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Large-scale preparation and labelling reactions of deuterated silanes

Jesús Campos, Miguel Rubio, Ana C. Esqueda, and Ernesto Carmona*

A catalytic synthesis of deuterated silanes $SiEt_3D$, $SiMe_2PhD$ and $SiPh_2D_2$ is reported that allows their facile generation in a 3–4 g scale, utilizing D_2 (0.5 bar) as the hydrogen isotope source and low catalyst loadings (0.01 mol%). The catalyst precursor is the rhodium (III) complex 1, which contains a (η^5-C_5Me_5)Rh cation stabilized by coordination to a cyclometallated phoshine $PMeXyl_2$ (Xyl = 2,6-$C_6H_3Me_2$). The same complex is also an active catalyst for the hydrosilylation of the C=O and C≡N bonds of various ketones, aldehydes and α,β-unsaturated nitriles. Hence, combination of these two properties permits development of a simple and proficient one-flask, two-step procedure for the deuterosilylation of these substrates.

Keywords: deuterium exchange; deuterium; silanes; deuterosilylation; catalysis; rhodium

Introduction

The growing demand for deuterium-labelled and tritium-labelled compounds stimulates the search for fast, selective, catalytic methods that allow efficient isotopic incorporation.[1] In general, ^{2}H-labelled and ^{3}H-labelled molecules can be prepared by the same basic procedures. In addition to H/D (or H/T) exchange at carbon centres,[2,3] a convenient labelling practice is reduction of C-X multiple bonds (X=C, N, O) with a hydride source such as a metal hydride derived from boron, aluminium or tin.[2a,4,5] However, use of these reagents, although common, encounters substantial limitations by the chemistry required (particularly for T-labelling) and by the generation of considerable amounts of waste products.

Hydrosilanes, $SiR_{4-n}H_n$ (n = 1−3), are an extraordinarily important class of reagents for chemical synthesis.[6–12] They are air and moisture stable and are viewed as environmentally friendly reductants, therefore representing suitable alternatives to the more toxic tin derivatives. Metal-catalysed hydrosilylation is a very important industrial and laboratory method,[7–10] widely employed in chemical synthesis (Figure 1) for the reduction of C-X (X=C, N, O) multiple bonds. Furthermore, hydrosilanes can also be utilized for the catalytic reduction of carbon–halogen bonds, including unreactive C-F bonds.[11,12]

Deuterated and tritiated commonly used silanes, for instance, $SiEt_3D$ and $SiEt_3T$, or $SiPh_2D_2$ and $SiPh_2T_2$, would therefore offer significant advantages in the solution of chemical and biochemical problems with the use of hydrogen isotopes. Thus, catalytic deuterosilylation and tritiosilylation will reduce C-O and C-N multiple bonds, placing the label at carbon while simultaneously protecting the resulting alcohol or amine moieties, allowing further multistep synthesis or the direct introduction of a second D or T label. Despite this great potential, deuterated and tritiated silanes have been hardly exploited as isotopic labelling reagents. Most probably, this is due to the scarcity of information on catalytic H/D (or H/T) exchanges at silicon centres,[13–15] which leaves reduction of the silicon–halogen bond of halosilanes with $NaBD_4$, $LiAlD_4$ or a similar deuteride agent as the more commonly used synthesis of deuterated silanes.[2a,16] For tritium, catalytic H/T exchange at carbon[2d,e,3] is preferred over the use of $LiBT_4$, $NaBT_4$ and LiT and related reagents.[4,5] Indeed, the high potential of tritiated silanes such as $SiEt_3T$ and $SiPh_2T_2$ was advanced by Saljoughian in 2002,[17] but almost 10 years later, it does not seem to have been accomplished, most likely because of unsolved problems in the preparation of these tritiating reagents[4,5] (see, e.g. the study by Neu and Andres[5] for difficulties in the preparation of $SiEt_3T$).

We have recently communicated a very efficient, rhodium-catalysed procedure for the synthesis of deuterated and tritiated silanes.[18a,b] Subsequently, the catalytic properties of this system to effect with great efficacy the deuterosilylation and tritiosilylation of a variety of ketones and aldehydes, by using $SiEt_3H$ under sub-atmospheric pressure of D_2 or T_2, have been exploited.[18c] In this contribution, we provide details for the synthesis in a several gramme scale of deuterated silanes catalysed by complex **1** (Figure 2), by using $SiEt_3D$, $SiMe_2PhD$ and $SiPh_2D_2$ as representative examples. It is most probable that the method can also be applied to the large-scale synthesis of corresponding tritiated silanes with high specific activity. Nevertheless, the lack of facilities in our laboratories to achieve such goal has limited our work to the preparation of $SiEt_3T$ and tritiated complex **1**, in both cases with low specific activity.[18] In view of the efficacy of our method, microwave enhancement[1b,19] of the labelling procedure has not been considered.

Departamento de Química Inorgánica, Instituto de Investigaciones Químicas (IIQ), Universidad de Sevilla, Consejo Superior de Investigaciones Científicas, Avda. Américo Vespucio 49, 41092 Sevilla, Spain

**Correspondence to: Ernesto Carmona, Departamento de Química Inorgánica, Instituto de Investigaciones Químicas (IIQ), Universidad de Sevilla, Consejo Superior de Investigaciones Científicas, Avda. Américo Vespucio 49, 41092 Sevilla, Spain.*
E-mail: guzman@us.es

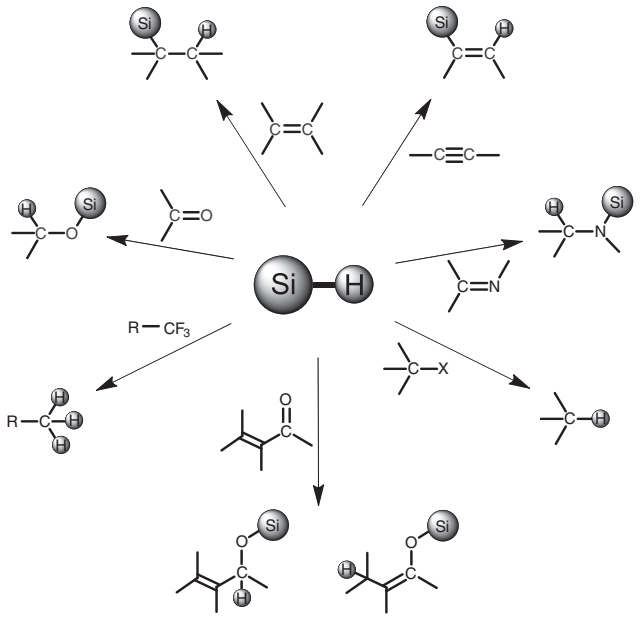


Figure 1. Some synthetic applications of hydrosilanes.

