VIP **Cobalt Catalysts**

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Mild and Homogeneous Cobalt-Catalyzed Hydrogenation of C=C, C=O, and C=N Bonds**

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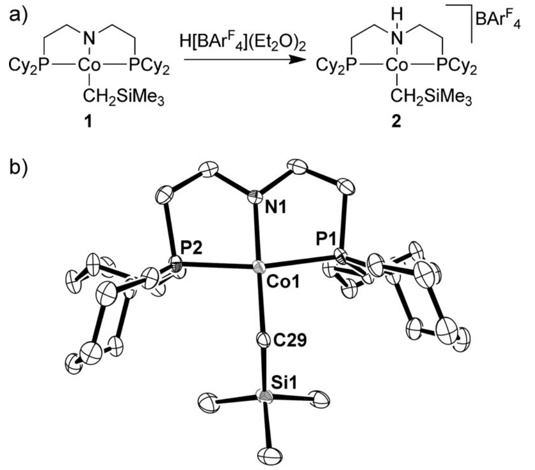
The replacement of precious-metal catalysts with cheap and abundant metals is a major goal of sustainable chemistry.[1] Hydrogenation catalysts have diverse and widespread applications, including the production of biorenewable chemicals and fuels, commodity chemicals, and the synthesis of fine chemicals and pharmaceuticals.[2–4] Homogeneous rhodium, ruthenium, and iridium catalysts are also of critical importance in asymmetric hydrogenation.[5] Despite significant recent advances, the design of earth-abundant-metal hydrogenation catalysts has lagged behind, perhaps because of the tendency of 3d metals to engage in one-electron or radical chemistry. Several iron catalysts have been developed for the hydrogenation of ketones or alkenes, but they are typically chemoselective, reducing only one class of substrate.[6–9] Furthermore, iron catalysts are often quite sensitive to additional oxygen- and nitrogen-containing functional groups and water.[10]

There is growing evidence that cobalt complexes can be effective catalysts for homogeneous hydrogenation. Cobalt(I) complexes, such as $[Co(H)(CO)_4]$ and $[Co(H)(CO)(PnBu_3)_3]$, are known to catalyze the hydrogenation of alkenes and arenes under hydroformylation conditions (> 120 °C, > 30 atm H_2/CO).[11–13] Diiminopyridine cobalt complexes and the dinitrogen complex $[Co(H)(N_2)(PPh_3)_3]$ catalyze olefin hydrogenation at room temperature,[14,15] and an asymmetric hydrogenation of substituted styrenes was recently developed.[16] However, prior examples of cobalt hydrogenation catalysts have been quite limited in substrate scope, and nearly all have involved cobalt(I).[17,18] Herein, we report a cobalt-based catalytic system for the homogeneous hydrogenation of alkenes, aldehydes, ketones, and imines. The hydrogenation reactions take place under very mild conditions and require no base additives. The ability to hydrogenate multiple classes of substrates and broad functional-group tolerance make this cobalt system a significant advance over previously reported earth-abundant-metal hydrogenation catalysts.

We synthesized cobalt(II) complexes of the tridentate ligand bis[2-(dicyclohexylphosphino)ethyl]amine ($PNHP^{Cy}$) (Scheme 1). Previous work by Fryzuk et al. had shown that a related pincer amidodiphosphine ligand stabilized a square-planar 15-electron d^7-cobalt(II)–alkyl complex,[19] and we were interested in exploring the reactivity of this type of unusual odd-electron cobalt–alkyl species. Reaction of $PNHP^{Cy}$ with $[(pyr)_2Co(CH_2SiMe_3)_2]$[20] (pyr = pyridine) afforded the new cobalt(II)–alkyl complex $[(PNP^{Cy})Co(CH_2SiMe_3)]$ (**1**) as dark-yellow crystals. In the solid state, paramagnetic complex **1** has a square-planar geometry, and solution-state magnetic-moment measurements are also consistent with a square-planar low-spin d^7 configuration ($\mu_{eff} = 2.2\ \mu_B$).[21,22] The solution-state magnetic moment of complex **1** is quite similar to that of the related square-planar complex $[(N(SiMe_2CH_2PPh_2)_2)Co(CH_2SiMe_3)]$ (2.1 μ_B), which was reported by Fryzuk et al.[19]



Scheme 1. a) Complexes **1** and **2**. b) X-ray structure of complex **1** (thermal ellipsoids at 50% probability, hydrogen atoms omitted for clarity). Two crystallographically independent molecules were present in the unit cell for complex **1**, one of which is shown above. Selected bond distances [Å] and angles [°]: Co1–N1 1.880(3), Co1–P1 2.202(1), Co1–P2 2.204(1), Co1–C29 2.005(3); N1-Co1-C29 172.2(1), N1-Co1-P1 84.9(1), C29-Co1-P1 95.4(1), N1-Co1-P2 84.6(1), C29-Co1-P2 95.7(1), P1-Co1-P2 168.7(4).

