

# Organic Synthesis in Water Mediated By Silyl Radicals

Sebastián Barata-Vallejo<sup>b</sup>, Norma Sbarbati Nudelman<sup>b</sup> and Al Postigo<sup>\*a</sup>

<sup>a</sup>Department of Chemistry-Faculty of Science. University of Belgrano. Villanueva 1324 CP 1426-Buenos Aires-Argentina

<sup>b</sup>Sebastián Barata-Vallejo and Norma Sbarbati Nudelman. Departamento de Química Orgánica-Facultad de Ciencias Exactas y Naturales. Universidad de Buenos Aires, Pabellón II, 3er piso, Ciudad Universitaria, 1428-Buenos Aires-Argentina

**Abstract:** This account is focused on highlighting the recent advances on synthetically-useful organic reactions employing silicon-centered radicals in water, and presenting new reactions in water, mediated by silyl radicals. In doing so, several types of organic radical transformations will be discussed, such as reduction of organic halides utilizing non toxic organosilane reducing agents in water, transformation of azides into amines, synthesis of protecting silyl ethers in water, hydrosilylation reactions of carbon-carbon double and triple bonds, and radical cyclization reactions in water induced by silicon-centered radicals. More recently, intermolecular radical carbon-carbon bond formation reactions mediated by silyl radicals have allowed the synthesis of perfluoroalkyl-substituted compounds in water, widening the scope for the syntheses of fluorophores. These silicon radical-mediated chain reactions in water are initiated through different methods, among which, thermal, photochemical, and dioxygen initiations are reported to be the most successful methods in water. A versatile aspect of the radical methodology employed in water will be presented in terms of dealing with water-soluble and organic solvent-soluble substrates in these silicon radical-mediated reactions in water. In this regard, for an efficient chain process to take place in water, a chain carrier must be used when water-soluble substrates are employed, whereas organic solvent-soluble materials do not require a chain transporter when silyl radicals are used in water.

**Keywords:** Silyl radicals,  $(\text{Me}_3\text{Si})_3\text{SiH}$ , silyl radicals in water, radical carbon-carbon bond formation in water, chain carrier.

## I. INTRODUCTION

The majority of organic radical reactions employing Si-centred radicals take place in organic solvents, neat media, and on surface chemistry, and only recently has water been used as a convenient reaction medium for these radicals [1,2].

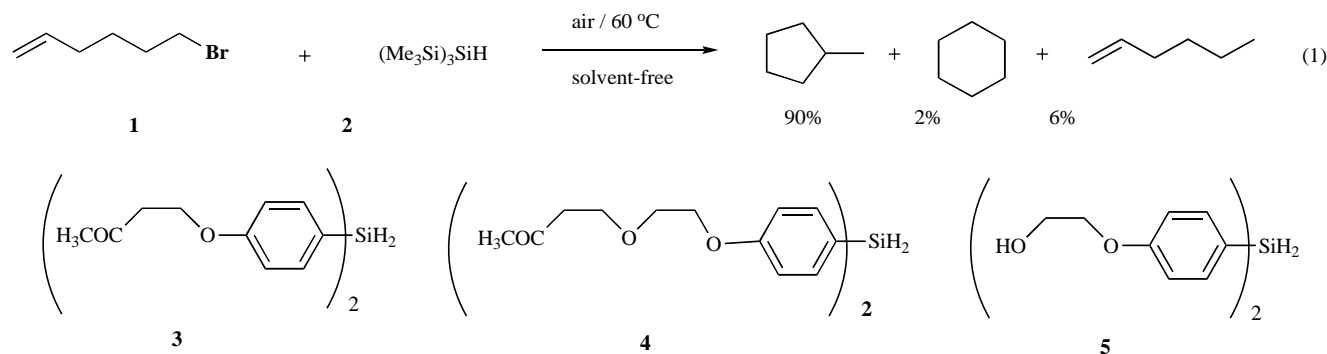
The development of novel water-soluble organosilane compounds and their applications to radical reactions in water is constantly being paid attention to, as a means to producing effective radical organic transformations in water, such as reductions of hydrophilic organic halides.

In the radical chain processes, the initial silyl radicals are generated by some initiation. The most popular initiator is 2',2'-azobisisobutyronitrile (AIBN), with a half-life of 1 h at 81 °C, generating the incipient radicals that commence the radical chain reaction. Other azo-compounds are used from time to time [3] as well as the thermal decomposition of di-*tert*-butyl peroxide [4] depending on the reaction conditions. Triethyl borane ( $\text{Et}_3\text{B}$ ) in the presence of

very small amounts of oxygen is an excellent initiator for low temperature reactions (down to  $-78$  °C). Also air-initiated reactions have recently been reported (eq 1) [4b].

Togo and Yokoyama [5] have dealt with the necessity of performing reduction reactions in water of water-soluble halides. They have shown that the reactivity of water-soluble arylsilanes, as reducing agents, is much higher than that of alkylsilanes, and that the reactivity of diarylsilanes was higher than that of monoarylsilanes and triarylsilanes. Thus, the solubility of bis[4-(2-methoxyethoxy)phenyl]silane **3** and bis{4-[2-(2-methoxyethoxy)ethoxy]phenyl} silane **4** were about  $1.0 \times 10^{-2}$  M and  $1.5 \times 10^{-2}$  M, respectively.

The reduction of potassium *o*-bromobenzoate and potassium *o*-iodobenzoate, which form the  $\text{sp}^2$  carbon radicals, showed that the bromine atom abstraction is somewhat difficult, whereas the iodine atom of potassium *o*-iodobenzoate is easily removed by the silyl radical. These results and others obtained by the same authors showed that organosilanes **3** and **4** (Fig. (1)) can promote radical



**Fig. (1).** Water-Soluble Arylsilanes Utilized in Radical Reductions of Hydrophilic Organic Halides.

\*Address all correspondence to this author at the Department of Chemistry-Faculty of Science. University of Belgrano. Villanueva 1324 CP 1426-Buenos Aires-Argentina; Tel: +54 11 4511-4700; Fax: (+) 54 11 4511-4700; E-mail: alberto.postigo@ub.edu.ar.

reductions of alkyl bromides, alkyl iodides, and aryl iodides, initiated by  $\text{Et}_3\text{B}$ , in aqueous media under aerobic conditions.

Radical cyclizations in water using organosilanes **4** and **5** have also been studied. The radical cyclization of potassium 7-bromo-2-heptenoate with **4** and **5** was carried out to afford 48 and 82% yields of cyclopentyl acetic acid, respectively, while no direct reduction product, *i.e.* 2-heptenoic acid, was formed. This clearly demonstrated the radical nature of the process [5].

Water is also a choice of solvent for free-radical polymerization. The high heat capacity of water allows effective transfer of the heat from polymerization. Compared to organic solvents, the high polarity of water distinguishes remarkably the miscibility of many monomers from polymers. Today, aqueous free-radical polymerization is applied in industries [6].

Several interesting photoinitiators based on the silyl radical chemistry have been proposed as a means to effecting polymerization in aqueous suspensions [7]. Among these compounds, (4-tris(trimethylsilyl)silyloxy)benzophenone generates silyl radicals under light irradiation that produce high rates of polymerization. A water-soluble poly(methylphenylsilylene) derivative has been used as a photoinitiator of radical polymerization of hydrophilic vinyl monomers with great success [8]. Following, we shall describe different radical triggering events that have recently been used for generating silicon-centered radicals in water that will be used throughout this chapter.

### 1. A.-INITIATION BY THERMAL DECOMPOSITION OF AN AZO COMPOUND

The water-insoluble radical initiator 1,1'-azobis(cyclohexanecarbonitrile) (ACCN; half-life of 2.33 h at 100 °C) has been found to give the best performance for both hydrophobic and hydrophilic substrates in initial studies and this trend has been confirmed by successive experiments. The procedure is the following: In a 5 mL Wheaton-vial<sup>®</sup>, provided with a stir bar, a heterogeneous aqueous mixture of the substrate (10 mM),  $(\text{Me}_3\text{Si})_3\text{SiH}$  (1.2 – 2.0 equiv., or other hydrosilane) and ACCN (0.3 equiv.) is flushed with Ar for ten minutes before heating at 100 °C for 2-4 hours or otherwise indicated. After the reaction time elapsed, addition of pentane and extraction, the organic-phase is analyzed.

### 1. B.-PHOTOCHEMICAL RADICAL INITIATION

The initiation of the hydrosilylation reactions in water can be accomplished directly with light (low pressure Hg lamp, 254 nm) in the absence of a radical chemical precursor (*e.g.* peroxide), where most of the light is absorbed by  $(\text{Me}_3\text{Si})_3\text{SiH}$ . To this effect, for all substrates studied, the absorption of  $(\text{Me}_3\text{Si})_3\text{SiH}$  (12 mM) at the irradiation wavelength (254 nm) should represent *ca.* 95%-97% of the total absorption of the mixture (substrate and reagents). Nevertheless, as  $(\text{Me}_3\text{Si})_3\text{SiH}$  is not soluble in water, it is assumed that its local droplet-concentration could be much higher, and therefore results in higher local UV-absorbances.

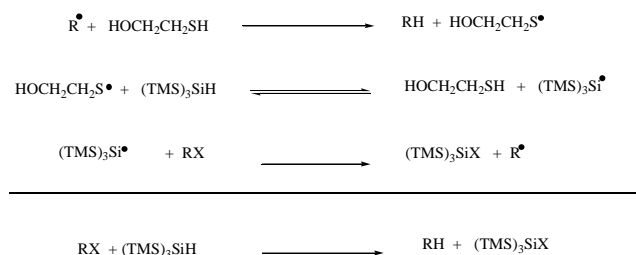
A volume of Ar-degassed water (3 mL) is placed in a quartz cell provided with a stir bar, with subsequent addition of  $(\text{Me}_3\text{Si})_3\text{SiH}$  ( $3 \times 10^{-5}$  moles) and the substrate ( $3 \times 10^{-5}$  moles) by syringe. The cell is mounted on a stir plate very near the lamp (1 cm) and stirred vigorously throughout the irradiation (1.5 – 2 h). The temperature is controlled thermostatically at 20 °C. At the working concentrations, most of the light (254 nm) is absorbed by  $(\text{Me}_3\text{Si})_3\text{SiH}$ .

## 1. C.-RADICAL INITIATION BY DIOXYGEN

A balloon filled with pure oxygen connected to the vessel where no apparent bubbling resulted, allowed dioxygen to be introduced up to its solubility limits in water. The dioxygen-initiated radical-induced reactions in Ar-degassed water is carried out by adding subsequently  $(\text{Me}_3\text{Si})_3\text{SiH}$  ( $6 \times 10^{-5}$  moles) and the substrate ( $5 \times 10^{-5}$  moles). The vessel is tight-sealed, connected with a balloon filled with 99.99 % dioxygen, and vigorously stirred at 20 °C (24 h). As a slight positive oxygen-pressure is exerted on the reaction vessel, air does not leak in the system. For hydrophilic alkynes,  $\text{HOCH}_2\text{CH}_2\text{SH}$  (0.3 equiv.) is employed as the chain propagating agent (*vide infra*).

## 2. REDUCTION OF ORGANIC COMPOUNDS AND HYDROSILYLATION REACTIONS OF DOUBLE BONDS

It is known that in organic solvents, *tris*(trimethylsilyl)silane,  $(\text{Me}_3\text{Si})_3\text{SiH}$ , is an efficient reducing agent for organic halides. Also, the reported methodology of polarity-reversal catalysis is well documented in organic solvents. The thiol/silane couple shows not only an efficient synergy of radical production and regeneration, but could also provide for the use of an amphiphilic thiol, in order to enhance the radical reactivity at the interface. For the reduction of an organic halide (RX) by the couple  $(\text{Me}_3\text{Si})_3\text{SiH}$  /  $\text{HOCH}_2\text{CH}_2\text{SH}$  under radical conditions, the propagation steps depicted in Scheme 1 are expected. That is, the alkyl radicals abstract hydrogen from the thiol and the resulting thiyl radicals abstract hydrogen from the silane, so that the thiol is regenerated along with the chain carrying silyl radical for a given RX [9,10].



**Scheme 1.** Polarity Reversal Catalysis of Silanes with Thiols.

The proposal of  $(\text{Me}_3\text{Si})_3\text{SiH}$  in water is attractive from the point of view of its commercial availability. Recently, Postigo and Chatgialiloglu[11] tested the reducing agent  $(\text{Me}_3\text{Si})_3\text{SiH}$  in water and observed its high stability in deaerated aqueous media and high temperatures. They subjected a series of organic halides to reduction with  $(\text{Me}_3\text{Si})_3\text{SiH}$  in water with different initiators, azo compounds and  $\text{Et}_3\text{B}$ . The initiators studied that afforded the best reduction yields with  $(\text{Me}_3\text{Si})_3\text{SiH}$  were the water soluble 2,2'-azobis(2-amidinopropane) dihydrochloride (AAPH) and 1,1'-azobis(cyclohexanecarbonitrile) (ACCN, organic-solvent soluble, see section 1.A.-). The half-life of ACCN at 100 °C is 2.33 h, while that of AAPH is *ca.* 1.1 h at 73 °C.

The reduction of hydrophilic 4-iodobutyric acid and hydrophobic 5-iodouracil, afforded the corresponding reduced products in yields >90 %, with both initiators.

