

# An Immobilized Homogeneous Catalyst for Efficient and Selective Hydrogenation of Functionalized Aldehydes, Alkenes, and Alkynes

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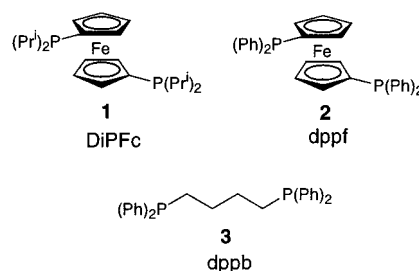
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An immobilized cationic rhodium(I) catalyst bearing the diphosphine 1,1'-bis(diisopropylphosphino)-ferrocene (DiPFc, **1**) allows efficient and chemoselective hydrogenation of a range of functionalized aldehydes, as well as alkenes and alkynes, under mild conditions. This heterogenized catalyst system is convenient to prepare, is stable to air and moisture over extended periods, and is readily recycled.

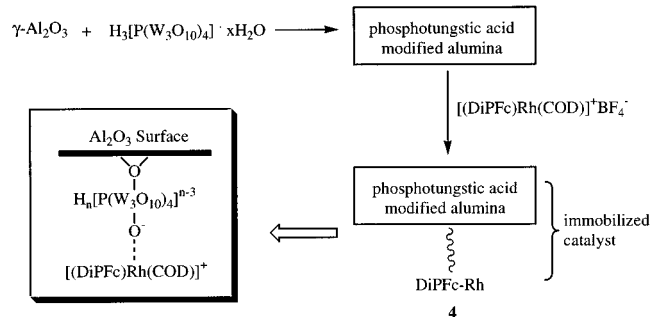
## Introduction

Homogeneous catalysts can offer high molar catalytic efficiencies and rates under mild conditions, tolerance to many types of organic functionality, and high selectivity in reactions that allow formation of a specific desired reaction product.<sup>1</sup> Heterogeneous catalysts are usually more robust and easy to handle and can be completely removed from a reaction and reused in a subsequent transformation.<sup>2</sup> An ideal catalyst would possess the beneficial aspects of both homogeneous and heterogeneous systems. Toward this objective, significant effort has been expended in an attempt to develop homogeneous catalysts that are anchored to a solid support, but practical success has been relatively limited to date.<sup>3</sup> Systems of this type suffer from numerous difficulties, including tedious and/or expensive syntheses of polymeric ligands, reduced catalytic activities and selectivities relative to the homogeneous catalyst, and excessive leaching of the catalytic species from the solid support.<sup>4,5</sup> Recently, Augustine and co-workers described an innovative strategy for immobilizing homogeneous catalysts on support materials modified with heteropoly acids.<sup>6</sup> Herein, we describe a useful application of this approach, which has allowed the development of an efficient immobilized catalyst system for the selective hydrogenation of a variety of functionalized aldehydes, alkenes and alkynes.



**Figure 1.** Diphosphine ligands used to prepared immobilized catalysts.

## Scheme 1. Immobilization of DiPFc-Rh Catalyst Precursor on Modified Alumina



## Results and Discussion

**Immobilized Rhodium Catalysts.** For the current study, heterogenized rhodium–diphosphine catalysts were prepared by a procedure slightly modified from that previously reported by Augustine.<sup>6</sup> Three different diphosphine ligand systems (**1–3**, Figure 1) and two different support materials ( $\gamma\text{-Al}_2\text{O}_3$  and  $\text{SiO}_2$ ) were employed, and the resulting catalyst systems were comparatively tested for activity and selectivity in hydrogenation reactions.

For instance, the immobilized catalyst **4** was formed by mixing neutral  $\gamma$ -alumina with phosphotungstic acid in methanol, followed by addition of the known homogeneous catalyst precursor  $[(\text{DiPFc})\text{Rh}(\text{COD})]^+\text{BF}_4^-$  (see Scheme 1). This precursor and analogous rhodium complexes bearing the DiPFc ligand previously have been shown to afford reactive hydrogenation catalysts in solution.<sup>7,8</sup> After allowing the mixture to stir for 16 h,

(1) (a) Pignolet, L. H., Ed. *Homogeneous Catalysis with Metal Phosphine Complexes*; Plenum Press: New York, 1983. (b) Masters, C. *Homogeneous Transition-Metal Catalysis*; Chapman and Hall: London, 1981. (c) Parshall, G. W.; Ittel, S. D. *Homogeneous Catalysis*; John Wiley & Sons: New York, 1992.

(2) (a) Ertl, G.; Knozinger, H.; Weitkamp, J., Eds. *Handbook of Heterogeneous Catalysis*; Wiley-VCH: Weinheim, 1997. (b) Blaser, H. U.; Steiner, H.; Studer, M. In *Transition Metals for Organic Synthesis*; Beller, M.; Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998; Vol. 2, Chapter 1.2.

(3) Hartley, F. R. *Supported Metal Complexes*; Reidel: Dordrecht, 1985.

(4) (a) Pittman, C. U. In *Comprehensive Organometallic Chemistry*; Wilkinson, G.; Stone, F. G.; Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, pp 553–611. (b) Keim, W.; Dreissen, Holscher, B. In *Handbook of Heterogeneous Catalysis*; Ertl, G.; Knozinger, H.; Weitkamp, J., Eds.; Wiley-VCH: Weinheim, 1997; Vol. 1, pp 231–240.

(5) (a) Herrmann, W. A.; Cornils, B. *Angew. Chem., Int. Ed.* **1997**, *36*, 1048. (b) Lindner, E.; Schneller, T.; Auer, F.; Mayer, H. A. *Angew. Chem., Int. Ed.* **1999**, *38*, 2155.