Results and discussion

Catalytic synthesis of $SiEt_3D$, $SiMe_2PhD$ and $SiPh_2D_2$

Figure 2 contains a general representation of the synthesis of deuterosilanes catalysed by compound **1**. As already noted,[18a] this catalytic procedure is based on the following considerations: (a) there is no observable reaction between **1** and H_2 or $SiEt_3H$, but exposure of solutions of **1** to D_2 yields $\mathbf{1(D_{11})^+}$, as a consequence of fast exchange involving all sp^3-hybridized C-H bonds of the phosphine xylyl groups; (b) treatment of $\mathbf{1(D_{11})^+}$ with an excess of $SiEt_3H$ exchanges the label and affords $SiEt_3D$. We have taken profit of this reactivity to effect the deuteration of some common hydrosilane reagents, namely $SiEt_3H$, $SiMe_2PhH$ and $SiPh_2H_2$ in a large scale (3–4 g). In all probabilities, this synthesis can be scaled up further and can also be applied to other tertiary or secondary silanes, and even to primary silanes.[18a] As a general precaution, water must be thoroughly excluded, for compound **1** catalyses also with high efficiency the production of H_2 from H_2O and hydrosilanes.[20]

Using $SiEt_3H$ as a representative example, we dissolved 4.2 mg of compound **1** (3.1×10^{-3} mmol) in 5 mL of $SiEt_3H$ (31.3 mmol; catalyst concentration 0.01 mol%) in an ~220-mL flask and stirred at 50 °C, under 0.5 bar of D_2, for a total time of 16 h. Although the H/D exchange is fast at 20 °C in CH_2Cl_2 solution, heating at 50 °C permits complete solubilization of the catalyst into the neat silane and hence catalysis performance in the absence of solvent. On the other hand, because an equilibrium between reactants and products in Figure 2 is established, to ensure complete deuteration of the silane (≥99%) in this 5-mL-scale synthesis, the reaction was periodically stopped by cooling at 0 °C. The flask atmosphere was evacuated by application of vacuum (0.1 bar for ~20 s) and the reaction vessel charged again with 0.5 bar of D_2. This cycle was repeated a total of five times during the global reaction period and the pure $SiEt_3D$ then obtained by trap-to-trap distillation. The same procedure was utilized for the synthesis of $SiMe_2PhD$ and $SiPh_2D_2$. Pure $SiMe_2PhD$ was separated by trap-to-trap distillation too, whereas for $SiPh_2D_2$, a Kugelrohr vacuum distillation apparatus was employed.

The course of the reaction was followed by ^1H and $^{29}Si\{^1H\}$ NMR spectroscopy and by IR spectroscopy to monitor the hydrogen isotope exchange. The ^1H NMR spectrum of $SiEt_3H$ ($CDCl_3$) exhibits a septet at δ 3.68 ppm that corresponds to the hydrogen atom bonded to silicon. Upon deuteration, this resonance gradually disappears, and it is completely absent in the ^1H NMR of the final product, which shows instead the corresponding signal in the ^2H NMR spectrum. Deuteration of the silane ethyl substituents does not occur. As shown in Figure 3(a), the $^{29}Si\{^1H\}$ NMR spectrum of $SiEt_3H$ is a singlet with δ 0.8 p.p.m. that experiences an isotopic displacement to δ 0.4 p.p.m. ($^1J_{SiD} = 28$ Hz) upon deuteration (Figure 3(c)). The spectrum of an ~45:55 mixture of the two isotopologues has been included in Figure 3(b). On the other hand, the IR spectrum of $SiEt_3H$ features a band at ~2100 cm^{-1} due to ν(Si-H) (Figure 4) that shifts to about 1530 cm^{-1} in the spectrum of $SiEt_3D$. The relative intensities of these IR bands along the course of the H/D exchange match closely the results obtained from ^1H and $^{29}Si\{^1H\}$ NMR studies.

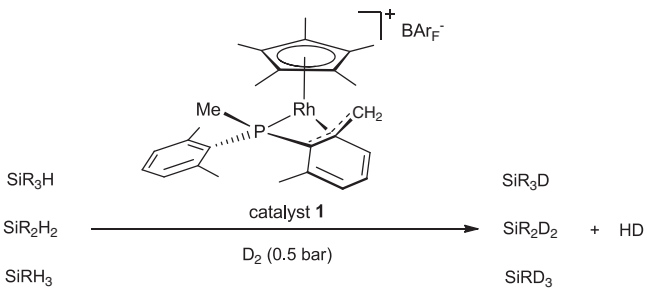


Figure 2. Si-H/Si-D exchange catalysed by the rhodium(III) complex **1** (BAr_F = B[3,5-$(CF_3)_2C_6H_3$]).

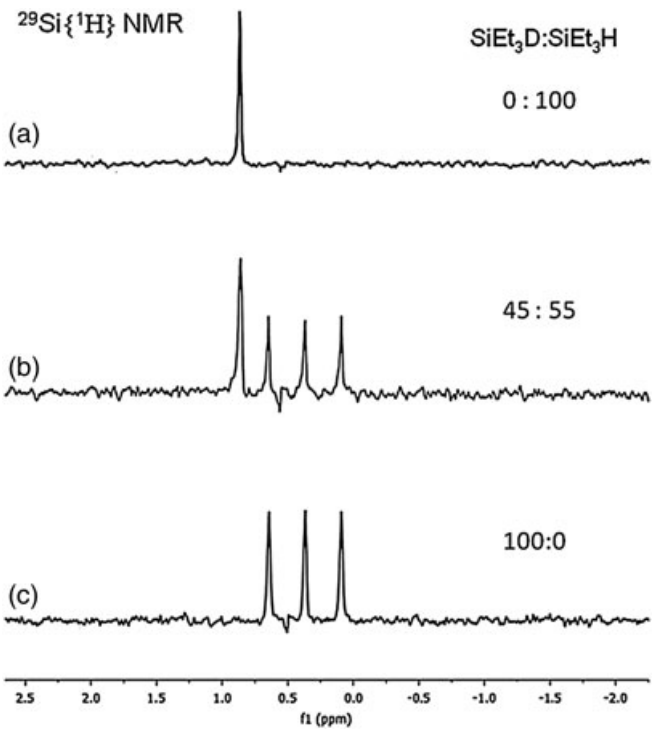


Figure 3. $^{29}Si\{^1H\}$ NRM spectrum of $SiEt_3H$ (a), $SiEt_3D$ (c) and an ~45:55 mixture of the two isotopologues (b).