The reduction of hydrophilic (1S)-bromocamphor-10-sulfonic acid and 5-bromouridine were also considered under similar reaction conditions. Using the water-soluble AAPH initiator no reaction occurred for the camphor derivative, whereas 5-bromouridine afforded uridine in 82% yield (based on 17% converted substrate).

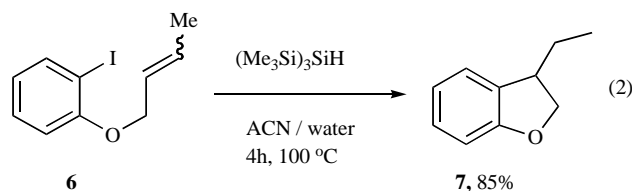
However, when 3 mM ACCN is used as initiator, both substrates afforded 90% yields of the corresponding reduction products, although the conversion of the starting material was as low as 10%. By increasing the amount of ACCN, however, the disappearance of starting material increased in favor of reduction product [11]. In this work, the relevance of 2-mercaptoethanol in the reduction process was revealed. For the reduction of 5-bromouridine, the optimal ratio of substrate / 2-mercaptoethanol was found to be 3-3.5 [11].

Other substrates of biological relevance bearing halogen atoms such as 8-bromoadenosine and 8-bromoguanosine were also subjected to reduction with  $(\text{Me}_3\text{Si})_3\text{SiH}$  /  $\text{HOCH}_2\text{CH}_2\text{SH}$  in water initiated by ACCN. Very high yields of reduced products were obtained under these reaction conditions (>80 %) [11b].

Later on, Postigo and Chatgililoglu [12] reported on two methods for the use of  $(\text{Me}_3\text{Si})_3\text{SiH}$  in water, depending on the hydrophilic or hydrophobic character of the substrates.

The reduction of water-insoluble organic substrates proceeded in a heterogeneous mixture of substrate,  $(\text{Me}_3\text{Si})_3\text{SiH}$ , and ACCN, in water which is previously de-oxygenated with Ar and heated at 100 °C for 4 h. For water-soluble substrates,  $\text{HOCH}_2\text{CH}_2\text{SH}$  is used. Thus, reduction of 5-bromo-nicotinic acid, 5'-iodo-5'-deoxyadenosine, and other hydrophilic halides do proceed by the couple  $(\text{Me}_3\text{Si})_3\text{SiH}$  /  $\text{HOCH}_2\text{CH}_2\text{SH}$ , where the alkyl or aryl radicals (R) abstract hydrogen from the thiol in the water phase, and the resulting thiyl radicals migrate into the lipophilic dispersion of the silane and abstract a hydrogen atom, thus regenerating the thiol along with the chain-carrying silyl radical for a given RX (Scheme 1). The reaction of the silyl radical is expected to occur at the interface of the organic dispersion with the aqueous phase. It is worth mentioning that the reaction of thiyl radicals with silane is estimated to be exothermic by *ca.* -3.5 Kcal mol<sup>-1</sup> [13].

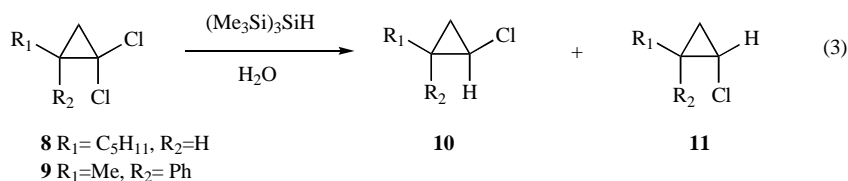
The same reaction conditions were also applied to the radical cyclization of 1-allyloxy-2-iodobenzene derivative **6**, as shown in eq 2, but in this case, 2-mercaptoethanol was not needed.



The reaction afforded 85 % yield of cyclized product **7**.

There is little knowledge on the reduction of *gem*-dichlorides by  $(\text{Me}_3\text{Si})_3\text{SiH}$  in organic solvents, and this knowledge was limited to some stereoselective examples [14a]. Reduction of *gem*-dichlorides **8** and **9** in water (eq 3) with  $(\text{Me}_3\text{Si})_3\text{SiH}$  and ACCN under the usual experimental conditions (see section 1.A.-, this time at 70 °C, 2 h) proceeded smoothly affording the corresponding monochloride derivatives, in quantitative yields, as a diastereoisomeric mixture of compounds **10/11** in a 1.7:1 ratio for both cases (**8** and **9**).

The diastereoselectivity outcome of this reaction is likely due to the influence of the substituents on the rate of the cyclopropyl radi-



cal and on the shielding of the two faces of the cyclopropyl ring [14a,15,16].

Another successful class of radical reductions in water has been obtained by the transformation of azides into primary amines under the same experimental conditions. The results are reported in Table 1.

**Table 1. Reduction of water-soluble azides**

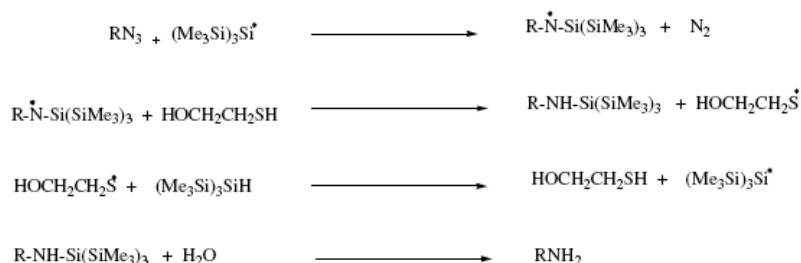
| RN <sub>3</sub> | conversion (%) | RNH <sub>2</sub> , (%) |
|-----------------|----------------|------------------------|
| <b>12</b>       | 70             | 99                     |
| <b>13</b>       | >99            | 90                     |
| <b>14</b>       | >99            | 95                     |
| <b>15</b>       | >99            | 99                     |

Again, no reaction was observed in the absence of amphiphilic 2-mercaptoethanol. The mechanistic steps of this reaction are shown in Scheme 2, in analogy with the pathways reported for the radical reduction of aromatic azides with triethylsilane in toluene [12,17,18].

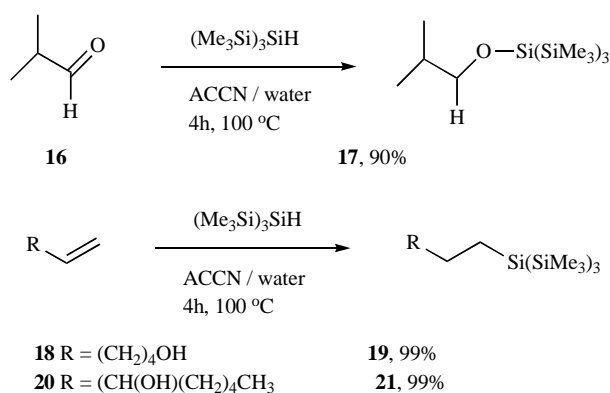
De-oxygenation reactions in water (Barton-McCombie reaction) have also been attempted using  $(\text{Me}_3\text{Si})_3\text{SiH}$  as reducing agent [12]. As observed in organic solvents, the reaction is independent of the type of the thiocarbonyl derivative (e.g.: *O*-arylthiocarbonate, *O*-thiocarbamate, thiocarbonyl imidazole or xanthate). On the other hand, the water-soluble material does require the presence of the chain-carrier 2-mercaptoethanol.

The radical-base hydrosilylation reactions are generally performed in organic solvents, or under solvent free conditions [14]. More recently, these reactions are also performed in continuous-flow microreactors [15]. Lately, these reactions are performed in water [12].

Postigo *et al.* [12] effected the hydrosilylation reaction of unsaturated bonds in water, using different hydrophobic compounds, such as aldehydes (**16**), alkenes (**18,20**), under the same reaction conditions reported previously (section 1.A.-, and Scheme 3).



**Scheme 2.** Proposed Reaction Steps for the Reduction of Azides in Water.



**Scheme 3.** Hydrosilylation Reactions of Multiple Bonds Using  $(\text{Me}_3\text{Si})_3\text{SiH}$  in Water.

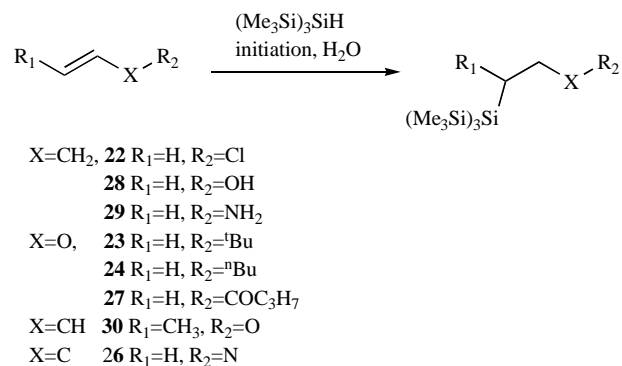
The efficiency of the reaction was very good, and in all cases, good to quantitative formation of the hydrosilylation products was achieved. These results showed that the nature of the reaction medium does not play an important role either in influencing the efficiency of the radical transformation or in the ability to dissolve the reagents. The authors attribute the success of the radical transformations of all water-insoluble material suspended in the aqueous medium to the vigorous stirring that creates an efficient vortex and dispersion. Probably, the radical initiation benefits from the enhanced contact surface of tiny drops containing  $(\text{Me}_3\text{Si})_3\text{SiH}$  and ACCN [12].

For water-soluble material, hydrosilylation of multiple bonds in water is reported by the same authors to vary slightly. In this case, as referred to before, the reducing system  $(\text{Me}_3\text{Si})_3\text{SiH}$  /  $\text{HOCH}_2\text{CH}_2\text{SH}$  in water is used. The amphiphilic thiol is successfully employed for radical reactions in the heterogeneous system of vesicle suspensions [16]. Excellent results of hydrosilylation of multiple bonds were achieved by adding this amphiphilic thiol to the system. The treatment of hydrophilic substrates in water has the additional advantage of an easy separation of the silane by-products by partition between water and organic phases.

More recently, Calandra *et al.* [21] undertook the hydrosilylation reaction of a series of alkenes (Scheme 4) in water with  $(\text{Me}_3\text{Si})_3\text{SiH}$  (e.g.: 3-chloroprop-1-ene, prop-2-en-1-ol, prop-2-en-1-amine, *tert*-butyl vinyl ether, and *n*-butyl vinyl ether) initiated thermally and by light (*vide infra*, sections 1.A.- and 1.B.-) and found very good yields of hydrosilylated alkanes. In Table 2, columns 3 and 4, yields of the hydrosilylation products derived from alkenes obtained by ACCN initiation and photochemical initiation are given for the series of alkenes (Scheme 4) studied. Interestingly, under thermal initiation, the hydrosilylated product derived from hydrophobic 3-chloroprop-1-ene (**22**) is obtained in 65% relative yield (Table 2, column 3, entry 1, product **22a**, 2-(3-chloropropyl)-

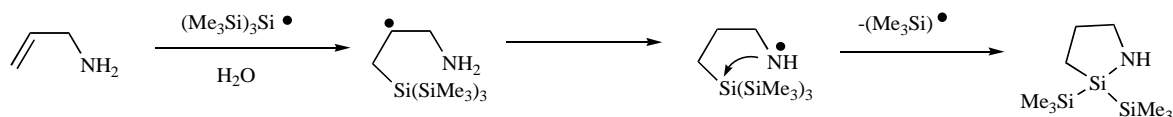
1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane, without chlorine atom reduction). There is also a product derived from the chlorine atom substitution by the  $(\text{Me}_3\text{Si})_3\text{Si}$  group (product **22b**, 2-allyl-1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane), which is obtained in 35% relative yield. These relative yields were calculated from  $^1\text{H}$  NMR integration. The hydrosilylated product derived from *tert*-butyl vinyl ether is also obtained in high yield (substrate **23**, 74%). High yields of hydrosilylation are obtained from *n*-butyl vinyl ether (**24**) [12] (isolated in 99% yield) in water under ACCN initiation [21].

Hydrosilylation products derived from methylenecyclobutane (**25**), acrylonitrile [9,12] (**26**), and vinyl butyrate (**27**), are obtained in water in yields ranging from 68% to quantitative, when the reactions are initiated by ACCN (entries 4,5, and 6, column 3, Table 2) [21].



**Scheme 4.** Hydrosilylation Reactions of Alkenes in Water By Various Initiating Techniques.

When the water soluble prop-2-en-1-ol (**28**), prop-2-en-1-amine (**29**), and organic solvent-soluble crotonaldehyde (**30**) are treated with  $(\text{Me}_3\text{Si})_3\text{SiH}$  in the presence of a thiol under ACCN initiation in water, the corresponding hydrosilylated products are obtained in higher than 75% yields (Table 2, column 3, entries 7, 8, and 9). In the absence of the thiol 2-mercaptoethanol, poor yields of hydrosilylated products are obtained. A notable case is that from substrate **29** (isolated global product yield 75%), which renders both a product derived from simple radical hydrosilylation of the C-C double bond (product **29a**, 15 % relative yield) and a ring-closed product (**29b**, *i.e.*: 2-(1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane-2-yl)ethanamine 85 % relative yield). The formation of product **29b** is accounted for in Scheme 5, where the incipient carbon centered radical derived from the addition of the  $(\text{Me}_3\text{Si})_3\text{Si}$  radical to the C-C double bond of the allylamine abstracts a hydrogen atom from the NH<sub>2</sub> group, rendering the aminyl radical that attacks the Si atom of the ancillary  $(\text{Me}_3\text{Si})_3\text{Si}$  group and undergoes intramolecular radical cyclization with loss of  $\text{Me}_3\text{Si}$  radical [21].