(6) Augustine, R.; Tanielyan, S.; Anderson, S.; Yang, H. *Chem. Commun.* **1999**, 1257

the orange rhodium complex was completely absorbed onto the solid support, as evidenced by transference of color from solution to the insoluble support material. The immobilized catalyst **4** was then filtered and extensively washed with methanol or ethanol (Soxhlet extraction, 12–16 h), dried in vacuo, and then used directly in catalysis.

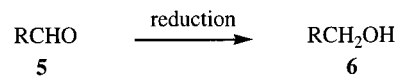
The mechanism of absorption and the exact nature of the tethered complex remain undefined. Evidence suggests that cationic, rather than neutral, transition metal complexes may be required, as they are most effectively absorbed onto the heteropoly acid-modified supports. This notion is corroborated by the observation that anionic species such as halides and carboxylates effectively strip the anchored metal complex from the support of catalysts of type **4**. This presumably occurs by coordination of the anion to the cationic metal center, which renders the complex neutral and incapable of interacting with the modified support. The nature of heteropoly acids allows one to postulate that a relatively robust linkage between the heteropoly acid and the alumina (or silica) support may form through intercalation or insertion of an oxygen atom (or atoms) of the heteropoly acid molecule into the surface lattice of the support.<sup>9</sup> Given the high acidity of phosphotungstic acid, one may hypothesize that the tethered heteropoly acid/anion could play a role as a counteranion analogous to triflate for the cationic DiPFc-Rh catalyst. In this context, the nature of catalyst attachment may be entirely electrostatic. However, the presence of a weak coordinate covalent interaction between an oxygen atom of the phosphotungstic acid component and the rhodium atom of the pre-catalyst also is plausible (see box in Scheme 1). A bonding interaction of this type previously has been observed directly in solution between heteropoly acids and rhodium and iridium complexes.<sup>10</sup>

All tethered homogeneous catalysts used in this study were prepared by the simple procedure outlined in Scheme 1. Immobilized catalyst variants were fabricated by changing either the support material (e.g., SiO<sub>2</sub>) or homogeneous metal complex used. It is important to note that little tethering of homogeneous rhodium catalysts occurs in the absence of the phosphotungstic acid component.<sup>6</sup>

We next sought to examine the catalytic competence of immobilized catalyst **4** and the analogous silica-supported system. It is important to note that these immobilized homogeneous catalysts apparently are stable to atmospheric oxygen and moisture over extended periods. The immobilized catalyst **4**, which was used in the hydrogenation processes described below, was stored for over 1 year in the air, with no apparent loss of catalytic activity.

**Hydrogenation of Aldehydes.** Recently, we required a mild, efficient, and selective procedure for reducing aldehydes **5** to alcohols **6** on commercial scale (1 kg-ton quantities). Aldehydes are large volume products that derive from various sources, including catalytic hydro-

formylation of alkenes.<sup>11</sup> Aldehyde reduction often is a desirable step in this sequence which affords valuable alcohol products from inexpensive starting materials (e.g., alkenes, hydrogen, and carbon monoxide in the case of hydroformylation).



Despite the importance of aldehyde reduction in organic chemistry, surprisingly few generally applicable manufacturing methods are available for this transformation. Reduction of **5** through the use of hydride reagents (e.g., LiAlH<sub>4</sub>, NaBH<sub>4</sub>, etc.) often is quite facile and selective, and arguably is the most widely practiced procedure of this type.<sup>12</sup> Unfortunately, hydride reducing agents are moisture-sensitive reagents that are not economically attractive for manufacturing since they are employed in stoichiometric quantities. Moreover, their use requires tedious workup procedures and generates substantial quantities of waste (boron or aluminum salts).

Numerous heterogeneous catalysts, such as PtO<sub>2</sub>, Raney Ni, and Pd/C, can catalyze the hydrogenation of aldehydes.<sup>12</sup> However, heterogeneous catalysts are not broadly applicable since they tend to be intolerant of various organic groups, such as divalent sulfide moieties. Moreover, heterogeneous catalysts generally do not actuate hydrogenation of aldehydes with a high degree of chemical selectivity (e.g., other sensitive groups such as nitro, oxime, ketone, arylhalide, benzyloxy, etc. also are reduced). Another serious problem encountered when reducing aromatic aldehydes using heterogeneous catalysts is that any formed hydroxymethyl group may be further reduced to a methyl substituent. For example, heterogeneous hydrogenation of benzaldehyde often affords toluene due to facile hydrogenolysis of the intermediate benzyl alcohol.

We previously demonstrated that the homogeneous DiPFc-Rh catalyst is effective for the hydrogenation of a range of aldehydes under mild conditions.<sup>7,13</sup> We now sought to assess the utility of immobilized catalyst **4** in the hydrogenation of aldehydes bearing different functional groups. These studies were aimed at demonstrating the combined properties of high catalytic efficiency under mild conditions, selectivity in the reduction process, and tolerance of the catalyst to certain functionality. The robust nature of the catalyst system also was important. Moreover, comparisons have been made with the commonly employed heterogeneous catalysts palladium-on-carbon (Pd/C) and platinum oxide (PtO<sub>2</sub>).

Preliminary screening experiments using the immobilized catalyst **4** were conducted using the representative substrate valeraldehyde. All hydrogenations were performed under a standard set of mild reaction conditions: hydrogen pressure = 100 psi, temperature = 20 °C, reaction time = 16 h, mol aldehyde/mol Rh (S/C) = 320 (based upon analysis of Rh content by atomic

(7) Burk, M. J.; Harper, T. G. P.; Lee, J. R.; Kalberg, C. *Tetrahedron Lett.* **1994**, *35*, 4963.