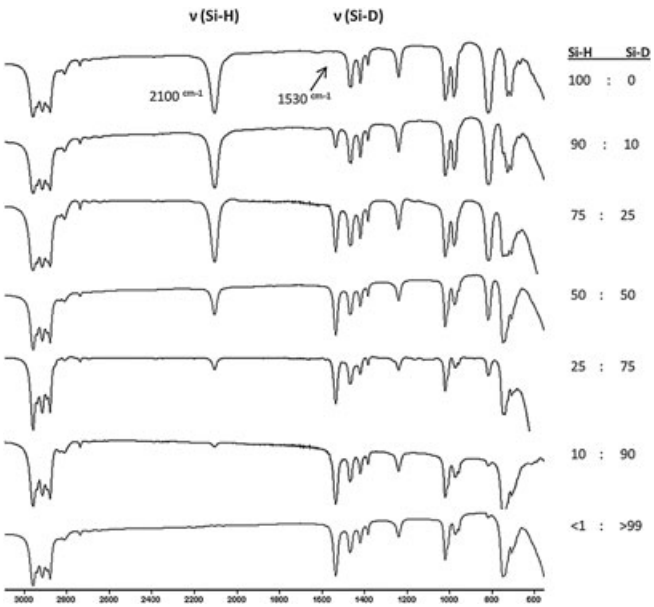


Figure 4. IR spectra (neat silanes) of mixtures of $SiEt_3H$ (ν(Si-H) = 2100 cm^{-1}) and $SiEt_3D$ (ν(Si-D) = 1530 cm^{-1}).

Hydrosilylation and deuterosilylation of >C=O bonds

As an extension of previous work from our group in this area,[18b] we have studied the reduction of a common natural product with biological activity, the (R)-camphor molecule that contains a sterically congested ketone functionality. Reduction of its carbonyl group can give rise to *exo* or *endo* isomers. Entries 3–7 in Table 1 contain the results of this study that encompassed the use of $SiEt_3H$, $SiPh_2H_2$, $SiMe_2PhH$, $SiEt_3D$ and $SiMe_2PhD$. For comparative purposes, entries 1 and 2 summarize previous results obtained for acetophenone and $SiEt_3H$ and $SiEt_3D$.[18b] Both $SiEt_3H$ and $SiPh_2H_2$ led to little or no control of diastereoselectivity, although the latter favoured formation of the *exo* product (~7:3 ratio of *exo*:*endo*). This selectivity is comparable with that reported when $RhH(PPh_3)_4$ was used as a catalyst[21] for this reduction (1.8:1 ratio) but is opposite to catalysis by the iridium cation $[IrH(POCOP)(acetone)]^+$ (POCOP = 2,6-*bis*(di-*tert*-butylphosphinito)phenyl) that produced an approximate 1:4 ratio of *exo* and *endo* isomers.[8a] Our reaction is less efficient than the latter process, which proceeds quantitatively at 0 °C.[8a] However, for our system, direct deuterosilylation was achieved by application of the one-flask, two-step procedure described earlier,[18b] which makes use of D_2 as the hydrogen isotope source. Firstly, a dichloromethane solution of catalyst **1** and $SiEt_3H$ (entry 7) or $SiMe_2PhH$ (entry 8) was stirred in the presence of D_2 (0.5 bar) for 2–3 min, whereby D-incorporation to $SiEt_3H$ and **1** took place. The gas atmosphere was then replaced by fresh D_2 (0.5 bar) and the process repeated a total of three times, to ensure a D-content in the silane product of ≥99%. Then, camphor was added and the mixture stirred at 50 °C for 24 h to yield the isotopically labelled silylborneols in good yields (entries 7 and 8), with diastereoselectivity similar to that observed for the non-labelled product.

To analyse competition between the 1,2-addition and 1,4-addition of the hydrosilane to α,β-unsaturated carbonyl compounds, we also employed benzylideneacetone (entries 8–10) and cinnamaldehyde (entries 11–14) for this study. For the former, there was a clear preference for the 1,4-addition with respect to the 1,2-addition of about 9:1, regardless of the use of $SiEt_3H$ or $SiMe_2PhH$ as the reductant, although the corresponding silyl enols resulted as comparable mixtures of their *Z* and *E* isomers. The more accessible carbonyl group of cinnamaldehyde led to an almost 1:1 ratio of 1,2-addition and 1,4-addition products, although for the latter reactivity almost only the *E* isomers of the silyl enols were obtained.

Less reactive carbonyl species like esters and amides were also investigated. Reactions of several tertiary and secondary silanes with esters ethylbenzoate and ethylbutyrate were unsuccessful, even after prolonged heating at 60 °C. Similarly, hydrosilylation of benzamide and *N*,*N*-dimethylacetamide proved fruitless. Nevertheless, a positive consequence of these results is that selective reduction of the ketone functionality in α-ketoesters and α-ketoamides should be feasible. In accord with expectations, $SiEt_3H$ added chemoselectively to the keto carbonyl group of ethyl pyruvate (entry 16) to give the corresponding silyl ethers. Thus, compound **1** seems to be a good candidate for the selective hydrosilylation of aldehydes and ketones in the presence of the less reactive ester and amide functional groups.

Hydrosilylation and deuterosilylation of C-N multiple bonds

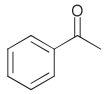
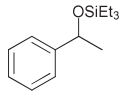
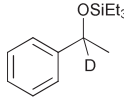
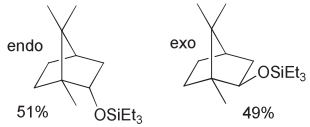
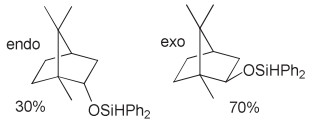
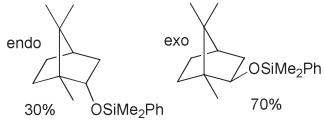
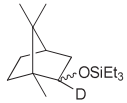
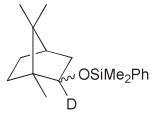
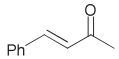
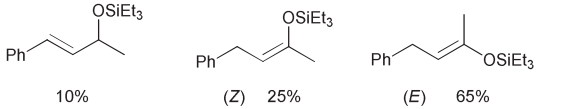
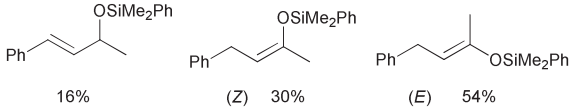
Reaction of *N*-benzylidene aniline with 2.2 eq of $SiEt_3H$ at 50 °C for 2 h, in the presence of 1 mol% concentration of **1**, gave the expected silylamine product in quantitative yield (Table 2, entry 1). With the use of the procedure described previously for direct deuterations, the D-isotopologue was generated also quantitatively. In this case, to ensure full deuterosilylation, we employed a non-optimized time of 12 h.