When one equivalent of the acid $H[BAr^F_4]\cdot(Et_2O)_2$ ($BAr^F_4 = B(3,5\text{-}(CF_3)_2C_6H_3)_4$) was added to a solution of **1** in [D$_8$]THF, a new paramagnetic product, $[(PNHP^{Cy})Co(CH_2SiMe_3)]BAr^F_4$ (**2**), was detected by ^1H NMR spectroscopy in 90% yield (integration against an internal standard). Complex **2** was isolated and characterized by NMR and IR spectroscopy, X-ray crystallography, and elemental analysis.

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The ^{1}H NMR spectrum of **2** showed a broad signal at -20.88 ppm, corresponding to the $Si(CH_3)_3$ protons on the alkyl ligand, and the IR spectrum of **2** showed an N−H stretch at 3147 cm^{-1}. In the solid state, complex **2** has a distorted square-planar geometry.

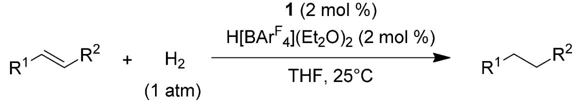
Initially, we tested the reactivity of cobalt complexes **1** and **2** with H_2, evaluating the catalytic hydrogenation of styrene. Only very slow hydrogenation occurred using complex **1** (2 mol%), with around 2% conversion of styrene to ethylbenzene observed after 24 hours at 60 °C under H_2 (1 atm). In contrast, complex **2** was a highly active precatalyst. Complete conversion (50 turnovers) was observed within two hours at room temperature under just 1 atm of H_2 using **2** (2 mol%, generated in situ from **1** and $H[BAr^F{}_4]\cdot(Et_2O)_2$). Using an isolated sample of complex **2** for the hydrogenation of styrene afforded identical results as when complex **2** was generated in situ. The hydrogenation of styrene with precatalyst **2** was unaffected by the addition of excess Hg metal, which is consistent with an active homogeneous catalyst. With a lower catalyst loading (0.05 mol% **1** and 0.05 mol% $H[BAr^F{}_4]\cdot(Et_2O)_2$), a total of 1100 turnovers were observed after 24 hours at room temperature (1 atm H_2).

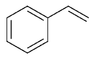
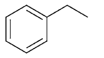
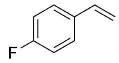
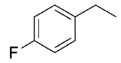
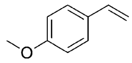
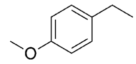
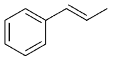
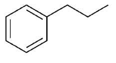
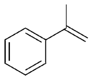
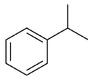
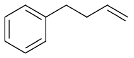
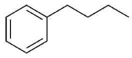
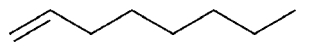
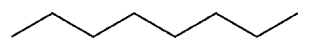
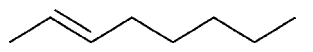
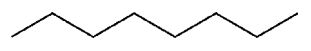
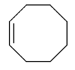
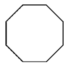
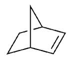
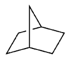
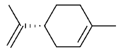
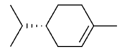
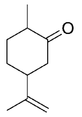
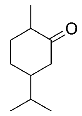
Encouraged by the observation of high activity under such mild conditions, we explored the substrate scope of this hydrogenation using cobalt precatalyst **2**. The hydrogenation of a variety of alkenes was tested by employing a combination of **1** (2 mol%) and $H[BAr^F{}_4]\cdot(Et_2O)_2$ (2 mol%) in THF (Table 1). Hydrogenation of terminal and internal alkenes proceeded readily within 24 hours at room temperature with excellent yields (Table 1, entries 5–11). Addition of D_2 to norbornylene occurred with *syn* stereochemistry, affording *exo*,*exo*-2,3-d_2-norbornane. Hydrogenation of (*R*)-(+)-limonene occurred selectively at the terminal position and the internal trisubstituted C=C bond was not hydrogenated (Table 1, entry 11), even under 4 atm H_2.[23] At room temperature, hydrogenation of dihydrocarvone occurred only at the C=C bond, affording 5-isopropyl-2-methylcyclohexanone in 99% yield (Table 1, entry 12).

