CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200701415

$(Me_3Si)_3SiH$: Twenty Years After Its Discovery as a Radical-Based Reducing Agent

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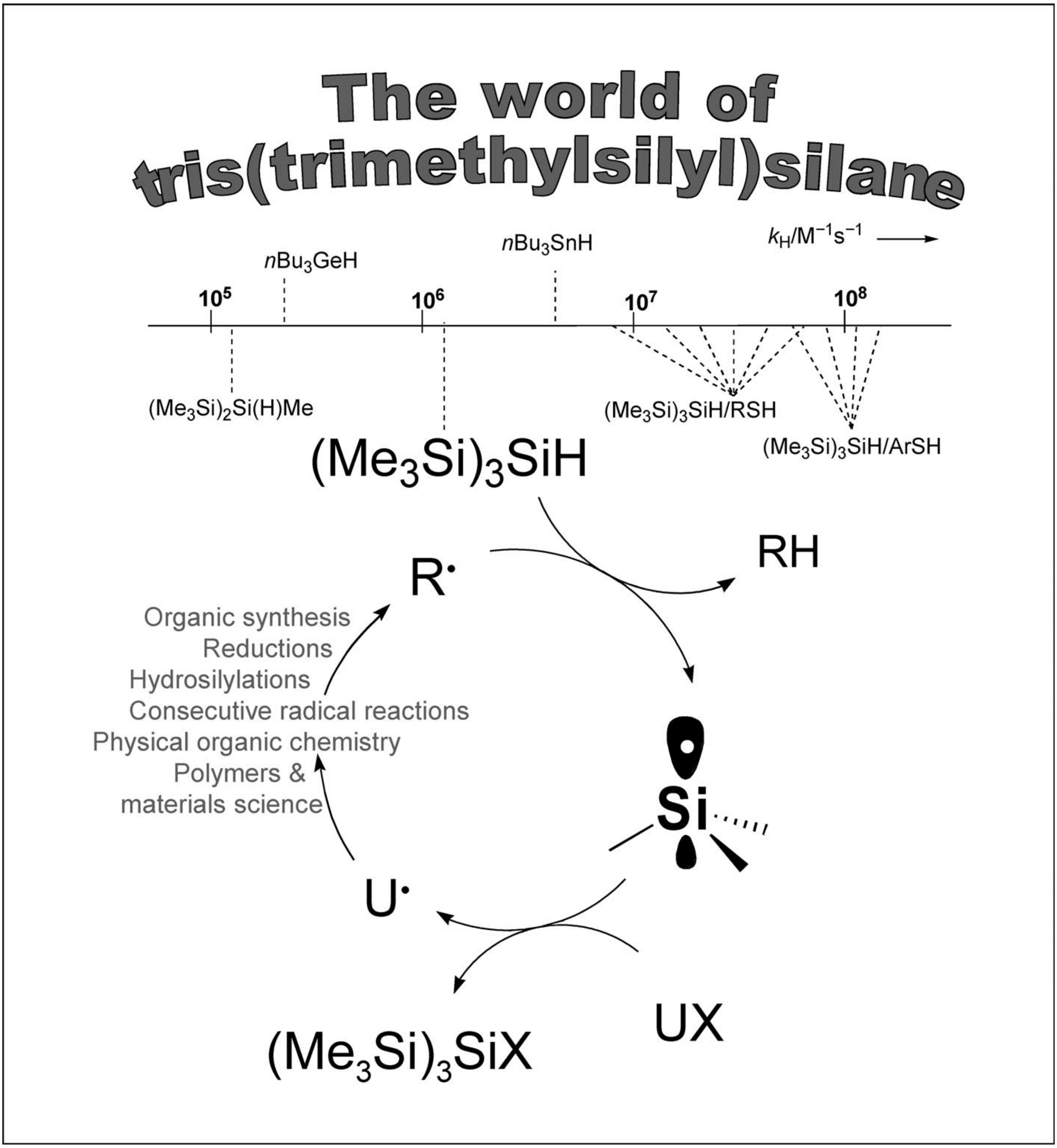


Abstract: This Concept shows the flexibility and applicability of $(Me_3Si)_3SiH$ in several synthetic transformations, such as radical reductions, consecutive radical reactions and hydrosilylation. The reactivity of $(Me_3Si)_3SiH$ combines the multidisciplinary aspects of physical organic chemistry and organic synthesis, extending to polymers and materials science, as in the functionalization of flat silicon surfaces.

Keywords: hydrosilylation • radical reactions • reduction • silicon surfaces • tris(trimethylsilyl)silane

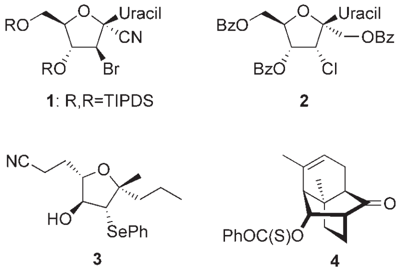
Introduction

Tris(trimethylsilyl)silane, $(Me_3Si)_3SiH$, was synthesized by Gilman and co-workers in 1965 and was then almost totally forgotten for the next 20 years,[1] until our laboratory discovered that this material could serve as a radical-based reducing agent. The rebirth of $(Me_3Si)_3SiH$ represents one example of Sleeping Beauty in chemistry! My lecture on "Novel Silanes as Radical Reducing Agents" was presented at the Gordon Research Conference on Free Radical Reactions in 1987 and was followed by two relevant communications.[2,3] In 1990, this discovery was awarded with the Fluka prize as "Reagent of the Year".

Twenty years of use of the $(Me_3Si)_3SiH$ reagent in various laboratories world-wide have revealed the potential of this reagent, thereby stimulating further interest in organosilanes as safe and efficient reagents for radical chemistry. Overall, organic free radical chemistry has suffered (and still does) due to the use of toxic tin compounds. New reagents and reactions have been introduced and new modus operandi revealed, which will certainly motivate the abandon of traditional choices. Additionally, the radical chemistry associated with $(Me_3Si)_3SiH$ has been applied to polymers and in materials science. For example, radical reactions have been found to be the most convenient method for the organic modification of hydrogen-terminated silicon surfaces.

The radical chemistry of organosilanes has been the subject of periodical reviews, which mainly focused on $(Me_3Si)_3SiH$.[4–9] In this article, some recent examples of $(Me_3Si)_3SiH$ as a mediator, attractive either from the synthetic or mechanistic point of view, will be presented, and based on the state-of-the-art the future potential of this reagent will be indicated. Silicon surfaces will be included, expanding the area to the synthetic architecture of monolayers.

