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Letters

Dual Si–H effects in platinum-catalyzed silane reduction of carboxamides leading to a practical synthetic process of tertiary-amines involving self-encapsulation of the catalyst species into the insoluble silicone resin formed

Shiori Hanada, Yukihiro Motoyama and Hideo Nagashima*

Institute for Materials Chemistry and Engineering, Graduate School of Engineering Sciences, Kyushu University, Kasuga, Fukuoka 816-8580, Japan

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Abstract—Combination of commercially available platinum catalysts with siloxanes containing more than two Si–H groups is found to be an efficient catalyst system for the reduction of carboxamides to amines. In particular, facile removal of silicon and platinum residues from the product can be achieved by the use of polymethylhydrosiloxanes as reducing reagents.

Synthetic procedures using environmentally benign reagents under mild conditions have lately been receiving much attention from organic chemists.[1] In particular, easy separation of the products from the reaction mixture is a key point in the production of large quantities of organic molecules. We have recently reported that a certain ruthenium cluster catalyzes the reduction of carboxamides with trialkylsilanes.[2] This realizes production of gram-quantities of amines with non-pyrophoric metal hydrides under mild conditions, and the product can be separated from the siloxane by-products and most of the ruthenium residues by acid–base treatment of the reaction mixture.[2b] Although removal of ruthenium residues from the amine product of this reaction required further improvement of the process, we have lately discovered an epoch-making method of the separation procedure using polymethylhydrosiloxane (PMHS) as the reducing reagent; the reduction is accompanied with cross-linking of the silicon-polymer to produce insoluble silicon resin, to which the ruthenium species is efficiently soaked up.[3] This actually results in facile separation of the amine product from the by-products, that is, ruthenium and silicon residues, by simple extraction and filtration, providing an ideal method of synthesizing silicon- and ruthenium-free amines from amides. In the course of these studies, we were interested in the possibility that similar reduction of amides with PMHS involving self-encapsulation of the metal species may also take place with other transition metal catalysts. One candidate is H_2PtCl_6 and other platinum compounds, which are easily available from commercial sources and widely used for catalytic hydrosilylation of alkenes in both laboratory and industrial scales.[4] However, the literature suggests that platinum catalysts are extremely useful for reactions of a wide variety of hydrosilanes with alkenes and alkynes, but not active for the reduction of carbonyl compounds. To our best knowledge, the possibility of platinum-catalyzed silane reduction of amides is only briefly suggested in a paper by Igarashi and Fuchikami, in which amides were converted to the corresponding amines by hydrosilanes in the presence of ruthenium and osmium carbonyl complexes.[5] In this report, *N*-acetylpyrrolidine was reduced to *N*-ethylpyrrolidine at 100 °C for 16 h in the presence of $PtCl_2$ (1 mol %) and Et_2NH as a cocatalyst (5 mol %); the reaction giving the product at lower temperature in short reaction time is apparently desirable for organic synthesis. In this letter, we wish to report a breakthrough on this problem by an interesting 'dual Si–H effect' in the platinum-catalyzed silane reduction of amides. Platinum catalysts are not active for the reduction of amides with hydrosilanes containing only one

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Keywords: Carboxamide; Dual Si–H effect; Platinum; Reduction; Self-encapsulation.

* Corresponding author. Tel./fax: +81 92 583 7819; e-mail: nagasima@cm.kyushu-u.ac.jp

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Si–H group in the molecule as the literature suggested; however, siloxanes containing more than two Si–H groups facilely reduce the amides under mild conditions. As an extension of this, use of PMHS having many Si–H groups in the polymer chain contributes to both facile reduction of amides and formation of insoluble siloxane resins to which almost all platinum residues are encapsulated. This discovery provides a practical synthetic method of silicon and metal-free amines by easily available platinum catalysts.