(8) Appleton, T. D.; Cullen, W. R.; Evans, S.-V.; Kim, T.-J.; Trotter, J. *J. Organomet. Chem.* **1985**, *279*, 5.

(9) (a) Izumi, Y.; Hasere, R.; Urabe, K. *J. Catal.* **1983**, *84*, 402. (b) Izumi, Y.; Urabe, K.; Onaka, M. *Zeolite, Clay, and Heteropoly Acids in Organic Reactions*; VCH: New York, 1992.

(10) Pohl, M.; Lyon, D. K.; Mizuno, K.; Nomiya, K.; Finke, R. G. *Inorg. Chem.* **1995**, *34*, 1413.

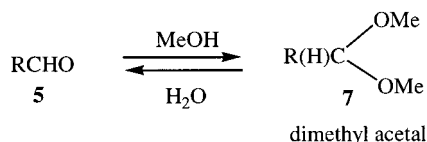
(11) Parshall, G. W.; Ittel, S. D. *Homogeneous Catalysis*; John Wiley & Sons: New York, 1992; pp. 106–111.

(12) Hudlicky, M. *Reductions in Organic Chemistry*; Halsted Press: New York, 1984.

(13) A cationic rhodium catalyst bearing the ligand 1,3-bis(diisopropylphosphino)propane was also shown to promote efficient hydrogenation of two model aldehydes under mild conditions; see: Tani, K.; Suwa, K.; Tanigawa, E.; Yoshida, T.; Okano, T.; Otsuka, S. *Chem. Lett.* **1982**, 261.

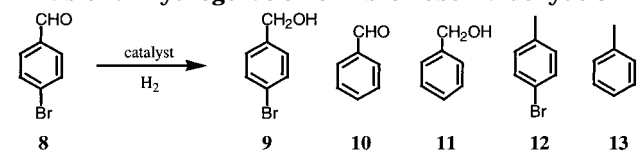
absorption spectroscopy), concentration = 0.1 M. Under these conditions, little conversion to 1-pentanol occurred in the nonprotic solvent THF. Similarly, little conversion to the desired product (<5% pentanol formed) was observed in methanol or ethanol. These results are discordant with those achieved using the homogeneous DiPFc-Rh catalyst, whereupon hydrogenation of valeraldehyde proceeded readily in these solvents. In the case of immobilized catalyst **4**, conversion and product yields were limited by the formation of acetals of type **7**, which were identified by <sup>1</sup>H NMR spectroscopy and confirmed by GC-MS. It is likely that acetal formation is accelerated by the acidic support (i.e., phosphotungstic acid modified alumina) employed to immobilize the DiPFc-Rh catalyst.

In the presence of water, the formation of acetals **7** is reversible, and it was reasoned that an alcohol/water mixture may be necessary in order to permit in situ regeneration of the aldehyde, which serves as a substrate for hydrogenation. A survey of different alcohol/water mixtures revealed that the combination of 2-propanol/water in 1:1 v/v ratio was preferred with regard to hydrogenation rates, percent conversion, and yields of the desired alcohol products. Under the above-noted conditions, the immobilized DiPFc-Rh catalyst **4** was found to operate efficiently in a 2-propanol/water (1:1) solvent mixture to allow facile and complete hydrogenation of valeraldehyde to 1-pentanol in high yield.



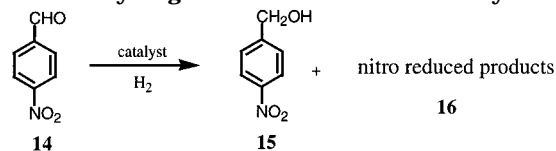
It was of particular interest to demonstrate the superiority of immobilized catalyst **4** relative to other commonly employed heterogeneous catalysts. Accordingly, we examined a range of aldehydes bearing specific functionality such as aromatic bromide, sulfur, nitro, and benzyloxy groups. In all cases, we found that when **4** was used, complete and selective hydrogenation of the aldehyde function occurred to furnish *exclusively* the desired alcohols **6** in high yield. By contrast, the heterogeneous catalysts often rendered product mixtures, or were inhibited by the pendant functionality. Very mild conditions were employed for reactions involving heterogeneous catalysts in an attempt to achieve optimal selectivity in the reduction of each substrate. In such cases, complete conversion of substrate was not always achieved. Under conditions required for complete conversion of substrate, the heterogeneous catalysts generally produced greater percentages of byproducts. The results of these studies are shown below.

In the first series of experiments, we found that hydrogenation of 4-bromobenzaldehyde **8** using catalyst **4** provided solely 4-bromobenzyl alcohol **9** (Table 1). Hydrogenation of substrate **8** using the DiPFc-Rh catalyst immobilized on silica, rather than alumina, furnished the identical result (entry 2). In all cases studied thus far, the alumina- and silica-supported DiPFc-Rh catalysts were found indistinguishable in terms of activity and selectivity. Other immobilized rhodium catalysts displayed only low catalytic activity for hydrogenation of **8** (entries 3–4). Under mild conditions, the heterogeneous catalyst Pd/C afforded only the debrominated product

**Table 1. Hydrogenation of 4-bromobenzaldehyde **8**<sup>a</sup>**

entry	catalyst/support <sup>b</sup>	% <b>8</b>	% <b>9</b>	% <b>10</b>	% <b>11</b>	% <b>12</b>	% <b>13</b>
1	DiPFc-Rh/Al <sub>2</sub> O <sub>3</sub> , <b>4</b>		100				
2	DiPFc-Rh/SiO <sub>2</sub>		100				
3	dppf-Rh/SiO <sub>2</sub>	88	12				
4	dppb-Rh/SiO <sub>2</sub>	93	7				
5	Pd/C	80		20			
6	Pd/C <sup>c</sup>						100
7	PtO <sub>2</sub>	1	90	1	4	4	

<sup>a</sup> Conditions for immobilized catalysts: 100 psi H<sub>2</sub>; S/C = 300–350 (based on Rh content); [**8**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. Conditions for Pd/C: 14 psi H<sub>2</sub>; 5 mg of 10% Pd w/w catalyst; [**8**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 30 min. Conditions for PtO<sub>2</sub>: 14 psi H<sub>2</sub>; 5 mg of catalyst; [**8**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. <sup>b</sup> In entries 1–4, the supports used were modified with phosphotungstic acid as shown in Scheme 1. <sup>c</sup> Reaction conducted using 10 mg 10% Pd/C at 100 psi H<sub>2</sub> over 1 h.

