

ChemComm

Accepted Manuscript



This article can be cited before page numbers have been issued, to do this please use: A. Tahara, Y. Sunada, T. Takeshita, R. Inoue and H. Nagashima, *Chem. Commun.*, 2018, DOI: 10.1039/C8CC04780D.



This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the [author guidelines](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the ethical guidelines, outlined in our [author and reviewer resource centre](#), still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.



Journal Name

COMMUNICATION

Remarkably High Catalyst Efficiency of a Disilaruthenacyclic Complex for Hydrosilane Reduction of Carbonyl Compounds

 Atsushi Tahara,^a Yusuke Sunada,^{a,c} Takashi Takeshita,^b Ryoko Inoue,^b and Hideo Nagashima^{*a,b}

 Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

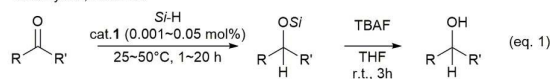
www.rsc.org/

A disilaruthenacyclic complex (**1**) showed extremely high catalytic activity for hydrosilane reduction of aldehydes and ketones to silyl ethers and secondary and tertiary amides to the corresponding amines. An σ -CAM mechanism was proposed to explain the activity.

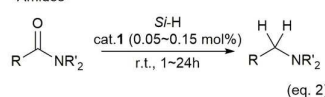
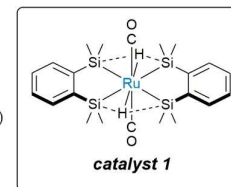
Hydrosilanes are air- and moisture-stable, yet act as hydrides for efficient reduction of carbonyl compounds by the action of transition metals or acids.¹ Recent investigations into new catalysts have realized not only reduction of ketones and aldehydes to the corresponding silyl ethers but also reduction of esters to silyl or alkyl ethers, and amides to amines or enamines.^{1b,1c} Some hydrosilanes, typically 1,1,3,3-tetramethyldisiloxane (TMDS), are easily obtained from commercial sources at reasonable prices, can be stored under aerobic conditions, and are easy to handle.^{1c,2} However, facile removal of catalyst residues from the product is difficult, but is important for the process to be environmentally friendly and safe. One approach to overcome this limitation is the development of highly active catalysts.³ For example, Tilley's group reported the reduction of benzophenone with $\text{PhMe}_2\text{SiH}_2$ in the presence of a ruthenium complex catalyst, which achieved TON = 46,000 at room temperature at 48 h (TOF = 958/h), when 46% of the substrate was converted.^{3d} For full conversion of the substrate, 0.01 mol% of the catalyst was necessary, which corresponds to TON = 10,000. Other reports described highly active catalysts that achieved TON values of up to 10^4 for the reduction of ketones.^{3a-3c,3e} The present report describes a disilaruthenacyclic complex (**1**) as a catalyst with extremely high catalytic activity for the hydrosilane reduction of aldehydes, ketones, and amides (Scheme 1).

General Schemes

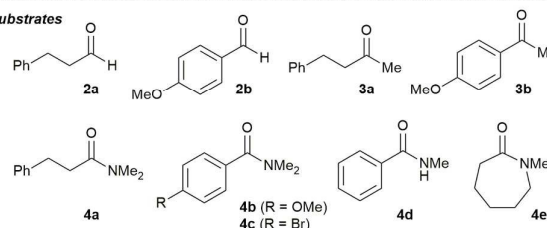
<Aldehydes, Ketones>



<Amides>


 Si-H = $\text{Me}_2\text{HSiOSiHMe}_2$ (TMDS),
 $\text{Me}_2\text{HSi}(\text{CH}_2)_2\text{SiHMe}_2$ (BDMSE)
 Ph_2SiH_2 , PhMe_2SiH


Substrates



Scheme 1. Hydrosilane reduction of aldehydes, ketones, and amides catalyzed by disilaruthenacyclic complex **1**.

