



Accepted Article

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This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: ChemCatChem 10.1002/cctc.201801605

Link to VoR: http://dx.doi.org/10.1002/cctc.201801605



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Bench-Stable Cobalt Pre-Catalysts for Mild Hydrosilative Reduction of Tertiary Amides to Amines and Beyond

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Abstract: The readily synthesized and bench-stable cobalt dichloride complex (dpephos)CoCl₂ is employed as a pre-catalyst for a diversity of silane additions to unsaturated organic molecules, including the normally challenging reduction of amides to amines. With regard to hydrosilative reduction of amides even more effective and activator free catalytic systems can be generated from the bench-stable, commercially available Co(acac)₂ and Co(OAc)₂ with dpephos and PPh₃ ligands. These systems operate under mild conditions (<100 °C), with many examples of room temperature transformations, presenting a first example of mild cobalt-catalyzed hydrosilylation of amides.

Introduction

Catalytic hydrosilylation of unsaturated organic molecules is a fundamental transformation in synthetic organic chemistry, relevant to production of both commodity and fine chemicals, medicinal chemistry, silicone industry and materials science.^[1] Moreover, addition of hydrosilanes to unsaturated C-C and C-X (X = heteroatom) bonds constitutes a straightforward methodology for preparation of Si-containing molecules, which find a broad range of applications, including protecting groups in organic synthesis,^[1,2] precursors for Si-based dielectric materials,^[3,4a] additives in perfumery and personal care products,^[1a,f,4a] monomers for production of silicone polymers^[4,5] and many others.^[1a,f,4]

Historically, catalytic systems for hydrosilylation reactions have been based on heavy late transition metals, such as Rh, Ir, Ru, Pt, Pd, etc.^[1] Due to the skyrocketing prices of these metals, the development of more economical non-precious metal based catalysts has been an intensive area of research in the last decade.^[6-9] In this regard, earth abundant base transition metal catalysts (Mn, Fe, Co, Ni) have become very attractive alternatives to conventional precious metal systems^[6a,d,e,7]

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Whereas, a series of base metal catalysts have been developed for hydrosilylation of alkenes, alkynes, aldehydes, ketones^[6a,d,e-8] and even esters^[8j,9] the examples of application of simple commercially available bench-stable systems are still scarce.^{[8} e,h,i]</sup> Base-metal catalyzed hydrosilative reduction of amides is even more challenging^[10,11] and there is only a handful of reported examples, most of which require rather high temperatures (≥100 °C) and long reaction times^[10,12-16]

The first examples of base-metal-catalyzed reduction of tertiary amides to amines were reported in 2009 by Beller^[12a] and Nagashima^[12b] for Fe(CO)₅ and Fe₃(CO)₁₂, which were found to mediate the reductions under either thermal (100 °C, 24 h) or photochemical (25 °C, 9 h) conditions with rather high catalyst loadings (6-30 mol. % of Fe). Since then, a few similar Fe-catalyzed reactions have been reported,^[13] but no startling improvement of the reaction conditions was seen. Concerning the other base metal systems, not much has been done outside of iron. Thus, the related Mn-catalyzed reductions are limited to only three reports. One describes the reduction of HC(O)NR₂ (R = Me, Et) with tertiary silanes in the presence of $CpMn(CO)_3$ (5 mol%), activated either thermally (120 °C, 24 h) or photochemically (70 °C, 12-18 h).^[14a] Another example involves the reduction of *N*-acetylpiperidine with HSiEt₃ in the presence of Mn₂(CO)₁₀ (1 mol%) and Et₃N (5 mol%) at 100 °C (16 h).^[14b] The third report was recently disclosed by Sydora, Stradiotto and Turculet^[14c] and presents the first example of mild (25 °C, 18 h or 75 °C, 1 h) base-metal-catalyzed reduction of tertiary amides to amines using a manganese amide precursor supported by Nphosphinoamidinate ligand, $(\kappa^2-P,N)Mn(N(SiMe_3)_2)$. Ni and Co based systems are even less common in amide hysrosilylation reactions. For example, selective Ni-catalyzed reductions of amides are limited to the use of NiCl₂(dme) with PhSiH₃ (10 mol% of Ni, 115 °C, 24 h),^[15a] whereas reduction of both keto and amide groups of α -keto amides was accomplished with Ni(OAc)₂ (5 mol% of Ni) and Ph₂SiH₂ in the presence of TMEDA (10 mol%) and KO'Bu (10 mol%).[15b] For cobalt, the only example of reduction of amides was demonstrated by Darcel and Sortais^[16] using air-sensitive and thermally unstable Co₂(CO)₈ (1 mol%, 100 °C, 3-16 h) (Scheme 1). Notably, Co₂(CO)₈ was found to mediate the reduction of Nbenzylbenzamide with 68% conversion in 16 h at 100 °C, [Ошибка! Закладка не определена.] presenting a rare example of base-metalcatalyzed reduction of secondary amides.^[10,12-16]

Driven by our interests in developing efficient base metal pre-catalysts for reduction of unsaturated organic molecules, we herein describe the catalytic behavior of a series of bench-stable commercially available (or readily prepared) cobalt pre-catalysts (Scheme 1) in hydrosilylation reactions, including a rare example





Scheme 1. Co-catalyzed hydrosilative reduction of amides

of mild base-metal-catalyzed hydrosilative reduction of amides to amines.

