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Silyl Compounds

Chemoselective Catalytic Hydrosilylation of Nitriles**

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Dedicated to Professor Lyudmila G. Kuzmina on the occasion of her 65th birthday

Catalytic hydrosilylation of unsaturated substrates has emerged over recent decades as a powerful industrial and laboratory methodology for the preparation of a wide range of organosilicon products.[1] In the case of ketones and imines, it also serves as a convenient reduction method in that it provides protected alcohols and amines in one step.[2] Whereas diverse procedures have been developed for the hydrosilylation of C=X (X = C, N, O),[1] P=O,[3] S=O,[4] and C≡C bonds,[1,5] Si–H addition to the N≡C triple bond remains a great synthetic challenge.[1h,6] Hydrosilylation of nitriles also presents a difficult chemoselectivity problem in that the products of monoaddition, *N*-silylaldimines R'_3Si-N=CHR, are usually much more reactive than nitriles, so that the reaction proceeds further to give the disilylamines $(R'_3Si)_2NCH_2R$.[6c,7] Since the original report by Calas et al.[8] on the $ZnCl_2$-catalyzed condensation of $HSiEt_3$ with PhCN to give the imine $PhHC{=}NSiEt_3$ in moderate yield (54%, at 140–150°C), only a few catalytic monohydrosilylations of nitriles have been published.[9,10] These methods either require drastic reactions conditions or are very slow and give low yields, and in no case was the selectivity towards functional groups established. A handful of examples of stoichiometric mono-Si–H additions to nitriles have been published.[11]

Given the importance of silylimines in medicinal chemistry and organic synthesis, the selective formation of $R'_3SiN{=}$CHR from nitriles would be a significant addition to the current repertoire of synthetic chemistry.[9,12] This process also presents an attractive alternative to the current synthetic methods of reduction of nitriles to imines and aldehydes based on the use of expensive and often pyrophoric aluminum or boron hydrides, such as diisobutylaluminum hydride (DIBAL-H).[13] Also, silylaldimines have recently been found to be useful partners in N–C coupling with aryl halides to make substituted aldimines, which paves the way to a variety of secondary amines.[14]

Herein we report a convenient method for selective mono(hydrosilylation) of nitriles that occurs under very mild conditions and shows excellent tolerance to most common functional groups. Moreover, simply increasing the silane load allowed us to achieve the complete reduction to disilylamines. Other highlights of this catalytic system are that it can operate under solvent-free conditions and that the catalyst is recyclable.

We have recently reported that cationic Ru complexes $[Cp(R_3P)Ru(NCCH_3)_2]^+$ (**1**; Cp = cyclopentadienyl) catalyze a variety of hydrosilylation reactions, showing moderate to excellent activity.[15] Rewardingly, we found that complex $[Cp(iPr_3P)Ru(NCCH_3)_2]BAF$ (**1a**; $BAF = [B(C_6F_5)_4]^-$) also catalyzed the hydrosilylation of nitriles better than it does the hydrosilylation of C=O and C=C bonds (Table 1). Simple alkyl- and aryl-substituted nitriles RCN (Table 1, entries 1–4) are easily converted at room temperature into the corresponding *N*-silylimines. The reaction times appear to increase with the size of group R. Hydrosilylation of *t*BuCN is still selective, but requires slightly increased temperature (50°C) and a longer reaction time (Table 1, entry 3). The CN group in the homoallylic position is selectively reduced in the presence of C=C double bond (Table 1, entry 5). In contrast, the hydrosilylation of a conjugated alkenyl nitrile required much longer time and does not reach completion even after 24 h (Table 1, entry 6), suggesting possible catalyst poisoning by the chelating azabutadiene product. Previous reports on the hydrosilylation of unsaturated nitriles primarily showed selective Si–H addition to the C=C double bond[6b,16] with only a few examples of double hydrosilylation of the cyano group.[7b] Attempted hydrosilylation of a nonconjugated alkynyl nitrile (Table 1, entry 7) resulted in a very sluggish Si–H addition to the C≡C triple bond, in accord with the high propensity of half-sandwich complexes of Ru to activate alkynes.[17] Electron-poor aryl nitriles containing the usually reactive keto-, aldo-, nitro-, and ester functionalities in the aryl substituent are hydrosilylated exclusively on the cyano group (Table 1, entries 8–11), although the reaction times are significantly increased relative to that of benzonitrile (Table 1, entry 4). In contrast, $HSiMe_2Ph$ adds to the electron-rich *p*-cyanoanisole at the same rate (100% after 1 h in $[D_6]$acetone; Table 1, entry 12) as to PhCN (Table 1, entry 4). Finally, hydrosilylation of 3-cyanopyridine occurs selectively at the cyano group, but a long reaction time is required (Table 1, entry 13).