Imine hydrosilylation catalysed by **1** is very sensitive to steric hindrance around the C=N bond. Thus, hydrosilylation of the bulkier aldimine *N*-benzylidene-*t*-butylamine (entry 3), and ketimine (*E*)-*N*-(1-phenylethylidene)aniline (entry 4), occurred with low conversion and, in the former case, with partial formation of the opposite regioselectivity product (entry 3).

Whereas well-known procedures are available for the hydrosilylation of C=X bonds (X=C, N, O),[7–10] hydrosilylation of C≡N bonds remains comparatively unexplored because the cyano group behaves as inert under common hydrosilylation conditions.[7e,22] Murai and co-workers used $Co_2(CO)_8$ as catalyst for the reduction of nitriles by $SiMe_3H$ to *N*,*N*-disilylamines.[23a] Subsequently, a heterogeneous, Rh-catalysed process for the hydrosilylation of aromatic aldehydes was developed,[23b] and more recently, Gutsulyak and Nikonov have reported a very convenient method for the selective monosilylation and disilylation of nitriles, by action of a Ru catalyst.[23c]

Whereas acetonitrile (Table 2, entry 2) underwent only partial conversion in the presence of **1** and $SiEt_3H$ (<40%, 50 °C, 24 h) and benzonitrile remained unaltered even under somewhat more forcing conditions (entry 6), α,β-unsaturated nitriles experienced facile hydrosilylation to produce vinylamines protected with two silyl groups (entries 7–9). This observation, which finds scarce literature precedent,[23a,b] allowed isolation of vinyl *bis*(silylamines) as stable molecules. The parent vinylamines are usually unstable and decompose gradually even at low temperatures.[24] The use of this method permitted also facile D-labelling of the amine resulting from the double deuterosilylation of cinnamonitrile (Figure 5 and entry 8 of Table 2). At variance with previous reports,[23a,b] other possible products of this reaction, such as the protected aliphatic amine or the protected allylic amine, were not observed (Figure 5). Moreover, the double hydrosilylation of cinnamaldehyde by **1** is highly selective and gives exclusively the *E* isomer.

Table 1. Hydrodilylation and deuterosilylation of C-O double bonds

Entry	Substrate	S/C	Silane	*T* (°C)	*t* (h)	% Conv	Product
1		1000	$SiEt_3H$	25	1	99	
2		200	$DSiEt_3$	25	5	99	
3		200	$SiEt_3H$	50	24	50	
4		200	$SiPh_2H_2$	50	24	70	
5		200	$SiMe_2PhH$	50	40	99	
6		200	$SiEt_3D$	50	40	59	
7		200	$SiMe_2PhD$	50	40	70	
8		200	$SiEt_3H$	25	1	99	
9		200	$SiMe_2PhH$	25	1	99	
10		200	$SiEt_3D$	25	1	99	

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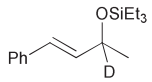
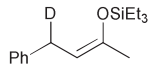
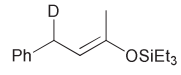
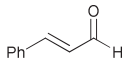
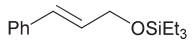
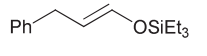
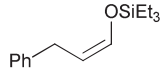
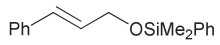
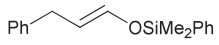
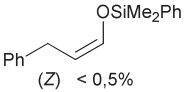
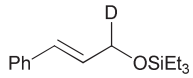
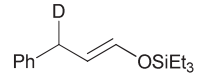
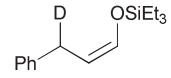
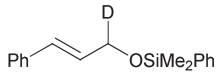
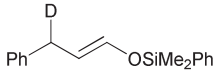
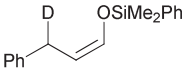
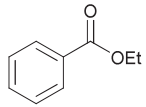
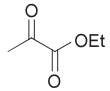
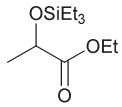
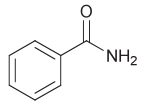
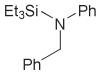
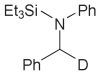
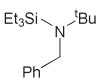
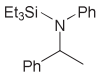
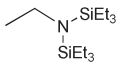
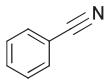
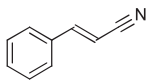
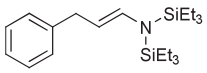
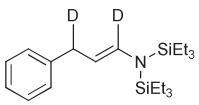
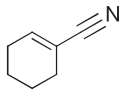
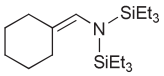
							 11%  (*Z*) 23%  (*E*) 66%
11		200	$SiEt_3H$	25	1	99	 48%  (*E*) 52%  (*Z*) < 0,5%
12		200	$SiMe_2PhH$	25	2	99	 50%  (*E*) 50%  (*Z*) < 0,5%
13		200	$SiEt_3D$	25	5	99	 48%  (*E*) 50%  (*Z*) 2%
14		200	$SiMe_2PhD$	25	5	99	 57%  (*E*) 34%  (*Z*) 9%
15		200	$SiEt_3H$	60	48	0	Only minor unidentified products
16		200	$SiEt_3H$	50	24	99	 < 10% dialkyl ether
17		100	$SiEt_3H$	60	48	0	No reaction

Table 2. Hydrosilylation and deuterosilylation of C-N multiple bonds

Entry	Substrate	S/C	Silane	*T* (°C)	*t* (h)	%Conv	Product
1		100	$SiEt_3H$	50	2	100	
2		100	$SiEt_3D$	50	12	100	
3		100	$SiEt_3H$	50	24	15	  75% 25%
4		100	$SiEt_3H$	50	24	40	
5	CH_3CN	100	$SiEt_3H$	50	24	38	
6		100	$SiEt_3H$	60	48	0	No reaction
7		100	$SiEt_3H$	50	6	100	
8		100	$SiEt_3D$	50	36	100	
9		100	$SiEt_3H$	80*	7	95	

Conditions: silane (2.2 eq for imines and 3 eq for nitriles) and solvent (CD_2Cl_2, 0.5 mL).
*Solvent $ClCH_2CH_2Cl$.

Experimental

General

All operations were performed under an argon atmosphere by using standard Schlenk techniques, employing dry solvents and glassware. High Resolution Mass Spectrometry (HRMS) data were obtained using a Jeol JMS-SX 102A mass spectrometer (JEOL Ltd., Tokyo, Japan) at the Analytical Services of the Universidad de Sevilla (CITIUS). Infrared spectra were recorded on Bruker Vector 22 spectrometer (Bruker Biospin S.A.S, Wissembourg Cédex, France). The NMR instruments used were Bruker DRX-500, DRX-400 and DRX-300 spectrometers. Spectra were referenced to external $SiMe_4$ (δ 0 p.p.m.) by using the residual proton solvent peaks as internal standards (^{1}H NMR experiments), or the characteristic resonances of the solvent nuclei (^{13}C NMR experiments). Spectral assignments were made by routine one-dimensional and two-dimensional NMR experiments where appropriate. Catalyst **1** was prepared as previously described.[18] All substrates were purchased from commercial sources and were distilled under vacuum from $CaCl_2$ or $MgSO_4$ before use. Silanes were purchased from commercial sources and used without further purification. $PMeXyl_2$ (Xyl = 2,6-$C_6H_3Me_2$) was prepared from PCl_3, MeMgBr and XylMgBr.[25a] The rhodium dimer and $ZnCp^*_2$ were also obtained using published procedures.[25b,c] $NaBAr_F$ can either be prepared[25d] or be obtained from commercial sources.