There have been few previous reports of cobalt catalysts capable of ketone or aldehyde hydrogenation. Aldehyde hydrogenation has been observed as a side reaction in the hydroformylation of olefins catalyzed by $[Co_2(CO)_8]$, but these reactions occur under extremely harsh conditions (300 atm syngas, 185 °C).[11,24,25] Ohgo and Weber developed a cobalt–dioxime-based system that catalyzed the asymmetric hydrogenation of benzil, but the substrate scope was limited to selected 1,2-dicarbonyl compounds.[26,27] Thus, we were surprised to find that cobalt precatalyst **2** was quite active for hydrogenation of both aldehydes and ketones under mild conditions.

Hydrogenation of acetophenone proceeded in nearly quantitative yield under 1 atm of H_2 (Table 2, entry 1). Aliphatic ketones 2-hexanone and 2-indanone were reduced in high yields at 60 °C (Table 2, entries 5 and 6). Benzaldehyde and substituted benzaldehydes were also reduced in excellent yields within 24 hours under 1 atm of H_2 (Table 2, entries 8–11). The unsubstituted aliphatic aldehyde 1-octanal was hydrogenated more slowly, and 1-octanol was isolated in 92% yield after 64 hours at 60 °C under 4 atm of H_2 (Table 2, entry 12). To gain insight into the chemoselectivity of the cobalt catalysis, a competition experiment was performed, in which a 1:1 mixture of styrene and benzaldehyde was hydrogenated at room temperature under 1 atm of H_2 using **2**. Benzaldehyde was hydrogenated more rapidly, with complete conversion of benzaldehyde and only 16% conversion of styrene observed after 24 hours.[23]

Table 1: Cobalt-catalyzed alkene hydrogenation.[a]



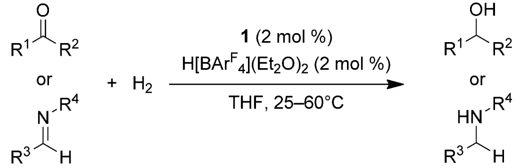
Entry	Substrate	Product	*t* [h]	Yield[b] [%]
1			24	100
2			24	100
3			24	99
4			24	100
5			24	99
6			24	100
7			24	99
8			24	100
9			24	100
10			24	100
11			40	80
12			42	99

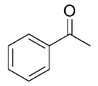
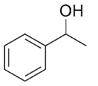
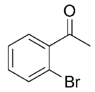
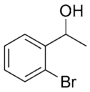
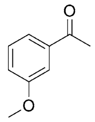
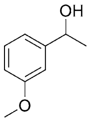
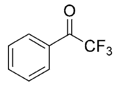
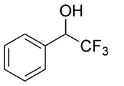
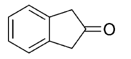
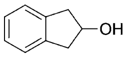
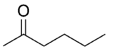
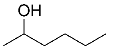
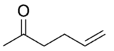
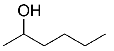
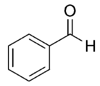
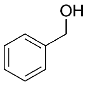
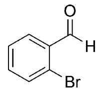
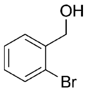
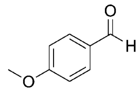
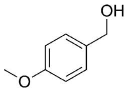
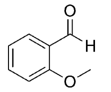
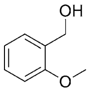
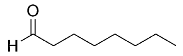
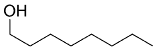
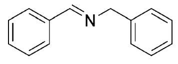
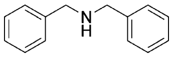
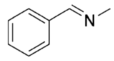
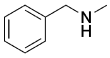
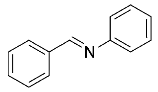
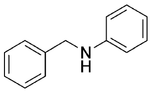
[a] Conditions: substrate (0.5 mmol) in THF (2 mL), H_2 (1 atm), 25 °C. [b] Yields determined by GC analysis.