Results and Discussion

Hydrosilylation of alkenes and alkynes. Testing cobalt precatalysts we started with (dpephos)CoCl₂ (dpephos = bis[(2dipenylphosphino)phenyl] ether), which was prepared using literature procedure^[17] from CoCl₂•6H₂O and dpephos in CH₂Cl₂/CH₃CN (ca. 1/1). Despite a number of Co(II) chloride pre-catalysts and their use in hydrosilylation of alkenes and alkynes have been reported,^[6-8] to the best of our knowledge, no efficient systems based on CoCl₂ in a combination with simple commercially available phosphine ligands have been disclosed. Although, we primarily targeted the hydrosilative reduction of amides, for comparison with the previously reported Co systems,^[6-8] catalytic activity of (dpephos)CoCl₂ was initially tested in hydrosilylation of alkenes and alkynes. Specifically, the reaction conditions as well as the catalyst activation protocols were evaluated for hydrosilylation of styrene with PhSiH₃. Co(II) dichloride pre-catalyst was converted in situ to reactive Co(I)-H species with the aid of external activators^[18] and, in general, hydrosilylation of styrene afforded the mixtures of Markovnikov silane addition product (1a), anti-Markovnikov product (2a) and ethylbenzene (3a). No products of dehydrogenative silation of styrene were detected. The selected results are summarized in Table 1, showing that styrene conversion and the products ratios are highly affected by the reaction conditions (solvent, temperature) and, to the higher extent, by the employed catalyst activation method. Thus at 5 mol% loading of (dpephos)CoCl₂, among a series of cobalt dihalide activators commonly used in catalytic alkene hydrofunctionalizations,^[18] only LiBHEt₃ (2 equiv. to Co) in benzene at 65 °C showed sufficient styrene conversion (91%) with the ratio 1a:2a:3a of 61:24:15 (Table 1, entry 6). Lowering the temperature of the reaction down to 35 °C and keeping the Co loading at 5 mol% resulted in the same styrene conversion but produced twice less amount of ethylbenzene (Table 1, entry 7). At ambient temperature, lower styrene conversion (71%) and longer reaction times (24 h) were observed (Table 1, entry 8). At 35 °C, the decrease in catalyst loading down to 1 mol% resulted in inefficient hydrosilylation reaction with only 17% conversion of styrene after 6 h and substantial formation of ethylbenzene by-product (Table 1, entry 9).

Ph + PhSiH ₃	(dpephos)Co activator A , solvent, te	Cl _{2,} x mol.% 2x mol.% mp., time	SiH ₂ Ph	Ph Sił 2a	$H_2Ph + Ph $
entry	x/A	solvent	T, ℃ / <i>t</i> , h	Conv. ^[b]	Ratio 1a:2a:3a ^[b]
1	5/MeLi	C ₆ D ₆	65 / 5	25%	35:19:46
2	5/NaO ^t Bu	C ₆ D ₆	65 / 5	53%	50:31:19
3	5/NaO ^t Bu	THF-d ₈	65 / 5	9%	42:28:30
4	5/KO [#] Bu	THF-d ₈	65 /5	34%	0:23:77
5	5/LiBHEt ₃	THF-d ₈	65 / 5	47%	44:25:31
6	5/LiBHEt₃	C ₆ D ₆	65 / 5	91%	61:24:15
7	5/LiBHEt₃	C ₆ D ₆	35 / 5	90%	68:25:7
8	5/LiBHEt₃	C ₆ D ₆	25 / 24	71%	65:25:10
9	1/LiBHEt ₃	C ₆ D ₆	35 / 6	17%	19:24:57

Table 1. Evaluation of conditions for (dpephos)CoCl₂-catalyzed hydrosilylation

[a] 0.48 M. [b] Determined by ¹H-NMR.

of styrene with PhSiH3[a]

Having identified the optimal catalyst activation method and reaction conditions (Table 1, entry 6) we then probed the catalytic activity of (dpephos)CoCl₂ in a variety of silane addition reactions. Rewardingly, (dpephos)CoCl₂/LiBHEt₃ system turned out to be active in hydrosilylation of a alkenes, alkynes, ketones, aldehydes, esters, and amides, being only the second example of a Co catalyst for hydrosilative reduction of amides^[16] and the first Co catalyst that reduces amides under mild conditions (<100 °C). Thus, terminal alkenes, with an exception of styrene, which showed preference for Markovnikov addition (Table 1), were exclusively converted to the linear alkylsilanes (Scheme 2).



Scheme 2. (dpephos)CoCl₂/LiBHEt₃-catalyzed hydrosilylation of alkenes and alkynes (C_{substrate} = 0.48 M). Yields were determined by ¹H-NMR. [a] 0.3 h at 60 °C. [b] 1 h, 60 °C. [c] 0.25 h.

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The reactions were performed with 5 mol% Co loading at 65 °C and analyzed by ¹H-NMR spectroscopy after 5 h, showing >99% conversion of hexene-1, octene-1 and 3,3-dimethylbutene-1 to the corresponding alkylsilanes 2b-2d. Although we did not explore shorter reaction times for all the substrates, complete of hexene-1, 3,3-dimethylbutene-1 conversion and allyltrimethylsilane was also observed after 0.3 h, 1 h and 1 h respectively (Scheme 2), suggesting that the reaction time of 5 h might not be necessary for hydrosilylation of terminal aliphatic alkenes. In contrast, sterically demanding terminal alkenes, such as 9-vinylcarbazole and limonene, and internal alkenes, such as trans-2-octene, cyclohexene and 2-methyl-1-phenylpropene, did not undergo hydrosilylation even at elevated temperatures (up to 100 °C, sealed NMR tube).

Similar to (dpephos)CoCl₂/LiBHEt₃, regioselective Markovnikov hydrosilylation of aryl alkenes and anti-Markovnikov hydrosilylation of aliphatic alkenes with PhSiH₃ was recently reported by Ge et al. for Co(acac)₂/xantphos (xantphos = 4,5bis(diphenylphosphino)-9,9-dimethylxanthene).[8e] Using dpephos in place of xantphos, addition of PhSiH₃ to styrene at 25 °C resulted in reduced branched-to-linear (b/l) product ratio (76:24 vs 97:3 for xantphos) and lower styrene conversion (15% vs >98% for xantphos).[8e] Compared to Co(acac)₂/dpephos, (dpephos)CoCl₂/LiBHEt₃-catalyzed reactions showed verv similar b/l ratios (Table 1, entries 6-8); however, significantly higher conversion of styrene (71%) was observed at room temperature (Table 1, entry 8).[8e]