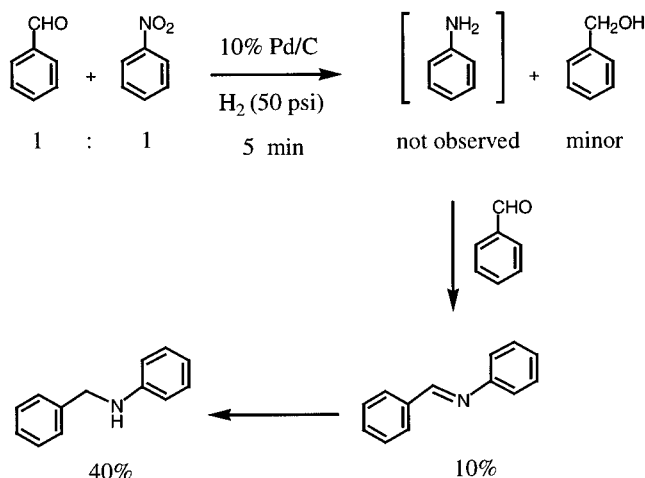
**Table 2. Hydrogenation of 4-Nitrobenzaldehyde **14**<sup>a</sup>**

entry	catalyst/support <sup>b</sup>	% <b>14</b>	% <b>15</b>	% <b>16</b>
1	DiPFc-Rh/Al <sub>2</sub> O <sub>3</sub> , <b>4</b>		100	
2	DiPFc-Rh/SiO <sub>2</sub>		100	
3	Pd/C	58		42
4	Pd/C <sup>c</sup>			100
5	PtO <sub>2</sub>	15		85

<sup>a</sup> Conditions for immobilized DiPFc-Rh catalysts: 100 psi H<sub>2</sub>; S/C = 320 (based on 0.21% w/w Rh content); [**14**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. Conditions for Pd/C: 50 psi H<sub>2</sub>; 5 mg of 10% Pd w/w catalyst; [**14**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 20 min. Conditions for PtO<sub>2</sub>: 14 psi H<sub>2</sub>; 5 mg of catalyst; [**14**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 1 h. <sup>b</sup> In entries 1–2, the supports used were modified with phosphotungstic acid as shown in Scheme 1. <sup>c</sup> Reaction conducted using 10 mg 10% Pd/C at 100 psi H<sub>2</sub> over 20 min.

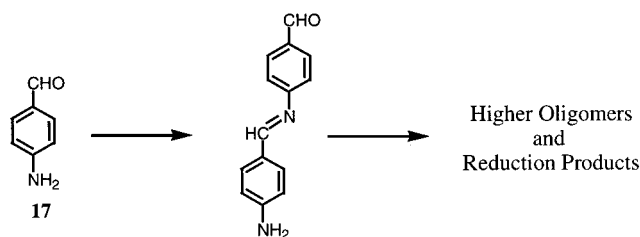
benzaldehyde. Under somewhat more forcing conditions, complete conversion to toluene **13** was observed (entry 6). While the desired product **9** predominated when heterogeneous PtO<sub>2</sub> was employed (entry 7), a wide range of byproducts derived from debromination and over-reduction also were formed.

The next substrates that we assessed for chemoselective reduction were those containing aromatic nitro groups, such as 4-nitrobenzaldehyde **14**. Functional substrates bearing nitro substituents represent a great challenge for most catalysts due to the propensity with which the sensitive nitro group is reduced.<sup>12</sup> The DiPFc-Rh/Al<sub>2</sub>O<sub>3</sub> catalyst **4** was shown to allow complete hydrogenation of **14** with 100% chemoselectivity to afford only the desired monoreduced alcohol product **15** (Table 2, entry 1). Identical results were achieved with the silica-supported homogeneous catalyst. In contrast, the heterogeneous catalysts Pd/C and PtO<sub>2</sub> rendered mixtures dominated by nitro-reduced species (entries 3–5). Under more forcing conditions, only nitro-reduced compounds were observed with the heterogeneous catalyst systems employed (see entry 4). In no case were

**Scheme 2. Competitive Hydrogenation of Nitrobenzene and Benzaldehyde**

products derived from primary aldehyde reduction identified when the heterogeneous systems were used.

The inferred nitro-reduced product 4-aminobenzaldehyde (**17**) generated initially in the heterogeneously catalyzed hydrogenation of **14** was impossible to analyze directly due to subsequent self-condensation leading to formation of higher oligomers and further reduction products.