The exceptional tolerance of this nitrile hydrosilylation to the presence of the carbonyl functionality was also manifested by performing the catalysis in acetone as a solvent, which significantly accelerates the reaction rate. Thus, the full conversion of benzonitrile into the silylated imine was four times faster in acetone than in chloroform. Hydrosilylation of acetonitrile is also faster in acetone, but is accompanied by some loss of selectivity. Moreover, after 6 h most of the initial product, the imine $CH_3CH{=}NSiMe_2Ph$, was converted into a mixture of compounds, the major component of which was an

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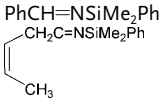
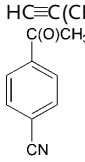
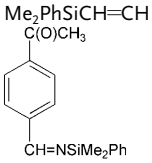
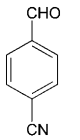
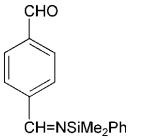
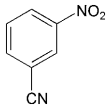
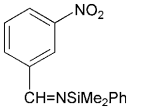
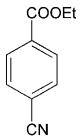
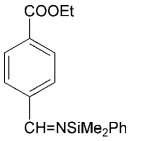
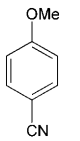
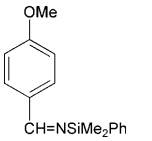
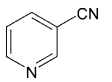
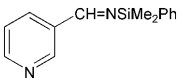
Table 1: Catalytic hydrosilylation of nitriles with $HSiMe_2Ph$.[a]

Entry	Substrate	TOF [h^{-1}][b]	Conv. (time)[c]	Products
1	CH_3CN	75 (100%)	100% (20 min)[d]	$CH_3CH{=}NSiMe_2Ph$ (90%)
2	*i*PrCN	16.6 (50%)	100% (2 h)	*i*PrCH=$NSiMe_2Ph$
3	*t*BuCN	0.04 (14%)	14% (24 h)	*t*BuCH=$NSiMe_2Ph$
4	PhCN	6.3 (50%)	100% (4 h)[e]	PhCH=$NSiMe_2Ph$
5		2.5 (100%)	100% (2.5 h)	
6	$CH_2{=}CHCN$	0.3 (30%)	30% (24 h)	$CH_2{=}CHCH{=}NSiMe_2Ph$
7	$HC{\equiv}C(CH_2)_3CN$	0.06 (40%)	40% (168 h)	$Me_2PhSiCH{=}CH(CH_2)_3CN$
8		4.4 (50%)	100% (8 h)	
9		4.6 (50%)	100% (14 h)	
10		19 (50%)	100% (4 h)	
11		0.5 (50%)	100% (48 h)[f]	
12		25 (100%)	100% (1 h)[d]	
13		6.9 (50%)	68% (14 h)	

[a] In a general procedure, 4–5 mol% of **1** was added to a solution of substrate and silane in $CDCl_3$. [b] Calculated at the conversion shown in parentheses. [c] Calculated from ^1H NMR data. [d] Reaction in [D_6]acetone. [e] 100% after 1 h in [D_6]acetone. [f] Reaction in CD_2Cl_2.

unusual coupling product $CH_3CH{=}N{-}CH(CH_3)N(SiMe_2Ph)_2$. It is tempting to speculate that this compound results from the so far unknown N–Si addition across the C=N bond, but the exact mechanism is not known yet.