In one extreme example, ketone reduction by **1** at 25°C for 5 h achieved TON = 100,000 and TOF = 20,000/h, which are among the greatest values achieved for catalytic hydrosilane reduction of ketones and aldehydes.³

Complex **1** was prepared according to a procedure reported previously.^{4,5c} Screening to identify the best hydrosilane was performed for the reduction of aldehydes, ketones, and amides, as shown in Table 1. Aldehyde **2a** and ketone **3a** were treated with four hydrosilanes, TMDS, Ph_2SiH_2 , $\text{Me}_2\text{HSi}(\text{CH}_2)_2\text{SiHMe}_2$ (BDMSE), and PhMe_2SiH , at room temperature for 1 h in the presence of 0.05 mol% catalyst. The corresponding silyl ether was obtained as a single product. For the reduction of both **2a** and **3a**, TMDS and Ph_2SiH_2 showed much greater activity than did the other two hydrosilanes. We also examined PhSiH_3 , PMHS and other three hydrosilanes. All of them were less effective than TMDS and Ph_2SiH_2 (See, ESI 2-1).

^a Institute for Materials Chemistry and Engineering, Kyushu University, Kasuga, Fukuoka 816-8580, Japan.

^b Interdisciplinary Graduate School of Engineering Sciences, Kyushu University, Kasuga, Fukuoka 816-8580, Japan.

^c Institute of Industrial Science, The University of Tokyo, 4-6-1 Komaba, Meguro-ku, Tokyo 153-8505, Japan.

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

COMMUNICATION

Journal Name

Table 1. Comparison of reactivity for reduction of aldehyde **2a**, ketone **3a**, amides **4a** and **4c** with a hydrosilane.^a

Entry	Substrate "Si-H"	Conv. (%) ^c			
		2a ^b	3a ^b	4a ^b	4c ^b
1	TMDS	72	>99	56	87
2	Ph ₂ SiH ₂	82	>99	<1	3
3	BDMSE	20	8	85	>99
4	PhMe ₂ SiH	11	6	10 (>99) ^d	62

^a All reactions were conducted with a carbonyl compound (1 mmol) and **1** (0.05 mol%) in dioxane (0.5 mL) at 25°C for 1 h. ^b Amounts of the hydrosilanes were 2.2 mmol for TMDS, Ph₂SiH₂ and BDMSE, and 4.4 mmol for PhMe₂SiH. ^c Conversions of substrates were determined by ¹H NMR based on a signal of the internal standard. ^d Yield of the product at 24 h.

TMDS is an inexpensive and safe reducing reagent for carbonyl compounds and is used for industrial processes.² Table 2 shows four examples for the hydrosilylation of ketones and aldehydes with TMDS. With 0.05 mol% catalyst loading and TMDS (5 eq. per Si-H to the substrate), reaction was complete within 30 min. at room temperature. After hydrolysis, the corresponding alcohol was obtained in 80–92% isolated yield. Experiments to achieve the highest TON with full conversion of the starting material (50 g scale) revealed that catalyst **1** promoted the hydrosilylation of **2b** and **3b** with TMDS (5.0 eq. Si-H to **2b** or **3b**) by the action of 0.001 mol% **1** (3.6 or 4.1 ppm of Ru based on **2b** or **3b**, respectively) to give the corresponding silyl ether quantitatively under optimal conditions (for **2b**, at 50°C for 20 h; for **3b**, at 25°C for 5 h as shown in Scheme 2). After distillation, the product was isolated in greater than 96% yield. In both cases, the TON was 100,000, whereas the TOF was 4,545/h for **2b** and 20,000/h for **3b**. The lower reactivity of the aldehyde compared to that of the ketone is an interesting difference from the reactivity of complex hydrides.[‡]

