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$(Me_3Si)_3SiH$-Mediated Intermolecular Radical Perfluoroalkylation Reactions of Olefins in Water

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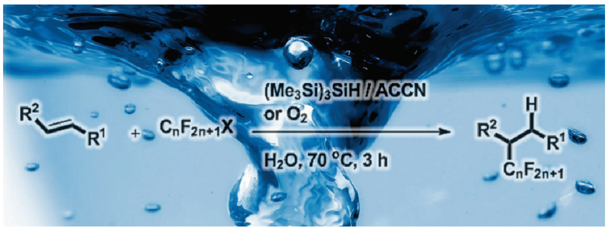

Perfluoroalkyl-substituted compounds are regarded as important components of fluorophors and for the introduction of fluorous tags into organic substrates. Their syntheses in organic solvents are achieved through different methods, among which, the addition of perfluoroalkyl radicals to unsaturated bonds represents a convenient choice. On the other hand, intermolecular radical reactions in water have attracted the attention of synthetic chemists as a strategic route to carbon−carbon bond formation reactions. In this paper we undertook the intermolecular addition of perfluoroalkyl radicals on electron rich alkenes and alkenes with electron withdrawing groups in water, mediated by silyl radicals, and obtained perfluoroalkyl-substituted compounds in fairly good yields. The radical triggering events employed consist of the thermal decomposition of an azo compound and the dioxygen initiation. Our results indicate that for intermolecular carbon−carbon bond formation reactions mediated by $(Me_3Si)_3SiH$, the decomposition of the azo compound 1,1′-azobis(cyclohexanecarbonitrile) (ACCN) is the best radical initiator. We also found that water exerts a relevant solvent effect on the rates of perfluoroalkyl radical additions onto double bonds and the H atom abstraction from the silane. Our account provides a versatile and 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. This is the first report where perfluoroalkyl-substituted alkanes are synthesized through intermolecular radical carbon−carbon bond formation reactions in water, mediated by silyl radicals.

1. Introduction

Perfluoroalkyl compounds have attracted much attention during the past twenty years for their wide applications in different fields of chemistry. In particular, recent advance in fluorous[1] combinatorial technique requires convenient methods for selective introduction of fluorous tags containing perfluoroalkyl groups[2] into various organic compounds.[3] The synthesis of these compounds cannot be achieved through classical nucleophilic substitutions on perfluoroalkyl halides, R_fX, as these substrates are impeded to react by the

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S_N1 mechanism, on account of the low stability of carbocations, and precluded to undergo S_N2 substitutions due to repulsion of the lone electron pairs of the fluorine atoms to the backside attack by the nucleophile.[4]

Compounds bearing the perfluoroalkyl moiety R_f-C bond, however, have been synthesized by different routes. One such route involves addition of $R_f^{\bullet}$ radicals to double bonds.[5−7] Perfluoroalkyl iodides and bromides are convenient perfluoroalkyl radical precursors in the presence of radical initiators.[8]

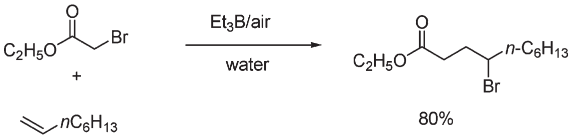
Because perfluoroalkyl iodides exhibit their absorption in UV and near-UV regions, the photoinitiation based on the homolytic dissociation of the R_f-I bond is also applicable for the iodoperfluoroalkylation of unsaturated compounds with R_fI.[9] Ogawa et al. undertook an iodoperfluoroalkylation of unsaturated carbon−carbon double and triple bonds in benzotrifluoride as solvent.[4,9] These authors also utilized nonconjugated 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.[4,10]

On the other hand, intermolecular radical carbon−carbon bond formation reactions, i.e., consecutive reactions, demand a careful synthetic design 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,[11] 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 adduct radical) than with the silicon hydride. This process has in due course been termed "*disciplined intermediates*".[12] 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.[13]

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.[14] Oshima et al.[14a] reported 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 1).