The $(Me_3Si)_3SiH$ reagent: The majority of radical reactions of interest to synthetic chemists are chain processes. In this context, $(Me_3Si)_3SiH$ is an effective reducing agent for the removal of a variety of functional groups. Examples of dehalogenation and reductive removal of chalcogen groups are shown in Scheme 1 for bromide **1**, chloride **2** and selenide **3**.[10–13] For the removal of the hydroxy group, the strategy starts from a thiocarbonyl derivative (e.g., *O*-arylthiocarbonate, *O*-thioxocarbamate, thiocarbonyl imidazole or xanthate) or a selenocarbonate. An example is provided using the *O*-phenylthiocarbonate **4** (Scheme 1).[14] This reaction has important applications in nucleoside chemistry, where it can be very useful in going from the ribose to the 2-deoxyribose series, a step often required in medicinal chemistry. The need for non-toxic reagents to achieve this step is evident, since the compounds have to be tested for biological assays and even traces of toxic by-products can affect results. From this simple example it is clear that the arrival of the silane reagent onto the scene resulted in a great advancement for radical chemistry, since chemical and biological issues were satisfied simultaneously.



Scheme 1. Removal of functional group (yields are in parentheses) of bromide **1** (94%), chloride **2** (92%), phenyl selenide **3** (97%), or *O*-phenylthiocarbonate **4** (88%) by reaction with $(Me_3Si)_3SiH$ at 80°C (or 110°C for **3**) in toluene using AIBN (2,2′-azobisisobutyronitrile) as the radical initiator [Bz: C(O)Ph, TIPDS: $Si(iPr)_2OSi(iPr)_2$].

A variety of acyl derivatives (such as acyl chlorides,[15] phenylseleno esters[16] or *N*-hydroxypyridine-2-thione esters[17]) can be used for decarbonylation and reductive decarboxylation with $(Me_3Si)_3SiH$. Together with the decarboxylation step, as in the case of the chiral *cis*-cyclopropane structure **5** designed for antidopaminergic activity (Scheme 2),[17] another feature of the radical reactivity of $(Me_3Si)_3SiH$ is the diastereoselective outcome. The hydrogen abstraction from the sterically demanding $(Me_3Si)_3SiH$ preferably occurs from the less-hindered side of the intermediate cyclopropyl radical, thus affording a very high *cis*-selectivity. The wide range of functional groups that can react with $(Me_3Si)_3SiH$ includes isocyanides, reduced to the corresponding hydrocarbons.[18] Synthesis of secondary amines

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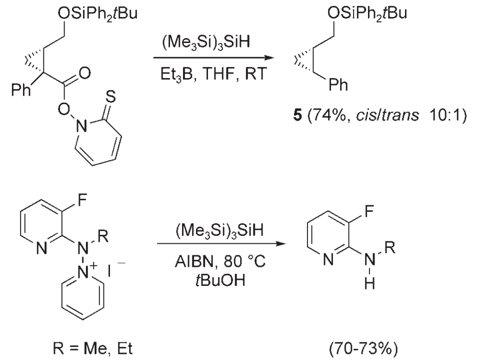
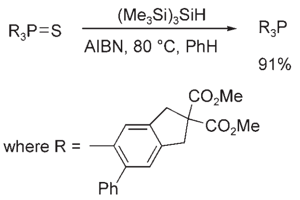


Scheme 2. Removal of functional group by reaction with $(Me_3Si)_3SiH$.

can be achieved either by replacement of a pyridinium moiety with hydrogen (Scheme 2)[19] or by reduction of nitroxides.[20]

$(Me_3Si)_3SiH$ is useful for the reduction of phosphine sulfides and phosphine selenides under free radical conditions to give the corresponding phosphines or, after treatment with BH_3•THF, the corresponding phosphine–borane complex in good to excellent yields.[21] Stereochemical studies on P-chiral phosphine sulphides have shown that these reductions proceed with retention of configuration. This desulfidation protocol has recently been applied with success for the synthesis of bulky phosphines (e.g., Scheme 3)[22] or (*Z*)-1,2-diphosphino-1-alkenes.[23] It is worth underlining that in these reactions the ejected silanethiyl radical undergoes a fast 1,2-migration of silyl group from silicon to sulfur, affording a new silyl radical that either reacts with $(Me_3Si)_3SiH$, completing the reaction cycle (Scheme 4), or replaces the $(Me_3Si)_3Si^{\bullet}$ radical in the reaction sequence.[24]



Scheme 3. Desulfidation of a bulky phosphine.

$$(Me_3Si)_3SiS^{\bullet} \longrightarrow (Me_3Si)_2\dot{Si}SSiMe_3$$

$$(Me_3Si)_2\dot{Si}SSiMe_3 + (Me_3Si)_3SiH \longrightarrow (Me_3Si)_2Si(H)SSiMe_3 + (Me_3Si)_3Si^{\bullet}$$

Scheme 4. Reaction sequence indicating how the $(Me_3Si)_3SiS^{\bullet}$ radical rearranges and allows for propapagation of the chain reaction.

All the reduction processes described above, include a propagation step where hydrogen is abstracted from the Si-H moiety. For such a fundamental step, kinetic studies have been performed with a large variety of radicals towards $(Me_3Si)_3SiH$.[25] In Figure 1, the scale of rate constants of hydrogen abstraction from a few Group 14 hydrides by primary alkyl radicals at about 80 °C is provided. The rate constant for $(Me_3Si)_3SiH$ is only about five times slower than that of nBu$_3$SnH. The contribution of Me_3Si groups on the reactivity of $(Me_3Si)_3SiH$ can be appreciated in the analogous silane, where one Me_3Si group is replaced by Me[26] that is 10 times slower.

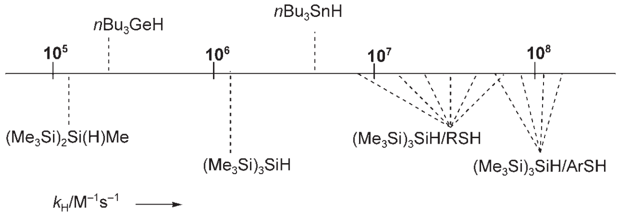


Figure 1. Rate constants for H-atom abstraction from a variety of reducing systems by primary alkyl radicals at 80 °C.