The mechanism of Co/diphosphine-catalyzed hydrosilylation of alkenes with PhSiH₃ was studied by Ge et al.[8e] and the reactions were suggested to proceed via Chalk-Harrod (with a Co-H intermediate)^[19], mechanism and the regioselectivity of the silane addition was rationalized by the preferential 2,1-migratory insertion of the vinylarenes into the Co-H bond (electronic preference)^[20] vs 1,2-insertion for aliphatic alkenes (driven by steric preference).[8e,21] Indeed, our variable temperature NMR studies of the reaction of (dpephos)CoCl₂ with 2.5 equiv. of LiBHEt₃ in PhMe-d₈ revealed formation of a diamagnetic hydride species 4 (mixture of two isomers, 3.2:1 ratio by ¹H-NMR) at 0 °C.^[22] The ¹H-NMR spectrum of the major isomer of **4** shows a Co*H* resonance at δ -19.89 ppm (dt, ${}^{2}J_{H-P}$ = 60.5 Hz, 44.5 Hz),^[23] coupled to two non-equivalent phosphine signals (2:1 integral ratio; δ 42.5 ppm and 48.2 ppm) in the ³¹P{¹H}-NMR. Unfortunately, thermal instability of 4 and its formation in a complex mixture of decomposition products hampered its isolation and full characterization. However, based on the NMR features, 4 was tentatively assigned to [(dpephos)Co(H)]₂(μ -dpephos), a dimer having tetracoordinate Co(I) centres and a bridging dpephos ligand. Notably, no formation of silyl species, akin to (dpephos)Co(SiH₂Ph), was observed when the NMR reaction of (dpephos)CoCl₂ with LiBHEt₃ (2.5 equiv) was repeated in the presence of excess PhSiH₃ (ca. 5 equiv). The intermediacy of Co-H species is consistent with the fact that no alkenylsilanes, products of dehydrogenative silation of alkenes, were detected during (dpephos)CoCl₂/LiBHEt₃-catalyzed hydrosilation of olefins (Table 1 and Scheme 2).^[24]

The alkylcobalt species produced from the Co hydride by 2,1- and 1,2-insertion of olefins can be interconverted *via* β -H elimination and reinsertion of the alkene into the Co-H bond. For styrene, keeping in mind the preferential formation of the

secondary benzylcobalt intermediate,[8e,20] lower b/l ratio of hydrosilylation products for dpephos (bite angle of 102.2 °) vs xantphos (bite angle of 111.7 °)[25] can be rationalized by the competing rates of β -H elimination and silane addition upon reducing the bite angle of the ligand. In contrast, for unhindered aliphatic alkenes, undergoing 1,2-insertion to form primary alkylcobalt species,^[8e,21] addition of PhSiH₃ appears preferential over β -H elimination and results in exclusive formation of anti-Markovnikov products (2b-2d, Scheme 2). For (dpephos)CoCl₂/LiBHEt₃-catalyzed hydrosilylation of allylbenzene and allyltrymethylsilane with PhSiH₃, 14% and 3% of internal alkenes were observed by ¹H-NMR, respectively (Scheme 2), whereas the use of more sterically hindered PhMeSiH₂ in hydrosilylation of allylbenzene results in almost exclusive formation of PhCH=CHCH₃.

(dpephos)CoCl₂/LiBHEt₃-catalyzed (5 mol% of Co) hydrosilvlation of alkynes (phenylacetylene, 3-cyclohexyl-1-propyne, hexyne-1 and trimethylsilylacetylene) with PhSiH₃ is fast and proceeds at room temperature to give a complete conversion (>99%, 0.25-0.5 h) of substrates with a preference for anti-Markovnikov silane addition products, trans-*β*-vinylsilanes (6a-6d, Scheme 2). After 30 min at room temperature, for hexyne-1 and trimethylsilylacetylene, the reactions also result in 18% and 12% of the products of double anti-Markovnikov PhSiH₃ addition, (PhH₂Si)₂C(H)CH₂Bu and (PhH₂Si)₂C(H)CH₂SiMe₃,^[26] respectively (Scheme 2), whereas treatment of hexyne-1 with 5 equiv. of PhSiH₃ for 24 h at 25 $^{\circ}$ C leads to 52% of (PhH₂Si)₂C(H)CH₂Bu 52% in a mixture with 48% of 6c. During preparation of this manuscript, similar (E)-selective anti-Markovnikov hydrosilylation of terminal alkynes to (E)- β vinylsilanes has been reported by Ge et al. for Co(acac)₂/dpephos system,^[8h] however no bis(silyl) products were detected, albeit the reactions were conducted with a slight excess of PhSiH₃ (ca. 1.5 equiv).^[8h]

Hydrosilylation of aldehydes, ketones and esters. $(dpephos)CoCl_2/LiBHEt_3$ also effected the hydrosilylation of aldehydes and ketones (Table 2). In contrast to alkynes the room temperature reactions were found to be sluggish and com-

Table 2. Hydrosilylation of aldehydes, ketones and esters ^[a]						
Entry	Substrate	Product(s)	Yield, % ^[b]			
1	PhC(O)H	PhHSi(OBn) ₂ ^[c]	>99			
2	octanal	PhSiH _n (OOct) _{3-n}	>99			
3	Me ₂ C(O)	PhSiH ₂ (O'Pr) / PhSiH(O'Pr) ₂ ^[d]	58 / 42			
4	PhC(O)Me	PhSiH ₂ (OCH(Me)Ph)	>99			
5	$Ph_2C(O)$	PhSiH ₂ (OC(H)Ph ₂)	>99			
6	cyclohexanone	PhSiH ₂ (OCy) / PhSiH(OCy) ₂	81 / 19			
7	EtOAc	PhSiH ₂ (OEt) / PhSiH(OEt) ₂ / PhSi(OEt) ₃	3 / 87 / 10			
8	PhC(O)OMe	PhCH ₂ OH ^[e] (MeOH)	>99			

[a] C_6D_6 (0.48 M), (dpephos)CoCl₂/LiBHEt₃ (5/10 mol%), 60 °C, 5 h. [b] NMR yields. [c] 2 equiv of PhSiH₃ were used. [d] 1.5 equiv of PhSiH₃ was used. [e] After hydrolysis with 20% NaOH (aq.) (18 h, 25 °C).

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plete conversions were achieved only at 60 °C. With an exception of ethyl acetate and methyl benzoate, which showed complete conversions in 5 hours at 60 °C (Table 2), (dpephos)CoCl₂/LiBHEt₃ showed poor activity in hydrosilylation of esters. Thus, only 62%, 25% and 46% conversions of phenyl acetate, *tert*-butyl acetate and ethyl tri-fluoroacetate, respectively, were observed after 40 h at 60 °C.