**Scheme 5.** Proposed Mechanism for Formation of Cyclic Product 29b from the Hydrosilylation Reaction of Allyl Amine (29) in Water.

**Table 2.** Hydrosilylation product yields from C-C multiple-bonded organic solvent-soluble substrates and hydrophilic substrates (10 mM) in deoxygenated water with  $(\text{Me}_3\text{Si})_3\text{SiH}$  (12 mM) under different initiation conditions (ACCN and  $h\nu$ ) [21]

| Entry                 | Substrate                           | ACCN (100 °C, 2h)<br>Yield, %                          | $h\nu$ (254 nm)<br>Yield, %                            |
|-----------------------|-------------------------------------|--|--|
| 1                     | 3-chloroprop-1-ene (22)             | (22a) 65 <sup>b</sup><br>(22b) 35 <sup>b</sup>         | -  |
| 2                     | <i>Tert</i> -butyl vinyl ether (23) | 74 <sup>a</sup>  | 60 <sup>a</sup>  |
| 3                     | <i>n</i> -Butyl vinyl ether (24)    | 99 <sup>a</sup>  | 31 <sup>a</sup>  |
| 4                     | Methylenecyclobutane (25)           | 68 <sup>a</sup>  | 54 <sup>a</sup>  |
| 5 <sup>ref.9,11</sup> | Acrylonitrile (26)                  | 80 <sup>a</sup>  | 82 <sup>a</sup>  |
| 6                     | Vinyl butyrate (27)                 | 99 <sup>a</sup>  | 88 <sup>a</sup>  |
| 7                     | Prop-2-en-1-ol (28)                 | 99 <sup>a,c</sup>                                      | 99 <sup>a,c</sup>                                      |
| 8                     | Prop-2-en-1-amine (29)              | (29a) 15 <sup>b,c,d</sup><br>(29b) 85 <sup>b,c,d</sup> | (29a) 50 <sup>b,c,d</sup><br>(29b) 50 <sup>b,c,d</sup> |
| 9                     | Crotonaldehyde (30)                 | 75 <sup>a,c</sup>                                      | 90 <sup>a,c</sup>                                      |

<sup>a</sup> Isolated Yield. <sup>b</sup> Relative product yield. <sup>c</sup> HOCH<sub>2</sub>CH<sub>2</sub>SH (0.3 equiv.) was added as chain carrier. <sup>d</sup> global Isolated yield; 65%.

From Table 2, column 4, the yields of hydrosilylation reactions of alkenes initiated by light in water are reported. Interestingly, the hydrosilylated product derived from hydrophobic 3-chloroprop-1-ene (22) is not obtained under photoinitiation. The hydrosilylated product derived from *tert*-butyl vinyl ether (23, Table 2, column 4, entry 2) is obtained in moderate yields (60%). The hydrosilylation product from *n*-butyl vinyl ether [12] is obtained in rather low yield (substrate 24, hydrosilylated product isolated in 31 % yield) in water [21].

When the water soluble prop-2-en-1-ol (28), prop-2-en-1-amine (29), and organic solvent-soluble crotonaldehyde (30) are treated with  $(\text{Me}_3\text{Si})_3\text{SiH}$  in the presence of a thiol under light initiation in water, the corresponding hydrosilylated products are obtained in high yields (Table 2, column 4, entries 7, 8, and 9). As observed in the thermal initiation (*vide supra*), substrate 29 (isolated global product yield 65 %), renders both a product derived from simple radical hydrosilylation of the C-C double bond (product 29a, 50% relative yield) and a ring-closed product (29b, *i.e.*: 2-(1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-yl)ethanamine 50% relative yield). The formation of product 29b is accounted for in Scheme 5. This behavior has been observed before in allyl and homoallyl alcohols [22]. The authors subjected the open chain hydrosilylated product derived from substrate 29, *i.e.*: 3-(1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-yl)propan-1-amine (29a), to photolysis (254-nm) and thermal treatment (ACCN, 100 °C) in water, as indicated in sections I.B.- and I.A.-, respectively. After two-hour reaction, no cyclic product 29b was formed. This experiment was performed in order to rule out the formation of 29b, as from a secondary reaction pathway (*i.e.*: 29a) [21].

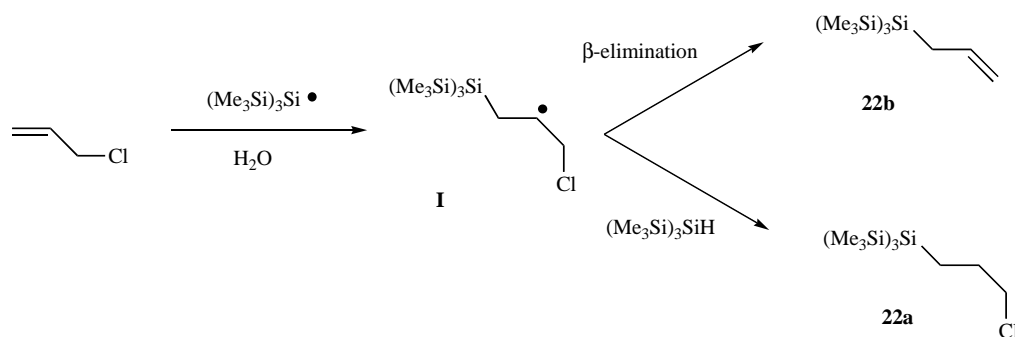
In order to give further support to the mechanism suggested in Scheme 4, the isolated open chain product 29a (4 mM) was treated in water (2 mL) with *t*-butylhydroperoxide (*t*-BuOOH, 10mM). The reaction was initiated by light (266 nm). After 40 min-reaction,

product 29b was obtained in *ca.*45% yield. This simple experiment shows that the aminyl radical II (Scheme 5) produced in this latter reaction from H-abstraction from 29a by *t*-BuO• radical, can trigger an intramolecular cyclization with displacement of the TMS group to render product 29b. Therefore, 1,3-H atom migration to render II (Scheme 5) could be suggested to take place along the reaction coordinate. In other works, the intramolecular substitution reaction at silicon, S<sub>Hi</sub> mechanism [23], has been suggested to yield ring-closure products [24].

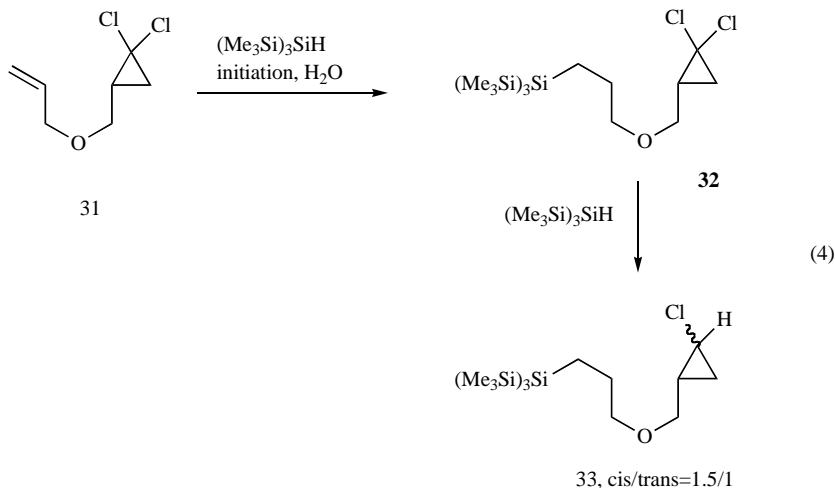
Notably, the hydrosilylation product derived from substrate 28, allylic alcohol, only affords an open chain product (99% isolated yield), as opposed to allylamine 29 where products 29a and 29b are observed. This difference could be related to the difference in the nucleophilicity of oxygen- and nitrogen-centered radicals in water, as opposed to organic solvents [22].

When the reaction is carried out in the absence of the thiol 2-mercaptoethanol, poor yields of hydrosilylated products are obtained from water-soluble substrates 28 and 29. Water-soluble hydrosilylated products are isolated by mixing the aqueous layer with pentane, the pentane layers discarded (to exclude excess of silane) and the aqueous phase lyophilized.

Hydrosilylation products derived from methylenecyclobutane (25), acrylonitrile [9,12] (26), and vinyl butyrate (27), are obtained in water in yields ranging from 54% to 88%, when the reactions are initiated photochemically (entries 4,5, and 6, column 4, Table 2). The authors suggest that UV-irradiation of  $(\text{Me}_3\text{Si})_3\text{SiH}$  generates silyl radicals from homolysis of the Si-H bond. The silyl radicals in turn add to the unsaturated C-C bonds generating carbon-centered radicals that abstract hydrogen atoms from  $(\text{Me}_3\text{Si})_3\text{SiH}$ , thus regenerating the silyl radicals. The hydrosilylation of prop-2-en-1-ol 28 and 3-chloroprop-1-ene 22 in the absence of solvent [10,11] and in the presence of air has also been attempted. A neat mixture (50 x 10<sup>-5</sup> moles of substrate and 50 x 10<sup>-5</sup> moles of  $(\text{Me}_3\text{Si})_3\text{SiH}$  was



**Scheme 6.** Proposed Mechanism for Formation of Products 22a and 22b in Water.



allowed to stir for 48 hrs in an open vessel. After the reaction time elapsed, no hydrosilylation product is observed, and the substrate is recovered unaltered. From these results, water can be regarded as a good support medium for carrying out the radical chain transformation, as the solubility of oxygen in the neat substrate is compromised. In a recent report [19], the radical chain hydrosilylation reaction of C-C multiple-bonded compounds in water has been initiated with dioxygen, and found that this radical initiation is very sensitive to the dioxygen concentration. However, yields of hydrosilylated products derived from alkenes under dioxygen radical initiation are rather low [19].

In the present study [21], it was found that substrate **22**, forms products **22a** and **22b** under thermal initiation. Formation of product **22a** and product **22b** can be accounted for from Scheme 6 [21]. Product **22a** arises from an ordinary hydrosilylation of the C-C double bond of **22**, while product **22b** is the result of a  $\beta$ -elimination of the chlorine atom from the intermediate radical species I (Scheme 6).

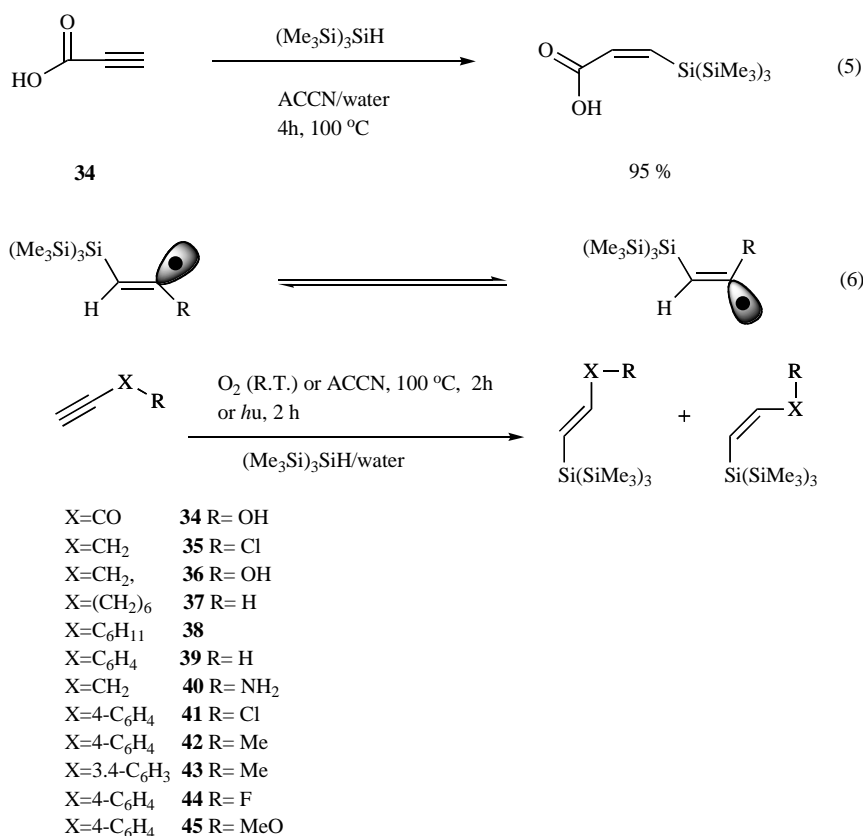
In alkenyl-substituted 1,1-dichlorocyclopropane ring systems [19], the hydrosilylation of C-C double bonds under radical thermal initiation precedes the chlorine atom reduction in water; that is, the hydrosilylation of C-C double bonds is faster than the chlorine atom removal by the  $(\text{Me}_3\text{Si})_3\text{Si}$  radical and that the one-chlorine atom reduction occurs under forced reaction conditions. Thus the authors [19] investigated the competition reaction between the *gem*-dichlorocyclopropane moiety reduction and hydrosilylation of double bonds in alkenyl-substituted *gem*-dichlorocyclopropane derivatives in water. The authors found that the hydrosilylation of the double bonds in alkenyl-substituted *gem*-dichlorocyclopropane derivatives precedes the chloro atom reduction in water. The substrate studied was **31** (eq 4). Reaction of **31** in water according to

the usual protocol (section 1.A.- at 70 °C) afforded the hydrosilylated product **32** with retention of both chlorine atoms. Prolonged reaction times showed the formation of monochloride **33**.