The particular reactivity of $(Me_3Si)_3SiH$ has promoted further advancement for fast trapping reducing systems. The $(Me_3Si)_3SiH$/thiol pair is a brilliant example of such systems.[27,28] The mechanism in Scheme 5 illustrates the propagation steps with 2-mercaptoethanol as the thiol. Its role is to act as hydrogen donor and then to be regenerated by reaction of thiyl radical with silane. This reactivity can be employed to study the fast reaction of carbon-centered radicals with thiols, using the free-radical clock methodology.[27] The rate constants of primary alkyl radicals with $(Me_3Si)_3SiH$/RSH and $(Me_3Si)_3SiH$/ArSH are in the range of $0.9–8 \times 10^7$ and $0.75–1.5 \times 10^8\,\text{M}^{-1}\,\text{s}^{-1}$, respectively, at 80 °C (Figure 1). Therefore, the $(Me_3Si)_3SiH$-based methodology covers a few orders of magnitude in terms of hydrogen-atom donation, allowing for the selection of the best system to achieve the desired synthetic transformation. The fact that $(Me_3Si)_3SiH$ was developed with a strong contribution from physical organic chemistry in determining rate constants and thermodynamic parameters, has certainly contributed to the confidence in its application due to the predictability of its behavior.

$$(Me_3Si)_3Si^{\bullet} + RX \longrightarrow (Me_3Si)_3SiX + R^{\bullet}$$

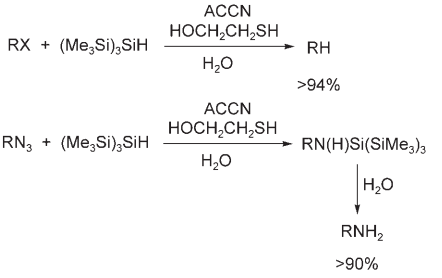
$$R^{\bullet} + HOCH_2CH_2SH \longrightarrow RH + HOCH_2CH_2S^{\bullet}$$

$$HOCH_2CH_2S^{\bullet} + (Me_3Si)_3SiH \longrightarrow HOCH_2CH_2SH + (Me_3Si)_3Si^{\bullet}$$

Scheme 5. Propagation steps for the removal of the X group from the $(Me_3Si)_3SiH/HOCH_2CH_2SH$ reducing system.

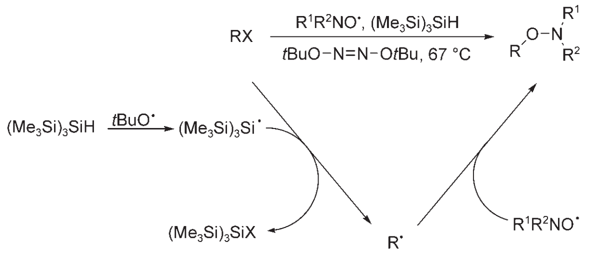
Some physical and chemical characteristics of $(Me_3Si)_3SiH$ have also been important in its further development. $(Me_3Si)_3SiH$ is not soluble in water and does not suffer significantly after reaction with water at 100 °C for several hours, motivating interest in applying it to radical reactions in water. Water-insoluble substrates, suspended with

$(Me_3Si)_3SiH$ and the radical initiator ACCN [1,1′-azobis(cyclohexanecarbonitrile)], in aqueous medium at 100 °C under vigorous stirring, can be reduced in good yields.[29] This procedure does not work with water-soluble substrates, however when a catalytic amount of the amphiphilic 2-mercaptoethanol is coupled to $(Me_3Si)_3SiH$, it becomes a very efficient system for the reduction of different organohalides (Scheme 6). This protocol has successfully been extended to the reduction of aliphatic and aromatic azides to the corresponding primary amines, in yields ranging from 90 % to quantitative (Scheme 6).[29] The reaction mechanism is analogous to that in Scheme 5, that is, after the addition of $(Me_3Si)_3Si^{\bullet}$ radical to the azide moiety, liberation of nitrogen, and formation of a silyl-substituted aminyl radical, the thiol serves as the hydrogen atom donor. Hydrolysis of the silylamine afforded the amine as the final product. These procedures illustrate the flexibility of $(Me_3Si)_3SiH$ as the radical-based reducing agent of choice in different media, as well as additional benefits, including the possibility to work with unprotected substrates, its purification and satisfactory environmental impact.



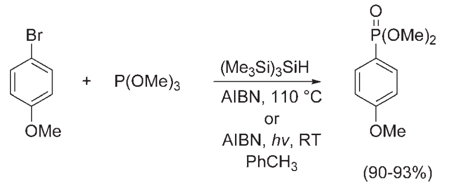
Scheme 6. Reduction of water-soluble halides or azides using the $(Me_3Si)_3SiH/HOCH_2CH_2SH$ pair [ACCN: 1,1′-azobis(cyclohexanecarbonitrile)].

The large reactivity of $(Me_3Si)_3SiH$ can be useful in generating a variety of carbon-centered radicals, for example, primary, secondary, tertiary, benzylic, allylic, and α-carbonyl, to be trapped by the desired agent. This method can be used to access otherwise structurally poor reagents. The *N*-alkoxylamines, a class of initiators in "living" radical polymerization (Scheme 7), represent an example.[30] The synthesis is mediated by $(Me_3Si)_3SiH$, used to generate C-centered radicals from alkyl bromides or iodides that are trapped in situ by stable nitroxide radicals. However, the reaction is not a radical chain process and stoichiometric quantities of the radical initiator (*t*BuONNO*t*Bu) are required.



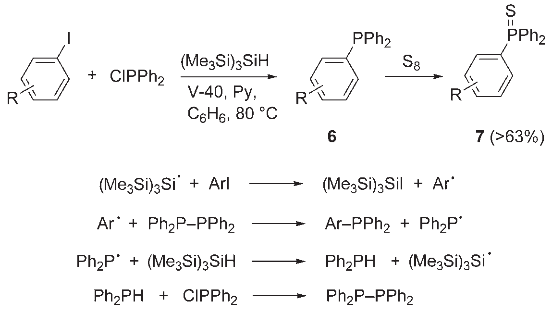
Scheme 7. Synthesis of *N*-alkoxyamines mediated by $(Me_3Si)_3SiH$ using stoichiometric quantities of initiator.

Other C−heteroatom bonds can be similarly prepared. The intermolecular C−P bond formation via radical phosphonation[31] and phosphination[32] has been achieved by reaction of aryl halides with trialkyl phosphites and chlorodiphenylphosphine, respectively, in the presence of $(Me_3Si)_3SiH$ under standard radical conditions. The phosphonation reaction worked well either under UV irradiation at room temperature or in refluxing toluene (Scheme 8).



Scheme 8. Radical phosphonation mediated by $(Me_3Si)_3SiH$.