Hydrosilative reduction of amides. The most intriguing question remained was whether (dpephos)CoCl₂ can serve as pre-catalysts for hydrosilative reduction of amides to amines. Rewardingly, applying the working conditions found for alkenes, aldehydes and ketones (5 mol% of Co, 60 °C, 5 h), (dpephos)CoCl₂ showed complete conversion (>99%) of a diversity of tertiary amides to the corresponding tertiary amines 7a-i (Table 3). To our delight, the reduction dimethylformamide (DMF) with 1.5 equiv of PhSiH₃^[27]and (dpephos)CoCl₂ (5 mol%)/LiBHEt₃ (10 mol%) reached the completion in 5 h even at 25 °C, being, after (κ^2 -P,N)Mn(N(SiMe₃)₂), reported in 2017 by Sydora, Stradiotto and Turculet,^[14c] only the second example of a base metal catalyst for the room temperature reduction of tertiary amides in the absence of photochemical activation.^[28]

Although amide substrates were added after pre-catalyst activation with LiBHEt₃,^[29] due to the well-known ability of LiBHEt₃ to add to the carbonyl function of amides,^[30,31] we

sought of a system that does not require external activation and the reaction can be initiated by the silane. Inspired by the recent achievements in Co(acac)₂/bisphosphine-catalyzed hydrosilylation of alkenes^[8e] and alkynes^[8h] we explored the catalytic activity of Co(acac)₂ and Co(OAc)₂ in reduction of DMF with PhSiH₃. Turned out, at 5 mol% loading of Co, with dpephos (1 equiv to Co), both Co(acac)₂ and Co(OAc)₂ have a comparable to (dpephos)CoCl₂/LiBHEt₃ activity in converting DMF to trimethylamine at both 60 °C and room temperature (>99% in 5 h, 7a, Table 3). For Co(acac)₂/dpephos, decreasing the pre-catalyst loading from 5 mol% to 0.5 mol% results in a slightly slower reaction at room temperature (92% conversion of DMF in 5 h); however, at 60 °C leads to quantitative conversion of DMF to trimethylamine within 5 h (TON = 200, TOF = 40 h^{-1} ; Table 3, 7a, system E). The activity of Co(OAc)₂ in the reduction of DMF remains high even upon substitution of dpephos with two equivalents of PPh₃ (>99% in 5 h at 60 °C and 25 °C; Table 3, catalytic system F), whereas Co(acac)₂/PPh₃ (5 mol% of Co) showed lower activity and 79% and 80%^[32] conversions of DMF and N,N-dibenzylacetamide, respectively, were observed at room temperature after 24 h (Table 3, 7c, system D). Based on these observations, the following systems were chosen for further comparative reactivity testing: (dpephos)CoCl₂/LiBHEt₃ (5 mol% of Co) at 60 °C (Table 3, A), Co(acac)₂/dpephos (5 mol% of Co) at room temperature and 60 °C (Table 3, B), and

Table 3. Co-catalyzed hydrosilative reduction of primary, secondary and tertiary amides to amines^[a]

$R^{1} \xrightarrow{O}_{R^{3}} R^{2} \xrightarrow{I.5 \text{ PhSiH}_{3}}_{\text{ligand or activator}} R^{1} \xrightarrow{H}_{R^{3}} R^{2} + oligosiloxane $ $R^{1} \xrightarrow{O}_{R^{3}} R^{2} \xrightarrow{I.5 \text{ PhSiH}_{3}}_{\text{ligand or activator}} R^{1} \xrightarrow{H}_{R^{3}} R^{2} + oligosiloxane $ $R^{2} \xrightarrow{O}_{R^{3}} R^{2} \xrightarrow{CoX_{2} (x \text{ mol.}\%)}_{\text{ligand or activator}} R^{2} \xrightarrow{R^{3}} R^{3} \xrightarrow{I.5 \text{ PhSiH}_{3}}_{\text{ligand or activator}} R^{2} \xrightarrow{H}_{R^{3}} R^{2} \xrightarrow{I.5 \text{ PhSiH}_{3}}_{\text{ligand or activator}} R^{2} \xrightarrow{I.5 \text{ PhSH}_{3}}_{\text{ligand or activator}} R^{2} \xrightarrow{I.5 \text{ PhSH}_{3}}_{ligand or act$											
Product	Catalytic system	T, °C / <i>t</i> , h	Yield, %	Product	Catalytic system	T, °C / <i>t</i> , h	Yield, %	Product	Catalytic system	T, °C / <i>t</i> , h	Yield, %
H H H N	A-F A-C, F E D	60 / 5 25 / 5 25 / 6.5 25 / 24	>99 >99 >99 ^[b] 79		A B B E	60 / 5 25 / 17 60 / 5 60 / 24	>99 >99 (93) >99 72		A A B	60 / 5 65 / 16 100 / 24	28 44 ^[k] 15
H H X N 7b	A B E E	60 / 5 25 / 17 60 / 5 60 / 24	>99 >99 82 94		A B B E	60 / 5 25 / 17 60 / 5 60 / 24	>99 87 85 87 ^[f]	H H N ^H 7j	B B B	75 / 24 75 / 48 75 / 72	45 73 >99
	A B ^{Ph} D E E	60 / 5 25 / 3 25 / 24 25 / 32 60 / 5	>99 >99 (95) 80 ^[c] 68 >99	$ \begin{array}{c} H \\ H \\ 7g \\ H \end{array} $	A B E	60 / 5 25 / 17 60 / 24	>99 >99 61 ^[g]	Ph N R R = H,	7k: B 7I: B 7I: B 7k; Me, 7I	100 / 24 75 / 24 75 / 48	83 ^[1] 89 ^{[m} >99 ^{[m}
H H Ph N I 7d	A B E E	60 / 16 60 / 24 60 / 24 60 / 48	91 ^[d] >99 ^[e] 28 37		A A B E	60 / 5 65 / 16 25 / 24 60 / 24	>99 96 ^[h] 90 ^[i] 43 ^[j]	Et N ^{Ph}	В	60 / 60	>99[^{n]}

