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Selective Hydrosilylation of *N*-Allylimines using a (3-Iminophosphine)Palladium Precatalyst

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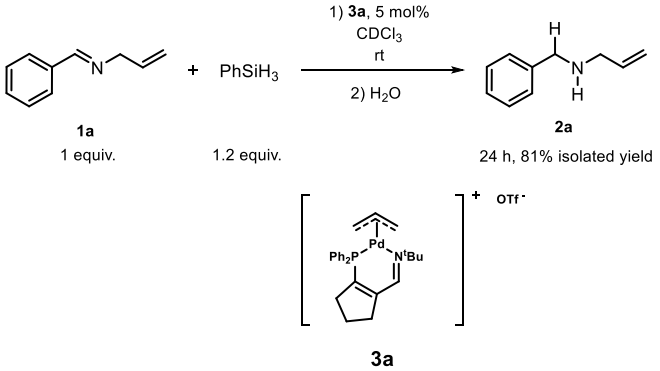
Hydrosilylation utilizing a (3-iminophosphine)palladium catalyst leads to the selective reduction of the imine unit of allylimines. Successful reduction of twenty-five different substituted aromatic and alkyl allylimines demonstrated the scope and selectivity of this catalytic system.

Allylamines are fundamentally important organic building blocks, especially as moieties within chiral amines because of their occurrence in natural products and pharmaceuticals.[1, 2] Many modern efforts in the development of new synthetic strategies facilitating amine synthesis have targeted catalytic hydroamination reactions for the addition of primary and secondary amines to C-C unsaturated bonds.[2-9] Alternatively, catalytic hydrosilylation has been extensively used to form new C-Si bonds[10-14] with many examples utilizing catalytic hydrosilylation or hydrogenation as a means to form amines from imines or amides.[15-21] Overall, successes in functional group tolerance, chemoselectivity, and enantioselectivity in imine hydrosilylation/reduction demonstrated by various research groups have garnered much interest in this field.[22-27] To date, numerous examples of metal catalyzed imine hydrosilylation/reduction have been reported, often utilizing titanium,[28] iron,[21, 27] zinc,[20, 29] ruthenium,[30] rhodium, or iridium.[17, 18, 31, 32] Although highly active metal and even metal-free examples of imine hydrosilylation have been reported, they often suffer from a lack of selectivity for the imine in reduction reactions or very poor overall functional group tolerance.[27, 33, 34] Furthermore, there are only a few examples of palladium-catalyzed hydrosilylation of imines, and no comprehensive study of substrate scope with palladium catalysts for this transformation has been undertaken.[31, 35] With regard to palladium-catalyzed imine reduction, many recent hydrogenation examples, especially those involving the asymmetric hydrogenation of imines, require PMP or tosyl protected imines while displaying a relatively limited substrate scope.[36] This raises the need for the development of useful new catalysts with broad substrate tolerance in the palladium-catalyzed reduction of imines.

Recently, we demonstrated that cationic complexes of the type [(3-iminophosphine)Pd(allyl)]$^+$ successfully catalyze the efficient and regioselective hydrosilylation of allenes.[14] We also postulated that in this process, the catalyst activated primary and secondary hydrosilanes to form a Pd-H intermediate, an assertion that was further supported by an H/D crossover experiment.[14] Since allylamines have broad significance in synthetic chemistry, we hoped to utilize the hydrosilane activation in our system to effect the catalytic hydrosilylation of allylimines in order to reduce them to allylamines following hydrolysis. Herein, we report palladium-catalyzed selective hydrosilylation/reduction of various allylimines under mild conditions (Scheme 1). All catalytic reactions were performed in NMR tubes with ^{1}H NMR spectra observed frequently to monitor reaction completion.