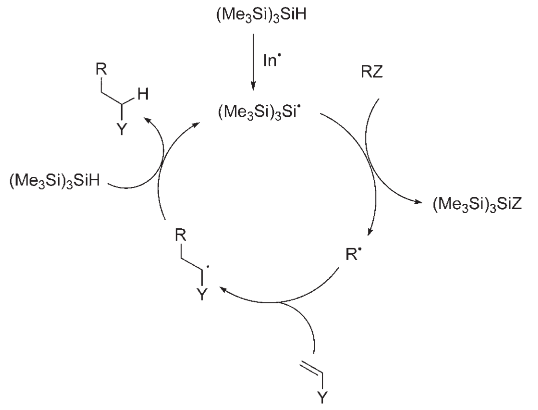
The radical phosphination required pyridine in boiling benzene for 20 h. Phosphinated products **6** were handled as phosphine sulfides **7** (Scheme 9). The reaction mechanism for the phosphination procedure involving the in situ formation of tetraphenylbiphosphine is also shown in Scheme 9. This approach has been extended to the phosphination of alkyl halides and the sequential radical cyclization/phosphination reaction.[32]



Scheme 9. Radical phosphination mediated by $(Me_3Si)_3SiH$.

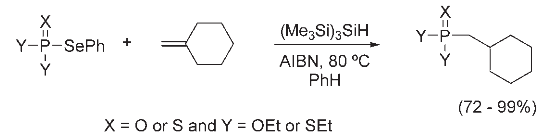
$(Me_3Si)_3SiH$ in consecutive radical reactions: Synthetic strategies based on multi-step radical reactions have steadily grown in popularity. $(Me_3Si)_3SiH$ as a mediator has contributed substantially to this area, often giving the best results, compared to other reducing reagents, by coupling reactivity with stereoselectivity,.[5–7] Nicolaou and co-workers found $(Me_3Si)_3SiH$ to be a superior reagent in the radical-based approach towards the synthesis of azadirachtin, an antifeedant agent used as insecticide, as well as in other related systems.[33]

The radical chain reaction for the reductive alkylation of alkenes by $(Me_3Si)_3SiH$ is reported in Scheme 10.[34] The key step in these consecutive reactions generally involves the intra- or intermolecular addition of $R^\bullet$ to a multiple-bonded carbon acceptor. This sequence requires a radical reagent which is fast to abstract the group Z from the starting material, but not too fast to reduce the corresponding $R^\bullet$ prior its addition to the multiple bonds. $(Me_3Si)_3SiH$ characteristics correspond well with these features, since the reagent is a slightly slower hydrogen donor than nBu$_3$SnH (cf. Figure 1).



Scheme 10. Propagation steps for the reductive alkylation of alkenes by $(Me_3Si)_3SiH$. The carbon-centered radical $R^\bullet$, resulting from the initial atom (or group) removal by a silyl radical, can be designed to undergo a number of consecutive reactions prior to H-atom transfer ($In^\bullet$ is the radical derived from the initiator).

Some examples have been chosen from the recent literature to illustrate the synthetic and mechanistic peculiarities of the $(Me_3Si)_3SiH$ reagent. Phosphorous–carbon bond formation using four structurally different phenylseleno derivatives with 3 equiv of $(Me_3Si)_3SiH$ and AIBN in refluxing benzene for 2 h is depicted in Scheme 11. The reaction

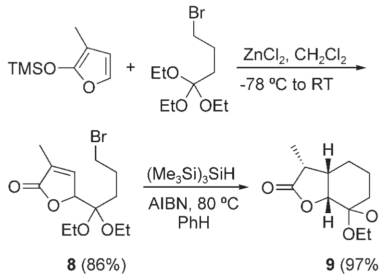


Scheme 11. Reductive phosphorylation of alkenes by $(Me_3Si)_3SiH$.

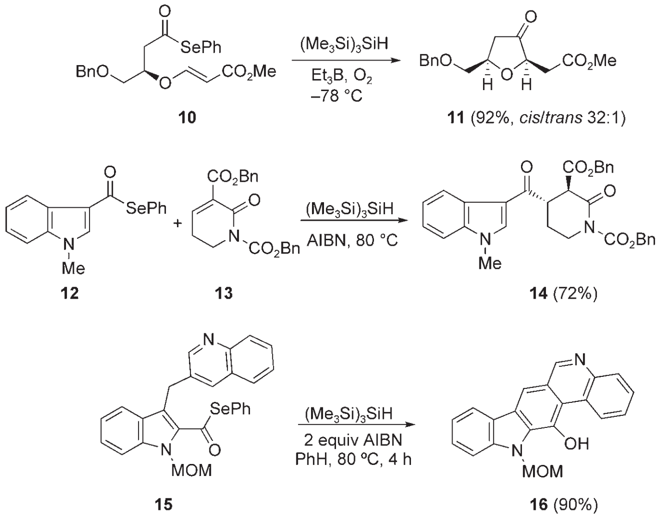
mechanism is analogous to the one reported in Scheme 10. Comparative studies on the reaction of the four phosphorus-centered radicals have been obtained. Although the reaction with 1-methylene cyclohexane is efficient with all four derivatives, a different selectivity is observed with electron-rich or electron-poor alkenes.[35]

An example of efficient two-step annelation of functionalized orthoesters with trimethylsilyloxyfuran derivatives to produce bicyclo[3.n.0]lactones[36] is given in Scheme 12. The radical cyclization and the subsequent hydrogen abstraction to afford **9** occurs efficiently and with complete diastereocontrol, resulting in two contiguous stereocenters generated with >95% stereoselectivity.

The removal of PhSe group can be employed in strategies where the generated acyl radicals can lead to C–C bond formation under diverse experimental conditions, as shown in Scheme 13. This sequence has been widely used both for the construction of heterocyclic natural products and for its stereochemical potential. The cyclization of **10** is the key step for the enantioselective synthesis of nonisoprenoid sesquiterpene (−)-kumausallene by radical cyclization at −78 °C. The product is obtained in a 32:1 mixture in favor of the 2,5-*cis* diastereoisomer.[37] The intermolecular C–C bond formation with the lactam ester **13** affording ketone **14** can be envisaged as potentially useful for the synthesis of 2-acylindole alkaloids.[38] Both the effects of H-donating ability and steric hindrance by the silane are evident, even at 80 °C.



Scheme 12. An example of two-step annelation that produces bicyclo[3.n.0]lactones.

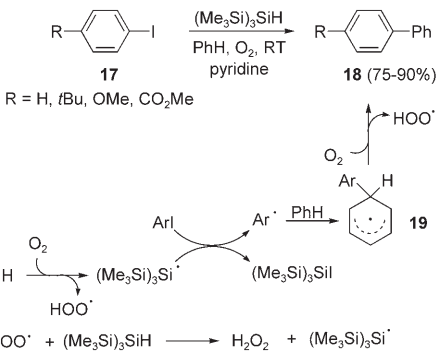


Scheme 13. Carbon-carbon bond formation mediated by $(Me_3Si)_3SiH$ using phenylseleno esters under a variety of experimental conditions [Bn: CH_2Ph and MOM: CH_2OCH_3].