Analogous behavior also was observed in the reduction of 3-nitrobenzaldehyde, where complete conversion to the desired 3-nitrobenzyl alcohol was accomplished exclusively with the immobilized catalyst **4**. The heterogeneous catalysts Pd/C and PtO<sub>2</sub> again rendered only products arising from primary reduction of the nitro group. Further corroboration of these results was achieved through a competition experiment, whereby equimolar quantities of benzaldehyde and nitrobenzene were subjected to the hydrogenation conditions outlined above. With the immobilized catalyst **4**, only the aldehyde was reduced to afford benzyl alcohol, and no aniline was seen. When 10% Pd/C was utilized as catalyst, after 5 min (ca. 50% conversion) the major products formed emanated from preliminary reduction of nitrobenzene (Scheme 2). The primary product, aniline, was not observed since apparently it condensed further with benzaldehyde to form *N*-benzylideneaniline, which under the conditions was reduced to *N*-phenylbenzylamine. These secondary products were directly observed (10% and 40%, respectively) and characterized through comparison with authentic material. Allowing the Pd/C-catalyzed reaction to proceed for a longer period (20 min) resulted in complete reduction and formation of benzyl alcohol and *N*-phenylbenzylamine.

Substrate **18** was examined in order to assess the tolerance of the immobilized DiPFc-Rh catalysts toward sulfur functionality. Many heterogeneous catalysts are

**Table 3. Hydrogenation of 4-Methylthiobenzaldehyde **18**<sup>a</sup>**

entry	catalyst/support <sup>b</sup>	% <b>18</b>	% <b>19</b>
1	DiPFc-Rh/Al <sub>2</sub> O <sub>3</sub> , <b>4</b>		100
2	DiPFc-Rh/SiO <sub>2</sub>		100
3	DiPFc-Rh/SiO <sub>2</sub> <sup>c</sup>		100
4	dppf-Rh/SiO <sub>2</sub>	99	1
5	dppb-Rh/SiO <sub>2</sub>	100	
6	Pd/C	95	5
7	PtO <sub>2</sub>	3	97

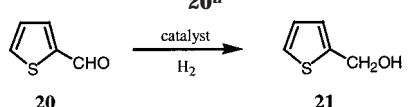
<sup>a</sup> Conditions for immobilized homogeneous catalysts: 100 psi H<sub>2</sub>; S/C = 300–350 (based Rh content); [**18**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. Conditions for Pd/C: 100 psi H<sub>2</sub>; 10 mg of 10% Pd w/w catalyst; [**18**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. Conditions for PtO<sub>2</sub>: 100 psi H<sub>2</sub>; 10 mg of catalyst; [**18**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. <sup>b</sup> In entries 1–5, the supports used were modified with phosphotungstic acid as shown in Scheme 1. <sup>c</sup> Reaction conducted at S/C = 500 at 60 °C over 20 h.

strongly inhibited by sulfur-containing substrates or sulfur contaminated substrates.<sup>2,12</sup> This constitutes a serious problem in the fine chemical and specialty chemical industries and also in the processing of petroleum-derived products.

As can be seen in Table 3, the methylthio substituent of **18** did not vitiate the catalytic activity of immobilized DiPFc-Rh catalyst **4**, which allowed complete conversion to **19**. Likewise, the silica-supported DiPFc-Rh catalyst was equally effective for this transformation under mild conditions. However, the other immobilized homogeneous catalysts derived from dppf and dppb were found ineffectual for hydrogenation of **18**. Because these experiments are aimed at testing functional group tolerance rather than chemoselectivity, reactions involving heterogeneous catalysts could be performed under more forcing reaction conditions (i.e., 10 mg catalyst, 100 psi H<sub>2</sub>, 16 h reaction time). Even under these conditions, the Pd/C catalyst system allowed only 5% conversion to the desired product. The platinum oxide catalyst was found to be more effective and furnished 97% of the desired product **19**.

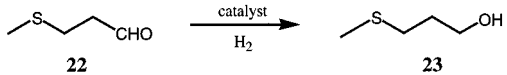
With regard to sulfur tolerance, we have examined two additional substrates in order to examine this property in further detail. The first substrate was thiophene-2-carboxaldehyde **20**, which was hydrogenated smoothly to the expected product **21** using the immobilized DiPFc-Rh catalyst. Both heterogeneous catalysts that we assessed struggled to reduce this substrate under the conditions tested (Table 4).

The last sulfur-containing substrate surveyed, 3-thio-methylpropionaldehyde (**22**), was perhaps the most challenging substrate that we examined. Substrate **22** possesses a dialkylsulfide unit that may be expected to serve as a strong catalyst inhibitor through coordination of the electron-rich S atom to the catalyst metal center. As can be seen in Table 5, the immobilized catalyst **4** allowed facile and complete hydrogenation of **22** to the alcohol **23**, while neither heterogeneous catalyst screened was effective. The immobilized catalyst **4** even allowed complete reduction of substrate **22** that was purchased as a technical grade mixture containing only 90% of the

**Table 4. Hydrogenation of Thiophene-2-carboxaldehyde**


entry	catalyst/support <sup>b</sup>	% <b>20</b>	% <b>21</b>
1	DiPFc-Rh/Al <sub>2</sub> O <sub>3</sub> , <b>4</b>		100
2	Pd/C	92	8
3	PtO <sub>2</sub>	87	13

<sup>a</sup> Conditions for immobilized homogeneous catalysts: 100 psi H<sub>2</sub>; S/C = 320 (based on 0.21% w/w Rh content); [**20**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. Conditions for Pd/C: 100 psi H<sub>2</sub>; 10 mg of 10% Pd w/w catalyst; [**20**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. Conditions for PtO<sub>2</sub>: 100 psi H<sub>2</sub>; 10 mg of catalyst; [**20**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. <sup>b</sup> In entry 1, the support used was modified with phosphotungstic acid as shown in Scheme 1.