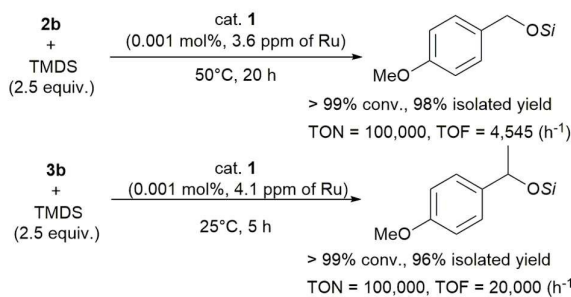
The reduction of amides is more difficult than that of ketones and aldehydes with conventional hydride reagents.¹ Although several transition metal catalysts have been reported for hydrosilane reduction of amides under mild conditions,^{2,5a} selective reduction of amides to amines with a catalyst loading less than 0.1 mol% has not been reported. As shown in Table 1, complex **1** efficiently catalyzed the reduction of two amides, **4a** and **4c**. In the presence of 0.05 mol% of **1**, reaction was complete at room temperature within 1 h when TMDS or BDMSE was used for the reduction. The PhMe₂SiH was less effective but worked well when the reaction time was prolonged. No reaction occurred with Ph₂SiH₂ under the same conditions. Table 3 shows the reduction of five amides, including aliphatic and aromatic tertiary amides **4a–4c**, a secondary amide **4d**, and a lactam **4e**, on a preparative scale. The BDMSE was the best hydrosilane for most of the substrates; however, the less expensive TMDS or PhMe₂SiH could be used after optimizing the reaction conditions. In all cases, the corresponding amine was obtained as a single product. Four tertiary amides underwent reduction with 0.05 mol% of **1** to achieve TON = 2,000. Secondary amide reduction required 0.15 mol% of the catalyst (entries 10–12). An attempt to reduce the catalyst loading to less than 0.01 mol% did not

achieve full conversion of the starting material. The best TON available in

Table 2. Conversion of aldehydes **2a** and **2b** or ketones **3a** and **3b** to alcohols by catalytic hydrosilylation with TMDS and subsequent hydrolysis with TBAF.^a

Entry	Substrate	¹ H NMR	Isolated	TON	TOF (h ⁻¹)
		Yield (%) ^b	Yield (%) ^c		
1	2a	>99	91	2,000	4,000
2	2b	>99	86	2,000	4,000
3	3a	>99	92	2,000	4,000
4	3b	>99	80	2,000	4,000

^a All reactions were conducted with a carbonyl compound (3 mmol), **1** (0.05 mol%), and TMDS (7.5 mmol) under neat conditions at 25°C for 0.5 h. ^b Yields of the silyl ether were estimated by ¹H NMR based on a signal of the internal standard. ^c Isolated yield of the alcohol after hydrolysis.

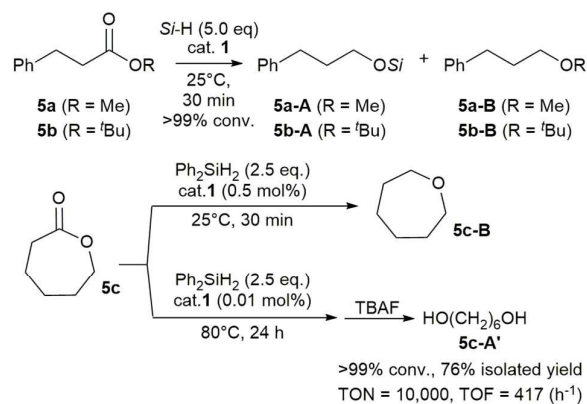
**Scheme 2.** Hydrosilylation of **2b** and **3b** with low catalyst loadings to achieve extremely high TON and TOF values (Si = Me₂SiOSiMe₂H).**Table 3.** Hydrosilane reduction of amides **4a–4e** to amines catalyzed by **1**.^a