The ester **15** was treated with $(Me_3Si)_3SiH$ and a large excess of AIBN in benzene to give the pentacyclic alkaloid

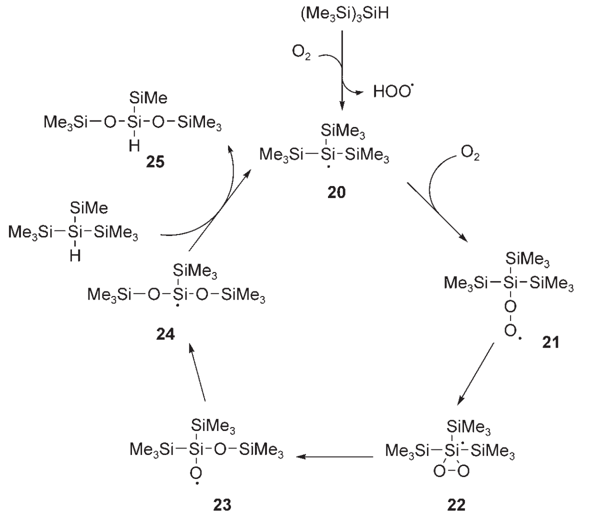
16 in good yield.[39] However, the whole process is not the result of a radical chain reaction. The radical derived from the decomposition of AIBN also participates in the oxidation or rearomatization of the intermediate radical upon completion of the chain.

Curran and Keller found that the $(Me_3Si)_3SiH$-mediated addition of aryl iodides (**17**) to benzene can be facilitated by oxidative rearomatization with oxygen.[40] The reaction also proceeds well in intramolecular cases. Some *para*-substituted derivatives **18** obtained in good yields are reported in Scheme 14. A radical initiator is not necessary for the good performance of the reaction, since the oxygen serves to initiate the reaction. The reaction mechanism is outlined in Scheme 14. Silyl radicals, initially generated by reaction with oxygen, abstract iodine with formation of aryl radical that undergoes intermolecular addition to benzene to form cyclohexadienyl radical **19**. Oxidative rearomatization with oxygen, affords the products and additional $HOO^\bullet$ radical. Hydrogen abstraction from the silane by $HOO^\bullet$ radical should regenerate $(Me_3Si)_3Si^\bullet$ radical, thus completing this chain reaction.



Scheme 14. $(Me_3Si)_3SiH$-mediated radical addition of aryl iodides to benzene and reaction mechanism.

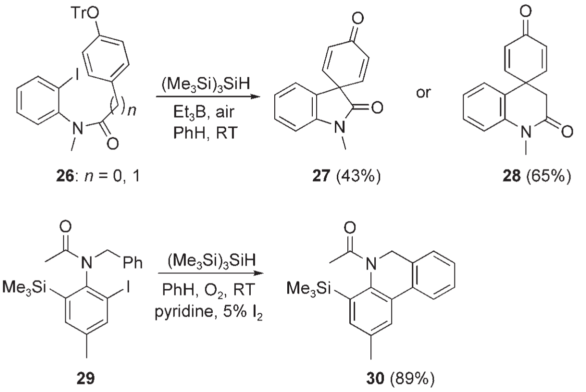
The reaction of $(Me_3Si)_3SiH$ with either oxygen or air is worthy of additional comment. From our initial studies, we found that this reaction occurs spontaneously and slowly at ambient temperature to form siloxane as the sole product.[42] The mechanism of this unusual process has been studied in some detail.[42] The absolute rate constant for the spontaneous reaction of $(Me_3Si)_3SiH$ with molecular oxygen was determined to be $\sim 3.5\times10^{-5}\,\text{M}^{-1}\text{s}^{-1}$ at 70 °C[42] and theoretical studies elucidated the reaction coordinates.[43] The propagation sequence shown in Scheme 15 corroborates all findings.[41,42] Silyl radical **20** adds to oxygen to form the peroxyl radical **21**. This silylperoxyl radical undergoes three consecutive unimolecular steps: **21**→**22**→**23**→**24**. Hydrogen abstraction from $(Me_3Si)_3SiH$ by radical **24** gives the final product **25** and another silyl radical **20**, thus completing the cycle of this chain reaction. There is strong evidence that the formation of the dioxirane-like pentacoordinated silyl radical **22** is the rate determining step ($\sim 10^3\,\text{s}^{-1}$ at 70 °C) of the three consecutive unimolecular steps.



Scheme 15. Reaction mechanism for the autoxidation of $(Me_3Si)_3SiH$.

A few aspects of the autoxidation of $(Me_3Si)_3SiH$ are of interest to synthetic chemists: i) in some cases oxygen can serve to initiate radical chain reactions, therefore no additional radical initiator is needed; ii) the oxidized product **25** does not interfere with radical reactions; and (iii) GC analysis can be used for a titration of the reagent, thus giving the exact concentration of silane if necessary.

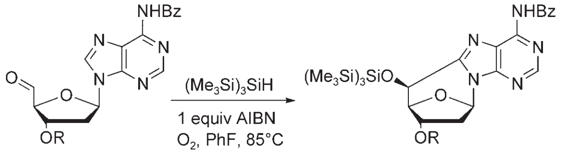
Thus, $(Me_3Si)_3SiH$ can be employed under a variety of aerobic conditions as well as in the presence or absence of other initiators, as in the case of Et_3B in the intramolecular addition of aryl iodides to arenes (Scheme 16). A solution of the appropriate trityl precursor **26** in benzene (0.15 M) was treated with 1.2 equiv of $(Me_3Si)_3SiH$ and 1.2 equiv of Et_3B, and the resulting mixture was stirred in open air at room temperature until the starting material was consumed (typically 3 h). The reactions proceed via *ipso* cyclization of aryl radicals to the oxygen-substituted aromatic ring, followed by β-fragmentation of the trityl substituent to give spirooxindole **27** and spirodihydroquinolone **28**.[44] Under the same



Scheme 16. $(Me_3Si)_3SiH$-mediated intramolecular addition of aryl iodides to arenes.

conditions but in the absence of Et_3B, iodide **29** afforded **30** in good yield.[40] Radical initiator is not necessary for the good performance of the reaction since oxygen plays this role and simultaneously facilitates the oxidative rearomatization. Harrowven et al. completed the first total synthesis of cavicularin,[45] in which an analogous reaction was used with an aryl iodide for a radical-induced transannular ring contraction. For this key step, $(Me_3Si)_3SiH$ was used together with AIBN in toluene at 90 °C.