[a] THF-d₈ (0.48 M) for Co(acac)₂ and Co(OAc)₂ and C₆D₆ (0.48 M) for (dpephos)CoCl₂/LiBHEt₃. Yields were determined by ¹H-NMR (see Supporting Information for details). Yields of isolated products are given with parentheses. [b] 92% of **7a** was observed in 5 h at 25 °C. [c] >99% of **7c** was observed in 10 h at 60 °C. [d] 19% of **7d** was observed after 24 h at 25 °C and >99% of **7d** was observed after 24 h at 60 °C. [e] 38% of **7d** was observed after 24 h at 25 °C. [f] 83% of **7f** observed in 5 h at 60 °C. [g] 45% of **7g** was observed in 5 h at 60 °C. [h] PhMeSiH₂ (4 equiv) was used instead of PhSiH₃ and 71% of **7h** was observed in 5 h at 65 °C. [i] 81% of **7h** was observed after 5 h at 60 °C. [k] PhMeSiH₂ (3 equiv) was used instead of PhSiH₃ and 32% of **7i** was observed in 5 h at 65 °C. [l] Determined by GC-MS after hydrolysis with 20% NaOH (aq). [m] A mixture of **7I** and silylated products **7I-Si** was produced; overall yield for the mixture.

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Co(acac)₂/dpephos (0.5 mol% of Co) at 60 °C (Table 3, E). With PhSiH₃, all three systems were found to catalyze reduction of a diversity of aliphatic, aromatic and cyclic tertiary amides to the corresponding tertiary amines (Table 3). Interestingly, despite a large bite angle of dpephos ligand (102.2°), [25] steric hindrance of the amide substrate does not seem to play a big role and very similar, conversions of N,N-diisopropylbenzamide and 4benzoylmorpholine and were obtained with 5 mol% of (dpephos)-CoCl₂/LiBHEt₃ (7e and 7f, Table 3). Moreover the reduction of less crowded N,N-dimethylbenzamide with PhSiH₃ (7d, Table 3) proved more difficult than the analogous reaction with N,N-diisopropylbenzamide, which is surprising and can not be rationalized only by the steric considerations. On the other hand, substitution of PhSiH₃ with PhMeSiH₂ in the reduction of N-methylsuccinimide results in slower reaction (94% in 16 h at 65 °C; 7h, Table 3), suggesting that steric hindrance of the silane reductant has a significant influence on the reactivity. Similar observations were reported by Darcel and Sortais for the Co₂(CO)₈-catalyzed reduction of amides with PMHS (polymethylhydrosiloxane) in place of PhSiH₃.^[16]

Notably, Co(acac)₂/dpephos (5 mol% of Co) also catalyzes the reduction of secondary and primary amides with PhSiH₃, constituting a rare example of a base metal catalytic system for direct hydrosilylation of primary and secondary amides to amines.^[15a,33,34] Compared to tertiary amides, the reactions require higher temperatures (75-100 °C) and longer times (Table 3). Thus at 75 °C, full conversion of acetamide to ethylamine could be achieved within 72 hours (**7j**, Table 3), whereas the reduction of benzamide requires heating at 100 °C for 24 hours. (**7k**, Table 3).^[35] The reduction of secondary amides is slightly faster than for primary amides and full conversion of *N*methylbenzamide and *N*-phenylpropionamide could be achieved within 48 h at 75 °C and 60 h at 60 °C, respectively (**71** and **7m**, Table 3).

Finally, taking into account slow Co/dpephos-catalyzed hydrosilylation of alkenes, aldehydes, ketones and esters at room temperature (see the discussion above) we explored the chemoselectivity of the reduction of amides in the presence of compounds having potent reductive functional groups. Chemoselectivity tests for Co(acac)₂/dpephos system were performed on NMR scale with DMF and N.N-dibenzylacetamide combined with 1 equiv of a competing substrate (benzaldehvde, acetophenone, styrene, cyclohexene, octyne-4, ethyl acetate and benzonitrile). The results of these trials are summarized in Table 4. With PhSiH₃, the reactions showed excellent chemoselectivities (>99% conversion) in favor of the reduction of amide substrates with internal alkenes and esters (Table 4, entries 5 and 8). For a mixture of N.N-dibenzylacetamide and styrene, despite 1 equiv of PhSiH₃ was used, complete conversion of both substrates was observed with the formation of a 1:4 mixture of anti-Markovnikov and Markovnikov styrene hydrosilylation products, respectively (Table 4, entry 3), suggesting participation of the hydrosiloxane by-products in hydrosilylation reactions. Very similar outcome with the formation of a mixture of vinylsilanes, was observed upon competing reduction of a mixture of DMF and octyne-4. To avoid further hydrosilylation of competing substrates with hydrosiloxanes, formed upon reduction of amides with PhSiH₃, the reactions of DMF/styrene and DMF/octyne-4 mixtures were attempted with PhMe₂SiH, but showed no conversion of either substrates at room temperature and at 60 °C (Table 4, entries 4 and 7), presumably due to the steric hindrance of the silane.^[16] In contrast, treatment of the mixture of 1-methyl-2-pyrrolidinone and allylbenzene with PhMeSiH₂ and Co(acac)₂/dpephos (5 mol% of Co) showed chemoselective but slow (47% conv. in 16 h at 65 °C) reduction of the amide (Table 4, entry 6).

Table 4.	Competitive	Co(acac) ₂ /dpephos-catalyzed	hydrosilative	reduction
of amides	[a]			

Entry	Amide	Competing substrate	Silane	<i>t</i> , h	Conv., % ^[b]
1	MeC(O)NBn ₂	PhC(O)H	PhSiH₃	5	49 / >99 ^[c]
2	MeC(O)NBn ₂	PhC(O)Me	PhSiH₃	5	54 / >99 ^[d]
3	MeC(O)NBn ₂	PhCH=CH ₂	PhSiH₃	24	>99 / >99 ^[e]
4 ^[f]	HC(O)NMe ₂	PhCH=CH ₂	PhMe ₂ SiH	24	0 / 0
5	HC(O)NMe ₂	cyclohexene	PhSiH₃	5	>99 / 0
6 ^[g]	1-methyl-2- pyrrolidinone	allylbenzene	PhMeSiH ₂	16	47 / 0
7 ^[f]	HC(O)NMe ₂	octyne-4	PhMe ₂ SiH	24	0 / 0
8	MeC(O)NBn ₂	EtOAc	PhSiH₃	24	>99 / 0
9	MeC(O)NBn ₂	PhCN	PhSiH₃	24	23 / 0