(1)

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 that converts alkenyl silanes into ketones has been elegantly described by Oshima et al.[15] Other types of intermolecular radical carbon−carbon bond formation reactions in water have been reported lately, describing radical additions to radical acceptors such as imines and their derivatives.[16−18] These latter consecutive radical reactions are also initiated by BEt_3/air.

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.[19]

We have attempted several radical reactions in water mediated by silyl radicals, among them, reduction of organic halides,[20] reduction of azides,[21] hydrosilylation reactions of multiple-bonded substrates,[22] intramolecular carbon−carbon bond formation reactions,[23] etc., either by azo compounds decomposition, photochemically or through dioxygen initiation.

Dolbier et al.[24] have found that perfluorinated radicals were much more reactive than their hydrocarbon counterparts in addition to normal, electron rich alkenes such as

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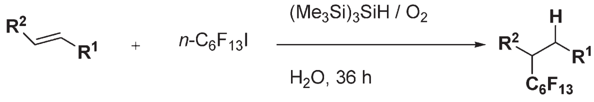
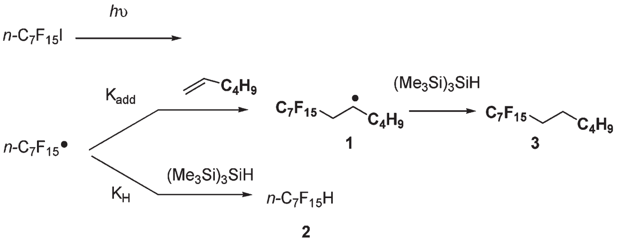
SCHEME 1. Intermolecular Radical Carbon−Carbon Bond Formation in Water[a]



$R^1 = C_4H_9$, $R^2 = H$	**1a, 65%**
$R^1 = C_6H_{13}$, $R^2 = H$	**2a, 71%**
$R^1 = C_8H_{17}$, $R^2 = H$	**3a, 74%**
$R^1 = Ph$, $R^2 = H$	**4a, 54%**
$R^1 = p\text{-}CH_3C_6H_4$, $R^2 = H$	**5a, 63%**
$R^1 = CN$, $R^2 = H$	**6a, 77%**
$R^1 = CHO$, $R^2 = CH_3$	**7a, 59%**
$R^1 = COOMe$, $R^2 = H$	**8a, 75%**
$R^1 = COMe$, $R^2 = H$	**9a, 76%**

[a]Reactions of different alkenes with *n*-1-iodoperfluorohexane initiated by $(Me_3Si)_3SiH$/dioxygen.

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 $n\text{-}C_7F_{15}CH_2CH^{\bullet}C_4H_9$ was 110 times more rapid than that to the analogous hydrocarbon radicals (eq 2).



(2)

Thus the authors determined that k_{add} (eq 2) has a value of $7.9 \times 10^6\ M^{-1}\ s^{-1}$ in benzene-d_6 at 298 K, and the value of k_H is ca. $50 \times 10^6\ M^{-1}\ s^{-1}$ in benzene-d_6 at 303 K.

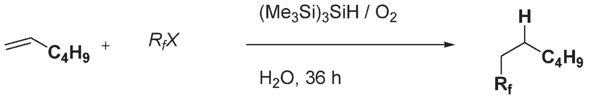
Given the known rate acceleration effects of radical reactions in water,[23] it becomes challenging at this time to attempt intermolecular carbon−carbon bond formation radical reactions in this medium, mediated by silyl radicals. Therefore, we herein embark on a study of the perfluoroalkylation of electron 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 to be employed are azo compounds and dioxygen which up to now gave us the best results in previous studies.[18−21]

Moreover, the scope of this paper is on the syntheses of perfluoroalkyl-substituted alkanes, which are currently employed in fluorous syntheses. Our results are meant to contribute with a versatile methodology for the synthesis of perfluoroalkyl-substituted compounds in water.