Synthesis of catalyst 1[18] (Figure 6)

Preparation of [(η^5-C_5Me_5)Rh(Cl){PMe(2,6-CH_2(Me)C_6H_3)(2,6-$Me_2C_6H_3$)}] (1-Cl)

A solution of $PMe(Xyl)_2$ (131 mg, 0.5 mmol) in 2 mL of THF is added, at −40 °C, to a solution of $[RhCl(C_2H_4)_2]_2$ (100 mg,

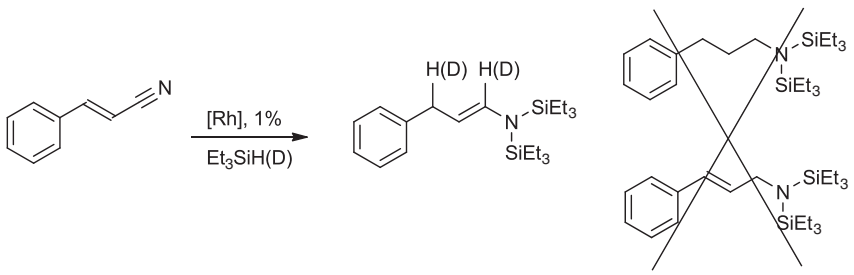


Figure 5. Selective hydrosilylation of cynamonitrile with catalyst **1**. Common by-products found in hydrosilylation of α,β-unsaturated nitriles have not been detected.

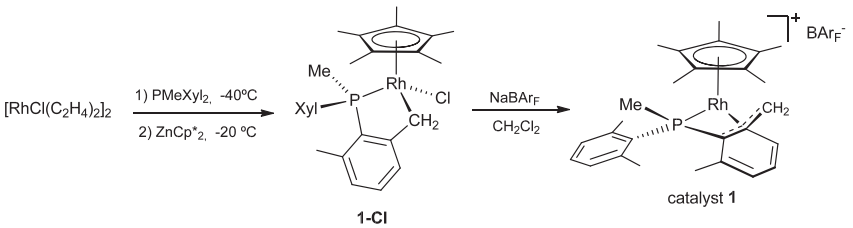


Figure 6. Synthesis of catalyst **1** (Xyl = 2,6-$C_6H_3Me_2$; BAr_F = B[3,5-$(CF_3)_2C_6H_3$]).

0.25 mmol) in 3 mL of THF. The reaction mixture is stirred for 3 h at this temperature. Then, a solution of $ZnCp_2$* (84 mg, 0.25 mmol) in 1 mL of THF is added, and the mixture is stirred for 5 h while allowing the temperature to reach −25 °C. The solvent is removed under vacuum and the residue extracted with diethyl ether and then evaporated to dryness. The crude is dissolved in 5 mL of CH_2Cl_2 and stirred for 3 h at room temperature. The solvent is removed under vacuum and the crude product washed with pentane to yield complex **1-Cl** as an orange solid in 83% yield. Anal. calc. for $C_{27}H_{35}ClPRh$: C, 61.3; H, 6.7. Found: C, 61.2; H, 6.6. ^1H, ^{13}C and ^{31}P NMR data can be found in the study by Campos *et al.*[18a]

*Synthesis of [(η^5-C_5Me_5)Rh{PMe(2,6-CH_2(Me)C_6H_3)(2,6-$Me_2C_6H_3$)}]$^+BAr_F^-$, (**1**)*

To a solid mixture of **1-Cl** (150 mg, 0.28 mmol) and $NaBAr_F$ (252 mg, 0.28 mmol) was added 5 mL of CH_2Cl_2. The reaction mixture was stirred for 10 min at room temperature, and after this time, the solution was filtered and the solvent evaporated under reduced pressure, to obtain an orange solid (350 mg, 95%). This complex can be crystallized from a 1:1 mixture of CH_2Cl_2 : pentane. Anal. calc. for $C_{59}H_{47}BF_{24}PRh$: C, 52.6; H, 3.5. Found: C, 53.0; H, 3.3. ^1H, ^{13}C and ^{31}P NMR data can be found in the study by Campos *et al.*[18a]

High-scale synthesis of deuterosilanes

[1-^2H]Triethylsilane ($SiEt_3D$)

Triethylsilane (5 mL, 31.30 mmol) was added under nitrogen to a pressure vessel (volume ~220 mL) containing catalyst **1** (4.2 mg, 3.1×10^{-3} mmol). The solution was cooled to 0 °C and nitrogen pumped out. Then, the flask was charged with deuterium (0.5 bar), and the mixture was vigorously stirred at 50 °C for 16 h. To exchange quantitatively the Si-H bond, we repeated the cooling at 0 °C/vacuum (0.1 bar)/D_2 (0.5 bar) process five times. The solution was transferred to a Young's ampoule and the deuterosilane purified by trap-to-trap distillation to obtain $SiEt_3D$ as a colourless liquid (3.49 g, 96% yield; 99% D-incorporation). IR (neat silane): 1530 cm^{-1}. ^1H NMR (500 MHz, C_6D_6, 25 °C) δ: 0.96 (t, 9H, $^3J_{HH}$ = 7.9 Hz, $3CH_3$), 0.53 (q, 6H, $^3J_{HH}$ = 7.9 Hz, $3CH_2$). $^{29}Si\{^1H\}$ NMR (99 MHz, C_6D_6) δ: 0.4 (t, $^1J_{SiD}$ = 28 Hz).

[1-^2H]dimethylphenylsilane ($SiMe_2PhD$)

The same procedure utilized to deuterate triethylsilane was employed but using dimethylphenylsilane (5 mL, 32.66 mmol) and catalyst **1** (4.4 mg, 3.2×10^{-3} mmol). Deuterated dimethylphenylsilane was purified by trap-to-trap distillation, and $SiMe_2PhD$ was obtained as a colourless liquid (4.15 g, 93% yield; 99% D-incorporation). IR (neat silane): 1540 cm^{-1}. ^1H NMR (500 MHz, C_6D_6, 25 °C) δ: 7.54 (m, 2H, Ph), 7.28 (m, 3H, Ph), 0.34 (s, 6H, $2CH_3$). $^{29}Si\{^1H\}$ NMR (99 MHz, C_6D_6) δ: −17.2 (t, $^1J_{SiD}$ = 29 Hz).