### 3-HYDROSILYLATION REACTIONS OF ALKYNES IN WATER

Recently, Zhou *et al.* [4b] reported that phenylacetylene is hydrosilylated in water in 1 hour through air initiation to render the hydrosilylated product in 85 % yield. It is well-known that the hydrosilylation of alkynes [10] in organic solvents takes place efficaciously under thermal initiation (AIBN), with the hydrosilylation products being obtained in high isolated yield, albeit in *E:Z* varying isomeric ratios. However, hydrosilylation of alkynes in water is very efficient and stereoselective under thermal initiation, as has been reported before [12]. For example, the *Z:E* ratio for the hydrosilylated product derived from 1-cyclohexylacetylene changes from 45:55 in toluene (80 °C) to 74:26 in water (100 °C) [16]. Thus, in organic solvents the initiation with AIBN takes place efficaciously albeit with poor stereoselectivity, while in water, ACCN is preferably used as initiator, and the stereoselectivity is much higher [12,19].

The hydrosilylation of water-soluble propiolic acid **34** (eq 5) [12,19] was tested under thermal-initiation conditions (section 1.A.-). The reaction proceeded efficiently giving the *Z*-alkene with optimal yield (99%, eq 5). It is worth noting that the hydrosilylation has recently been reported to be efficient also under neat conditions, where the initiation was linked to the presence of adventitious oxygen [18]. The authors [19] postulate that the higher stereoselectivity in favor of the *Z* isomer, under the experimental conditions, suggests that additional factors are playing a role in



**Scheme 7.** Hydrosilylation ((Me<sub>3</sub>Si)<sub>3</sub>SiH) Reactions of Triple-bonded Substrates in Water by Different Initiation Methods.



water. It could be hypothesized that the hindrance of approach of the bulky silane to the radicals may also be influenced by the organization of the organic material dispersed in water.

Unconjugated vinyl radicals are known to be sp<sup>2</sup> hybridized and to invert with a very low barrier (eq 6). Therefore, Z-hydrosilylated alkene products are preferentially obtained.

The hydrosilylation reaction of propiolic acid (**34**) and 3-chloroprop-1-yne (**35**) have also been tested under photochemical initiation conditions (Scheme 7), although in the former case, 2-mercaptoethanol is added as the chain carrier. The reactions proceed efficaciously affording the respective hydrosilylated alkenes in optimal reaction yields (95 %, Scheme 7, Table 3, column 5, entries 1 and 2). These hydrosilylated alkenes are obtained with varying Z:E isomeric ratios higher than 93:7. The retention of the chlorine atom is observed in this hydrosilylated alkene product derived from substrate **35** [12].

The hydrosilylation reaction of organic solvent-soluble 3-chloroprop-1-yne **35** and water-soluble prop-2-yn-1-ol **36** initiated by ACCN have been tested under the conditions described above (using in this latter case, 2-mercaptoethanol as the chain carrier). The reactions proceed efficaciously affording the respective hydrosilylated alkenes in optimal reaction yields (89 % and 98 %, respectively, Scheme 7, Table 3, column 4, entries 2, and 3). These alkenes are obtained with Z:E isomeric ratios varying from 89:11 (that from alkyne **35**) and 88:12 (that from alkyne **36**), determined by <sup>1</sup>H NMR spectroscopy [12].

(Me<sub>3</sub>Si)<sub>3</sub>SiH as a pure material or in solution reacts spontaneously and slowly at ambient temperature with molecular oxygen

from air, to form the siloxane. The mechanism of this unusual process has been studied in some detail [14]. Absolute rate constants for the spontaneous reaction of (Me<sub>3</sub>Si)<sub>3</sub>SiH with molecular oxygen (reaction 7) have been determined to be 3.5 × 10<sup>-5</sup> M<sup>-1</sup> s<sup>-1</sup> at 70 °C, and theoretical studies elucidated the reaction co-ordinates [25].

In organic solvents (benzene), Curran *et al.* [26] reported the (Me<sub>3</sub>Si)<sub>3</sub>SiH / dioxygen-mediated radical initiation reaction in the absence of an azo compound or light. Thus it was shown that (Me<sub>3</sub>Si)<sub>3</sub>SiH mediates in the radical addition reaction of aryl iodides to benzene, and the rearomatization is achieved through oxygen. The mechanism of this reaction in benzene is described in Scheme 8.

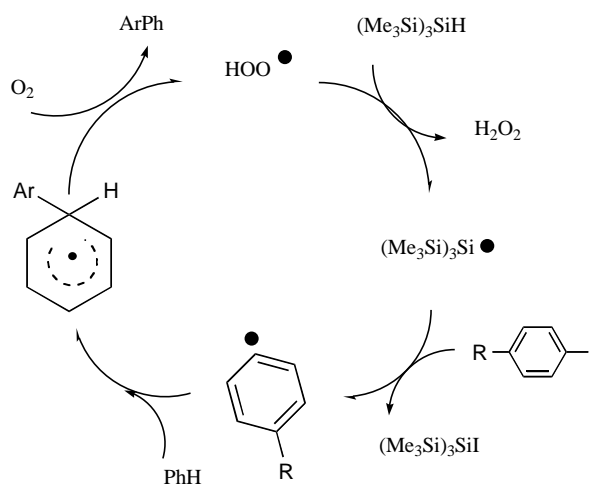
Silyl radicals, generated from reaction of (Me<sub>3</sub>Si)<sub>3</sub>SiH with oxygen, abstract the iodine atom from iodobenzene generating aryl radicals that suffer intramolecular addition to benzene (solvent) to form the cyclohexadienyl radical. Oxygen-induced rearomatization affords products along with hydroperoxyl radicals (HOO•). This radical abstracts hydrogen from the silane yielding (Me<sub>3</sub>Si)<sub>3</sub>Si• radicals completing the chain reaction.

Though it has been established that the thermal decomposition of ACCN is an excellent method for initiating the hydrosilylation reaction of unsaturated organic compounds in water (*vide supra*), the high temperature needed for the decomposition of the initiator (ACCN, 70 – 100 °C) precludes the treatment of thermally labile substrates and compromises the stability of products. Also, the photochemical initiation is very sensitive to the nature of the alkyne studied, since only alkynes with low absorptivities at 254 nm can be

**Table 3.** Hydrosilylation reactions of C-C triple bonds. Organic solvent-soluble substrates and hydrophilic substrates (10 mM) in water with  $(\text{Me}_3\text{Si})_3\text{SiH}$  (12 mM) under different initiation conditions [27a]

| Entry                   | Substrate                         | O <sub>2</sub> (R.T.)<br>Isolated Yield, % (Z:E<br>ratio) | ACCN<br>Isolated Yield, % (Z:E<br>ratio) | hν<br>Isolated Yield, % (Z:E<br>ratio) |
|-------------------------|-----------------------------------|---|--|--|
| 1 <sup>ref. 10,11</sup> | Propiolic acid (34)               | 99 (99:1)   | 95 (99:1)                                | 95 (97:3)                              |
| 2                       | 3-chloroprop-1-yne (35)           | 97 (99:1)   | 89 (89:11)                               | 95 (93:7)                              |
| 3 <sup>ref. 10</sup>    | Prop-2-yn-1-ol (36)               | 98 (99:1)   | 98 (88:12)                               | 99 (95:5)                              |
| 4 <sup>ref. 10,11</sup> | Phenylacetylene (39)              | 99 (99:1)   | 93 (70:30)                               | 98 (75:25)                             |
| 5 <sup>c</sup>          | Prop-2-yn-1-amine (40)            | 98 (96:4)   | 89 (88:12)                               | 99 (91:9)                              |
| 6                       | 1-chloro-4-ethynylbenzene (41)    | 88 (95:5)   | 90 (71:29)                               | 91 (79:21)                             |
| 7 <sup>ref. 16</sup>    | 4-ethynyl toluene (42)            | 96 (99:1)   | 90 (85:15)                               | 83 (79:21)                             |
| 8 <sup>b</sup>          | 3,4-dimethyl-ethynyl benzene (43) | 75 (99:1)   | 71 (80:20)                               | 67 (66:34)                             |
| 9 <sup>ref. 17</sup>    | 1-ethynyl-4-fluorobenzene (44)    | 89 (95:5)   | 85 (87:13)                               | 80 (85:15)                             |
| 10                      | 4-ethynyl anisole (45)            | 95 (99:1)   | 89 (85:15)                               | 90 (79:21)                             |

<sup>a</sup> HOCH<sub>2</sub>CH<sub>2</sub>SH (0.3 equiv.) was added as chain carrier. <sup>b</sup> 24 mM  $(\text{Me}_3\text{Si})_3\text{SiH}$  used, 4h-reaction. <sup>c</sup> Isolated yield.

**Scheme 8.** Dioxxygen Initiation in  $(\text{Me}_3\text{Si})_3\text{SiH}$ -mediated Reactions in Benzene.

employed. The photostability of the hydrosilylated alkenes at the irradiation wavelength is also a compromising and limiting factor in choosing this latter initiation technique.

Alkynes, are more effectively hydrosilylated in water by  $(\text{Me}_3\text{Si})_3\text{SiH}$  through dioxxygen initiation than alkenes are, where this condition affords only moderate to low yields of hydrosilylated alkanes (*vide supra*). Remarkably, the hydrosilylation of alkynes in water by  $(\text{Me}_3\text{Si})_3\text{SiH}$  proceeds with the highest Z-stereoselectivity when the reactions are initiated by dioxxygen (Table 3, column 3). In a recent report [19] alkynes such as 1-octyne (37), 1-cyclohexylacetylene (38), 1-phenylacetylene (39) and propiolic acid (34) are treated with  $(\text{Me}_3\text{Si})_3\text{SiH}$  in water under dioxxygen (see Section 1.C.-) initiation and yield the respective alkenes stereoselectively in high yields. Normally Z alkenes (Z:E ratios >99:1, isolated alkene yields >95 %) are formed. The hydrosilylation reactions of alkynes in water under dioxxygen initiation have shown the highest degree of stereoselectivity achieved under this milder initiation technique [19,27]. For example, the Z:E ratio from hydrosilylation of 1-cyclohexylacetylene varies from 96:4 in toluene (25 °C, with Et<sub>3</sub>B/air as initiator) to >99:1 in water (22 °C), under dioxxygen

initiation. More recently, these reactions are also performed in continuous-flow microreactors [14]. Comparison of these data with the analogous reactions carried out in toluene at 80-90 °C and AIBN as initiator [20], not only shows better product yields but also a higher stereoselectivity in favor of the Z isomer. Unconjugated vinyl radicals are known to be sp<sup>2</sup> hybridized and to invert with a very low barrier (eq 6). Therefore, Z-hydrosilylated alkene products are preferentially obtained.

A new series of light and thermal sensitive alkyne substrates and hydrosilylated products were studied through the dioxxygen initiation, as this latter was deemed the most convenient radical triggering event [27], providing further mechanistic evidence for the dioxxygen-radical initiation in water.

The water-soluble prop-2-yn-1-ol [21] (36), and prop-2-yn-1-amine (40) have been tested under dioxxygen initiation conditions employing the amphiphilic 2-mercaptoethanol as the chain carrier. The reactions proceed efficaciously (24 hrs) affording the respective hydrosilylated alkenes in optimal reaction yields (98%, Scheme 9, Table 3, column 3, entries 3 and 5, respectively). These hydrosilylated alkenes are obtained with Z:E isomeric ratios equal to 99:1 and 96:4 respectively. Water-soluble hydrosilylated alkene products are rinsed with pentane (to discard silane excess), lyophilized, and column-chromatographed by reverse-phase silica gel.

The hydrosilylation of water-insoluble 3-chloroprop-1-yne (35) with  $(\text{Me}_3\text{Si})_3\text{SiH}$  initiated by dioxxygen (24 hrs) affords a high yield of the corresponding hydrosilylated alkene product (97 %), in a Z:E ratio equal to 99:1 (Table 3, column 3, entry 2). Retention of the chlorine atom is observed in this hydrosilylated alkene product. It should be pointed out that a small minor by-product (*ca.* 5%) detected from the oxygen-initiated reactions in water corresponds to a compound observed by mass spectrometry of mass 280 and formula minima C<sub>9</sub>H<sub>28</sub>Si<sub>3</sub>O<sub>2</sub> whose structure has been assigned to  $(\text{Me}_3\text{SiO})_2\text{Si}(\text{H})\text{SiMe}_3$ , arising from the autoxidation of silane [20]. This by-product was confirmed by GC-co-injection with an authentic sample which has been synthesized according to a reported procedure [20].

When hydrosilylation reactions of substituted phenylacetylenes (41-45) are attempted under dioxxygen initiation (Table 3, column 3, entries 6-10) in water, the respective hydrosilylated styrene derivatives are obtained in high yields, ranging from 88% yield (that de-



rived from 1-chloro-4-ethynylbenzene (**41**) to 96 % yield (that from 4-ethynyltoluene (**42**)), and 75% yield from 3,4-dimethyl-ethynylbenzene (**43**). Notably, the stereoselectivity observed in all *tris*(trimethylsilyl)silyl-substituted styrenes are  $\geq 95\%$  in favor of the *Z* isomers. For comparison, the hydrosilylation in water of the parent phenylacetylene (**39**) initiated by dioxygen is shown in Table 3, where the hydrosilylated styrene is obtained quantitatively in the *Z* geometric isomer exclusively (Table 3, column 3, entry 4) [27].