Entry	Amide	"Si-H"	Cat. (mol%)	Time (h)	Yield (%) ^d	TON
1	4a	PhMe ₂ SiH	0.05	7	79 [>99]	2,000
2 ^b		TMDS	0.05	1	[56] ^e	1,120
3 ^b		BDMSE	0.05	1	[85] ^e	1,700
4	4b	PhMe ₂ SiH	0.05	5	90 [>99] ^e	2,000
5		TMDS	0.15	3	67 [>99] ^e	667
6 ^b		BDMSE	0.05	24	[>99] ^e	2,000
7 ^c	4c	PhMe ₂ SiH	0.45	23	86 [>99] ^e	222
8		TMDS	0.05	3	84 [>99] ^e	2,000
9 ^b		BDMSE	0.05	1	[>99] ^e	2,000
10	4d	PhMe ₂ SiH	0.15	3	92 [>99] ^e	667
11		TMDS	0.15	3	82 [>99] ^e	667
12 ^b		BDMSE	0.15	3	86 [>99] ^e	667
13	4e	PhMe ₂ SiH	0.05	7	87 [>99] ^e	2,000
14		TMDS	0.05	3	75 [>99] ^e	2,000
15		BDMSE	0.02	3	86 [>99] ^e	5,000

^a All reactions were conducted using amide (1 mmol), **1** (0.05–0.45 mol%), and hydrosilane (4.4 mmol per a Si-H moiety) under neat conditions at 25°C. ^b Reactions were performed in dioxane (0.5 mL). ^c Reaction was performed at 50°C. ^d Isolated yield. ^e Determined by ¹H NMR in the presence of an internal standard.

the trials was reaction of lactam **4e** with BDMSE in the presence of 0.02 mol% of **1** at room temperature, which achieved complete conversion of **4e** to the corresponding amine in 3 h. The product was isolated by distillation in 86% yield. The calculated TON was 5,000 and TOF was 1,667/h. Reaction of primary amides with hydrosilanes often results in dehydration to form nitriles.^{1c,4} Treatment of *p*-

MeOC₆H₄CONH₂ with PhMe₂SiH and 0.15 mol% of **1** at 23°C for



23 h gave *p*-MeOC₆H₄CN in 67% yield.

Scheme 3. Hydrosilane reduction of esters catalyzed by **1**.

Table 4. Hydrosilane reduction of **5a** and **5b** with TMDS or Ph₂SiH₂.^a

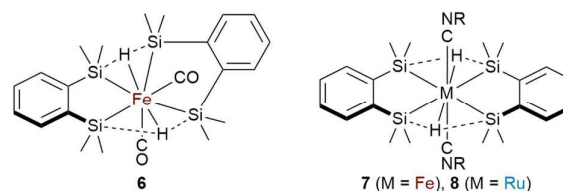
Entry	Ester	"Si-H"	Cat. (mol%)	5-A : 5-B ^b	Product (%) ^d
1	5a	TMDS	1.5	95 : 5	5a-A (84) ^e
2		Ph ₂ SiH ₂		<1 : >99	5a-B (93)
3 ^c	5b	TMDS	4	<1 : >99	5b-B (85)
4 ^c		Ph ₂ SiH ₂		<1 : >99	5b-B (90)

^a All reactions were conducted with an ester (1 mmol for **5a**, 0.5 mmol for **5b**), catalytic amount of **1**, and a hydrosilane (2.5 mmol for **5a**, 1.25 mmol for **5b**) under neat conditions at 25°C for 0.5 h. ^b Estimated by ¹H NMR. ^c 4 mol% of **1** was used. ^d Isolated yield. ^e Isolated as 3-phenyl-1-propanol (**5a-A'**) after hydrolysis.