[1-$^2H_2$]Diphenylsilane ($SiPh_2D_2$)

The same procedure utilized to deuterate triethylsilane was employed but using diphenylsilane (5 mL, 26.86 mmol) and catalyst **1** (7.3 mg, 5.4×10^{-3} mmol). Deuterated diphenylsilane was purified by Kugelrohr distillation to obtain $SiPh_2D_2$ as a colourless oil (4.17 g, 84% yield; 99% D-incorporation). IR (Nujol): 1550 cm^{-1}. ^1H NMR (500 MHz, C_6D_6, 25 °C) δ: 7.30 (d, 4H, $^3J_{HH}$ = 7.8 Hz, *o*-Ph), 6.91 (m, 6H, *m*,*p*-Ph). $^{29}Si\{^1H\}$ NMR (99 MHz, C_6D_6) δ: −33.8 (quintet, $^1J_{SiD}$ = 30 Hz).

Determination of deuterium incorporation

The levels of deuteration exchange were checked by ^1H NMR, ^{29}Si NMR and IR spectroscopy. The level of deuteration was monitored by ^1H NMR spectroscopy. Exchange reactions were considered to be complete when no integrable ^1H signal for the Si-*H* atom could be detected. These results were confirmed by the disappearance of the characteristic signals in the ^{29}Si NMR and IR spectra. Signals for the hydrosilane and deuterosilane appear perfectly well resolved in the ^{29}Si NMR spectra because of the isotope effect on the chemical shift (Figure 3). The calculation of the deuterium percentage by ^{29}Si NMR is totally in accordance with the results obtained from the ^1H NMR analysis. The integration of the bands for ν(Si-H) (~2100 cm^{-1}) and ν(Si-D) (~1500 cm^{-1}) match up with the results obtained by ^1H and ^{29}Si NMR (Figure 4).

General method for the hydrosilylation of C-O and C-N multiple bonds

In a typical experiment, a 2-mL screwcap glass vial was charged with catalyst **1** (0.7 mg, 0.5×10^{-3} mmol), the hydrosilane (1.1 mmol), the organic substrate (0.5 mmol) and CD_2Cl_2 (0.5 mL) in a glove box. After stirring for 1 h, we transferred the reaction mixture to a screwcap NMR tube and checked the reaction progress by ^1H NMR spectroscopy.

General method for the direct deuterosilylation of C-O and C-N multiple bonds

In a typical experiment, a Young's ampoule was charged with catalyst **1** (0.7 mg, 0.5×10^{-3} mmol), triethylsilane (89 μL, 0.55 mmol) and CD_2Cl_2. The solution was cooled to 0 °C, argon pumped out and replaced by D_2 (0.5 bar). The solution was stirred at room temperature for 10 min and then cooled at 0 °C, the gas atmosphere pumped out and replaced by D_2 (0.5 bar). After repeating this cycle for a total of three times, the organic substrate (0.25 mmol) was added and the mixture transferred to a screwcap NMR tube. The reaction progress was monitored by ^1H NMR spectroscopy.

Characterization of compounds

Hydrosilylation of (R)-camphor by hydrosilanes R_nSiH_{4-n} (entries 3–7, Table 1)

Using the general procedure at 50 °C, we hydrosilylated *R*-camphor (0.015 g, 0.1 mmol). Spectroscopic data of the reaction mixture were consistent with previously reported data for these compounds.[26]

^{1}H NMR (500 MHz, CD_2Cl_2): **$SiEt_3H$** (entry 3, Table 1; 46% *endo*, 54% *exo*): characteristic signals, δ 3.94 (m, 1H, *endo* isomer), 3.57 (dd, $^3J_{HH}$ = 7.9, 3.5 Hz, 1H, *exo* isomer). **$SiPh_2H_2$** (entry 4, Table 1; 30% *endo*, 70% *exo*): characteristic signals, δ 4.26 (m, 1H, *endo* isomer), 3.85 (dd, $^3J_{HH}$ = 7.8, 3.2 Hz, 1H, *exo* isomer). **$SiMe_2PhH$** (entry 6, Table 1; 30% *endo*, 70% *exo*): characteristic signals, δ 4.03 (m, 1H, *endo* isomer), 3.65 (dd, $^3J_{HH}$ = 7.5, 3.0 Hz; 1H, *exo* isomer).

Hydrosilylation of benzylideneacetone (entries 8 and 9, Table 1)

Using the general procedure at 50 °C, we hydrosilylated benzylideneacetone (0.015 g, 0.1 mmol). Spectroscopic data of the 1,2-addition and 1,4-addition products were consistent with previously reported data for these compounds.[27]

^{1}H NMR (400 MHz, CD_2Cl_2): **$SiEt_3H$** (entry 8, Table 1): characteristic signals, δ 6.56 (d, $^3J_{HH}$ = 16.0 Hz; =*CH*, 1,2-addition product), 6.27 (dd, $^3J_{HH}$ = 16.0, 6.0 Hz; =*CH*, 1,2-addition product), 4.90 (t, $^3J_{HH}$ = 7.5 Hz, =*CH*, *E*-1,4-addition product), 4.64 (t, $^3J_{HH}$ = 7.0 Hz, =*CH*, *Z*-1,4-addition product), 4.52 (m, *CH*, 1,2-addition product), 3.42 (d, $^3J_{HH}$ = 7.0 Hz, CH_2, *Z*-1,4-addition product), 3.34 (d, $^3J_{HH}$ = 8.0 Hz, CH_2, *E*-1,4-addition product). **$SiMe_2PhH$** (entry 9, Table 1): characteristic signals, δ 6.49 (d, $^3J_{HH}$ = 16.0 Hz; =*CH*, 1,2-addition product), 6.25 (dd, $^3J_{HH}$ = 16.0, 6.0 Hz; =*CH*, 1,2-addition product), 4.88 (t, $^3J_{HH}$ = 7.5 Hz, =*CH*, *E*-1,4-addition product), 4.69 (d, $^3J_{HH}$ = 7.0 Hz, =*CH*, *Z*-1,4-addition product), 4.53 (m, *CH*, 1,2-addition product), 3.39 (d, $^3J_{HH}$ = 7.0 Hz, CH_2, *Z*-1,4-addition product), 3.30 (d, $^3J_{HH}$ = 7.5 Hz, CH_2, *E*-1,4-addition product).

Deuterosilylation of benzylideneacetone (entry 10, Table 1)

Using the general procedure at 25 °C, we hydrosilylated benzylideneacetone (0.015 g, 0.1 mmol) by [1-^{2}H]-triethylsilane. Spectroscopic data of the non-deuterated 1,2-addition[27a] and 1,4-addition products[27b] were consistent with previously reported data for these compounds.