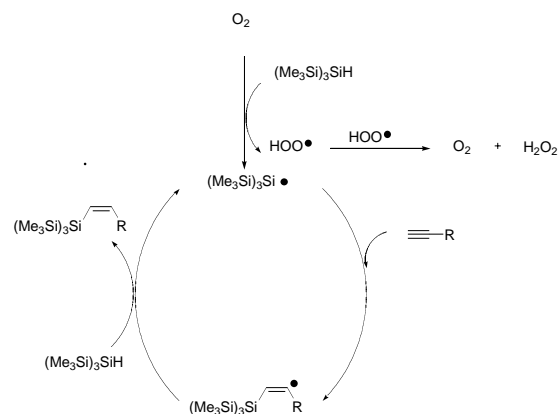
When substituted phenylacetylenes (**41-45**) are subjected to hydrosilylation reactions in water initiated by ACCN, the respective hydrosilylated styryl derivatives are obtained in good yields albeit with lower stereoselectivities than those observed under dioxygen initiation (Table 3, column 4, entries 6-10). The stereoselectivities are nevertheless in favor of the *Z* alkenes, ranging from 71:29 to 87:13. Notably, the stereoselectivities are lower than those obtained under dioxygen initiation. (*cf.* Table 3, columns 3 and 4). For comparison, the hydrosilylation in water of the parent phenylacetylene (**39**) initiated by ACCN is reported in Table 3 (entry 4, column 4) from previous studies, where the hydrosilylated styrene is obtained almost quantitatively (93%) with a *Z:E* stereoisomeric ratio equal to 70:20 [10].

The hydrosilylation reaction of water-soluble (**36**), and (**40**) have also been tested under photochemical initiation conditions employing 2-mercaptoethanol as the chain carrier. The reactions proceed efficaciously affording the respective hydrosilylated alkenes in optimal reaction yields (99 %, Scheme 9, Table 3, column 5, entries 3 and 5, respectively). These hydrosilylated alkenes are obtained with *Z:E* isomeric ratios equal to 95:5 and 91:9, respectively, determined by  $^1\text{H}$  NMR spectroscopy [19,21].

When substituted phenylacetylenes (**41-45**) are subjected to hydrosilylation reactions in water initiated by light, the respective hydrosilylated styryl derivatives are obtained in good yields albeit with poorer stereoselectivities as compared to those obtained under dioxygen (Table 3, column 5, entries 6-10). The stereoselectivities in favor of the *Z* alkenes range from 66:34 to 85:15. For comparison, the hydrosilylation yield in water of the parent phenylacetylene (**39**) induced by light is shown in Table 3 (entry 4, column 5), where the hydrosilylated styrene is obtained almost quantitatively (98%) with a *Z:E* stereoisomeric ratio equal to 75:25 [27].

For the dioxygen initiation, the authors postulate a mechanism as shown in Scheme 9 as operative in water for the hydrosilylation of C-C triple bonds. Upon reaction of dioxygen with  $(\text{Me}_3\text{Si})_3\text{SiH}$  (in water), silyl radicals along with hydroperoxyl radicals are generated. Hydroperoxyl radicals are known to be poorly reactive towards closed-shell compounds, and probably expected to recombine to form oxygen and hydrogen peroxide (or else abstract hydrogen from the silane to render  $(\text{Me}_3\text{Si})_3\text{Si}\cdot$  radicals that add to C-C triple bonds). No product derived from an addition reaction of hydroperoxyl radicals on C-C triple bonds has been detected under the reaction conditions. Nevertheless, hydrogen peroxide is expected to be a by-product of the reaction [27]. This latter was detected by adding to the aqueous reaction mixture (24 hour-reaction of 2-chloro-1-propyne or phenylacetylene,  $(\text{Me}_3\text{Si})_3\text{SiH}$ , dioxygen and water, where the hydrosilylated alkene product was previously detected by GC) a fresh colorless solution of  $\text{Fe}(\text{SCN})^+$  (10 mM) which turned immediately light orange due to the formation of  $\text{Fe}(\text{SCN})^+ \cdot$ . A blank experiment considering a freshly-prepared oxygen-saturated aqueous mixture of the respective alkyne and  $(\text{Me}_3\text{Si})_3\text{SiH}$ , did not lead to a change in color when  $\text{Fe}(\text{SCN})^+$  was added to the aqueous mixture, purporting that the chain reaction initiates very slowly. As a matter of fact, the radical chain reaction

under oxygen initiation is known to have a poor initiation yield, and the effectiveness of the overall radical hydrosilylation transformation relies on a very efficient propagation step. Another experiment carried out by adding  $\text{H}_2\text{O}_2$  (5%) to a 10 mM solution of  $\text{Fe}(\text{SCN})^+$ , isolated hydrosilylated alkene product (10 mM) and  $(\text{Me}_3\text{Si})_3\text{SiH}$  (10 mM) produced an orange solution [27].

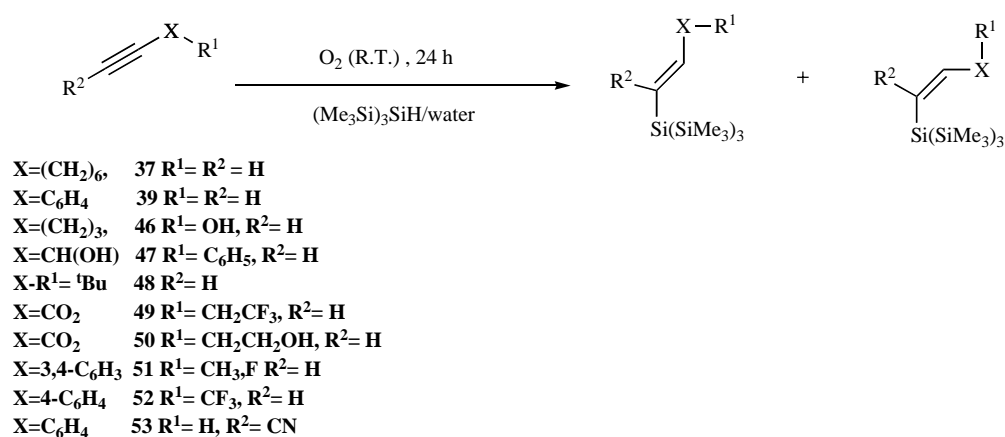


**Scheme 9.** Mechanism for the Dioxygen-Initiated Hydrosilylation Reactions of C-C triple Bonds in Water.

The silyl radicals perform the wellknown addition reaction to C-C triple bonds. Unconjugated  $\sigma$  vinyl radicals are known to be  $\text{sp}^2$  hybridized and to invert with a very low barrier (eq 6). Although  $(\text{Me}_3\text{Si})_3\text{Si}\cdot$  radicals have been shown to isomerize alkenes, the post-isomerization of the hydrosilylation adduct is not observed due to steric hindrance. The higher *Z*-stereoselectivity observed upon addition of  $(\text{Me}_3\text{Si})_3\text{Si}\cdot$  to triple bonds is rationalized in terms of the *E*  $\sigma$  vinyl silylated radical being more hindered to abstract hydrogen from  $(\text{Me}_3\text{Si})_3\text{SiH}$  than the *Z*  $\sigma$  vinyl silylated radical (eq 6). It is evident that the higher *Z* stereoselectivity observed upon dioxygen initiation in water (as compared to light-induced or thermal) is related to the stability of substrates and products under the experimental conditions. The milder dioxygen-initiated hydrosilylation reaction in water, as compared to the thermal and light-induced methods, circumvents issues associated with stability of substrates and products under the reaction conditions. In the photochemical initiation, light is partially absorbed by the substrate (*e.g.*: phenylacetylenes).

It is worth mentioning that under the experimental procedure, initiation with oxygen does not take place under  $\text{O}_2$  purging of the solution, nor with slow, continuous bubbling of  $\text{O}_2$  or air. Oxygen or air introduced slowly by syringe-pump techniques resulted in a less efficient initiation of the chain radical reaction. Probably, the slow oxygen addition into the solution with the balloon technique described above allows for sufficient oxygen to be dissolved in the water environment, thus initiating the radical chain (the solubility of oxygen in water is  $1.34 \times 10^{-3}$  M at 22 °C; taking into account that the substrate and  $(\text{Me}_3\text{Si})_3\text{SiH}$  concentrations are *ca.* 10 times higher, limiting working initiator concentrations could be reached by the methodology).

The water-soluble pent-4-yn-1-ol (**46**), and 2-hydroxyethyl propiolate (**50**) have been tested under dioxygen initiation conditions employing the amphiphilic 2-mercaptoethanol as the chain carrier (Table 4). The reactions proceed efficaciously (24 hrs) affording the respective hydrosilylated alkenes in optimal reaction yields (98% and 96%, respectively, Scheme 10, Table 4, column 3, entries 3 and 7, respectively). These hydrosilylated alkenes are obtained with *Z:E* isomeric ratios equal to 99:1.



**Scheme 10.** Hydrosilylation (( $Me_3Si$ ) $_3SiH$ ) Reactions of Triple-bonded Substrates in Water by the Dioxygen Initiation Method.

**Table 4.** Hydrosilylation reactions of C-C triple bonds. Organic solvent-soluble substrates and hydrophilic substrates (10 mM) in water with ( $Me_3Si$ ) $_3SiH$  (12 mM) under di-oxygen initiation conditions

| Entry                | Substrate                                   | O <sub>2</sub> (R.T.)<br>Isolated Product Yield, % (Z:E ratio) |
|----------------------|---|--|
| 1 <sup>ref.3</sup>   | Oct-1-yne (37)                              | 97 (99:1)  |
| 2                    | Phenylacetylene (39)                        | 99 (99:1)  |
| 3 <sup>ref.2</sup>   | Pent-4-yn-1-ol <sup>a</sup> (46)            | 98 (99:1)  |
| 4 <sup>ref.4b</sup>  | 1-phenylprop-2-yn-1-ol (47)                 | 75 (99:1)  |
| 5 <sup>ref.20</sup>  | 3,3-dimethylbut-1-yne (48)                  | 98 (96:4)  |
| 6 <sup>ref.27b</sup> | 2,2,2-trifluoroethylpropionate (49)         | 99 (99:1)  |
| 7 <sup>ref.27b</sup> | 2-hydroxyethyl propionate <sup>a</sup> (50) | 96 (99:1)  |
| 8 <sup>ref.4b</sup>  | 4-ethynyl-1-fluoro-3-methylbenzene (51)     | 89 (95:5)  |
| 9 <sup>ref.27c</sup> | 1-ethynyl-4-trifluoromethylbenzene (52)     | 95 (99:1)  |
| 10 <sup>ref.20</sup> | 3-phenylpropionitrile <sup>b</sup> (53)     | 88 (95:5)  |

<sup>a</sup> HOCH<sub>2</sub>CH<sub>2</sub>SH (0.3 equiv.) was added as chain carrier.

<sup>b</sup> 24 mM ( $Me_3Si$ ) $_3SiH$  used. Isolated yield.

For comparison, the hydrosilylation reaction of propiolic acid (**34**) with ( $Me_3Si$ ) $_3SiH$  in water initiated by dioxygen is reported, where a high Z:E stereoselectivity ratio is obtained (Table 3, column 3, entry 1) [19,12].

The hydrosilylation of water-insoluble oct-1-yne (**37**) with ( $Me_3Si$ ) $_3SiH$  initiated by dioxygen (24 hrs) affords a high yield of the corresponding hydrosilylated alkene product (97 %), in a Z:E ratio equal to 99:1, (Table 4, column 3, entry 1).

When hydrosilylation reactions of substituted phenylacetylenes (**51-53**) are attempted under dioxygen initiation (Table 4, column 3, entries 8, 9, and 10, respectively) in water, the respective hydrosilylated styrene derivatives are obtained in high yields, ranging from 89% yield (that derived from 4-ethynyl-1-fluoro-3-methylbenzene (**51**)) to 95 % yield (that from 1-ethynyl-4-trifluoromethylbenzene (**52**)), and 88% yield from 3-phenylpropionitrile (**53**). Notably, the stereoselectivity observed in all *tris*(trimethylsilyl)silyl-substituted styrenes are  $\geq 95\%$  in favor of the Z isomers.

#### 4. ( $Me_3Si$ ) $_3SiH$ CARBON-CARBON BOND FORMATION IN WATER

Perfluoroalkyl compounds have been the subject of intense studies during the past twenty years for their wide applications in different fields of chemistry. The development of fluorous combi-

natorial techniques have driven the search for convenient ways for introducing fluorous tags [28] containing perfluoroalkyl groups into various organic compounds [29]. The synthesis of these compounds cannot be achieved through classical nucleophilic substitutions on perfluoroalkyl halides,  $R_fX$ , as these substrates are thwarted from reacting by the  $S_N1$  mechanism, on account of the low stability of carbocations, and impeded to undergo  $S_N2$  substitutions due to repulsion of the lone electron pairs of the fluorine atoms to the back-side attack by the nucleophile [30].

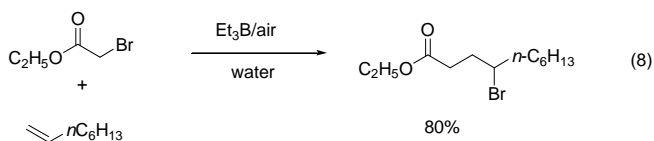
Compounds bearing the perfluoroalkyl moiety  $R_f-C$  bond, however, have been synthesized by different routes. One such route involves addition of  $R_f\cdot$  radicals to double bonds [31]. Perfluoroalkyl iodides and bromides are convenient sources of perfluoroalkyl radicals in the presence of radical initiators [32].