The hydrogenation of imines is a valuable synthetic route for the preparation of amines, and thus we tested in situ generated **2** for the hydrogenation of several imines. Hydrogenation of *N*-benzylidenebenzylamine proceeded under 4 atm H_2 at 60 °C to afford dibenzylamine in high yield (84% yield of isolated product) using 2 mol% of **2** (Table 2, entry 13). *N*-Benzylidenemethylamine and *N*-benzylideneaniline were also hydrogenated by the cobalt catalyst (Table 2, entries 14 and 15). Previous examples of cobalt-catalyzed imine hydrogenation are scarce.[28]

Given the broad substrate scope, we performed further experiments to assess the functional-group tolerance of the catalytic cobalt system (Table 3). According to GC analysis, 4-penten-1-ol was hydrogenated quantitatively within 24 hours at room temperature (1 atm H_2, Table 3, entry 3). Complex **2** catalyzed the hydrogenation of 4-pentenoic acid to afford pentanoic acid (82% yield of isolated product) (Table 3, entry 2). The cobalt catalyst was also active in the presence of

Table 2: Cobalt-catalyzed hydrogenation of C=O and C=N bonds.[a]



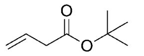
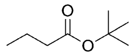
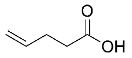
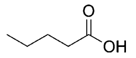
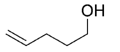
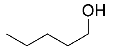
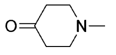
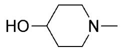
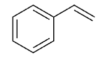
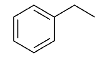
Entry	Substrate	Product	t [h]	Yield[f] [%] (NMR)[g] {GC}[h]
1			24	89 (98)
2[b]			43	86 (94)
3[b]			24	92 (98)
4[b]			48	91 (99)
5[b]			48	97 (99)
6[b]			24	{100}
7[c]			65	{99}
8			24	86 (92)
9			24	96 (100)
10[d]			24	92 (98)
11[d]			24	91 (99)
12[e]			64	92 (100)
13[e]			42	84 (89)
14[e]			72	88 (98)
15[e]			48	65 (70)

[a] Conditions: substrate (0.5 mmol) in THF (2 mL), H_2 (1 atm), 25 °C. [b] Reactions run at 60 °C. [c] Reactions run at 25 °C under 4 atm of H_2. [d] Reactions run at 50 °C. [e] Reactions run at 60 °C under 4 atm of H_2. [f] Yields of isolated products. [g] Yields determined by NMR spectroscopy. [h] Yields determined by GC analysis.

an amine, hydrogenating *N*-methyl-4-piperidone to *N*-methyl-4-piperidinol in 66 % yield, according to GC analysis (Table 3, entry 4).

Water is a common adventitious impurity in reagents and solvents, and thus we tested the activity of cobalt precatalyst **2** (2 mol %) for the hydrogenation of styrene in the presence of intentionally added water (10 mol %). Although the cobalt catalyst was inhibited by water, the hydrogenation reaction still occurred, affording ethylbenzene in 99 % yield after 24 hours at room temperature (Table 3, entry 5). The tolerance of the cobalt catalytic system to an array of functional groups and added water is remarkable, and is much more typical of precious-metal hydrogenation catalysts than those based on earth-abundant metals.[29,30]

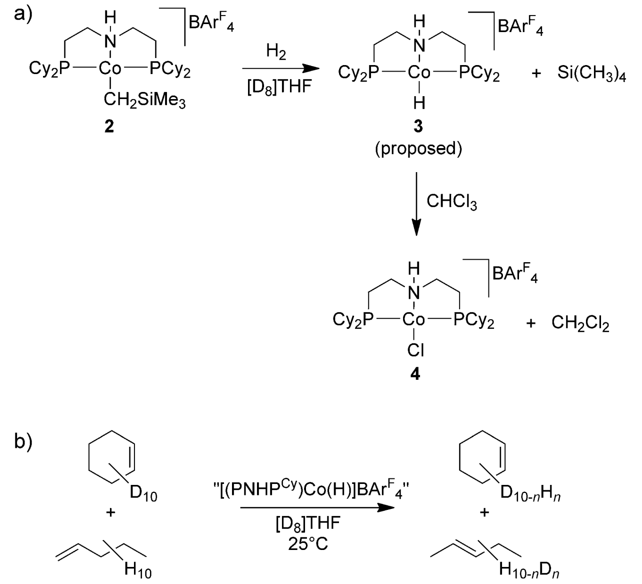
Table 3: Functional-group tolerance of cobalt-catalyzed hydrogenation.[a]

Entry	Substrate	Product	t [h]	Yield[b] [%]
1			24	99
2[c]			24	99 (82)[d]
3			24	99
4[c]			65	66
5	 + H_2O (10 mol %)	 + H_2O (10 mol %)	24	99

[a] Conditions: substrate (0.5 mmol) in THF (2 mL), **1** (2 mol%), H[BAr$^F_4$]·$(Et_2O)_2$ (2 mol%), H_2 (1 atm), 25 °C. [b] Yields determined by GC-MS analysis. [c] Reactions run at 60 °C under 1 atm of H_2. [d] Yield of isolated product.