We reported earlier that a ruthenium cluster catalyst reduces the amides to amines with various hydrosilanes at room temperature to 50 °C. Attempts to replace the ruthenium catalyst by $H_2PtCl_6{\cdot}6H_2O$ were unsuccessful as long as we used trialkylsilanes, alkoxysilanes, and hydrosiloxanes containing only one Si–H group in a molecule (Scheme 1). For example, no platinum-catalyzed reduction of *N*,*N*-dimethyl dihydrocinnamamide took place at 50 °C with Me_2PhSiH, Me_2EtSiH, $(EtO)_3SiH$, and $Me_3SiOSiMe_2H$. In sharp contrast, the reduction proceeds with $HSiMe_2OSiMe_2H$ or $Me_3Si(OSiHMe)_2OSiMe_3$ at that temperature to afford the corresponding amine in 90% or 63% yields, respectively (Table 1, entries 1 and 2). Dual Si–H groups in $HSiMe_2OSiMe_2H$ or $Me_3Si(OSiHMe)_2OSiMe_3$ apparently enhance the reactivity. In contrast to the fact that the reduction of these two hydrosiloxanes is homogeneous, the reduction with commercially available PMHS (Azmax: average $n = 25$) at 50 °C led to both production of amines and formation of insoluble silicon resins to which the platinum species was encapsulated (Fig. 1). Extraction of the reaction mixture with ether gave the desired amines (quantitative by NMR and GC analysis) containing only a tiny amount of silicon residue and platinum species, which could be removed by passing the extracts through a short pad of alumina (entry 3). Other commercially available platinum catalysts, $PtCl_2(COD)$ and ‘$Pt[\{(CH_2{=}CH)Me_2Si\}_2O]_n$’ (Karstedt’s catalyst)[6] are also useful for this reduction at lower than 50 °C (entries 4 and 5). In particular, a xylene solution of Karstedt’s catalyst (Aldrich) is active enough to perform the reaction with PMHS even at 0 °C for 3 h to give the desired amine in 86% isolated yield.[7] A notable side reaction of this process is the formation of enamine [*N*,*N*-dimethyl-(3-phenylpropen-1-yl)amine], which is typically seen with lower catalyst concentration

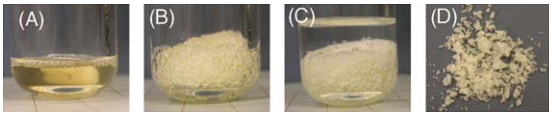
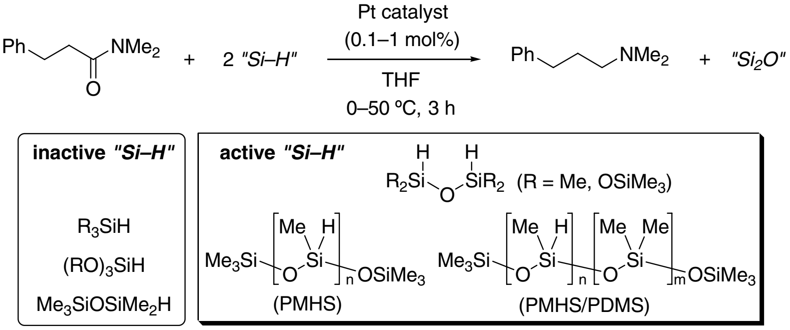


Figure 1. Photos of the Pt-catalyzed reaction; A: initial homogeneous solution, B: after the reaction (gel), C: extraction with ether, D: insoluble silicone resin containing platinum residue.



Scheme 1. Active vs. inactive hydrosilanes for the platinum-catalyzed reduction of amides.

Table 1. Pt-catalyzed reduction of *N*,*N*-dimethyl dihydrocinnamamide[a]

Entry	Catalyst [mol %]	Silane [Si–H: mmol]	Temperature (°C)	Yield[b] (%)
1	$H_2PtCl_6{\cdot}6H_2O$ [1]	$HSiMe_2OSiMe_2H$ [3.0]	50	90
2[c]	$H_2PtCl_6{\cdot}6H_2O$ [1]	$Me_3Si(OSiHMe)_2OSiMe_3$ [3.0]	50	63
3	$H_2PtCl_6{\cdot}6H_2O$ [1]	PMHS [3.7]	50	84
4	$PtCl_2(COD)$ [1]	PMHS [3.7]	40	77
5	$Pt[\{(CH_2{=}CH)Me_2Si\}_2O]_n$ [1]	PMHS [3.7]	0	86
6[d]	$H_2PtCl_6{\cdot}6H_2O$ [0.1]	PMHS [3.7]	90	72[e,f]
7[d]	$H_2PtCl_6{\cdot}6H_2O$ [0.1]	PMHS/PDMS [2.2]	90	80[e]
8[g]	$H_2PtCl_6{\cdot}6H_2O$ [0.1]	PMHS [3.7]	80	76[h]

[a] All reactions were carried out using 1 mmol of amide, 2.2–3.7 mmol of silane, 0.001–0.01 mmol of platinum catalyst in 0.6 mL of THF for 3 h.