The photoinitiation based on the homolytic dissociation of perfluoroalkyl iodides,  $R_f-I$ , (the  $CF_2-I$  bond) is also applicable for the iodoperfluoroalkylation of unsaturated compounds with  $R_fI$  [33]. Ogawa *et al.* undertook an iodoperfluoroalkylation of unsaturated carbon-carbon double and triple bonds in benzotrifluoride as solvent [33]. These authors also utilized non-conjugated dienes, conjugated dienes, allenes, vinylcyclopropanes, and isocyanides as radical-acceptor substrates for the radical iodoperfluoroalkylation reactions in benzotrifluoride, affording good yields of the corresponding iodoperfluoroalkylated derivatives. Another route to the synthesis

of compounds with perfluoroalkyl moieties is through the  $S_{RN}1$  mechanism, which involves radicals and radical ions as intermediates [30,34].

On the other hand, intermolecular radical carbon-carbon bond formation reactions, *i.e.*: consecutive reactions, demand a careful synthetic planning to achieve carbon-carbon coupling products in fairly good yields. The key step in these consecutive reactions generally involves the intermolecular addition of  $R\bullet$  radicals to a multiple-bonded carbon acceptor. When a hydride chain carrier is involved, care has to be exercised in order to ensure that the effective rate of the radical addition is higher than the rate of H atom transfer.

When silicon-centered radicals are used [35], for an efficient chain process it is important that (i) the  $R'_3Si\bullet$  radical reacts faster with RZ (the precursor of radical  $R\bullet$ ) than with the alkene, and (ii) that the alkyl radical reacts faster with the alkene (to form the radical adduct) than with the silicon hydride. This process has in due course been termed “disciplined intermediates” [36]. The hydrogen donation step controls the radical sequence and the concentration of silicon hydride often serves as the variable by which the product distribution can be influenced. The majority of sequential radical reactions using silanes as mediators for the intermolecular carbon-carbon bond formation deals with tris(trimethylsilyl)silane,  $(Me_3Si)_3SiH$ , in organic solvents [37]. The need to resort to more environmentally friendly solvents opened the scope of radical carbon-carbon bond formation reactions in water, and other aqueous mixtures. Atom transfer intermolecular carbon-carbon bond formation reactions in water have been investigated in detail by many authors [38,39]. It has been reported [40] the intermolecular carbon-carbon bond formation reaction in water from ethyl bromoacetate and 1-octene affording ethyl 4-bromodecanoate in 80% yield when the reaction is initiated by triethylborane ( $BEt_3$ ) / air (eq 8).



Other radical precursors such as bromomalonate and bromoacetonitrile give excellent results of bromine atom transfer products in water. A tandem radical addition-oxidation sequence in water which converts alkenyl silanes into ketones has been elegantly described by Oshima *et al.* [40] Other types of intermolecular radical carbon-carbon bond formation reactions in water have been lately reported, describing radical additions to radical acceptors such as imines and their derivatives [41,42,43]. These latter consecutive radical reactions are also initiated by  $BEt_3$  / air.

As has been shown in section 3.-, the dioxygen-radical initiation has recently been successfully applied in water for the hydrosilylation of alkynes employing  $(Me_3Si)_3SiH$  / oxygen, rendering high yields of the respective hydrosilylated alkene products

with excellent Z stereoselectivity [19a,27]. In sections 2.- and 3.- the attempted radical reactions in water mediated by silyl radicals have been illustrated, among them, reduction of organic halides [11,12], reduction of azides [12], hydrosilylation reactions of multiple-bonded substrates [12,19a,21], intramolecular carbon-carbon bond formation reactions [12] etc., either by azo compounds decomposition, photochemically or through dioxygen initiation [44].

Dolbier *et al.* [45] have found that perfluorinated radicals were much more reactive than their hydrocarbon counterparts in addition to normal, electron rich alkenes such as 1-hexene (40 000 times more reactive) in organic solvents, and that H transfer from  $(Me_3Si)_3SiH$  to a perfluoro-*n*-alkyl radical such as  $n-C_7F_{15}CH_2CH(\bullet)C_4H_9$  was 110 times more rapid than to the analogous hydrocarbon radicals (eq 9).

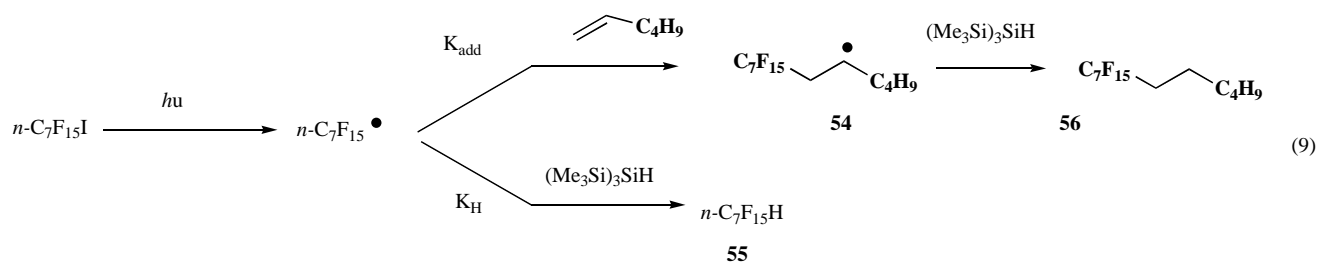
Thus the authors determined that  $k_{add}$  (eq 9) has a value of  $7.9 \times 10^6 \text{ M}^{-1}\text{s}^{-1}$  in benzene- $d_6$  at 298 K, and the value of  $k_H$  is *ca.*  $50 \times 10^6 \text{ M}^{-1}\text{s}^{-1}$  in benzene- $d_6$  at 303 K.

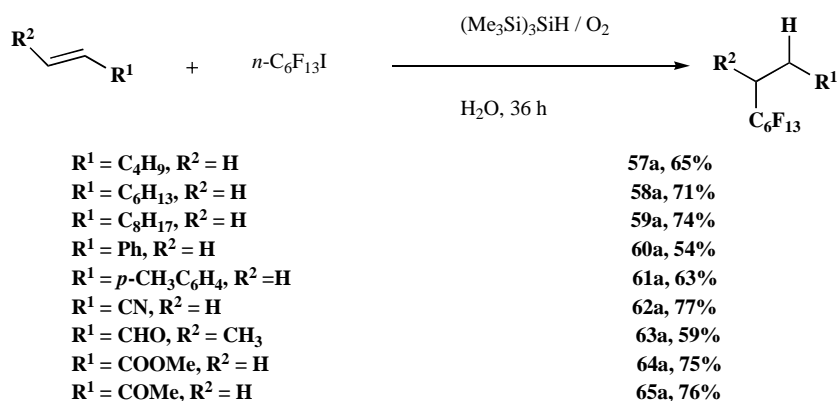
Given the known rate acceleration effects of radical reactions in water [42,44], it became worthwhile studying intermolecular carbon-carbon bond formation radical reactions in this medium, mediated by silyl radicals. Barata-Vallejo and Postigo [46] embarked on a study of the perfluoroalkylation reactions of electron rich alkenes and alkenes with electron withdrawing groups, to explore the scope and limitations of the intermolecular addition reactions of perfluoroalkylated radicals on alkenes in water mediated by  $(Me_3Si)_3SiH$ . The initiators employed are azo compounds and dioxygen which upto then had given the best results in previous studies [11,12,19a, 21,27].

A preliminary set of experiments was conducted [46] in order to adjust the right stoichiometry of the radical addition reactions of  $R_f\bullet$  radicals to alkenes so as to favor the radical addition product over the reduction product in water (as in products **55** and **56**, equation 9). For this preliminary experiment, 1-hexene was used as the radical acceptor, and  $n-C_6F_{13}I$ , as the source of  $R_f\bullet$  radicals. Reduction product  $n-C_6F_{13}H$  and addition product  $C_6F_{13}-C_6H_{13}$  were both obtained under different reaction conditions (by incremental amounts of  $(Me_3Si)_3SiH$ , and keeping alkene and  $n-C_6F_{13}I$  concentrations constant), under thermal initiation. The most favorable reaction conditions were obtained by using a molar ratio of *alkene* :  $(Me_3Si)_3SiH$  :  $R_fI$  equal to 25:2.5:5 and this ratio was chosen as optimal [47].

When 1-hexene is allowed to react with *n*-1-iodoheptafluorohexane,  $n-C_6F_{13}I$ , in water, initiated by  $(Me_3Si)_3SiH$  / dioxygen, 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorododecane **57a** [47,48] is obtained in 65% yield (Scheme 11, Table 5, entry 1). Analogously, 1-octene and 1-decene afford, upon reaction with  $n-C_6F_{13}I$  under the same radical conditions, products **58a** [48a,b] and **59a** [48b] in 71 and 74% yields (isolated yields), respectively (Scheme 11, Table 5, entries 2 and 3).

Styrene and *p*-methylstyrene when reacted with  $n-C_6F_{13}I$  in water under  $(Me_3Si)_3SiH$  / dioxygen initiation, give products **60a**[49]





**Scheme 11.** Intermolecular Radical Carbon-Carbon Bond Formation in Water. Reactions of Different Alkenes with *n*-1-Iodoperfluorohexane initiated by  $(\text{Me}_3\text{Si})_3\text{SiH}$  / dioxygen.

**Table 5.** Intermolecular radical carbon-carbon bond reactions in water. Reactions of different alkenes (40-50 mM) with *n*-1-iodoperfluorohexane (10 mM), initiated by  $(\text{Me}_3\text{Si})_3\text{SiH}$  (5 mM) / dioxygen

| Entry                   | Alkene              | Product, (%) <sup>a</sup> |
|-------------------------|---------------------|---------------------------|
| 1 <sup>ref.48c</sup>    | 1-Hexene            | 57a, (65)                 |
| 2 <sup>ref.50c</sup>    | 1-Octene            | 58a, (71)                 |
| 3 <sup>ref.48b</sup>    | 1-Decene            | 59a, (74)                 |
| 4 <sup>ref.51</sup>     | Styrene             | 60a <sup>b</sup> , (54)   |
| 5 <sup>ref.48b</sup>    | 4-Methylstyrene     | 61a <sup>b</sup> , (63)   |
| 6 <sup>ref.48c,51</sup> | Acrylonitrile       | 62a, (77)                 |
| 7                       | Crotonaldehyde      | 63a, (59)                 |
| 8 <sup>ref.51</sup>     | Methylacrylate      | 64a, (75)                 |
| 9 <sup>ref.48b</sup>    | Vinyl methyl ketone | 65a, (76)                 |

<sup>a</sup> Isolated yield after purification, based on  $\text{C}_6\text{F}_{13}\text{I}$

<sup>b</sup> 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorohexane,  $\text{CHF}_2(\text{CF}_2)_4\text{CF}_3$  was also obtained in 30-40 %.

and **61a** [50] in 54 and 63% yields respectively (Scheme 11, Table 5, entries 4 and 5). In these latter cases, reduction of the iodo compound (*i.e.*: 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorohexane,  $\text{CHF}_2(\text{CF}_2)_4\text{CF}_3$ ) was concomitantly obtained, as determined from the  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectra of the crude reaction mixtures (centered triplet at 6.29 ppm,  $J = 22$  Hz, from terminal  $\text{HCF}_2$ , in the  $^1\text{H}$  NMR spectrum and from the  $^{19}\text{F}$  NMR spectrum, the  $\text{CF}_2\text{H}$  peak at  $\delta = -114.05$  ppm). Alkenes with electron withdrawing groups such acrylonitrile (**26**), crotonaldehyde (**30**), methylacrylate, and vinyl methyl ketone also react with  $n\text{-C}_6\text{F}_{13}\text{I}$  under the same radical conditions, to afford the respective perfluoroalkylated products **62a** [48c,51], **63a**, **64a**, and **65a** [51-54] in yields ranging from 60 to 77% (Scheme 11, Table 5, entries 6-9).

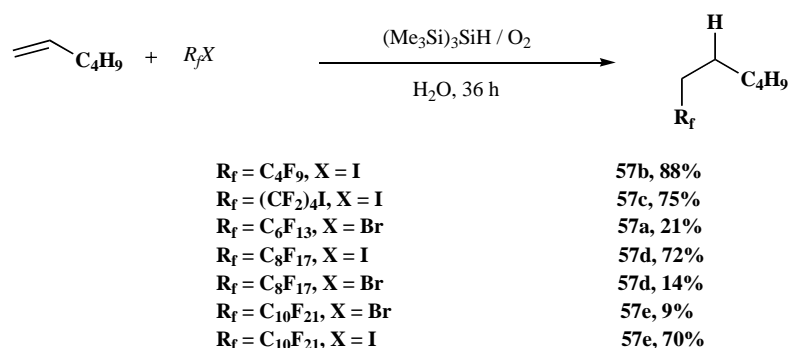
Encouraged by the above results obtained from reactions in water with  $n\text{-C}_6\text{F}_{13}\text{I}$  and different alkenes initiated by  $(\text{Me}_3\text{Si})_3\text{SiH}$  / dioxygen, the same authors proceeded with the perfluoroalkylation reactions of electron rich 1-hexene with an array of perfluoroalkyl halides (iodides and bromides) under the same radical conditions in water.