[a] THF-d₈ (0.48 M), Co(acac)₂/dpephos (5/5.5 mol%), amide:competing substrate:silane = 1:1:1, 25 °C unless mentioned otherwise. [b] Conversion by ¹H-NMR (conv. of amide / conv. of competing substrate). [c] Formation of a 1:1 mixture of PhHSi(OBn)₂ and EtNBn₂ was observed. [d] A mixture of PhH₂Si[OC(H)PhMe] (23%), PhHSi[OC(H)PhMe]₂ (13%), PhSi[OC(H)PhMe]₃ (12%) and EtNBn₂ (52%) was observed. [e] Complete conversion of both substrates was observed to give a mixture of markovnikov (11%) and Markovnikov (40%) styrene hydrosilylation products and EtNBn₂ (49%). [f] PhMe₂SiH was used both at 25 °C and 60 °C. [g] PhMeSiH₂ was observed.

Selective, albeit slow (23% conversion in 24 h), reduction of N,N-dibenzylacetamide with PhSiH₃ was observed also in the presence of 1 equiv. of PhCN (Table 4, entry 9). In contrast, the reactions in the presence of benzaldehyde and acetophenone result in only app. 50% conversion of N,N-dibenzylacetamide and formation of a 1:1 mixture of PhSiH(OBn)₂ and N-ethyldibenzylamine and a mixture of N-ethyldibenzylamine (52%) with PhH₂Si[OC(H)PhMe] (23%), PhHSi[OC(H)PhMe]₂ (13%) and PhSi[OC(H)PhMe]₃ (12%), respectively (Table 4, entries 1 and 2).

On the basis of literature precedents on Co(acac)₂-catalyzed hydrosilylation of alkenes and alkynes^[8e,h] and our variable temperature NMR studies of the reaction of (dpephos)CoCl₂ with LiBHEt₃, we propose the mechanism of hydrosilative reduction of tertiary amides to tertiary amines depicted in Scheme 3A. Activation of (dpephos)CoCl₂ with 2 equiv of LiBHEt₃ or activation of Co(acac)₂/L or Co(OAc)₂/L (L = dpephos, PPh₃) with PhSiH₃ lead to the formation of a Co(I) hydride species **8**,^[36] followed by the migratory insertion of an amide into the Co-H bond to give an intermediate **9** or its *N*-stabilized 16ē derivative **9'**. Further reaction with PhSiH₃ produces silyl ether **10**, which in

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the presence of the hydride 8 reacts with PhSiH₃ to produce an amine and the siloxane by-product.^[12a] An intermediacy of the silvlcobalt species does not seem likely since no formation of this species was observed during the stoichiometric reactivity studies of (dpephos)CoCl₂ with LiBHEt₃ (2.5 equiv) in the presence of excess PhSiH₃ and no formation of alkenylsilanes detected during (dpephos)CoCl₂/LiBHEt₃-catalyzed was hydrosilylation of alkenes.[37] In addition, the detailed mechanistic studies and deuterium labeling experiments reported by Ge et al. for the related Co(acac)₂/xantphoscatalyzed hydrosilylation of alkenes and alkynes^[8e,h] suggest the intermediacy of the CoH species rather than silylcobalt derivatives. Unfortunately, all attempts to trap the hydride species as amide insertion products of the type 9 or 9' via the reaction between (dpephos)CoCl₂ with 2 equiv of LiBHEt₃ in the presence of either DMF or N,N-dimethylacetamide (ca. 5-fold excess of the amides was used) were unsuccessful. However, (dpephos)CoCl₂/LiBHEt₃-catalyzed (5 mol% of Co) hydrosilative reduction of N,N-dimethylacetamide with PhSiD₃ results in 93% saturation of the methylene moiety of EtNMe2 with deuterium (Scheme 3B), suggesting that the two newly added hydrogen atoms in the amine product originate from the hydrosilane reductant and the hydrosilane is involved in the regeneration of the catalytically active species. A similar mechanism with the formation of the silvlated N,O-acetal 10 was proposed by Nagashima^[38] and Beller^[12a] for the ruthenium and iron-catalysed reactions, respectively. Analogously to our system, the reported Fe-catalyzed hydrosilylation of N,N-dibenzyl-4- Ph_2SiD_2 methoxybenzamide with resulted in selective incorporation of the deuterium atoms in the methylene moiety of the reduced amine product.[12a]

The mechanism of the reduction of secondary and primary amides could be more complicated due to possible competing formation of cobalt amidate species **11a** *vs* alkoxy intermediate **11b** (Eq. 1)^[39] and competing dehydration of primary amides to





nitriles^[13a,33] and secondary amides to imines, followed by their hydrosilylation reactions.^[33,40] Mechanistic studies for Co/dpephos-catalyzed reduction of primary and secondary amides are currently being conducted in our laboratories and will be reported in a due course.



Conclusions

We have developed simple and effective protocols for a diversity of silane addition reactions to unsaturated organic molecules and hydrosilative reduction of amides to amines, using benchstable commercially available or easily accessible cobalt precatalysts with commercially available phosphine ligands. For (dpephos)CoCl₂, activation with LiBHEt₃ is required to produce catalytically active Co(I) hydride species. For Co(acac)₂ and Co(OAc)₂, external activator-free systems were developed and the catalysts are activated by the reaction with hydrosilanes. Operating at temperatures below 100 °C, the developed Co/phosphine systems represent only the second example of mild base-metal-catalyzed hydrosilative reduction of amides, including a rare example of a base metal catalyst for direct hydrosilylation of secondary and primary amides. The reduction of tertiary amides in most cases can be performed at room temperature, tolerating alkene, nitrile, and ester functionalities, allowing for preparation of functionalized tertiary amines. Our future research will concentrate on expanding the scope of primary and secondary amides and on better understating of mechanistic aspects of these transformations.