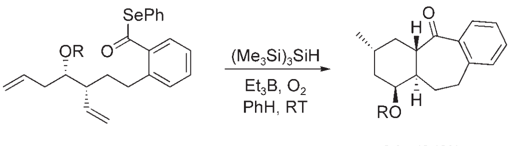
The rearomatization can also be used in the case of aromatic purine bases. The protected 5′-carbaldehyde **31** was treated with 5 equiv of $(Me_3Si)_3SiH$ and stoichiometric amounts of AIBN at 85 °C under air and was converted quantitatively in 2 h to the cyclonucleoside **32** as the sole product in 75 % yield (Scheme 17).[46] The reaction is highly stereoselective affording only the (5′*S*)-diastereomer. The mechanism includes the attack of the alkyl radical, derived from addition of $(Me_3Si)_3Si^{\bullet}$ radical to the unsaturated bond, to the adenine moiety. The rearomatization step is probably a synergism of two reactions, that is, the reaction with the radical derived from the decomposition of AIBN and the reaction with oxygen.



31: R = $SiMe_2tBu$ **32** (75%)

Scheme 17. One-step synthesis of protected (5′*S*)-5′,8-cyclo-2′-deoxyadenosine, a prototype of the well-known DNA lesion.

Multistep sequences are favored by the unique reactivity of $(Me_3Si)_3SiH$. Two examples are described below. Radical cascades that feature a 7-*exo* acyl radical cyclization followed by a 6-*exo* or 5-*exo* alkyl radical cyclization, lead to very good yields and diastereoselectivities.[47] The treatment of **33** with E_3B, air, and $(Me_3Si)_3SiH$ that provided the tricycle **34** in excellent yields as a single diastereomer (Scheme 18). Interestingly, the bulky tert-butylsilyl ether moiety is not a requirement for stereoselectivity in this process, which is mainly driven by the $(Me_3Si)_3Si$ group.

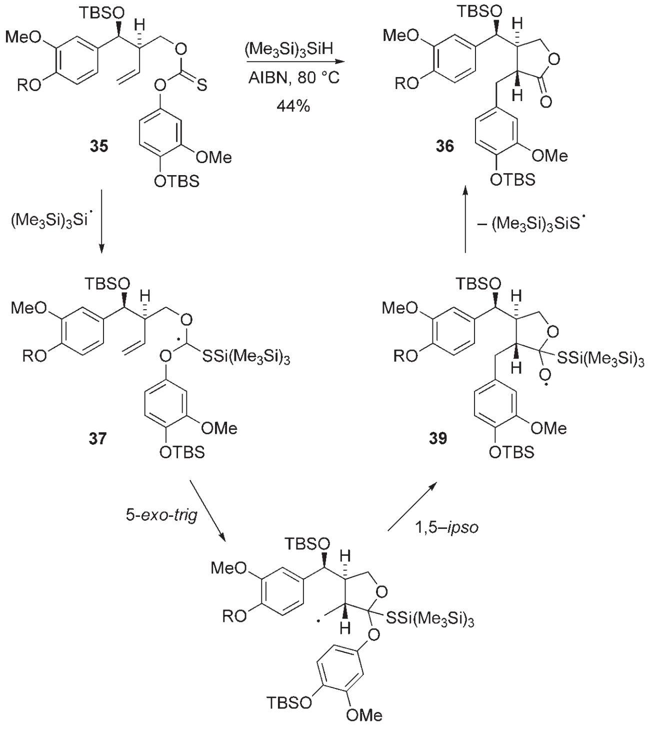


33a: R = H
33b: R = TBS

34a (84%)
34b (93%)

Scheme 18. Radical cascade including a 7-*exo* acyl radical cyclization followed by a 6-*exo* alkyl radical cyclization [TBS: $SiMe_2tBu$].

A radical carboxyarylation approach was introduced by Sherburn and co-workers as the key step in the total synthesis of the aromatic series of (−)-podophyllotoxin and its enantiomer (Scheme 19).[48,49] The thiocarbonate derivatives **35** (R = Me or TBS) are treated with 1.1 equiv of $(Me_3Si)_3SiH$ in refluxing benzene and in the presence of AIBN (0.4 equiv added over 6 h) as the radical initiator. The result is compound **36** in 44 % yield. This remarkable transformation resulted from a radical cascade, involving $(Me_3Si)_3Si^{\bullet}$ radical addition to the thiocarbonyl function (**35**→**37**), 5-*exo* cyclization (**37**→**38**) and intramolecular 1,5-*ipso* substitution (**38**→**39**) with the final ejection of the $(Me_3Si)_3SiS^{\bullet}$ radical.



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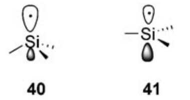
Scheme 19. Radical cascade mediated by $(Me_3Si)_3SiH$-denominated carboxyarylation [TBS: $SiMe_2tBu$].

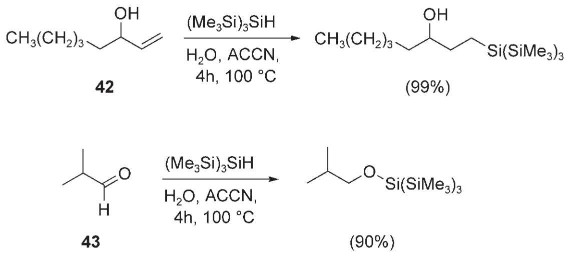
In this mechanism we suggest an additional role for the silane thiyl radical cleaved from **39**. It can undergo a fast 1,2-migration of silyl group from silicon to sulfur, affording a new silyl radical that either reacts with $(Me_3Si)_3SiH$ (cf. Scheme 4) completing the reaction cycle, or replaces the $(Me_3Si)_3Si^{\bullet}$ radical in the previously described reaction sequence.[24]

The influence of $(Me_3Si)_3SiH$ on the reactivity and geometry of silicon substituents: Trialkylsubstituted silicon-centered radicals are bent, as depicted in the σ-type structure **40** (Scheme 20). However, the nature of the substituents can have a profound influence on the geometry and half-lives of silyl radicals. For example, when Me_3Si groups progressively replace methyl groups, the degree of pyramidalization decreases.[50] Bulkier trialkylsilyl substituents, like iPr_3Si or tBu_2MeSi groups, considerably increase the persistence of silyl radicals. Indeed, the (tBu$_2$MeSi)$_3$Si$^•$ radical is found to be stable and isolable in the crystal form. The radicals (Et$_3$Si)$_3$Si$^•$, (iPr$_3$Si)$_3$Si$^•$, (tBu-Me$_2$Si)$_3$Si$^•$ and (tBu$_2$MeSi)$_3$Si$^•$ have the practically planar structure **41**, due to the steric repulsions among the bulky silyl substituents.[51,52]



Scheme 20. Bent and planar silicon-centered radicals.