[b] Isolated yield by Al_2O_3 column.

[c] For 10 h.

[d] In heptane.

[e] Determined by ^1H NMR analysis.

[f] 28% of enamine was formed.

[g] 5 g (28.2 mmol) of amide was used in dimethoxyethane.

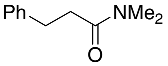
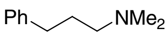
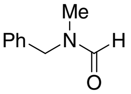
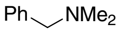
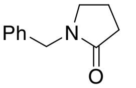
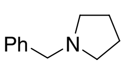
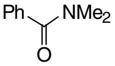
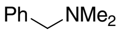
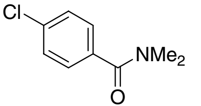
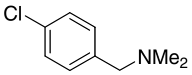
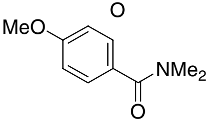
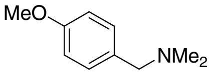
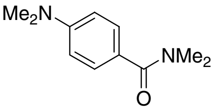
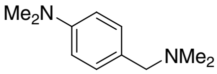
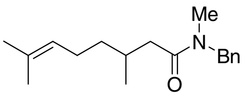
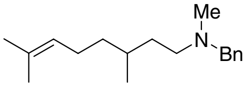
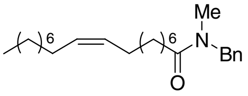
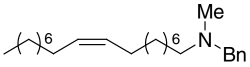
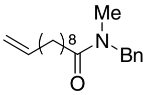
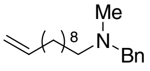
[h] Isolated by distillation.

(0.1 mol %) at higher temperature (90 °C) (entry 6). We found three clues to suppress the enamine formation, that is, higher catalyst loading (>1 mol %), lower reaction temperature (<80 °C), and use of polymethylhydrosiloxane (PMHS)/polydimethylsiloxane (PDMS) copolymer. In fact, use of PMHS/PDMS copolymer, $Me_3Si(OSiHMe)_n(OSiMe_2)_mOSiMe_3$ ($n = 13$, $m = 12$), effectively suppress the formation of the enamine (entry 7). Careful control of the reaction temperature below 80 °C resulted in successful isolation of a gram-quantity of the desired amine by 0.1 mol % of H_2PtCl_6 as shown in entry 8.

Self-encapsulation of the platinum residue to the insoluble siloxane resin is another important aspect for this platinum-catalyzed reduction, which takes part in facile removing the metallic species from the amine product. In fact, ICP-mass analyses of the product shown in entry 3 revealed that 97.9–98.9% of platinum species was soaked up to the insoluble silicon resin to give the crude product, of which purification by a short Al_2O_3 column afforded the amine with less than 1 ppm of platinum content. Furthermore, the platinum-containing silicon resin is reusable as the catalyst for the silane reduction of the amide with PMHS to form the desired amines, though the conversion of amide was somewhat decreased (first: 100%, second: 84%, third: 76%). Facile catalyst recycling and removal of the metallic residue is an important problem to be solved in the production of fine chemicals,[8] and this process offers a clear solution to this.

Application of this $H_2PtCl_6·6H_2O$-catalyzed process with PMHS to the reduction of various tertiary-amides is summarized in Table 2. All reactions resulted in good to high yields with both aliphatic and aromatic amides

Table 2. H_2PtCl_6-catalyzed reduction of various amides with PMHS[a]

Entry	Amide	Temperature (°C)	Product	Yield[b] (%)
1		50		84
2		50		72
3		25		92
4		60		75
5		60		94
6		60		88
7		60		55[c]
8[d]		80		89
9		50		95
10		50		80
11		50		Trace[e]

[a] All reactions were carried out using 1 mmol of amide, 250 μL (Si–H = 3.7 mmol) of PMHS, 0.01 mmol of $H_2PtCl_6·6H_2O$ in 0.6 mL of THF for 3 h.

[b] Isolated yield by column chromatography.

[c] Determined by ^1H NMR analysis.

[d] In dimethoxyethane.