**Table 5. Hydrogenation of 3-Methylthiopropionaldehyde **22**<sup>a</sup>**


entry	catalyst/support <sup>b</sup>	% <b>22</b>	% <b>23</b>
1	DiPFc-Rh/Al <sub>2</sub> O <sub>3</sub> , <b>4</b>		100
2	Pd/C	98	2
3	PtO <sub>2</sub>	97	3

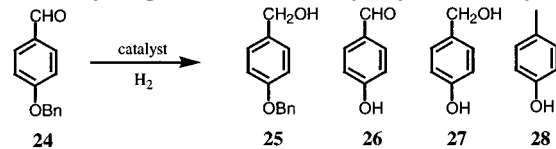
<sup>a</sup> Conditions for immobilized catalyst **4**: 100 psi H<sub>2</sub>; S/C = 320 (based on 0.21% w/w Rh content); [**22**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. Conditions for Pd/C: 100 psi H<sub>2</sub>; 10 mg of 10% Pd w/w catalyst; [**22**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. Conditions for PtO<sub>2</sub>: 100 psi H<sub>2</sub>; 10 mg of catalyst; [**22**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. <sup>b</sup> In entry 1, the support used was modified with phosphotungstic acid as shown in Scheme 1.

monomeric linear aldehyde, along with various unidentified species, and used without further purification.<sup>14</sup>

The final aldehyde substrate that we analyzed was 4-benzyloxybenzaldehyde (**24**) where we were searching for selective hydrogenation without cleavage of the sensitive O–Bn linkage. Complete chemoselectivity for aldehyde hydrogenation was achieved with the immobilized DiPFc-Rh catalyst **4** (Table 6). Mixtures of products were obtained with the heterogeneous noble metal catalysts Pd/C and PtO<sub>2</sub>, although the latter catalyst did display a fair degree of selectivity for aldehyde reduction.

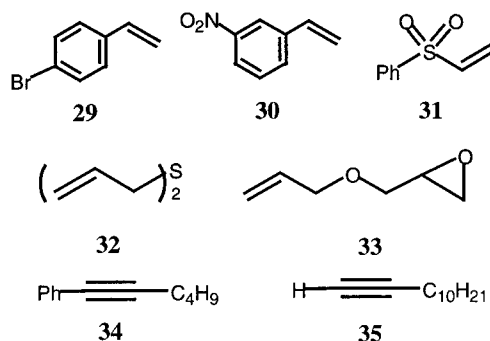
**Hydrogenation of Alkenes and Alkynes.** In addition to the above studies aimed at demonstrating the effectiveness of the immobilized DiPFc-Rh catalysts for chemoselective hydrogenation of functionalized aldehydes, we also have shown that these catalysts are useful for selective reduction of alkenes and alkynes. Figure 2 illustrates a selection of some of the alkenes and alkynes that have been hydrogenated using immobilized catalyst **4** in alcohol solvent and under the reaction conditions described above.

As with aldehydes, facile and highly selective reduction of the olefinic functionality occurred with no overreduction of aromatic bromide or aromatic nitro groups. Sulfur functionality was tolerated readily. Diallylsulfide (**32**), a particularly challenging substrate for heterogeneous catalysts, was smoothly and completely hydrogenated with the immobilized DiPFc-Rh catalyst **4** to afford di-

**Table 6. Hydrogenation of 4-Benzyloxybenzaldehyde **24**<sup>a</sup>**


entry	catalyst/support <sup>b</sup>	% <b>24</b>	% <b>25</b>	% <b>26</b>	% <b>27</b>	% <b>28</b>
1	DiPFc-Rh/Al <sub>2</sub> O <sub>3</sub> , <b>4</b>		100			
2	Pd/C	30	40	2	26	2
3	Pd/C <sup>c</sup>				40	60
4	PtO <sub>2</sub>	2	96	2		

<sup>a</sup> Conditions for immobilized homogeneous catalysts: 100 psi H<sub>2</sub>; S/C = 330 (based on 0.17% w/w Rh content); [**24**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 16 h. Conditions for Pd/C: 14 psi H<sub>2</sub>; 5 mg of 10% Pd w/w catalyst; [**24**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 2.5 h. Conditions for PtO<sub>2</sub>: 100 psi H<sub>2</sub>; 5 mg of catalyst; [**24**] = 0.1 M; solvent: 10 mL of 2-PrOH/H<sub>2</sub>O (1:1 v/v); 20 °C, 4 h. <sup>b</sup> In entry 1, the support used was modified with phosphotungstic acid as shown in Scheme 1. <sup>c</sup> Reaction conducted using 10 mg of 10% Pd/C at 100 psi H<sub>2</sub> over 16 h.

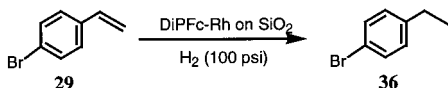
**Figure 2.** Assorted alkenes and alkynes hydrogenated with immobilized catalyst **4**.

*n*-propylsulfide. The latter reaction involving **32** also was conducted in the absence of solvent, and the same result was achieved. Interestingly, the sensitive epoxide unit of **33** remained intact during hydrogenation in diethyl ether to produce O-propylglycidol. Performing the hydrogenation of **33** in alcohol solvents led to epoxide ring-opened products. Examples of internal and terminal alkynes, **34** and **35**, were transformed into the fully reduced alkane products upon hydrogenation with immobilized catalyst **4**.

**Immobilized Catalyst Efficiency.** In an effort to gain a qualitative appreciation for the catalytic activity and efficiency that may be achievable using the immobilized DiPFc-Rh catalysts, we monitored hydrogen uptake during the hydrogenation of 4-bromostyrene **29** over time using a series of decreasing catalyst loadings. The results of this study are shown in Table 7. As can be seen, complete reduction of **29** occurred at S/C ratios up to 5000 (catalyst loading = 0.02 mol % based upon substrate) over 62 h. The last two reactions were not optimized, and it is likely that both processes were complete prior to the times listed. Moreover, while these studies were performed under mild conditions, it is important to realize that an increase of hydrogen pressure increases the rates of these reactions with no loss of chemoselectivity.