Experimental Section

General Details. All manipulations were carried out using conventional inert atmosphere glove-box and Schlenk techniques. All solvents were dried by distillation from appropriate drying agents. NMR spectra were obtained with a Bruker Avance 300, 400 and 600 MHz and JEOL ECA-500 MHz instruments (1H: 300, 400, 500 and 600 MHz; 13C: 75.5, 125.8 and 151 MHz; ³¹P: 121.5, 202.5 and 243 MHz; ²⁹Si: 99.4 and 119.2 MHz). Preparation of (dpephos)CoCl₂ was reported previously.^[17] PhSiD₃ was prepared by the reaction of PhSiCl₃ with LiAlD₄. Co(acac)₂. Co(OAc)₂. PPh₃, dpephos, LiBHEt₃ (1.0 M solution in THF), PhSiH₃, PhMeSiH₂, $\mathsf{PhMe}_2\mathsf{SiH},\,\mathsf{PhSiCl}_3,\,\mathsf{LiAlD}_4$ and organic substrates were purchased from Sigma-Aldrich and used without further purification unless specified. Octanal, benzaldehyde, acetone, acetophenone, ethyl acetate, DMF were additionally dried over 3Å molecular sieves. N,N-dibenzylacetamide, N,N-dimethylbenzamide, N,N-diisopropylbenzamide, 4synthesized benzovImorpholine were usina literature procedures.^[12a,13b,14c,41] All catalytic reactions were done under nitrogen or argon atmosphere using NMR tubes equipped with Teflon valves. Small amounts of Ph₂SiH₂, produced via redistribution of substituents in PhSiH₃, were observed in hydrosilylation reactions with PhSiH₃.^[42]

General procedure for hydrosilylation of alkenes and alkynes using (dpephos)CoCl₂. Organic substrate (0.24 mmol), PhSiH₃ (29.6 µL, 0.24

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mmol; excess PhSiH₃ was used in some reactions, which is indicated in the main text of the manuscript) and (dpephos)CoCl₂ (either 1 or 5 mol.%: 1.6 mg (2.4 µmol) or 8.0 mg (12.0 µmol), respectively) (note, (dpephos)CoCl₂ is only sparsely soluble in benzene) were mixed in a vial in 0.5 mL of C₆D₆. To this mixture, a solution of LiBHEt₃ (2 equivalents to (dpephos)CoCl₂) in THF (1.0 M) was added in one portion at room temperature with vigorous stirring. Immediately after addition of LiBHEt₃, gas evolution was observed and the initially blue suspension changed color to brown with complete dissolution of (dpephos)CoCl₂. The mixture was transferred to an NMR tube equipped with Teflon valve and sealed. Depending on the substrate used, the reaction was left at either 25 °C, 35 °C or 65 °C and was monitored by ¹H-NMR spectroscopy. Control experiments without LiBHEt₃ revealed no reaction between alkene and alkyne substrates and PhSiH₃.

General procedure for hydrosilylation of aldehydes, ketones and esters using (dpephos)CoCl₂. A solution of LiBHEt₃ in THF (1.0 M, 24.0 μ L, 24 μ mol), was added *via* syringe at room temperature with vigorous stirring to a suspension of (dpephos)CoCl₂ (8.0 mg, 12.0 μ mol) in 0.5 mL of C₆D₆ in a vial. Immediate dissolution of (dpephos)CoCl₂, gas evolution and change of color from blue to brown was observed. After addition of LiBHEt₃, a substrate (0.24 mmol) and PhSiH₃ (29.6 μ L, 0.24 mmol; excess PhSiH₃ was used for certain substrates and these cases are indicated in the main text of the manuscript) were added to the reaction. The resulting mixture was transferred to an NMR tube equipped with Teflon valve, sealed, heated at 60 °C for 5 hours and then analysed with NMR spectroscopy. For control experiments of hydrosilylation of ketones with PhSiH₃ in the absence of (dpephos)CoCl₂, using 10 mol% of LiBHEt₃, see the Supporting Information.

General procedures for hydrosilative reduction of amides. A: Using (dpephos)CoCl₂/LiBHEt₃ system.

Method 1. A solution of LiBHEt₃ in THF (1.0 M, 24.0 µL, 24 µmol), was added *via* syringe at room temperature with vigorous stirring to a suspension of (dpephos)CoCl₂ (8.0 mg, 12.0 µmol) in 0.5 mL of C₆D₆ in a vial. Immediate dissolution of (dpephos)CoCl₂, gas evolution and change of color from blue to brown was observed. After addition of LiBHEt₃, an amide substrate (0.24 mmol) and PhSiH₃ (44.4 µL, 0.36 mmol; larger excess PhSiH₃ was used for certain substrates and these cases are indicated in the main text of the manuscript) (for *N*-methylsuccinimide and 1-methylpyrrolidin-2-one, PhMeSiH₂ (49.4 µL, 0.36 mmol) was also used, see Table 3 in the main text of the manuscript) were added to the reaction. The resulting mixture was transferred to an NMR tube equipped with Teflon valve, sealed, and, depending on the amide substrate, was either left at 25 °C or heated at 60 °C. The reaction was monitored by ¹H-NMR.

Method 2. DMF (0.24 mmol), PhSiH₃ (44.4 µL, 0.36 mmol) and (dpephos)CoCl₂ (8.0 mg, 12.0 µmol) were mixed in a vial in 0.5 mL of C₆D₆. To this mixture, a solution of LiBHEt₃ (24.0 µL, 24 µmol) in THF (1.0 M) was added in one portion at room temperature with vigorous stirring. Immediately after addition of LiBHEt₃, gas evolution was observed and the initially blue suspension changed color to brown with complete dissolution of (dpephos)CoCl₂. The mixture was transferred to an NMR tube equipped with Teflon valve and sealed. Depending on the amide substrate, the mixture was either left at 25 °C or heated at 60 °C. The reaction was monitored by ¹H-NMR spectroscopy.

For a control experiment of hydrosilative reduction of N,Ndiisopropylbenzamide with PhSiH₃ and 10 mol% of LiBHEt₃ in the absence of (dpephos)CoCl₂, see the Supporting Information.