Importantly, we also discovered that the hydrosilylation of liquid substrates can be carried out under solvent-free conditions with reduced loadings of the catalyst (<1% mol). Taking advantage of the low solubility of the cationic catalyst in nonpolar solvents, the hydrosilylation products can be extracted with hexane or ether and the catalyst can easily be recovered and used again.[18]

Changing the phosphine ligand in the ruthenium complex or using a different silane has a drastic effect on the catalytic activity. The best results were achieved for the system iPr_3P/$HSiMe_2Ph$. All other combinations were much less active or completely inactive.[19] Since the precatalyst is a cationic complex, we also studied the influence of counteranion. Rewardingly, the substitution of the expensive BAF anion for the more readily available $[PF_6]^-$ or $[BF_4]^-$ counteranions resulted in only insignificant increase of reaction times, without any drastic effect on the selectivity of the reaction. Finally, the catalyst can be easily generated in the reaction flask by treating the commercially available and shelf-storable precursor $[CpRu(NCCH_3)_3]^+A^-$ ($A^- = [PF_6]^-$ or $[BF_4]^-$) with phosphine prior to catalysis.

Full reduction of nonfunctionalized nitriles to disilylamines can easily be achieved with the same catalyst (Table 2). Thus, bis(silyl)benzylamine is produced in the reaction of benzonitrile with two equivalents of silane (Table 2, entry 1).[20] For comparison, there was no hydrosilylation of the related imine PhMeC=NPh under the same reaction conditions. *p*-Cyanoanisole is converted cleanly into the bis(silylated)amine after 48 h (Table 1, entry 2), but the reaction stops at the imine stage for the electron-poor nitrile *meta*-$NO_2(C_6H_4)CN$ (Table 1, entry 3). Functionalized nitriles gave a mixture of products because of loss of chemoselectivity at the second stage of hydrosilylation (e.g. Table 1, entry 4). Finally, double hydrosilylation of an enolizable alkylnitrile

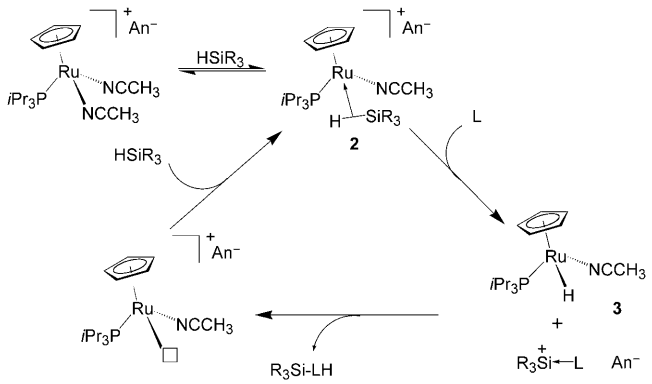
Table 2: Hydrosilylation of nitriles with two equivalents of $HSiMe_2Ph$ catalyzed by 5 mol% **1a**.[a]

Entry	Substrate	Conv. (time)	Products
1	PhCN	100% (66 h)	$PhCH_2N(SiMe_2Ph)_2$
2	$MeO(C_6H_4)CN$	100% (48 h)	$MeO(C_6H_4)CH_2N(SiMe_2Ph)_2$
3	*m*-$NO_2(C_6H_4)CN$	100% (48 h)	*m*-$NO_2(C_6H_4)CH{=}N(SiMe_2Ph)$
4	*p*-$CH_3(O)C(C_6H_4)CN$	100% (48 h)	*p*-$CH_2{=}C(OSiMe_2Ph)(C_6H_4)CH_2N(SiMe_2Ph)_2$ (40% in the mixture)
5	*i*PrCN	100% (24 h)	$(CH_3)_2CHCH_2N(SiMe_2Ph)_2$ (43%) $(CH_3)_2C{=}CHN(SiMe_2Ph)_2$ (57%)

[a] See Experimental Section for details.

was accompanied by the concomitant formation of an enamine (Table 1, entry 5).