In light of the high versatility and activity of cobalt precatalyst **2**, we performed additional experiments to gain insight into possible catalytic reaction mechanisms. The reaction of paramagnetic cobalt(II)–alkyl complex **2** with H_2 (1 atm) in [D$_8$]THF was monitored by ^{1}H NMR spectroscopy. Within one hour at room temperature, signals corresponding to complex **2** disappeared from the ^{1}H NMR spectrum, along with concomitant appearance of a new signal at 0 ppm, corresponding to tetramethylsilane (TMS). Although the solution had a yellow color that was consistent with the presence of a homogeneous cobalt complex, signals that could be attributed to a cobalt-containing product were not observed in the ^{1}H NMR spectrum of the reaction mixture. The magnetic moment of the solution was measured (Evans method) to be $\mu_{\text{eff}} \approx 2.7\ \mu_B$, consistent with (a) paramagnetic reaction product(s).

Several more experiments suggested that a cobalt(II)–hydride complex **3** might be formed upon the reaction of cobalt(II)–alkyl complex **2** with H_2. A solution of complex **2** in [D$_8$]THF was treated with H_2 (1 atm) for three hours, affording tetramethylsilane and the NMR-silent cobalt-containing product(s). Subsequent addition of $CHCl_3$ (2 equiv) caused an immediate color change from yellow to red, and formation of CH_2Cl_2 was detected by ^{1}H NMR spectroscopy. The cobalt-containing product of this reaction was isolated in 77 % yield and identified as the cobalt(II)–chloride complex [(PNHP^{Cy})Co(Cl)]BAr$^F_4$ (**4**) by X-ray crystallography, IR spectroscopy, and elemental analysis. The formation of chloride complex **4** upon trapping with $CHCl_3$ suggests that the hydride complex [(PNHP^{Cy})Co(H)]BAr$^F_4$ (**3**) is formed upon the reaction of **2** with H_2 (Scheme 2 a).



Scheme 2. a) Formation of cobalt(II)–chloride complex **4**. b) Cross-over experiment.

Solutions containing putative cobalt–hydride complex **3** catalyzed a rapid alkene isomerization at room temperature. When 1-octene (200 equiv) was added to a degassed solution of **3** in [D_8]THF, complete isomerization was observed within 20 minutes, affording a mixture of internal octenes. Previously, both metal–hydride and π-allyl mechanisms have been proposed for transition-metal-mediated olefin isomerization.[31,32] We performed a cross-over experiment to test for a metal–hydride intermediate in the cobalt system (Scheme 2b). Treatment of a mixture of complex **1** and $H[BAr^F_4]\cdot(Et_2O)_2$ in [D_8]THF with H_2 led to the generation of the active catalytic species. H_2 was removed, and then a 1:1 mixture of [D_{10}]cyclohexene and 1-pentene was added. Within 30 minutes, isomerization of 1-pentene to 2-pentene was observed by ^{1}H NMR spectroscopy. In addition, deuterium from [D_{10}]cyclohexene was incorporated into 2-pentene and resonances corresponding to [$D_{10-n}H_n$]cyclohexene emerged in the NMR spectrum, consistent with an isomerization pathway involving a discrete metal–hydride intermediate.

In conclusion, cobalt-catalyzed hydrogenation of alkenes, ketones, aldehydes, and imines has been achieved under mild conditions. While previous efforts to design cobalt catalysts have focused primarily on the synthesis of cobalt(I)–hydride and cobalt(I)–dihydrogen complexes,[16,33–35] the reactivity of cobalt(II)–hydride complexes has been largely unexplored.[36–42] The high catalytic activities reported herein and potential involvement of cobalt(II) suggest a new frontier in catalyst design. Future work will focus on further understanding the reactivity of these rare 15-electron alkyl and hydride complexes of cobalt(II).

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Keywords: cobalt · homogeneous catalysis · hydrogenation · synthetic methods

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