[e] Olefin-isomerized product was obtained.

below 60 °C for 3 h, except in the cases of dimethylaminobenzamide and 10-undecenamide. The reaction of *N*-benzylpyrrolidinone smoothly proceeds even at 25 °C to afford the *N*-benzylpyrrolidine in 92% yield (entry 3). Amides containing a chloride, MeO, or Me_2N as the functional group also underwent the reduction without problems: although the reactivity of *p*-$Me_2NC_6H_4$-$C(O)NMe_2$ was relatively lower than that of other amides (60 °C, 3 h: 55% yield), the reaction at 80 °C gave the product in satisfactory yield (entries 4–8). It is well known that $H_2PtCl_6{\cdot}6H_2O$ and other platinum compounds are effective catalysts for the reaction of Si–H groups in PMHS with olefins.[9] The reduction of amides proceeded with a di- or tri-substituted carbon–carbon double bond (C=C bond) existing in the same molecule intact; the desired alkenylamines were formed in high yields (entries 9 and 10). Only the case where the hydrosilylation of C=C bonds was competitive with the reduction of amide was seen in the reduction of *N*-benzyl-*N*-methyl-10-undecenamide (entry 11). Only a small amount (~5%) of *N*-benzyl-*N*-methylundecenamines with internal C=C bond, which could be formed by isomerization of the terminal C=C bond of the starting material followed by the reduction of the amide function, was isolated by extraction of the reaction mixture with ether. ^{29}Si CPMAS NMR suggested the immobilization of organic moieties derived from *N*-benzyl-*N*-methyl-10-undecenamide to the silicon resin via the platinum-catalyzed addition of Si–H groups to the C=C bond.[9] Attempted reduction of secondary and primary amides were not successful.

In summary, we have discovered a practical reduction procedure for tertiary-amines from carboxamides with hydrosilanes. This is achieved by catalysis of platinum, and the catalyst concentration, reaction time, and reaction temperature are apparently lower than the brief report by Igarashi and Fuchikami. The contamination of platinum residue to the product is minimum, because the silicon resin formed soaked up the catalyst platinum species simultaneously. Although these features are also achieved with the ruthenium catalyst reported earlier, this platinum catalyzed process has a special advantage for organic chemists due to the use of commercially available platinum compounds. The mechanisms of this remarkable 'dual Si–H effect' in the facile reduction of carboxamides involving efficient removal of silicon and platinum residues are presumably related to the $RhCl(PPh_3)_3$-catalyzed hydrosilylation of ketones with $HMe_2Si(CH_2)_2SiMe_2H$ previously reported by our group; there, interaction of two proximate Si–H groups to the rhodium center dramatically accelerated the reaction.[10] Since double oxidative addition of two Si–H groups to the platinum compounds has been studied by Shimada and Tanaka,[11] the dual Si–H group effect presented in this paper would be explained by interaction of dual Si–H groups in PMHS and other bi- or multi-functional siloxanes to platinum species which accelerate the reduction of amides. Detailed mechanistic studies on the interaction of platinum species with various organosilanes containing dual Si–H groups are now underway by our research group.[12]

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Supplementary data

Detailed experimental procedures and characterization data. See: http://www.sciencedirect.com/. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.06.165.

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7. A typical example: To a solution of $PhCH_2CH_2C(O)NMe_2$ and PMHS (Si–H = 3.7 equiv to the amide) in a small amount of THF was added 1 mol % of Karstedt's catalyst in xylene (Aldrich) at 0 °C. The solution rapidly became viscose and set to gel after 5 min. After 3 h, the mixture was extracted with ether to form crude dimethyl-3-phenylpropylamine, which was passed through a short pad of Al_2O_3 to give the amine (86%). ICP-mass analyses revealed the platinum content in the amine to be 36 ppm (crude) and <1 ppm (after purification).
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12. The formation of silicon resin containing platinum species is due to cross-linking of the PMHS chain, in which platinum catalyzes the reductive deoxygenation of amides leading to the formation of siloxane networks; this was clearly evidenced by ^{29}Si CPMAS NMR of the silicon

resin formed. It is not clear from the TEM analysis of the silicon resin containing platinum whether the encapsulated platinum species is molecular or colloidal, which has been discussed in terms of mechanisms of Pt-catalyzed hydrosilylation of olefins, see: Lewis, L. N.; Lewis, N. *J. Am. Chem. Soc.* **1986**, *108*, 7228.