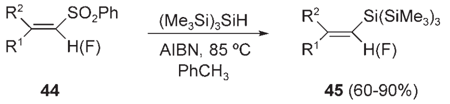
Hydrosilylation using (Me$_3$Si)$_3$SiH or silicon surfaces: The radical-based hydrosilylation of carbon-carbon or carbon-oxygen double bonds by (Me$_3$Si)$_3$SiH is an important class of reactions. The initially generated (Me$_3$Si)$_3$Si$^•$ radical adds to the double bond to give a radical adduct, which then reacts with (Me$_3$Si)$_3$SiH to give the addition product, together with "fresh" (Me$_3$Si)$_3$Si$^•$ radicals to perpetuate the chain.[53,54] Recently, the rate constants of (Me$_3$Si)$_3$Si$^•$ radical addition to a variety of monosubstituted olefins have been measured by laser flash photolysis, and the observed high reactivity and low selectivity are explained by antagonist polar and enthalpy effects.[55] Interestingly, the hydrosilylation of water-insoluble substrates is still an efficient process in aqueous medium as shown in Scheme 21 for olefin **42** and aldehyde **43**.[29b] It has been suggested that all water-insoluble materials (substrate, reagents and initiator) suspended in the aqueous medium can interact, due to the vigorous stirring that creates an efficient vortex and dispersion.



Scheme 21. Hydrosilylation of water-insoluble olefin and aldehyde in water.

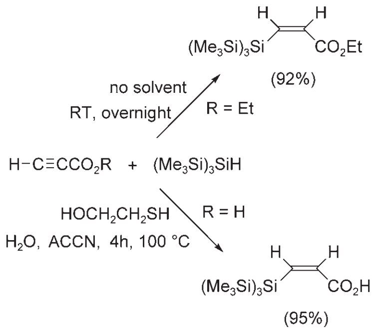
It is worth noting that tris(trimethylsilyl)silyl ethers are stable under conditions usually employed in organic synthesis for the deprotection of other silyl groups and can be deprotected using photolysis at 254 nm, in yields ranging from 62–95 %.[56] For example, the exposure of **32** (see Scheme 17) to UV irradiation for 30 min at room temperature in an 8:3 CH$_2$Cl$_2$/CH$_3$OH mixture gave the quantitative deprotection of the (Me$_3$Si)$_3$SiO group.[46] Although a simple hydrosilylation/deprotection combination is formally equivalent to the ionic reduction of carbonyl moieties, the use of an aldehyde functional group in consecutive radical reactions followed by photo-deprotection could be a new approach for the formation of new stereogenic centers based on the hindered properties of the (Me$_3$Si)$_3$Si group.

Radical-mediated silyldesulfonylation of various vinyl and (α-fluoro)vinyl sulfones **44** with (Me$_3$Si)$_3$SiH provides access to vinyl and (α-fluoro)vinyl silanes **45** (Scheme 22).[57] These reactions presumably occur via the addition of (Me$_3$Si)$_3$Si$^•$ radical followed by β-scission with the ejection of PhSO$_2^•$ radical. Hydrogen abstraction from (Me$_3$Si)$_3$SiH by PhSO$_2^•$ radical completes the cycle of these chain reactions. Such silyldesulfonylation provides a valid alternative to the hydrosilylation of alkynes with (Me$_3$Si)$_3$SiH (see below). Upon oxidative treatment with hydrogen peroxide in basic aqueous solution, compound **45** undergoes Pd-catalyzed cross-couplings with aryl halides. Apparently, H$_2$O$_2$-cleaved Si–Si bonds to generate siloxane intermediates, which are known to be good substrates for Hiyama coupling.



Scheme 22. Radical-mediated silyldesulfonylation (R^1, R^2=H, alkyl or aryl).

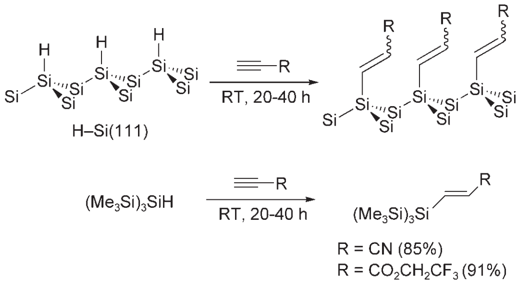
The addition of (Me$_3$Si)$_3$SiH to a number of monosubstituted acetylenes has also been studied in some detail.[50,58] These reactions are highly regioselective and give terminal (Me$_3$Si)$_3$Si-substituted alkenes in good yields. High *cis* or *trans* stereoselectivity is also observed, depending on the nature of the substituents at the acetylenic moiety and the experimental conditions. These reactions proceed without solvent[43] as well as in aqueous solutions, as shown in Scheme 23.[29b]



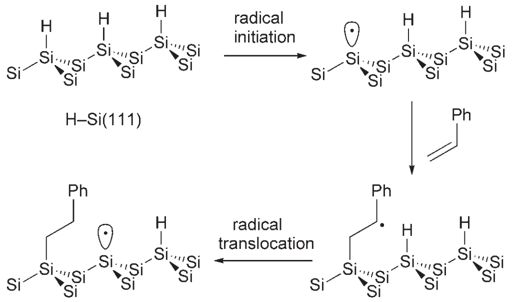
Scheme 23. Hydrosilylation of alkynes without solvent or in aqueous solution.

The understanding and control of silicon surfaces is of great importance for their technological applications. In the last decade, much attention has been directed towards the synthesis of organic monolayers, which can be tailored for specific requirements. Among the several existing methodologies, radical reactions have been found to be the most convenient method for achieving organic modifications of hydrogen-terminated silicon surfaces.[59] The two flat surfaces

H-Si(111) and H-Si(100)-2x1 resemble $(Me_3Si)_3SiH$ in that three silicon atoms are attached at the SiH moieties (cf. Schemes 24 and 26).[60] Therefore, it is not surprising that several $(Me_3Si)_3SiH$ reactions have been adopted and applied to surfaces, and that mechanistic schemes are often proposed in analogy with $(Me_3Si)_3SiH$ radical chemistry.[61] One example is illustrated in the modification of H-Si(111) surfaces by hydrosilylation of activated alkynes in comparison with $(Me_3Si)_3SiH$ under mild conditions.[62] When freshly prepared H-Si(111) surfaces are immersed in neat alkyne, or when$(Me_3Si)_3SiH$ is mixed with neat alkyne, the hydrosilylation proceeds smoothly in room light and ambient temperature (Scheme 24). Similar results were also obtained in the dark, suggesting that the radical initiation step in both systems is provided by traces of molecular oxygen (vide infra). The coverage ratio of the organic monolayer was estimated by X-ray photoelectron spectroscopy analysis at 51 % for R = CN and 56 % for $R = CO_2CH_2CF_3$, whereas the reaction yields with $(Me_3Si)_3SiH$ were 85 % and 91 %, respectively. Theoretical calculation at the B3LYP/6–31G*//HF/STO-3G* level showed that the Si–H bond dissociation energies of H-Si(111) and $(Me_3Si)_3Si$-H are very similar, further justifying the use of the well established radical-based $(Me_3Si)_3SiH$ reactivity as a model for surface reactions.[62]

