conditions: acetophenone (0.25 mmol), HBPIn (0.27 mmol), and catalyst (0.013 or 0.0025 mmol) in benzene-*d*<sub>6</sub> (0.50 mL) at 25 °C. <sup>b</sup> Determined by <sup>1</sup>H NMR spectroscopy.

**Scheme 1.** Ketone scope for hydroboration reactions.<sup>a</sup>

<sup>a</sup> Reaction conditions: ketone (0.25 mmol), HBPIn (0.27 mmol), and catalyst (0.0025 mmol) in benzene-*d*<sub>6</sub> (0.50 mL) at 25 °C for 15 min. Yields are based on <sup>1</sup>H NMR integration relative to a hexamethylbenzene internal standard. <sup>b</sup> 30 min.

Conversion of a variety of ketones (**3b–3m**) to their corresponding pinacol boronate esters (**4b–4m**) in the presence of 1 mol% of catalyst **1** or **2** was investigated (Scheme 1). Most hydroboration reactions reached near completion within 15 minutes using catalyst **1**. Acetophenone derivatives featuring electron-donating (**3b** and **3c**) or electron-withdrawing (**3d–3f**) substituents were tolerated. The electron-rich 4'-methoxyacetophenone (**3b**) underwent slower hydroboration than the electron-deficient acetophenone derivatives tested, requiring 30 minutes to achieve 97% yield using CDP catalyst **1** or 43% yield using phosphorus ylide catalyst **2**. Rapid hydroboration of benzophenone (**3h**), a non-enolizable substrate was observed. Cyclopropylphenylketone (**3j**) was converted to its corresponding boronate ester product (**4j**) without the formation of ring-opened product, suggesting that a ketyl radical intermediate is not formed in the reaction mechanism.<sup>14</sup> Alkyl-substituted ketones (**3k–3m**) also underwent efficient hydroboration using catalyst **1**, though diminished activity towards these substrates was observed using catalyst **2**. Chemoselective ketone hydroboration was observed in the presence of nitrile, pyridine, or alkene functional groups (substrates **3d**, **3g**, and **3m**).

We next explored reduction of imine substrates by catalysts **1** and **2**. Imine hydroboration is a convenient method to prepare amine products, which are important in pharmaceutical, agrochemical, and materials chemistry applications.<sup>15</sup> Hydroboration of *N*-benzylideneaniline (**5a**) was attempted using a range of potential Lewis basic catalysts (5 mol% loading), and catalytic activities were compared after 1 h at 25 °C (Table 2). IPr, IPrCH<sub>2</sub>, and resonance-stabilized phosphorus ylides were essentially inactive for *N*-benzylideneaniline hydroboration (entries 1–5). Phosphorus ylide **2** showed low activity for imine hydroboration (entry 6, 22% conversion), while the CDP catalyst **1** showed high catalytic activity for conversion of **5a** to the corresponding borylated amine product **6a** (entries 7 and 8).

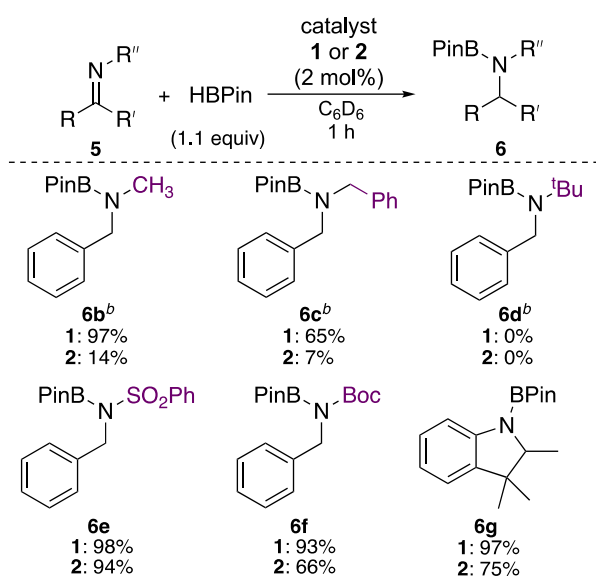
**Table 2.** Lewis basic catalyst comparison for *N*-benzylideneaniline hydroboration.<sup>a</sup>