Hydrosilane reduction of esters often affords a mixture of two products, a silyl ether and an alkyl ether.[‡] Hydrosilane reduction catalyzed by **1** gave alkyl ethers and silyl ethers, with the selectivity dependent on the substrate, hydrosilane used, and the amount of the catalyst. Scheme 3 and Table 4 show representative examples. With 1.5 mol% of **1**, methyl dihydrocinnamate **5a** was reduced at room temperature within 30 min. The corresponding silyl ether was obtained as the major product with TMDS, whereas the methyl ether was formed selectively with Ph₂SiH₂. Similar reactions of *t*-butyl dihydrocinnamate **5b** gave the *t*-butyl ether with both Ph₂SiH₂ and TMDS. Treatment of ϵ -caprolactone with Ph₂SiH₂ and 0.5 mol% of **1** gave oxepane as a single product, whereas selective formation of disilyl ethers of 1,6-hexanediol, which was converted to 1,6-hexanediol by TBAF, was achieved with 0.01 mol% of **1**. The TON value was 10,000 and the TOF was 417/h.

The key to understanding the extremely high catalytic performance of **1** is present in the disilametallacyclic structure. A series of disilametallacyclic compounds, which have structures analogous to **1**, have been reported recently.^{4,5} As shown in Chart 1, **6** is an iron analog of **1** with two CO ligands in a *cis*-configuration. The complexes, **7** and **8**, are isocyanide analogs of **1** and **6**, where the two isocyanide ligands are in a *trans*-configuration. The iron carbonyl complex **6** showed moderate to high catalytic activity towards hydrosilylation of carbonyl compounds, alkene hydrosilylation, and hydrogenation of alkenes.^{5a} The ruthenium carbonyl complex **1**

is a highly efficient catalyst for hydrosilane reduction, but is



less effective for the other two reactions.^{5c} Isocyanide

Chart 1. Three disilametallacyclic complexes analogous to **1**.

complexes **7** and **8** are excellent catalysts for hydrogenation of alkenes, including tri- and tetrasubstituted alkenes.^{5d} The reaction mechanisms for hydrogenation of alkenes catalyzed by **1**, **6–8** was investigated using DFT calculations, and the results showed that activation of H₂ occurs on the metal-silicon bond. Since mechanisms of hydrosilylation are considered similar to those of hydrogenation, activation of a Si-H bond possibly occurs on the Ru-Si bond in **1** during hydrosilane reduction of carbonyl compounds.

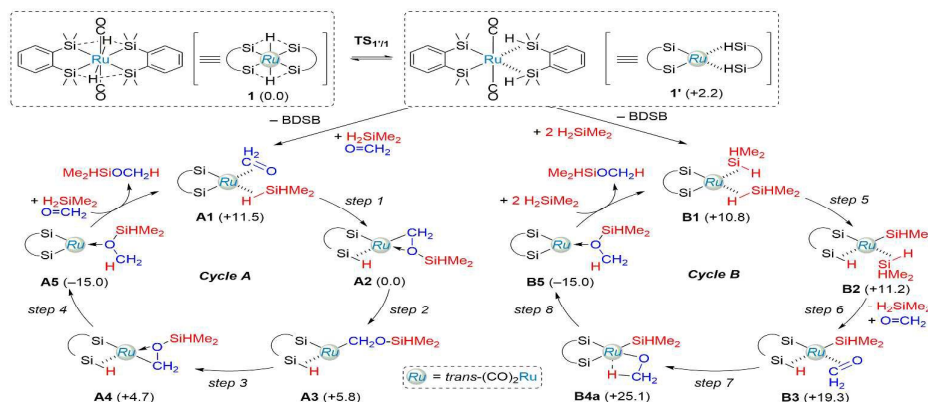
Scheme 4 illustrates two possible catalytic cycles for hydrosilane reduction of formaldehyde, which proceeds through pathways analogous to those proposed for hydrogenation of ethylene catalyzed by **1**, **6–8**.^{5c,5d} Since both TMDS and Ph₂SiH₂ were effective for the reduction (Table 1), Me₂SiH₂ was selected as the hydrosilane for DFT calculations.⁵ Complex **1** is a catalyst precursor, from which 1,2-bis(dimethylsilyl)benzene (BDSB) is dissociated to generate catalytically active species. In *Cycle A*, the BDSB ligand is replaced by CH₂=O and Me₂SiH₂ to form **A1**, in which both are bonded to the metal center in η^2 -mode. Oxidative hydrogen migration from the coordinated Me₂SiH₂ to a silicon atom in the disilametallacyclic moiety and concomitant Si-O bond formation to form **A2**. Subsequent dissociation of the oxygen atom from the metal center followed by rotation of the Ru-C bond results in formation of **A4** through **A3**. The second oxidative hydrogen migration of the hydride in **A4** from the silicon atom to the carbon bonded with ruthenium gives **A5**, from which coordination of CH₂O and Me₂SiH₂ liberates the product and regenerates **A1**. In *Cycle B*, BDSB in **1** are replaced by two Me₂SiH₂ molecules to form **B1**. Two oxidative hydrogen migrations occur in a concerted manner, which leads to formation of a Ru-Si bond and two η^2 -Si-H ligands to give **B2**. Replacement of the coordinated Me₂SiH₂ ligand in **B2** by CH₂=O forms **B3**, followed by the second oxidative hydrogen migration from the silicon atom to the carbon atom of coordinated formaldehyde to form **B5** via **B4a**. The intermediate **B5** is identical to **A5**. Liberation of the product is followed by regeneration of **B1** by coordination of two molecules of Me₂SiH₂. In both catalytic cycles, the energy barrier of the overall reaction is below 20 kcal/mol, which is low enough to promote the reaction at room temperature.