B: Using Co(acac)₂/dpephos, Co(OAC)₂/dpephos, Co(acac)₂/PPh₃ and Co(OAC)₂/PPh₃ systems. An amide substrate (0.24 mmol) and then PhSiH₃ (44.4 μ L, 0.36 mmol) were added to a mixture of cobalt precatalyst (Co(acac)₂ or Co(OAc)₂, 1.2 μ mol or 12.0 μ mol) and ligand (dpephos (1.1 equivalent to Co) or PPh₃ (2 equivalents to Co)) in 0.5 mL of THF-d₈ in an NMR tube equipped with Teflon valve. NMR tube with the mixture was shaken for a few seconds and, depending on the amide substrate and the pre-catalyst system, was either left at 25 °C or heated at 60 °C, 75 °C, or 100 °C. Within a few minutes, all cobalt pre-catalyst dissolved, gas evolution was observed and the color of the mixture became brown. The reaction was monitored by ¹H-NMR spectroscopy. The reduction of *N*,*N*-dibenzylacetamide and *N*,*N*-diisopropylbenzamide with PhSiH₃ using Co(acac)₂/dpephos (5 mol% of Co) in THF was also performed on 1 mmol scale. Full conversion of the amides to the corresponding amines was verified on the basis of ¹H- and ¹³C{¹H}-NMR spectroscopic analysis of the crude reaction mixture performed after 12 h and 24 h at room temperature, respectively. The amine products were isolated by filtration of the reaction mixtures on a short neutral alumina column followed by a short silica column, both washed with EtOAc:Hex (1:10). Dibenzylethylamine was additionally extracted with 15 mL of pentane. The isolated yields are given in parentheses in Table 3 and the detailed procedures are described in the Supporting Information.

General procedure for competitive Co(acac)₂/dpephos-catalyzed hydrosilative reduction of DMF, *N*,*N*-dibenzylacetamide and 1-methyl-2-pyrrolidinone. An amide substrate (0.24 mmol), a competing substrate (0.24 mmol) and then silane (PhSiH₃, PhMeSiH₂ or PhMe₂SiH) (0.24 mmol) were added to a mixture of Co(acac)₂ (3.1 mg, 12.0 µmol) and dpephos (7.1 mg, 13.2 µmol) in 0.5 mL of THF-d₈ in an NMR tube equipped with Teflon valve. NMR tube with the mixture was shaken for a few seconds and left at 25 °C. Within a few minutes, all Co(acac)₂ dissolved, gas evolution was observed and the color of the mixture turned brown. The reaction mixture was analyzed by NMR spectroscopy after 5 h and 24 hours.

Low temperature VT NMR reaction of (dpephos)CoCl₂ with LiBHEt₃. A solution of LiBHEt₃ (37.8 2 µL, 0.0378 mmol) in THF (1.0 M) was added via syringe to a frozen in liquid nitrogen suspension of (dpephos)CoCl₂ (10.1 mg, 0.0151 mmol) in toluene-d₈ in an NMR tube equipped with Teflon valve. The frozen sample was placed to an NMR machine precooled to -80 °C. The sample was slowly warmed up to 0 °C in the probe of the NMR machine and the reaction was monitored with ¹H and ³¹P NMR every 5 °C. At -5 °C - 0 °C, the reaction took place with the formation of a complex mixture of cobalt species, one of which was assigned to [(dpephos)Co(H)]2(µ-dpephos) (4; 3.2:1 mixture of two isomers). Further increase of the temperature to 25 °C leads to decomposition and formation of a mixture of unidentified paramagnetic cobalt species (formation of black precipitate was observed). Selected NMR data for [(dpephos)Co(H)]₂(µ-dpephos) (4): ¹H-NMR (600 MHz; PhMe-d₈; 273 K; δ, ppm): -19.89 (dt, ²J_{H-P} = 60.5 Hz, 44.5 Hz, 1H, CoH, major isomer); -20.15 (dt, ²J_{H-P} = 66.0 Hz, 42.0 Hz, 1H, CoH, minor isomer). ¹H{³¹P}-NMR (600 MHz; PhMe-d₈; 273 K; δ, ppm): -19.85 (s, 1H, CoH, major isomer); -20.10 (s, 1H, CoH, minor isomer). ³¹P-NMR (243 MHz; PhMe-d₈; 273 K; δ, ppm): 42.5 (m, 2P of major isomer and 2 P of minor isomer); 45.5 (m, 1P, minor isomer); 48.2 (m, 1P, major isomer). For the NMR spectra, see the Supporting Information.

Acknowledgements

This work was supported by Nazarbayev University through NU Research University Development Program (grant to AYK #2016023). We thank Prof. Dr. Georgii I. Nikonov (Brock University) for helpful discussions.

Keywords: cobalt • hydrosilylation • amides • homogeneous catalysis

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- [28] For the only example of Co-catalyzed hydrosilative reduction of amides, see ref. [16].
- [29] Our control experiments indicated that for DMF as a substrate the order of addition does not affect the yield of the amine produced and no byproducts of addition of LiBHEt₃ to DMF (see ref. [30]) were detected by NMR upon addition of LiBHEt₃ (10 mol.%) to a mixture of DMF, PhSiH₃ and (dpephos)CoCl₂ (5 mol%) in C₆D₆. An attempted hydrosilylation of *N*,*N*-diisopropylbenzamide with PhSiH₃ and 10 mol% LiBHEt₃ in the absence of (dpephos)CoCl₂ showed no amide conversion in 5 h at room temperature, whereas at 60 °C, only 22% conversion of the amide to diisopropylbenzylamine.
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- [34] For metal-free hydrosilylation of primary and secondary amides, see ref. [11a].
- [35] Bn₂NH (22%) and BnN=CHPh (16%) were detected by GC-MS.
- [36] The (dpephos)CoCl₂/LiBHEt₃-catalyzed reactions are accompanied by the release of H₂ (in small quantities also observed in the ¹H-NMR spectra), which presumably forms upon decomposition of the cobalt(II) dihydride species. An alternative scenario, generation of H₂ via dehydrogenative coupling of silanes, is not supported by NMR, which did not reveal any silane coupling products.
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(dpephos)CoCl₂ is employed as a pre-catalyst for a diversity of hydrosilylation reactions, including hydrosilative reduction of amides to amines. With regard to reduction of amides, more effective and activator free catalytic systems can be generated from Co(acac)₂ and Co(OAc)₂ with dpephos. These systems operate under mild conditions (<100 °C), with many examples of room temperature reactions, presenting a first example of mild Co-catalyzed hydrosilylation of amides

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