**Immobilized Catalyst Removal and Recycle.** A major economic advantage associated with a heterogeneous catalyst system is the possibility of catalyst reuse. We have examined the feasibility of recycling the im-

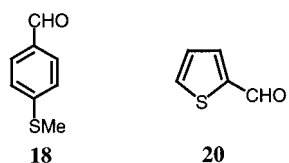
(14) This aldehyde is commercially available in technical grade from Fluka and contains various amounts of monomers and oligomers.

**Table 7. Hydrogenation of 4-bromostryrene 29 with DiPFc-Rh on Modified SiO<sub>2</sub><sup>a</sup>**

entry	S/C <sup>b</sup>	time <sup>c</sup> (h)	% convn
1	200	2	100
2	500	4	100
3	1000	16	100
4	5000	62	100

<sup>a</sup> Conditions for immobilized DiPFc-Rh catalyst on modified SiO<sub>2</sub>: 100 psi H<sub>2</sub>; [29] = 0.1 M; solvent: 10 mL of MeOH; 20 °C. <sup>b</sup> S/C ratio calculated based upon the assumption that all DiPFc-Rh catalyst was immobilized during catalyst preparation. <sup>c</sup> Time allowed for reaction to proceed.

mobilized DiPFc-Rh catalyst **4** in the hydrogenation of aldehydes **18** and **20**. Both aldehydes bear sulfur functionality, which we reasoned would test the robustness of immobilized catalyst **4** in the presence of potential coordinating groups. In these experiments, a 50 mL pressure reactor was charged with catalyst **4**, placed under a hydrogen atmosphere (100 psi), and the substrate (S/C = 320) in 2-PrOH/H<sub>2</sub>O (1:1 v/v, 10 mL) was added by syringe. After the reaction was allowed to stir for 6 h (hydrogen uptake was monitored), a small sample was removed, and complete conversion to alcohol product was confirmed by gas chromatography and <sup>1</sup>H NMR spectroscopy. The entire solution phase containing the product then was removed by syringe, the catalyst was washed twice with fresh solvent, and a subsequent aliquot of substrate in 2-PrOH/H<sub>2</sub>O was added. For both aldehydes **18** and **20**, the immobilized catalyst **4** was used successfully for four cycles of catalysis, and complete conversion to the alcohol products, **19** and **21**, was observed after each run. No reduction of catalytic activity was noted over the four cycles.



Catalyst **4** recycled 3 times for each substrate

The catalyst recycling results outlined above imply that leached rhodium catalyst is not responsible for the observed reduction activity. In addition to catalyst reuse, another chief benefit of immobilizing homogeneous catalysts is the potential to completely remove the catalyst from the reaction, thus eliminating noble metal contamination of the product. Through the use of atomic absorption spectroscopy (Inductively Coupled Plasma, ICP), we have analyzed the rhodium content remaining in solution after complete hydrogenation of thiophene-2-carboxaldehyde (**20**) and subsequent filtration of immobilized catalyst **4**. Rhodium content was assessed after each run over four sequential cycles of catalysis. In the first two runs, <2% of the total Rh content present in the original immobilized catalyst **4** was found in the reaction solution following removal of catalyst (17 μg of Rh and 15 μg of Rh, respectively, observed in first two runs of a recycled catalyst). After the second run of recycled catalyst, rhodium was no longer detected in the resulting organic product. These preliminary tests further indicate that

very little leaching of rhodium from the support occurs during hydrogenation processes involving immobilized catalyst **4**. These results are consistent with those reported by Augustine et al.<sup>6</sup>

## Summary and Conclusions

Despite the implicit advantages and significant effort that has been focused upon immobilizing homogeneous catalysts, few successful examples of practical catalyst systems have been described to date. We set out to develop a tethered hydrogenation catalyst that satisfied the following criteria: (1) the catalyst is easily and economically immobilized, (2) low metal leaching occurs during catalysis, (3) the immobilized catalyst displays high catalytic activity and efficiency for the desired transformation, (4) the immobilized catalyst operates under mild conditions (e.g., low temperatures and pressures), (5) the immobilized catalyst exhibits high levels of selectivity (e.g., chemoselectivity, stereoselectivity, etc.), (6) the immobilized catalyst exhibits broad tolerance to organic functionality (e.g., sulfur, alcohol, amine, etc.), (7) the immobilized catalyst precursor is robust (insensitive to air and moisture), and (8) the immobilized catalyst may be removed efficiently from the reaction mixture and recycled.

We have described a new immobilized homogeneous catalyst system that allows the rapid hydrogenation of functionalized aldehydes, alkenes, and alkynes. The immobilization method of Augustine and co-workers has been employed and demonstrated to be extremely useful for the current purpose. This is a practical system that is convenient to prepare and use, and which satisfies the strict criteria set forth. Accordingly, this system is likely to find wide application in both research and manufacturing, especially where chemoselectivity and functional group tolerance is desired.