When 1-hexene reacts with *n*-1-iodo-perfluorobutane,  $n\text{-C}_4\text{F}_9\text{I}$ , under the reaction conditions described above, 1,1,1,2,2,3,3,4,4-nonafluorodecane **57b** [53] is obtained in 88% yield (Scheme 12, Table 6, entry 1). The reaction of 1-hexene with 1,4-diiodo-1,1,2,2,3,3,4,4-octafluorobutane,  $n\text{-IC}_4\text{F}_8\text{I}$ , affords 1,1,2,2,3,3,4,4-

octafluoro-1-iodo-decane **57c**, obtained in 75% yield (Scheme 12, Table 6, entry 2), and 15% of reduced 1,1,2,2,3,3,4,4-octafluorodecane, as observed from the  $^{19}\text{F}$  NMR spectrum, the  $\text{CF}_2\text{H}$  peak at  $\delta = -114.15$  ppm.

When *n*-1-bromo perfluorohexane,  $n\text{-C}_6\text{F}_{13}\text{Br}$ , is allowed to react with 1-hexene, product **57a** is obtained in poor yield (21%, Scheme 12, Table 6, entry 3 *cf.* with the same reaction carried out with  $n\text{-C}_6\text{F}_{13}\text{I}$ , Scheme 11, Table 5, entry 1). Analogously, the reaction of 1-hexene with *n*-1-bromo perfluorooctane,  $n\text{-C}_8\text{F}_{17}\text{Br}$ , progresses poorly to give product **57d** in 14% yield, while the same reaction employing  $n\text{-C}_8\text{F}_{17}\text{I}$  affords **57d** in 72% yield (Scheme 12, Table 6, entries 3 and 4, respectively). In the same fashion, *n*-1-iodoperfluorodecane,  $n\text{-C}_{10}\text{F}_{21}\text{I}$ , reacts with 1-hexene to afford **57e** in 70% yield (Scheme 12, Table 6, entry 7), but with  $n\text{-C}_{10}\text{F}_{21}\text{Br}$ , product **57e** is obtained in 9% yield (Table 6, entry 6). This could be in agreement with a stronger BDE of the bond  $\text{R}_f\text{-Br}$  than that of  $\text{R}_f\text{-I}$ .

In order to cast some light into the efficiency of the chain reaction with dioxygen, and see whether the low yields obtained from 1-hexene and  $\text{R}_f\text{Br}$  and  $(\text{Me}_3\text{Si})_3\text{SiH}$  / dioxygen are due either to a slow initiation step or the retardation in the propagation step on account of the different BDE of bromo and iodo perfluoroalkanes, the authors undertook the radical chain initiation with the azo compound ACCN, at 70 °C in water.



**Scheme 12.** Inter-molecular Radical Carbon-Carbon Bond Formation in Water. Reactions of 1-Hexene with Haloperfluoroalkanes in Water, Initiated by  $(\text{Me}_3\text{Si})_3\text{SiH}$  / Dioxygen.

**Table 6.** Inter-molecular radical carbon-carbon bond formation in water. Reactions of different iodoperfluoroalkanes (10 mM) with 1-hexene (50 mM), initiated by  $(\text{Me}_3\text{Si})_3\text{SiH}$  (5 mM)/ dioxygen

| Entry                       | Perfluoroalkane                       | Product, (%) <sup>a</sup>    |
|-----------------------------|---------------------------------------|------------------------------|
| <b>1</b> <sup>ref.55</sup>  | $\text{C}_4\text{F}_9\text{I}$        | <b>57b, (88)</b>             |
| <b>2</b>                    | $\text{I}(\text{CF}_2)_4\text{I}$     | <b>57c<sup>b</sup>, (75)</b> |
| <b>3</b> <sup>ref.48c</sup> | $\text{C}_6\text{F}_{13}\text{Br}$    | <b>57a, (21)</b>             |
| <b>4</b> <sup>ref.48c</sup> | $\text{C}_8\text{F}_{17}\text{I}$     | <b>57d, (72)</b>             |
| <b>5</b> <sup>ref.48c</sup> | $\text{C}_8\text{F}_{17}\text{Br}$    | <b>57d, (14)</b>             |
| <b>6</b> <sup>ref.48b</sup> | $\text{C}_{10}\text{F}_{21}\text{Br}$ | <b>57e, (9)</b>              |
| <b>7</b> <sup>ref.48b</sup> | $\text{C}_{10}\text{F}_{21}\text{I}$  | <b>57e, (70)</b>             |

<sup>[a]</sup> Isolated yield based on  $\text{R}_f\text{X}$

<sup>[b]</sup> 15% of reduced 1,1,2,2,3,3,4,4-octafluoro-decane was also obtained, as observed from the <sup>19</sup>F NMR spectrum, the  $\text{CF}_2\text{H}$  peak at  $\delta = -114.15$  ppm.

When a series of alkenes are allowed to react with bromo perfluoroalkanes (*n*-1-bromo perfluorohexane, *n*-1-bromo perfluorooctane, and *n*-1-bromo perfluorodecane) in water as described above. for the thermal radical initiation reaction, the respective perfluoroalkylated products are obtained in yields ranging from 50 to 77% (Scheme 13, Table 7). Thus, 1-hexene reacts with *n*- $\text{C}_6\text{F}_{13}\text{Br}$ , *n*- $\text{C}_8\text{F}_{17}\text{Br}$ , and *n*- $\text{C}_{10}\text{F}_{21}\text{Br}$  to afford the corresponding perfluoroalkylated hexanes **57a** [51,47], **57d** [50,46], and **57e** [50,46] in 75, 70, and 62% yields, respectively (Scheme 13, Table 7, entry 1). 1-Octene (Table 7, entry 2) and 1-decene (Table 7, entry 3) also afford perfluoroalkylated alkenes in fairly good yields (50-77%). Styrene and 4-methylstyrene react with *n*- $\text{C}_6\text{F}_{13}\text{Br}$ , *n*- $\text{C}_8\text{F}_{17}\text{Br}$ , and *n*- $\text{C}_{10}\text{F}_{21}\text{Br}$  to afford the alkylated products in good yields, ranging from 46 to 81% (Scheme 13, Table 7, entries 4 and 5). Acrylonitrile, upon reaction with the series  $\text{C}_n\text{F}_{2n+1}\text{Br}$  (*n* = 6, 8, and 10) affords the perfluoroalkylated-substituted propionitriles **62a** [54], **62d** [54], and **62e** [54,50] in 51, 50, and 44% yields, respectively (Table 7, entry 6). Crotonaldehyde, upon reaction with *n*- $\text{C}_6\text{F}_{13}\text{Br}$ , *n*- $\text{C}_8\text{F}_{17}\text{Br}$ , and *n*- $\text{C}_{10}\text{F}_{21}\text{Br}$  under the reaction conditions described above, gives the perfluoroalkylated-substituted butyraldehydes **63a**, **63d**, and **63e** in 62, 60, and 55% yields, respectively (Scheme 13, Table 7, entry 7).

Methyl acrylate upon reaction with the series  $\text{C}_n\text{F}_{2n+1}\text{Br}$  (*n* = 6, 8, and 10) affords the perfluoroalkylated-substituted methyl propionates **64a**, **64d** [55], and **64e** in 55, 53, and 43% yields, respectively (Scheme 13, Table 7, entry 8), while vinyl methyl ketone when reacted with *n*- $\text{C}_6\text{F}_{13}\text{Br}$ , *n*- $\text{C}_8\text{F}_{17}\text{Br}$ , and *n*- $\text{C}_{10}\text{F}_{21}\text{Br}$  in water under ACCN /  $(\text{Me}_3\text{Si})_3\text{SiH}$  thermal initiation (Section 1.C.-), affords the 5-perfluoroalkylated-substituted 2-butanones **65a** [54,55],

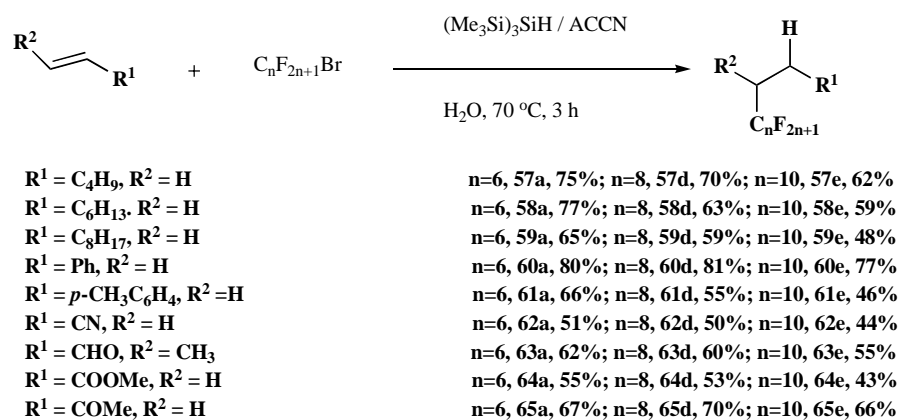
**65d** [56,54], and **65e** [54] in 67, 70, and 66% yields, respectively (Scheme 13, Table 7, entry 9).

The same authors also undertook the ACCN-radical initiated perfluoroalkylation of 1-hexene with  $\text{C}_n\text{H}_{2n+1}\text{I}$  (*n* = 8, and 10), and obtained compounds **57d** and **57e** [48d], respectively, in yields ranging from 90-95%, while the same yields under dioxygen-radical initiation were in the 70% range (*cf.*  $\text{O}_2$ -initiated radical yields of **57d** and **57e** from Table 6, entries 4 and 7, respectively).

These sets of experiments would reveal that the lower yields obtained with the bromo perfluoroalkanes and alkenes in water under dioxygen initiation than those obtained under ACCN initiation could be attributed to a slower initiation in the former rather than a retardation in the propagation step due to differences in BDE of  $\text{R}_f\text{-I}$  and  $\text{R}_f\text{-Br}$  bonds; however, some involvement of the BDE of  $\text{R}_f\text{-I}$  versus  $\text{R}_f\text{-Br}$  should also be considered.

It is observed that the yields of products **57a-65a** are much better under ACCN initiation (Table 7) than under dioxygen initiation (Table 5). It can be deduced that all water-insoluble material (substrates and reagents) suspended in the aqueous medium can interact due to the vigorous stirring that creates an efficient vortex and dispersion. In the dioxygen initiation, the chain mechanism probably benefits from the enhanced contact surface of tiny drops containing  $(\text{Me}_3\text{Si})_3\text{SiH}$  and dioxygen. The mechanism of the  $(\text{Me}_3\text{Si})_3\text{SiH}$ -mediated inter-molecular perfluoroalkylation of alkenes in water is depicted in Scheme 14.

The  $(\text{Me}_3\text{Si})_3\text{Si}\cdot$  radical, produced by some kind of radical initiation (either by dioxygen or thermal decomposition of ACCN initiator) in water, abstracts the halogen atom (iodine or bromine) from  $\text{R}_f\text{X}$ . This  $\text{R}_f\cdot$  radical reacts faster with the alkene than with



**Scheme 13.** Intermolecular Radical Carbon-Carbon Bond Formation in Water. Reactions of Alkenes with *n*-1-Bromoperfluoroalkanes ( $C_nF_{2n+1}Br$ ,  $n = 6, 8,$  and  $10$ ) in Water, Initiated by  $(Me_3Si)_3SiH / ACCN$ .

**Table 7.** Intermolecular radical carbon-carbon bond formation in Water. Reactions of different *n*-1-bromoperfluoroalkanes,  $C_nF_{2n+1}Br$  ( $n = 6, 8,$  and  $10$ ) (10 mM), with alkenes (40-50 mM), initiated by  $(Me_3Si)_3SiH$  (5 mM)/ ACCN (3 mM) at 70 °C.

| Entry   | Bromoperfluoroalkane |                                  |                              |                              |
|---|----------------------|----------------------------------|------------------------------|------------------------------|
|   | 1-Alkene             | <i>n</i> - $C_6F_{13}Br$         | <i>n</i> - $C_8F_{17}Br$     | <i>n</i> - $C_{10}F_{21}Br$  |
| Perfluoroalkylated Product, (%product) <sup>a</sup> |                      |                                  |                              |                              |
| 1   | 1-Hexene             | 57a <sup>ref.48c</sup> , (75)    | 57d, (70)                    | 57e, (62)                    |
| 2   | 1-Octene             | 58a <sup>ref.50</sup> , (77)     | 58d, (63)                    | 58e, (59)                    |
| 3   | 1-Decene             | 59a <sup>ref.48c</sup> , (65)    | 59d, (59)                    | 59e, (48)                    |
| 4   | Styrene              | 60a <sup>ref.51</sup> , (80)     | 60d, (81)                    | 60e, <sup>ref.51</sup> (77)  |
| 5   | 4-Methylstyrene      | 61a <sup>ref.48b</sup> , (66)    | 61d, (55)                    | 61e, (46)                    |
| 6   | Acrylonitrile        | 62a <sup>ref.48c,51</sup> , (51) | 62d, (50)                    | 62e <sup>ref.53</sup> , (44) |
| 7   | Crotonaldehyde       | 63a, (62)                        | 63d, (60)                    | 63e, (55)                    |
| 8   | Methylacrylate       | 64a, <sup>ref.51</sup> (55)      | 64d, (53)                    | 64e, (43)                    |
| 9   | Vinyl methyl ketone  | 65a <sup>ref.48b</sup> , (67)    | 65d <sup>ref.53</sup> , (70) | 65e <sup>ref.53</sup> , (66) |

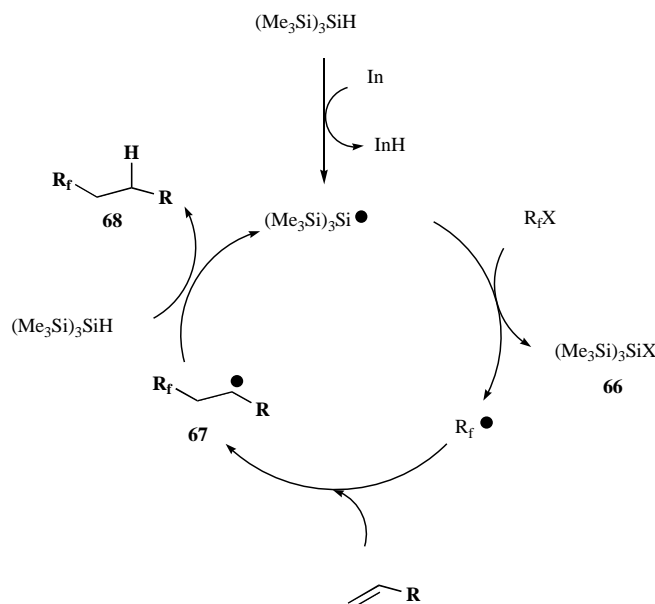
<sup>[a]</sup> Isolated yield after purification

the silicon hydride, affording the perfluoroalkylated radical adduct **67**. Radical adduct **67** abstracts hydrogen from the silane, affording the perfluoroalkyl-substituted alkane **68**, and regenerating the silyl radical, thus propagating the chain.