In summary, the disilarythene **1** was shown to be an excellent catalyst for hydrosilane reduction of aldehydes, ketones, and amides under mild conditions to a single product in high yield. Reduction of ketone **3b** with TMDS using a minimal amount of **1** (0.001 mol%, corresponding to 3–4 ppm

COMMUNICATION

Journal Name

Ru to starting material) achieved 100% conversion of the substrate, led to formation of a single product, and produced the highest TON values ever reported.³ The reduction of esters



Scheme 4. Possible catalytic cycles for hydrosilylation of HCHO with Me₂SiH₂ catalyzed by **1** [ΔG in parentheses (kcal/mol)]. The CO ligands are omitted for clarity.

experienced problems related to selectivity between the formation of alkyl ethers and silyl ethers; however, a TON of 10,000 was achieved for reaction of ϵ -caprolactone to disilyl ether of 1,6-hexane diol, which is the highest TON reported for hydrosilane reduction of esters. The DFT calculations suggested two catalytic cycles to explain such remarkably high catalytic activity. Activation of the Si-H bonds of hydrosilanes occurs on the Ru-Si bond in **1**. Perutz and Sabo-Etienne proposed a σ -CAM mechanism involving activation of H₂ on a transition metal that is assisted by an adjacent main group element.⁶ Hydrogenation reactions of alkenes catalyzed by complex **1** are exemplified by **6-8**, which are supported by both experimental and theoretical data.⁵ The present report suggests that the σ -CAM mechanism is applicable to hydrosilane reduction of carbonyl compounds, leading to the high catalytic performance of **1**.

This work was supported by the Core Research Evolutional Science and Technology (CREST) program of Japan Science and Technology Agency (JST), Japan, and a Grant-In-Aid for Scientific Research (B) (No. 18H01980 to H.N. and No. 16H04120 to Y.S.) from the Ministry of Education, Culture, and Sports, Science, and Technology, Japan. Help for DFT calculations by Ms. Konoka Hoshi is acknowledged.

Conflicts of interest

There are no conflicts to declare.