Scheme 1. First example of palladium-catalyzed hydrosilylation/reduction of allylimines**.**

Preliminary results showed that the hydrosilylation of **1a** at room temperature was moderately slow, therefore the reaction temperature was varied in order to find more optimal reaction conditions (Table 1). Acceptable reaction rates were observed with mild heating (40-50 ^{o}C), while higher temperatures resulted in the formation of a complex mixture of products due to uncharacterized competing side reactions.

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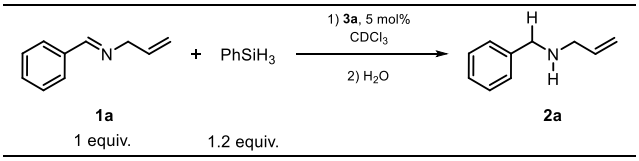
† Electronic supplementary information is available containing experimental details and spectroscopic data.

Table 1. Effect of reaction temperature.[a]

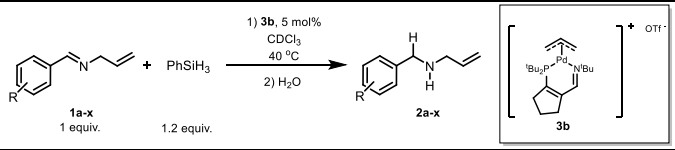


Temperature (°C)	Completion time[b] (h)
rt	24
30	16
40	8
50	6
60	4[c]

[a] Catalytic procedure: Reactions were carried out in NMR tubes prepared in a glovebox using $CDCl_3$ (800 µl), catalyst (0.025 mmol), $PhSiH_3$ (0.6 mmol, 1.2 equiv.), and allylimine (0.5 mmol, 1 equiv.); [b] Reaction completion was monitored and recorded by ^1H NMR spectroscopy by observation of the diminishing allylimine peaks. Hydrosilylated product was hydrolysed in 2 ml of H_2O to yield the secondary allylamine; [c] Formation of side-products was detected by ^1H NMR.

The best solvent was found to be $CDCl_3$ (see supporting information for more details). In an effort to further enhance the rate of the reaction, a stronger σ-donating di-tert-butyl phosphine unit was utilized on the 3IP ligand (**3b**) in place of the diphenylphosphine in **3a**. Using this improved ligand set reduced the completion time for the hydrosilylation of **1a** to 4 h at 40 °C. Having determined the better catalyst system and useful mild reaction conditions, we set out to investigate the functional group tolerance for this transformation. A variety of allylimines were synthesized via the Schiff base condensation of aromatic aldehydes with allylamine, which were then subsequently subjected to catalytic hydrosilylation (Table 2).

Table 2. Pd-catalyzed reduction of allylimines.[a]



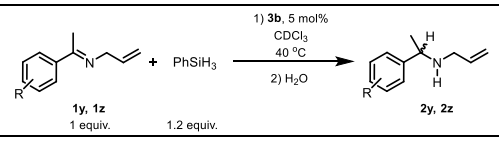
Entry	Allylimine	Product	t[b] (h)	yield[c] (%)
1	(1a)	(2a)	4	81
2	(1b)	(2b)	12	89
3	(1c)	(2c)	14	79
4	(1d)	(2d)	12	76
5	(1e)	(2e)	16	82
6	(1f)	(2f)	12	84
7	(1g)	(2g)	12	92
8	(1h)	(2h)	16	90
9	(1i)	(2i)	4	84
10	(1j)	(2j)	3	76
11	(1k)	(2k)	2	91
12	(1l)	(2l)	44	78
13	(1m)	(2m)	2	89
14	(1n)	(2n)	36	92
15	(1o)	(2o)	30	83
16	(1p)	(2p)	34	88
17	(1q)	- [d]	-	-
18	(1r)	(2r)	3	79
19	(1s)	(2s)	6	81
20	(1t)	(2t)	4	89
21	(1u)	(2u)	6	87
22	(1v)	(2v)	18	84
23	(1w)	(2w)	10	88
24	(1x)	(2x)	14	81