According to what has been observed and measured by Dolbier *et al.* [53], in benzene-*d*<sub>6</sub>, the ratio of products [**56**]/[**55**] (eq 9) should equal [47] the ratio of rate constants for addition (of perfluorinated heptyl radical on 1-hexene) and rate constant for H abstraction from  $(Me_3Si)_3SiH$  times the ratio of concentrations of alkene and silane [47]. According to the experimental conditions, employing equation in reference 47, a theoretical ratio of perfluoroalkylated alkane over reduced perfluoroalkane of *ca.* 1.3 would be obtained, which is not completely in agreement with the unobserved reduced perfluoroalkanes in these reaction systems in water (*i.e.*:  $CHF_2(CF_2)_4CF_3$ , when iodoperfluorohexane is employed). Transition state polar effects (in water) must be playing a decisive role in such radical addition reactions onto alkenes in water exerting an acceleration effect at the expense of the hydrogen atom transfer reaction [57].

The electrophilicity of  $R_f^\bullet$  radicals are the dominant factor giving rise to their high reactivity. The stronger carbon-carbon bond which forms when  $R_f^\bullet$  versus  $R^\bullet$  radicals add to an alkene is a driving force for the radical addition (the greater exothermicity of the

$R_f^\bullet$  radical addition is expected to lower the activation energy). It has been observed, in organic solvents, that the rates of addition of  $R_f^\bullet$  radicals onto alkenes correlate with the alkene IP (which reflects the *HOMO* energies) [53]. Indeed, the major transition state orbital interaction for the addition of the highly electrophilic  $R_f^\bullet$  radical to an alkene is that between the *SOMO* of the radical and the *HOMO* of the alkene. Thus, the rates of  $R_f^\bullet$  radical addition to electron deficient alkenes are slower than those to electron rich alkenes (as observed in organic solvents). From these results, however, it becomes apparent, that in water the rates for  $R_f^\bullet$  radical addition to both electron rich and electron deficient alkenes could be comparable, given the similar reaction yields (*cf.* in Table 7, entries 1-3 and 6-9, respectively). In order to clarify this subtle aspect of the reaction in water, a set of experiments designed to compare the ratios of  $(K_H/K_{add})_{1\text{-hexene}}$  and  $(K_H/K_{add})_{\text{acrylonitrile}}$  for the addition reaction of *n*- $C_6F_{13}I$  to the electron rich 1-hexene and electron deficient acrylonitrile, respectively was undertaken. These ratios of rate constants are obtained by plotting  $[n\text{-}C_6F_{13}H]/[57a]$  vs  $[(Me_3Si)_3SiH]/[1\text{-hexene}]$  and  $[n\text{-}C_6F_{13}H]/[62a]$  vs  $[(Me_3Si)_3SiH]/[\text{acrylonitrile}]$ , respectively, when the reactions are initiated thermally, by using incremental amounts of  $(Me_3Si)_3SiH$ , and keeping the alkene and *n*- $C_6F_{13}I$  concentrations constant. The authors obtained slopes for both plots equal to  $1.55 \pm 0.09$  ( $r^2 = 0.998$ ) and  $1.88 \pm 0.19$  ( $r^2 = 0.989$ ) for  $(K_H/K_{add})_{1\text{-hexene}}$  and  $(K_H/K_{add})_{\text{acrylonitrile}}$  respectively. This seems to



**Scheme 14.** Mechanism for Radical Carbon-Carbon Bond Formation Reactions from Alkenes and Perfluoroalkyl Iodides in Water, Mediated by  $(\text{Me}_3\text{Si})_3\text{SiH}$ .

indicate that the reactivities of electron rich and electron deficient alkenes towards  $\text{R}_f\cdot$  radicals in water are leveled off [46].

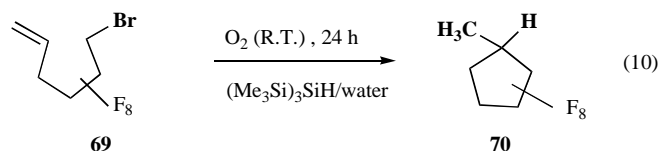
The ratio of rates constants  $(K_{\text{H}}/K_{\text{add}})_{1\text{-hexene}}$  obtained in benzotrifluoride as solvent [43] for the reaction of  $n\text{-C}_7\text{F}_{15}\text{I}$  and 1-hexene with  $(\text{Me}_3\text{Si})_3\text{SiH}$  as the hydrogen donor (eq 9) is 6.32, while that same ratio of rate constants for the reaction of  $n\text{-C}_6\text{F}_{13}\text{I}$  with 1-hexene in water is 1.55 (*vide supra*). Owing to the unavailability of the rate constant for  $\text{R}_f\cdot$  radical addition onto double bonds *in water* makes comparisons difficult; however, the results would seem to imply that the rate for hydrogen donation from  $(\text{Me}_3\text{Si})_3\text{SiH}$  to the  $\text{R}_f\cdot$  radical relative to the addition reaction is four times slower in *water* than in benzotrifluoride as solvent (*i.e.*:  $(K_{\text{H}}/K_{\text{add}})_{\text{water}} / (K_{\text{H}}/K_{\text{add}})_{\text{Benzotrifluoride}} = 0.25$ ).

The intermolecular radical carbon-carbon bond formation reactions presented herein in water take advantage of the halophilicity of silyl radicals towards iodine and bromine atoms. In this case, the halogen atom transfer reaction from **66** towards the perfluoroalkylated radical adduct **67** (Scheme 14) is slower than the hydrogen atom abstraction from the  $(\text{Me}_3\text{Si})_3\text{SiH}$ , thus providing the reduced perfluoroalkylated product **68**. As a support to the mechanism proposed (Scheme 14), 2-iodo-1,1,1,3,3,3-hexamethyl-2-(trimethyl)trisilane (**66**, X = I, Scheme 14) was isolated and characterized from the reaction mixtures described in Scheme 11. In the same fashion, from reactions described in Scheme 13, 2-bromo-1,1,1,3,3,3-hexamethyl-2-(trimethyl)trisilane (**66**, X = Br, Scheme 14) was detected by gas chromatography, isolated, and compared with an authentic sample. As mentioned above, by plotting  $[n\text{-C}_6\text{F}_{13}\text{H}]/[\mathbf{57a}]$  vs  $[(\text{Me}_3\text{Si})_3\text{SiH}]/[1\text{-hexene}]$ , a straight line, whose slope represents  $(K_{\text{H}}/K_{\text{add}})_{1\text{-hexene}}$  is obtained (with a value of  $1.55 \pm 0.09$ ,  $r^2 = 0.998$ ). The intercept of this plot, shows, remarkably, no deviation from the ideal value of zero, purporting that the only source of  $n\text{-C}_6\text{F}_{13}\cdot$  radical reduction (*i.e.*:  $n\text{-C}_6\text{F}_{13}\text{H}$ ) is the silane, and not the solvent or the alkene [53].

It is interesting to point out that the scope of the radical dioxygen initiation reactions with silanes in water has been extended from the use in hydrosilylation reactions of C-C multiple bonds [12,45] (section 1.2.-), to the intermolecular radical carbon-carbon bond formation. From results obtained in Tables 5, 6, and 7, the

thermal ACCN-initiation is deemed a better radical initiating technique than the dioxygen-initiation, as opposed to what has been observed in the radical hydrosilylation of alkynes in water [19a,27]. However, should thermally labile alkenes need be employed, the radical dioxygen initiation methodology is a good option of choice, as fairly good yields of carbon-carbon coupling products can be obtained in water under the mild dioxygen initiation technique, in the absence of reduced perfluorinated halides. Interesting and notorious solvent effects can be invoked in water on the rates of reactions of perfluoroalkyl radicals towards alkenes and silicon hydrides, respectively, as opposed to those found in benzene, where the latter rates are *ca.* six times faster at equal concentrations of silanes and alkenes. This account [46] provides also a convenient method to achieve perfluoroalkylation reactions of alkenes in water to render perfluoroalkylated alkanes as key intermediates in the synthesis of fluorophors and other fluorinated materials.

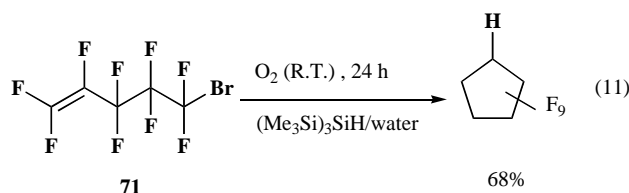
In a previous study [12], the radical cyclization in water of 1-((*E*)-but-2-enyloxy)-2-iodobenzene (**6**) to afford 3-ethyl-2,3-dihydrobenzofuran (**7**) in 85% yield (eq 2) has been reported, when  $(\text{Me}_3\text{Si})_3\text{SiH}$  and an azo initiator is employed. In this account, 6-bromo-3,3,4,4,5,5,6,6-octafluoro-1-hexene [45] (12 mM) **69** was subjected to reaction (24 h) with  $(\text{Me}_3\text{Si})_3\text{SiH}$  (8 mM) and dioxygen in water (5 mL), as described in Section 1.C., and obtained the *exo-trig* cyclization product 1,1,2,2,3,3,4,4-octafluoro-5-methylcyclopentane **70** (eq 10) in 76% yield (isolated) [58].



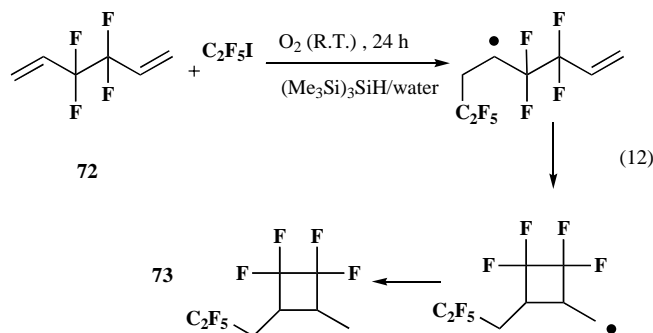
Though the measurement of the rate constant for cyclization in the heterogeneous water system is difficult to be obtained, the cyclohexane cyclized product has not been observed in water under the reaction conditions reported. No uncyclized-reduced product is neither observed [58].

Analogously, cyclization of 5-bromo-1,1,2,3,3,4,4,5,5-nonafluoro-pent-1-ene (12 mM) **71** in water triggered by

(Me<sub>3</sub>Si)<sub>3</sub>SiH (8 mM) / dioxygen leads to nonafluorocyclopentane, the *exo-trig* cyclization product in 68% yield (isolated). No reduced product could be isolated from the reaction mixture. The reaction carried out in benzene-*d*<sub>6</sub> does not lead to cyclization product (eq 11) [58].



When 3,3,4,4,1,5-hexadiene (40 mM) **72** is allowed to react (24 h) in water with (Me<sub>3</sub>Si)<sub>3</sub>SiH (5 mM) / dioxygen and C<sub>2</sub>F<sub>5</sub>I (10 mM), product **73** is obtained in 61% yield, based on C<sub>2</sub>F<sub>5</sub>I (eq 12).



## 5. SUMMARY AND OUTLOOK

The synthetically useful silyl radical-mediated transformations that can be accomplished in water encompass simple organic halide reductions, azide reductions, deoxygenation reactions, hydrosilylation reactions of carbon-carbon multiple bonds and carbon-oxygen double bonds, intramolecular carbon-carbon bond formation, and intermolecular consecutive radical reactions, and more recently, perfluoroalkylation reactions of multiple bonds. Future studies should be directed at the syntheses of more complex structures by intermolecular carbon carbon and carbon-heteroatom transformations in water mediated by silyl radicals.

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- Indeed, upon silyl radical attack on the C-C double bond of **29**, the 1-amino-3-(1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-yl)propan-2-yl radical would be formed. This latter radical, if Si<sub>H</sub> mechanism took place, would suffer bond cleavage and homolytic substitution at silicon to render, upon ulterior hydrogen abstraction, 3-(1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-yl)butan-1-amine product, which was not found in the reaction mixture.
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