^{1}H NMR (400 MHz, CD_2Cl_2): characteristic signals, δ 6.53 (d, $^3J_{HH}$ = 16.0 Hz; =*CH*, 1,2-addition product), 6.25 (d, $^3J_{HH}$ = 16.0 Hz; =*CH*, 1,2-addition product), 4.85 (d, $^3J_{HH}$ = 7.5 Hz, =*CH*, *E*-1,4-addition product), 4.61 (d, $^3J_{HH}$ = 7.0 Hz, =*CH*, *Z*-1,4-addition product), 3.36 (bd, $^3J_{HH}$ = 7.0 Hz, CH_2, *Z*-1,4-addition product), 3.29 (bd, $^3J_{HH}$ = 7.5 Hz, CH_2, *E*-1,4-addition product).

Hydrosilylation of cinnamaldehyde (entries 11 and 12, Table 1)

Using the general procedure at 25 °C, we hydrosilylated cinnamaldehyde (13 μL, 0.1 mmol). Spectroscopic data of the 1,2-addition and *E*-1,4-addition products were consistent with previously reported data for these compounds.[28]

$SiEt_3H$ (entry 11, Table 1) ^{1}H NMR (400 MHz, CD_2Cl_2): characteristic signals, δ 6.63 (d, $^3J_{HH}$ = 16.0 Hz; =*CH*, 1,2-addition product), 6.39 (dt, $^3J_{HH}$ = 12.0, 1.2 Hz; =*CH*, *E*-1,4-addition product), 6.33 (dt, $^3J_{HH}$ = 16.0, 5.2 Hz; =*CH*, 1,2-addition product), 5.19 (dt, $^3J_{HH}$ = 12.0, 7.5 Hz; =*CH*, *E*-1,4-addition product), 4.76 (m, =*CH*, *Z*-1,4-addition product), 4.37 (dd, $^3J_{HH}$ = 5.2, 1.6 Hz; CH_2, 1,2-addition product), 3.26 (d, $^3J_{HH}$ = 7.5; CH_2, *E*-1,4-addition product). **$SiMe_2PhH$** (entry 12, Table 1) ^{1}H NMR (500 MHz, CD_2Cl_2): characteristic signals, δ 6.60 (d, $^3J_{HH}$ = 16.0 Hz; =*CH*, 1,2-addition product), 6.39 (dt, $^3J_{HH}$ = 12.0, 1.2 Hz; =*CH*, *E*-1,4-addition product), 6.32 (dt, $^3J_{HH}$ = 16.0, 5.5 Hz; =*CH*, 1,2-addition product), 5.20 (dt, $^3J_{HH}$ = 12.0, 7.5 Hz; =*CH*, *E*-1,4-addition product), 4.75 (m, =*CH*, *Z*-1,4-addition product), 4.36 (dd, $^3J_{HH}$ = 5.5, 2.0 Hz; CH_2, 1,2-addition product), 3.20 (d, $^3J_{HH}$ = 7.5; CH_2, *E*-1,4-addition product).

Deuterosilylation of cinnamaldehyde (entries 13 and 14, Table 1)

Using the general procedure at 25 °C, we deuterosilylated cinnamaldehyde (13 μL, 0.1 mmol). Spectroscopic data of the products were consistent with those of the non-labelled compounds.

^{1}H NMR (400 MHz, CD_2Cl_2): **$SiEt_3D$** (entry 13, Table 1): characteristic signals, δ 6.60 (d, $^3J_{HH}$ = 16.0 Hz; =*CH*, 1,2-addition product), 6.39 (dd, $^3J_{HH}$ = 12.0, 1.2 Hz; =*CH*, *E*-1,4-addition product), 6.31 (dd, $^3J_{HH}$ = 16.0, 5.5 Hz; =*CH*, 1,2-addition product), 5.12 (dd, $^3J_{HH}$ = 12.0, 7.5 Hz; =*CH*, *E*-1,4-addition product), 4.70 (m, =*CH*, *Z*-1,4-addition product), 4.32 (bs, CH_2, 1,2-addition product), 3.21 (bd, $^3J_{HH}$ = 7.5; CH_2, *E*-1,4-addition product). **$SiMe_2PhD$** (entry 14, Table 1): characteristic signals, δ 6.60 (d, $^3J_{HH}$ = 16.0 Hz; =*CH*, 1,2-addition product), 6.38 (dd, $^3J_{HH}$ = 12.0, 1.2 Hz; =*CH*, *E*-1,4-addition product), 6.32 (dd, $^3J_{HH}$ = 16.0, 5.5 Hz; =*CH*, 1,2-addition product), 5.19 (dd, $^3J_{HH}$ = 12.0, 7.5 Hz; =*CH*, *E*-1,4-addition product), 4.74 (m, =*CH*, *Z*-1,4-addition product), 4.36 (bs, CH_2, 1,2-addition product), 3.20 (d, $^3J_{HH}$ = 7.5; CH_2, *E*-1,4-addition product).

Hydrosilylation of ethyl pyruvate (entry 16, Table 1)

Using the general procedure at 50 °C, we hydrosilylated ethyl pyruvate (0.012 g, 0.1 mmol) by triethylsilane. Spectroscopic data of the reaction mixture were consistent with previously reported data for this compound.[29]

^{1}H NMR (500 MHz, CD_2Cl_2): characteristic signals, δ 4.30 (q, $^3J_{HH}$ = 6.8 Hz, CH_3CH), 4.13 (q, $^3J_{HH}$ = 7.0 Hz, OCH_2CH_3), 1.36 (d, $^3J_{HH}$ = 6.8 Hz, CH_3CH), 1.26 (t, $^3J_{HH}$ = 7.0 Hz, OCH_2CH_3).

Hydrosilylation of N-benzylidene aniline (entry 1, Table 2)

Using the general procedure at 50 °C, we hydrosilylated *N*-benzylidene aniline (0.018 g, 0.1 mmol) by triethylsilane. Spectroscopic data of the reaction mixture were consistent with previously reported data for this compound.[18a]

^{1}H NMR (500 MHz, CD_2Cl_2): characteristic signals, δ 7.31 (d, $^3J_{HH}$ = 4.3 Hz, Ph), 7.22 (m, Ph), 7.17 (t, $^3J_{HH}$ = 7.9 Hz, Ph), 6.99 (d, $^3J_{HH}$ = 8.1 Hz, Ph), 6.83 (t, $^3J_{HH}$ = 7.3 Hz, Ph), 4.63 (s, CH_2N), 1.04 (t, $^3J_{HH}$ = 7.8 Hz, $SiCH_2CH_3$), 0.89 (q, $^3J_{HH}$ = 7.8 Hz, $SiCH_2CH_3$).