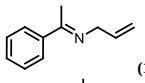
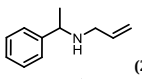
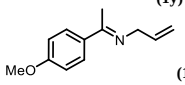
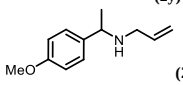
[a] Catalytic procedure: Reactions were carried out at 40 °C in NMR tubes prepared in a glovebox using $CDCl_3$ (800 µl), catalyst (0.025 mmol), $PhSiH_3$ (0.6 mmol, 1.2 equiv.), and allylimine (0.5 mmol, 1 equiv.); [b] Reaction completion was monitored and recorded by ^1H NMR spectroscopy by observation of the diminishing allylimine peaks. Hydrosilylated product was hydrolysed in 2 ml of H_2O to yield the secondary allylamine; [c] Isolated yield; [d] Catalyst decomposition occurred.

Previous reports have noted that a $PdCl_2$/hydrosilane system can result in the cleavage of C=N moieties,[35] but this reaction was not observed in our system. Instead, our system displayed clean hydrosilylation of the imine moiety for a wide range of aromatic imines, all of which underwent smooth hydrolysis in water. The necessary reaction times were highly dependent on the substituents on the aldimine aryl group with EDG requiring shorter reaction times compared to substrates bearing EWG. Representative secondary and tertiary alkyl *N*-allylimine substrates (**1w** and **1x**) showed that this hydrosilylation catalyst system also operated efficiently for alkyl derivatives. It was found that acetonitrile and benzonitrile did not react under these catalytic conditions, so this process is benign to alkyl and aryl nitriles. Further investigations revealed that ketimines were also relatively unreactive, with less than 5% conversion detected after 8 hours at room temperature using catalyst **3b**. Longer reaction times with ketimines proved somewhat

effective, although the crude product was contaminated with significant amounts of side-products (Table 3). Although the electronic character of the allylimines adequately explains the different reaction rates for aldimines, it does not clarify the low reactivity of ketimines. In our previous study, it was found that substrate sterics (in both the unsaturated substrate and the silane) play a major role in the reactivity of the system due to the necessary formation of a σ-complex within the catalytic mechanism in which the hydrosilane must approach the palladium center. Thus, in the hydrosilylation of ketimines, the presence of the second substituent (methyl) on the imine significantly hinders formation of this required σ-complex. Utilizing a ketimine bearing an electron-donating methoxy group did not significantly influence the reactivity and approximately the same reaction rate as the unsubstituted ketimine was observed. Thus, it seems that for ketimines, steric hinderance in the σ-complex formation step of the catalytic cycle is more important than electronic effects in the imine aryl unit.

Table 3. Investigation of ketimines.[a]



Entry	Allylimine	Product	t[b] (h)	yield[d] (%)
25	 (1y)	 (2y)	72[c]	68
26	 (1z)	 (2z)	72[c]	53

[a] Catalytic procedure: Reactions were carried out at 40 °C in NMR tubes prepared in a glovebox using $CDCl_3$ (800 µl), catalyst (0.025 mmol), $PhSiH_3$ (0.6 mmol, 1.2 equiv.), and allylimine (0.5 mmol, 1 equiv.); [b] Reaction completion was monitored and recorded by ^1H NMR spectroscopy by observation of the diminishing allylimine peaks. Hydrosilylated product was hydrolysed in 2 ml of H_2O to yield the secondary allylamine; [c] Formation of byproducts was detected by ^1H NMR spectroscopy; [d] Isolated yield.

Similar to our previous study involving the hydrosilylation of allenes,[14] we propose an analogous mechanism for the hydrosilylation of imines, in which formation of a Pd-H after treatment of the Pd-precatalyst with $PhSiH_3$ is essential. This is followed by insertion of the imine into the Pd-H bond to generate a Pd-amido complex. The relatively stable Pd-amido complex then forms a σ-complex with $PhSiH_3$ and produces the hydrosilylated product via a 4-centered transition state (Figure 1). Such interactions commonly play important roles in hydrosilylation processes.[37] It is plausible that the lone pair of nitrogen in the Pd-amido complex interacts with a d-orbital of silicon as (p-d)σ interactions are known, resulting in weakening of the Si-H bond and leading to formation of Si-N and Pd-H.[38] For the aldimines tested, the strong correlation between the electronic effects of the aryl substituents and the reaction rates can be attributed to conjugation of the aryl and imine fragments of the allylimine, which must undergo insertion into the Pd-H bond in order to produce the desired product.