Entry	Catalyst	Cat. Loading (mol%)	Time (min)	Conversion (%) <sup>b</sup>
1	IPr	5	60	0%
2	IPrCH <sub>2</sub>	5	60	0%
3	Ph <sub>3</sub> PCCO	5	60	3%
4	Ph <sub>3</sub> PCHCN	5	60	0%
5	Ph <sub>3</sub> PCHC(O)CH <sub>3</sub>	5	60	0%
6	Ph <sub>3</sub> PCH <sub>2</sub> ( <b>2</b> )	5	60	25%
7	cyclic CDP ( <b>1</b> )	5	60	98%
8	cyclic CDP ( <b>1</b> )	2	60	86%

<sup>a</sup> Reaction conditions: *N*-benzylideneaniline (0.25 mmol), HBPIn (0.27 mmol), and catalyst (0.013 or 0.0050 mmol) in benzene-*d*<sub>6</sub> (0.50 mL) at 25 °C. <sup>b</sup> Determined by <sup>1</sup>H NMR spectroscopy.

Hydroboration experiments using 2 mol% of catalyst **1** or **2** were performed for a series of imine substrates (**5b–5g**) with varied substituents on the imine nitrogen atom (Scheme 4). Phosphorus ylide **2** was an inefficient hydroboration catalyst for most imines tested (the *N*-sulfonyl substrate **5e** was an exception). Using CDP catalyst **1**, increasing the size of the *N*-alkyl substituent (substrates **5b–5d**) led to greatly diminished hydroboration activity. Imine substrates featuring *N*-sulfonyl (**5e**) and *N*-Boc (**5f**) functional groups were tolerated by catalyst **1**. Cyclic ketimine **5g** also underwent hydroboration to form product **6g** in 97% or 75% yield using catalyst **1** or **2**, respectively.

**Scheme 4.** Imine scope for hydroboration reactions.<sup>a</sup>



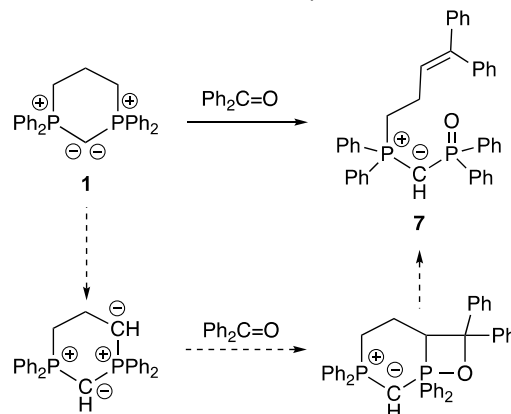
<sup>a</sup> Reaction conditions: imine (0.25 mmol), HBPIn (0.27 mmol), and catalyst (0.0050 mmol) in benzene-*d*<sub>6</sub> (0.50 mL) at 25 °C for 1 h. Yields are based on <sup>1</sup>H NMR integration relative to a hexamethylbenzene internal standard. <sup>b</sup> 1.5 equiv of HBPIn.

Stoichiometric experiments were performed between catalysts **1** or **2** and hydroboration substrates to gain insight into potential reaction mechanisms. Treatment of phosphorus ylide **2** with 1 equiv of HBPIn caused an upfield shift in the <sup>11</sup>B NMR signal and a diminished *J*<sub>BH</sub> coupling constant ( $\delta = 29.5$  ppm, *J*<sub>BH</sub> = 174 Hz for free pinacolborane vs  $\delta = 15.0$  ppm, *J*<sub>BH</sub> = 140 Hz upon treatment with 1 equiv of **2**). These spectroscopic changes are consistent with partial, reversible coordination of **2** to pinacolborane.<sup>16</sup> The reaction of CDP **1** with pinacolborane was more complex. Upon combination of equimolar **1** and HBPIn, an upfield shifted signal with reduced <sup>1</sup>H–<sup>11</sup>B coupling was observed by <sup>11</sup>B NMR spectroscopy ( $\delta = 5.4$  ppm, *J*<sub>BH</sub> = 109 Hz); however, a mixture of products was observed by <sup>31</sup>P NMR spectroscopy within minutes at 25 °C. Under catalytic conditions using CDP **1**, trace amounts of BH<sub>3</sub> can be observed by <sup>11</sup>B NMR spectroscopy, suggesting that **1** can mediate the formation of BH<sub>3</sub> from pinacolborane; however, previous work by Thomas and coworkers has shown that Lewis base-mediated ketone hydroboration does not proceed by hidden BH<sub>3</sub> catalysis.<sup>12a</sup>