Our previous mechanistic studies on the Ru-catalyzed hydrosilylation of carbonyls revealed a mechanism including the intermediate formation of a silane σ-complex **2**, which then undergoes nucleophilic abstraction of the silylium ion by the substrate L to form a neutral ruthenium hydride complex **3** (Scheme 1).[15] Although several complexes of type **2** have been isolated and characterized, our attempts at preparing the labile compound **3** have been so far unsuccessful.[21] We tentatively assign a similar mechanism for the hydrosilylation of nitriles.[22]



Scheme 1. Proposed mechanism for the Ru-catalyzed hydrosilylation. L is a carbonyl compound or nitrile, and the square represents an empty coordination site.

Attempts to extend this methodology to an open-flask setup were hampered by the sensitivity of the products to air. However, thorough exclusion of water is not required, as the silane reacts quickly with trace water in the presence of **1a** to give siloxane. The reactions can therefore be conveniently run on the bench in closed flasks that have been preflashed with inert gas.

In summary, we discovered a very efficient catalytic hydrosilylation of nitriles that shows unprecedented chemoselectivity and tolerates most common functional groups. The catalyst is air-stable and can easily be assembled prior to use starting from commercially available compounds. Moreover, the catalyst is recyclable, thus making it very attractable for practicable applications.

Experimental Section

Catalytic hydrosilylation of benzonitrile: Method 1: Complex **1a** (7 mg, 4% mol) was added to a solution of benzonitrile (16.6 μL, 0.16 mmol) and $HSiMe_2Ph$ (26 μL, 0.17 mmol) in $CDCl_3$. After 4 h at ambient temperature, 100% conversion of the starting nitrile to the *N*-silylimine was achieved.

Method 2: Complex $[Cp(iPr_3P)Ru(NCCH_3)_2][PF_6]$ (**1b**; 8.6 mg, 5 mol%) was added to a solution of $HSiMe_2Ph$ (47 μL, 0.30 mmol) and benzonitrile (30 μL, 0.29 mmol) in $[D_6]$acetone (0.6 mL). After 1 h at ambient temperature, 100% conversion of the starting nitrile to the *N*-silylimine was achieved.

Method 3 (reaction without solvent): Complex **1b** (106 mg, 1 mol%) was added to a mixture of $HSiMe_2Ph$ (3.0 mL, 19 mmol) and benzonitrile (2.0 mL, 19 mmol). After 24 h at ambient temperature, all benzonitrile was cleanly converted into the *N*-silylimine. The product was separated from the catalyst by extraction with hexane.

Catalytic hydrosilylation of isobutyronitrile (on the bench): Catalyst **1b** (0.054 g, 1.5% mol) was loaded in air into a 100 mL round-bottom flask. The flask was purged with nitrogen and charged with 30 mL of CH_2Cl_2. Isobutyronitrile (0.6 mL, 6.7 mmol) and then $HSiMe_2Ph$ (1.1 mL, 7.1 mmol) were added. The reaction mixture was stirred for 3 h at ambient temperature. Then hexane (30 mL) was added, and the yellow solution became cloudy. The volume was reduced to 30 mL resulting in precipitation of the catalyst as a brown oil (contaminated with siloxanes). The yellow solution was decanted from the precipitate and distilled under reduced pressure. Yield of the imine: 1.2 g (86%). ^1H NMR ($CDCl_3$): $\delta = 8.24$ (d, $^3J(H\text{-}H) = 4.4$ Hz, 1, CH = N), 7.55–7.50 (m, 2, Ph), 7.40–7.35 (m, 3, Ph), 2.37 (m, 1, CH), 1.07 (d, $^3J(H\text{-}H) = 6.6$ Hz, 6, CH_3), 0.44 ppm (s, 6, SiMe).

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[19] See the Supporting Information for details.
[20] When a second equivalent of silane was added after the monohydrosilylation of benzonitrile had completed, it took only 17 h to achieve the double hydrosilation. The reason for the discrepancy remains unknown.
[21] We did, however, succeed in the preparation of its pyridine (py) analogue, [Cp(*i*Pr_3P)RuH(py)]: D. V. Gutsulyak, G. I. Nikonov, manuscript in preparation.
[22] DFT studies show that silyl migration on the coordinated nitrile in **2** does not occur (see Ref. [15]).