In summary, we have reported a new system for metal-catalyzed hydrosilylation/reduction of imines in allylimines using mild conditions with high functional group tolerance as well as high selectivity for aldimines over ketimines and nitriles. In addition, this report is the only example of palladium-catalyzed allylimine hydrosilylation/reduction to date.

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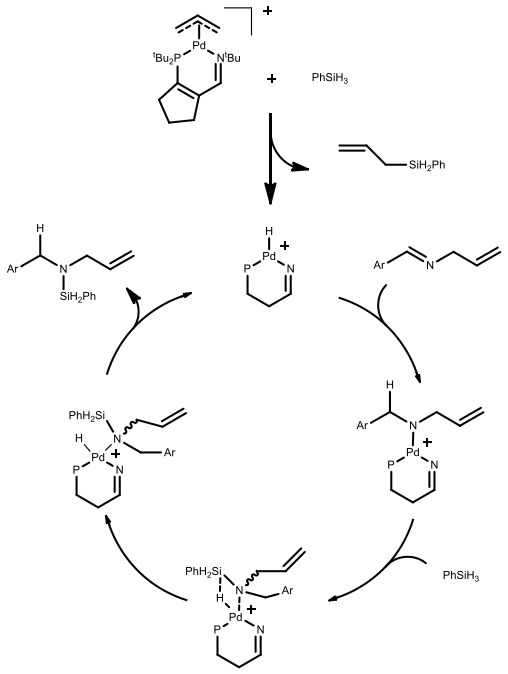

Figure 1. Proposed catalytic cycle for hydrosilylation of allylimines

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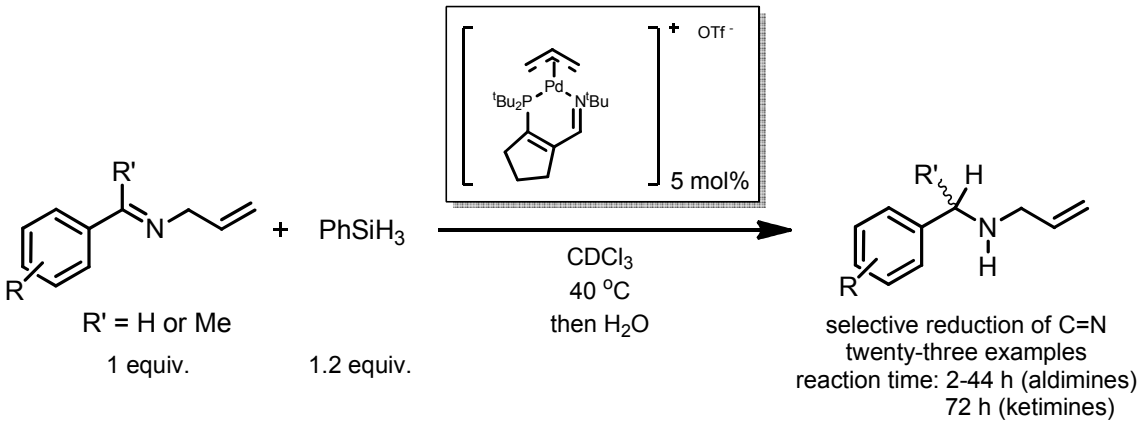

R' = H or Me

1 equiv. 1.2 equiv.

selective reduction of C=N
twenty-three examples
reaction time: 2-44 h (aldimines)
72 h (ketimines)