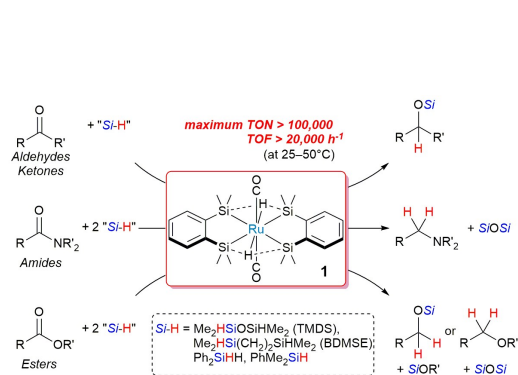
Notes and references

† Two interesting aspects were obtained on selectivities for hydrosilane reduction catalyzed by **1**. One is the reaction of ketone **3a**, which is faster than aldehyde **2a**. Another is two reaction pathways of esters **5** to form alkyl ethers and silyl ethers. We added three other examples for the reductions of esters (7-1, 7-2) and mechanistic considerations in ESI (2-2, 7-3).

§ We also performed both experiment and DFT calculations for hydrosilylation of acetophenone with Ph₂SiH₂. Similar to the

hydrogenation mechanisms reported earlier,^{5d} Cycle A is sensitive towards steric bulkiness of the substrate. Cycle B is more preferable for the acetophenone reduction mechanism to Cycle A. See details in ESI (11-3).

- (a) G. L. Larson and J. L. Fry, *Ionic and organometallic-catalyzed organosilane reductions*, John Wiley & Sons, 2009. (b) D. Addis, S. Das, K. Junge and M. Beller, *Angew. Chem. Int. Ed.*, 2011, **50**, 6004-6011. (c) H. Nagashima, *Synlett*, 2015, **26**, 866-890. (d) S. Chakraborty, P. Bhattacharya, H. Dai, H. Guan, *Acc. Chem. Res.*, 2015, **48**, 1995-2003. (e) B. Li, J. B. Sortais, C. Darcel, *RSC Adv.*, 2016, **6**, 57603-57625. See also, additional references described in ESI (references S3-S6).
- J. Pesti and G. L. Larson, *Org. Process Res. Dev.*, 2016, **20**, 1164-1181.
- (a) J. Yang and T. D. Tilley, *Angew. Chem. Int. Ed.*, 2010, **49**, 10186-10188. (b) S. Chakraborty, O. Blacque, T. Fox and H. Berke, *ACS Catal.*, 2013, **3**, 2208-2217. (c) A. J. Ruddy, C. M. Kelly, S. M. Crawford, C. A. Wheaton, O. L. Sydora, B. L. Small, M. Stradiotto and L. Turculet, *Organometallics*, 2013, **32**, 5581-5588. (d) M. C. Lipke and T. D. Tilley, *J. Am. Chem. Soc.*, 2014, **136**, 16387-16398. (e) R. J. Trovitch, *Acc. Chem. Res.*, 2017, **50**, 2842-2852.
- For an account on disilametallacyclic chemistry; Y. Sunada and H. Nagashima, *Dalton Trans.*, 2017, **46**, 7644-7655.
- (a) Y. Sunada, H. Tsutsumi, K. Shigeta, R. Yoshida, T. Hashimoto and H. Nagashima, *Dalton Trans.*, 2013, **42**, 16687-16692. (b) A. Tahara, H. Tanaka, Y. Sunada, Y. Shiota, K. Yoshizawa and H. Nagashima, *J. Org. Chem.*, 2016, **81**, 10900-10911. (c) K. Hoshi, A. Tahara, Y. Sunada, H. Tsutsumi, R. Inoue, H. Tanaka, Y. Shiota, K. Yoshizawa and H. Nagashima, *Bull. Chem. Soc. Jpn.*, 2017, **90**, 613-626. (d) Y. Sunada, H. Ogushi, T. Yamamoto, S. Uto, M. Sawano, A. Tahara, H. Tanaka, Y. Shiota, K. Yoshizawa and H. Nagashima, *J. Am. Chem. Soc.*, 2018, **140**, 4119-4134.
- R. N. Perutz and S. Sabo-Etienne, *Angew. Chem. Int. Ed.*, 2007, **46**, 2578-2592.



0.001 mol% of Ru catalyst for the hydrosilylation of carbonyl compounds (TON: up to 100,000)