The stoichiometric reactivity of catalysts **1** and **2** with imine and ketone substrates was also examined. No reaction was observed upon treatment of either compound **1** or **2** with 1 equiv of *N*-benzylidenemethylamine (**5a**) at 25 °C. Combining ylide **2** with 1 equiv of benzophenone (**3h**) resulted in Wittig olefination to form 1,1-diphenylethylene and triphenylphosphine oxide within 5 minutes at 25 °C, with no intermediates observed by <sup>1</sup>H or <sup>31</sup>P NMR spectroscopy. The triphenylphosphine oxide product does not catalyze acetophenone hydroboration.

CDP **1** reacts with 1 equiv of benzophenone at 25 °C to form the ring-opened ylide **7** (Scheme 5). Compound **7** does not catalyze acetophenone hydroboration. The <sup>1</sup>H-decoupled <sup>31</sup>P NMR spectrum of **7** exhibits two doublets ( $\delta = 28.4$  and 20.0 ppm, *J*<sub>PP</sub> = 21.3 Hz), which is similar to NMR data reported for Ph<sub>3</sub>PCHP(O)Ph<sub>2</sub>.<sup>17</sup> The ylidic carbon of **7** appears as a doublet of doublets (*J*<sub>CP</sub> = 120.9, 104 Hz) at  $\delta = 6.9$  ppm in <sup>13</sup>C NMR spectra. A plausible mechanism leading to the formation of **7** involves tautomerization of carbodiphosphorane **1** to an unsymmetrical double ylide form,<sup>18</sup> followed by Wittig olefination.

**Scheme 5.** Reaction of **1** with benzophenone.



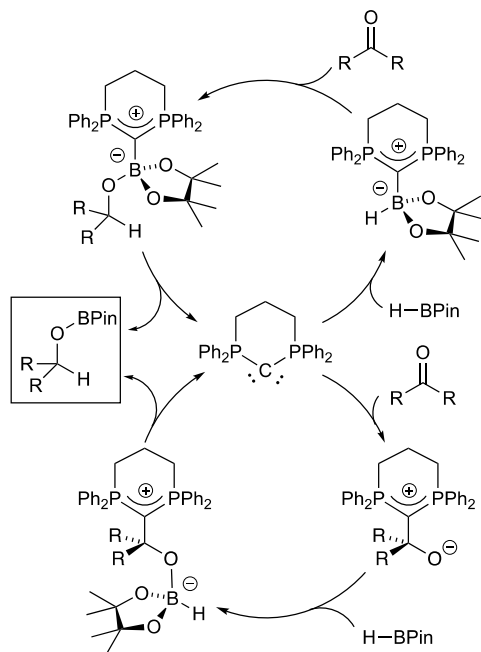
Based on the stoichiometric reactivity observed, two mechanistic pathways for ketone hydroboration are plausible (Scheme 6).<sup>3c</sup> Carbodiphosphorane **1** may coordinate to pinacolborane (Scheme 6, top), rendering the borane more hydridic. Hydroboration could then occur by hydride transfer to the ketone and B–O bond formation, followed by carbodiphosphorane dissociation. Alternatively, catalyst **1** could first coordinate to the ketone substrate (Scheme 6, bottom). Subsequent borane binding to oxygen followed by hydride transfer could furnish the pinacol boronate ester product. Analogous possible mechanisms can be envisioned for imine hydroboration. Although the carbodiphosphorane form of **1** is drawn in Scheme 6, the stoichiometric reactivity with benzophenone suggests that a tautomerized form of **1** may be accessible and could be the active catalyst. In future work, we hope to thoroughly investigate the hydroboration mechanisms of carbodiphosphorane catalysts.

In conclusion, cyclic carbodiphosphorane **1** is an efficient catalyst for ketone and imine hydroboration at 25 °C. To our knowledge, this is the first reported organocatalytic activity of a carbodiphosphorane. For comparison, we also surveyed the

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catalytic activity of phosphorus ylide **2**. Compared to **2**, carbodiphosphorane **1** affords higher yields of ketone hydroboration products and shows greatly enhanced activity in imine hydroboration reactions. Future work in our group will expand the use of carbodiphosphoranes and phosphorus ylides as Lewis basic organocatalysts.

**Scheme 6.** Plausible ketone hydroboration mechanisms.



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