## Experimental Section

**General Procedures.** Reactions and manipulations were performed using standard nitrogen-line or Schlenk-line techniques. Solvents were employed as supplied and degassed by sparging with nitrogen or argon prior to use. The complex [(COD)Rh(DiPFc)]BF<sub>4</sub> is known<sup>7,8</sup> and was prepared by reacting the known ligand 1,1'-bis(diisopropylphosphino)ferrocene (**1**)<sup>15</sup> with [(COD)<sub>2</sub>Rh]BF<sub>4</sub> by standard protocols that have been described previously.<sup>16</sup> This complex also is commercially available from Strem Chemical Co. The ligands dppf (**2**) and dppb (**3**) and the corresponding cationic Rh complexes were purchased from Aldrich Chemical Co. Hydrogen gas (99.999%) was purchased from Air Products and used as received directly from the cylinder. All aldehyde, alkene, and alkyne substrates used in this study were purchased from Aldrich Chemical Co. and were used as received. All reduction products described in this manuscript are known compounds, and for purposes of comparative identification, all but three were purchased commercially from Aldrich Chemical Co. Identification of the three noncommercial reduction products, 3-nitro-ethylbenzene,<sup>17</sup> ethylphenyl sulfone,<sup>18</sup> and *O*-propylglycidol,<sup>19</sup> arising from reduction of **30**, **31**, and **33**, respectively, was made by

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comparison with literature data obtained from references indicated for each compound. Palladium-on-carbon and platinum oxide were purchased from Lancaster Synthesis and Aldrich Chemical Co., respectively. Phosphotungstic acid hydrate was purchased from Fluka and used as received. Aluminum oxide, activated, neutral,  $\gamma$ , 96%, 60 mesh white powder was purchased from Strem Chemical Co. Silica gel 60, particle size 0.035–0.070 mm (220–440 mesh ASTM), activity according to Brockmann and Schroder: 2–3, was purchased from Fluka.

HPLC separations were performed using an achiral Prodigy ODS(3) column (150 mm  $\times$  3.2 mm) with 5  $\mu$ m particle size. Conditions employed were as follows: mobile phase: 90% H<sub>2</sub>O and 10% acetonitrile for 5 min, then ramp to 10% H<sub>2</sub>O and 90% acetonitrile over 15 min and hold; flow rate: 1.0 mL/min; injection volume: 20  $\mu$ L; detection: UV – 254 nm. GC chromatography was performed using Chrompack column CP-Sil 8CB (25 m  $\times$  0.25 mm i.d.), 60 °C (5 min), 10 °C/min up to 300 °C (10 min), flow rate: 1.4 mL/min, injector 250 °C, detector 280 °C.

**Immobilized [(DiPFc)Rh(COD)]<sup>+</sup> Catalyst 4.** A solution of phosphotungstic acid (PTA, 288 mg, 0.1 mmol, 1.0 equiv) in 25 mL of degassed methanol was added dropwise to a vigorously stirred (overhead stirrer was used to minimize grinding) suspension of 4.00 g of  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> in 30 mL of degassed methanol under nitrogen. The resulting mixture was stirred for 1 h at room temperature. Subsequently, a solution of [(DiPFc)Rh(COD)]BF<sub>4</sub> (64 mg, 0.09 mmol, 0.9 equiv) in 10 mL of methanol (degassed with nitrogen over 20 min) was added dropwise to the vigorously stirred slurry of the modified alumina. Stirring was continued for 20 h at room temperature. After solvent evaporation the remaining solid was placed in a Soxhlet apparatus and continuously extracted with degassed methanol under nitrogen for 16 h. The resulting orange powder (rhodium catalyst immobilized on modified alumina) was isolated, dried, and stored under nitrogen as a precaution. Yield: 3.78 g (89%). Rhodium analysis of several samples by atomic absorption spectroscopy consistently indicated a rhodium content of 0.19–0.21% Rh/g solid supported catalyst.

**Immobilized [(DiPFc)Rh(COD)]<sup>+</sup> Catalyst on Silica.** A solution of phosphotungstic acid (PTA, 288 mg, 0.1 mmol, 1.0 equiv) in 25 mL of degassed methanol was added dropwise to a vigorously stirred (overhead stirrer was used to minimize grinding) suspension of 4.00 g of silica in 30 mL of methanol (degassed with nitrogen over 20 min). The resulting mixture was stirred for 1 h at room temperature. Subsequently, a

solution of [(DiPFc)Rh(COD)]BF<sub>4</sub> (64 mg, 0.09 mmol, 0.9 equiv) in 10 mL of degassed methanol was dripped to the vigorously stirred slurry of the activated silica. Stirring was continued for 4.5 h at room temperature. After solvent evaporation the remaining solid was placed in a Soxhlet apparatus and continuously extracted with degassed methanol under nitrogen for 16 h. The orange silica powder was isolated, dried and stored under nitrogen. Yield: 3.64 g (86%).

**General Hydrogenation Procedure.** All reactions were carried out in a 50 mL Parr microreactor modified with an injection septum and valve. The microreactor was used in connection with a suitable glass liner. The solvent mixture (2-propanol/water, 1:1 v/v) was deoxygenated prior to use by bubbling nitrogen through it for 3 h with stirring.

The hydrogenation substrate and the immobilized catalyst precursor were added to a 50 mL glass liner, which was then immediately placed in a 50 mL Parr pressure vessel. This was then sealed and purged with hydrogen (5 pressurization/release cycles). Degassed solvent (2-propanol/water, 1:1 v/v, in the case of aldehydes) then was added via cannula and the reactor purged again with hydrogen (5 pressurization/release cycles at 100 psi), charged to the initial hydrogen pressure (100 psi), and vigorously stirred at a constant temperature (ambient temperature or heating bath). After an allocated period of time (hydrogen uptake was monitored), hydrogen pressure was released, and the reaction mixture was filtered (separation from the supported catalyst). The filtrate was then extracted several times with dichloromethane. The combined organic extracts were dried over sodium sulfate, filtered and evaporated. The product distribution of the crude product mixture was determined by NMR spectroscopy and GC–MS and was confirmed through comparison with authentic samples of all products. In cases where the formation of water-soluble or volatile products was likely, the hydrogenation mixture also was analyzed via HPLC prior to extractive workup.

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