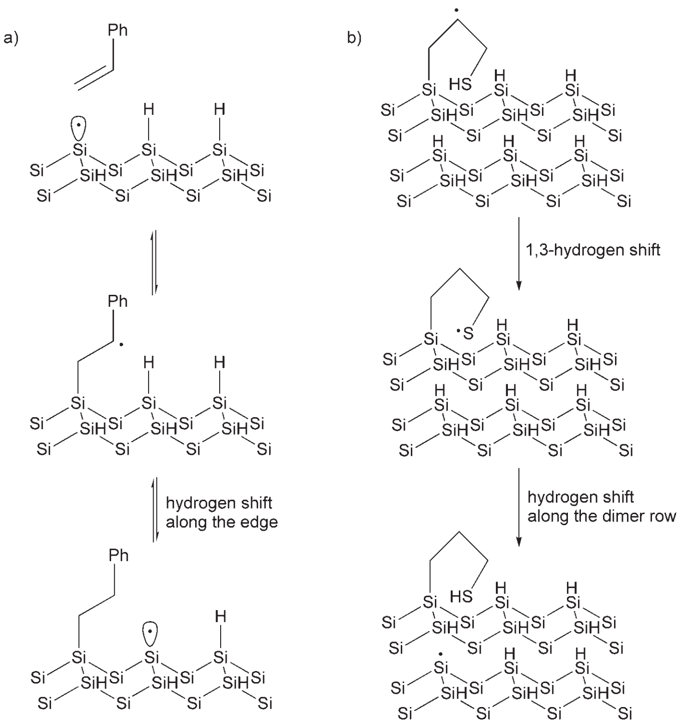


Scheme 24. Comparative hydrosilylation between H-Si(111) and $(Me_3Si)_3Si$-H under similar conditions; the coverage ratio of organic monolayer is estimated at 51 % for R = CN and 56 % for $R = CO_2CH_2CF_3$.



Scheme 25. Hydrosilylation of styrene by hydrogen-terminated Si(111) surfaces.

The structural properties of the H-Si(111) and H-Si(100)-2x1 surfaces are of critical importance thanks to their chemical behavior. They have two-dimensional rhombic and square lattices, respectively. Surface sites array in an isotropic style on H-Si(111) but adopt the anisotropic distribution on H-Si(100)-2x1 (cf. Schemes 25 and 26). Such behavior clearly influences the hydrosilylation of surfaces when using alkenes for preparing covalently bonded monolayer films. Reactions can be carried out in different conditions, for example, in neat deoxygenated alkenes using thermal decomposition of diacyl peroxides or UV irradiation as the radical initiation, or by creating isolated surface silyl radicals with the tip of the Scanning Tunneling Microscope (STM).



Scheme 26. a) Mechanism of radical chain reactions of the growth of styrene line along the edge of a dimer of a H-Si(100)-2x1 surface. b) Mechanism of radical chain reactions of the growth of allyl mercaptan line across the dimer rows of a H-Si(100)-2x1 surface.

The reaction of H-Si(111) surfaces with styrene, formally a hydrosilylation process,[63] is provided in Scheme 25. The initially formed surface silyl radical reacts with styrene to form a benzyl radical that abstracts hydrogen from a vicinal Si–H bond, thus creating another surface silyl radical. The best candidate for the radical translocation is the 1,5-hydrogen shift, which is also supported theoretically.[64] The lack of significant polymerization of styrene indicates the efficiency of the 1,5-hydrogen shift with respect to carbon-carbon bond formation. Due to the isotopic hexagonal arrangement of H-Si(111) surfaces, the reaction occurs with the formation of compact islands.

The reaction of styrene with H-Si(100)-2x1 surfaces proceeds in an analogous manner (Scheme 26a).[65] The C-centered radical translocates to the surface by a 1,5-hydrogen shift within the same row. However, evidence for reversible chain reactions in this system has been obtained by increasing the temperature from 300 to 400 K, leading to the complete desorption of the styrene line.[66] These results suggest that the appearance of a molecular line in an STM image is determined by the competing rates of the forward and reversed chain reactions at a given temperature. With the H-Si(100)-2x1 surfaces, another possibility involves growing the line across the dimer rows, as with allyl mercaptan (Scheme 26b).[67] The C-centered radical is thought initially to rearrange to an S-centered radical via a 1,3-hydrogen shift, followed by a radical translocation from sulfur to the silicon surface on the neighboring row. The abstraction of an H-atom from the neighboring row results in a dangling bond, which can now accept another allyl mercaptan molecule, leading to the cross-row chain reaction. This cross-row line is found to be more stable than that of the styrene line.

To date, numerous radical-induced hydrosilylations of terminal olefins or acetylenes, as well as aldehydes or ketones, have been reported for the H-Si(111) and H-Si(100)-2x1 surfaces under a variety of experimental conditions. The formation of benzaldehyde- and acetaldehyde-derived nanostructures on H-Si(100)-2x1 proceeds via a radical-mediated process that binds the aldehydes, through a strong Si–O covalent bond, to the surface.[68] Interestingly, the self-directed growth allows for the formation of organic-silicon nanostructures composed of single and double lines of molecules, suggesting that the intermediate C-centered radical faces two possibilities: reach and abstract the nearest H-atom within the same row or that of the neighboring row.

Conclusion

Over the last twenty years $(Me_3Si)_3SiH$ has become popular among organic chemists as a radical-based reducing agent. Unique transformations are possible, giving rise to structures otherwise very difficult to synthesize. The scope and breadth of the $(Me_3Si)_3SiH$ utility as a mediator of consecutive radical reactions is spectacular and we are convinced that many more diverse applications are yet to come.[69] We trust that the survey presented here will serve as a platform to expand silicon radical chemistry with new and exciting discoveries. $(Me_3Si)_3SiH$ exemplifies the role of multidisciplinarity in developing new chemical tools and combining knowledge from physical organic chemistry with theoretical methodologies, organic synthesis, and polymer and materials science.

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