Deuterosilylation of cinnamaldehyde (entry 2, Table 2)

Using the general procedure at 25 °C, we deuterosilylated *N*-benzylidene aniline (18 mg, 0.1 mmol) by [1-^{2}H]-triethylsilane. Spectroscopic data of the deuterosilylated product were consistent with those of the non-labelled compound.

^{1}H NMR (500 MHz, CD_2Cl_2): characteristic signals, δ 7.28 (d, $^3J_{HH}$ = 4.3 Hz, Ph), 7.20 (m, Ph), 7.15 (t, $^3J_{HH}$ = 7.8 Hz, Ph), 6.96 (d, $^3J_{HH}$ = 8.1 Hz, Ph), 6.80 (t, $^3J_{HH}$ = 7.5 Hz, Ph), 4.58 (br s, *CH*DN), 1.02 (t, $^3J_{HH}$ = 7.8 Hz), 0.86 (q, $^3J_{HH}$ = 7.8 Hz, 6H).

Hydrosilylation of N-benzyliden-*t*-butylamine (entry 3, Table 2)

Using the general procedure at 50 °C, we hydrosilylated *N*-benzyliden-*t*-butylamine (18 μL, 0.1 mmol) by triethylsilane.

^{1}H NMR (400 MHz, CD_2Cl_2): characteristic signals, δ 4.14 (s, N-C*H*-Si, C-Si isomer), 3.75 (s, CH_2-NSi, C-N isomer), 1.22 (s, ^{t}Bu, C-Si isomer), 1.19 (s, ^{t}Bu, C-N isomer).

Hydrosilylation of (E)-N-(1-phenylethylidene)aniline (entry 4, Table 2)

Using the general procedure at 50 °C, we hydrosilylated ketimine (*E*)-*N*-(1-phenylethylidene)aniline (0.020 mg, 0.1 mmol) by triethylsilane. Spectroscopic data of the reaction mixture were consistent with previously reported data for this compound.[30]

^{1}H NMR (300 MHz, CD_2Cl_2): characteristic signals, δ 6.7 (d, $^3J_{HH}$ = 8.2 Hz, N-Ph(*o*)), 4.52 (q, $^3J_{HH}$ = 6.7 Hz, CH_3C*H*-N), 1.62 (d, $^3J_{HH}$ = 6.7 Hz, CH_3CH-N).

Hydrosilylation of (E)-N-(1-phenylethylidene)aniline (entry 5, Table 2)

Using the general procedure at 50 °C, acetonitrile (5 μL, 0.1 mmol) was hydrosilylated by triethylsilane.

^{1}H NMR (500 MHz, CD_2Cl_2): characteristic signals, δ 2.88 (q, $^3J_{HH}$ = 7.4 Hz, CH_3CH_2N), 0.84 (t, $^3J_{HH}$ = 7.4 Hz, CH_3CH_2N).

Hydrosilylation of cinnamonitrile (entry 7, Table 2)

Using the general procedure at 50 °C, we hydrosilylated cinnamonitrile (0.013 mg, 0.1 mmol) by triethylsilane.

^{1}H NMR (400 MHz, CD_2Cl_2): characteristic signals, δ 7.29 (t, $^3J_{HH}$ = 7.4 Hz, Ph), 7.19 (m, Ph), 6.05 (d, $^3J_{HH}$ = 13.4 Hz, HC=C*H*-N), 5.22 (m, *H*C=CH-N), 3.30 (d, $^3J_{HH}$ = 12.9 Hz, CH_2), 0.96 (t, $^3J_{HH}$ = 7.9 Hz, SiCH$_2$CH_3), 0.67 (q, $^3J_{HH}$ = 7.9 Hz, SiCH_2CH$_3$). ^{13}C NMR (100 MHz, CD_2Cl_2): characteristic signals, δ 142.2 (*C* quat), 135.3 (HC=*C*H-N), 128.6 (*o*-*C*), 126.0 (*m*-*C*), 120.4 (*p*-*C*), 37.0 (H*C*=CH-N), 8.3 (Si*C*H$_2$CH$_3$), 5.2 (SiCH$_2$*C*H$_3$).

Deuterosilylation of cinnamonitrile (entry 8, Table 2)

Using the general procedure at 50 °C, we deuterosilylated cinnamonitrile (13 mg, 0.1 mmol) by [1-^{2}H]-triethylsilane. Spectroscopic data of the deuterosilylated product were consistent with those of the non-labelled compound.

^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.30 (t, $^3J_{HH}$ = 7.4 Hz, Ph), 7.21 (m, Ph), 5.22 (d, $^3J_{HH}$ = 6.7 Hz, *H*C=CH-N), 3.31 (d, $^3J_{HH}$ = 6.7 Hz, CH_2), 0.98 (t, $^3J_{HH}$ = 7.9 Hz, SiCH$_2$CH_3), 0.69 (q, $^3J_{HH}$ = 7.9 Hz, SiCH_2CH$_3$).

Hydrosilylation of ciclohex-1-ene-1-carbonitrle (entry 9, Table 2)

Using the general procedure at 80 °C, we hydrosilylated ciclohex-1-ene-1-carbonitrle (0.011 mg, 0.1 mmol) by triethylsilane.

^{1}H NMR (400 MHz, CD_2Cl_2): δ 5.64 (s, C=C*H*-N), 2.19 (m, *o*-CH_2), 2.05 (m, *o*-CH_2), 1.55 (m, *m*,*p*-CH_2), 4.63 (s, CH_2N), 0.97 (t, $^3J_{HH}$ = 7.6 Hz, SiCH_2CH$_3$), 0.64 (q, $^3J_{HH}$ = 7.6 Hz, SiCH$_2$CH_3). ^{13}C NMR (100 MHz, CD_2Cl_2): δ 136.7 (*C* quat), 125.4 (C=CH-N), 34.2 (*o*-*C*), 28.8 (*o*-*C*), 28.2 (*m*-*C*), 27.6 (*m*-*C*), 27.3 (*p*-*C*), 8.0 (SiCH$_2$CH$_3$), 6.2 (SiCH$_2$*C*H$_3$).

Conclusions

In summary, we have described a large-scale synthesis (3–4 g) of the D-isotopologues of three common and widely used hydrosilanes, namely $SiEt_3D$, $SiMe_2PhD$ and $SiPh_2D_2$. The simplicity of the process and its generality, along with the stability of the catalyst in air and its recyclability, make our system attractive for practical use. Extension of this procedure to the preparation of the tritium analogues with high specific activity should be feasible too, but it has not been attempted because of our lack of suitable experimental facilities. We have also developed some labelling reactions of the deuterated silanes with their application to the catalytic deuterosilylation of some organic molecules containing C=O, C=N and C≡N bonds.

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Conflict of Interest

The authors did not report any conflict of interest.

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