2. Results and Discussion

When 1-hexene is allowed to react with *n*-1-iodopefluorohexane, $n\text{-}C_6F_{13}I$, in water, initiated by $(Me_3Si)_3SiH$/dioxygen (see the Experimental Section), 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorododecane **1a**[25a] is obtained in 65% yield (Scheme 1). Analogously, 1-octene and 1-decene afford, upon reaction with $n\text{-}C_6F_{13}I$ under the same radical conditions, products **2a**[25b] and **3a**[25b] in 71% and 74% yields (isolated yields), respectively (Scheme 1).

SCHEME 2. Intermolecular Radical Carbon−Carbon Bond Formation in Water[a]



$R_f = C_4F_9$, X = I	**1b, 88%**
$R_f = (CF_2)_4I$, X = I	**1c, 75%**
$R_f = C_6F_{13}$, X = Br	**1a, 21%**
$R_f = C_8F_{17}$, X = I	**1d, 72%**
$R_f = C_8F_{17}$, X = Br	**1d, 14%**
$R_f = C_{10}F_{21}$, X = Br	**1e, 9%**
$R_f = C_{10}F_{21}$, X = I	**1e, 70%**

[a]Reactions of 1-hexene with haloperfluoroalkanes in water, initiated by $(Me_3Si)_3SiH$/dioxygen.

Styrene and *p*-methylstyrene when reacted with $n\text{-}C_6F_{13}I$ in water under $(Me_3Si)_3SiH$/dioxygen initiation give products **4a**[26] and **5a**[27] in 54% and 63% yields, respectively (Scheme 1). 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, $CHF_2(CF_2)_4CF_3$) was concomitantly obtained, as determined from the ^1H and ^{19}F NMR spectra of the crude reaction mixtures (centered triplet at 6.29 ppm, $J = 22$ Hz, from terminal HCF_2, in the ^1H NMR spectrum and from the ^{19}F NMR spectrum, the CF_2H peak at $\delta = -114.05$ ppm). Alkenes with electron withdrawing groups such acrylonitrile, crotonaldehyde, methyl acrylate, and vinyl methyl ketone also react with $n\text{-}C_6F_{13}I$ under the same radical conditions, to afford the respective perfluoroalkylated products **6a**,[28,25c] **7a**, **8a**, and **9a**[28,29] in yields ranging from 60% to 77% (Scheme 1). The products are isolated from the crude reaction mixture by extraction of the water phase with pentane (3×), drying of the pentane layers with anhydrous sodium sulfate, and filtering, and the evaporated pentane extracts are reduced-pressure distilled.

It should be pointed out that a small minor byproduct (ca. 5%) detected from the oxygen-initiated reactions in water corresponds to a compound observed by mass spectrometry of mass 280 and formula minima $C_9H_{28}Si_4O_2$ whose structure has been assigned to $(Me_3SiO)_2Si(H)SiMe_3$, arising from the autoxidation of silane.[30] This byproduct was confirmed by GC-co-injection with an authentic sample that has been synthesized according to a reported procedure.[30]

Encouraged by the above results obtained from reactions in water with $n\text{-}C_6F_{13}I$ and different alkenes initiated by $(Me_3Si)_3SiH$/dioxygen, we 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-iodoperfluorobutane, $n\text{-}C_4F_9I$, under the reaction conditions described above, 1,1,1,2,2,3,3,4,4-nonafluorodecane **1b**[31] is obtained in 88%

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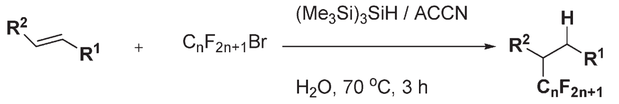
SCHEME 3. Intermolecular Radical Carbon−Carbon Bond Formation in Water[a]



$R^1 = C_4H_9$, $R^2 = H$	n=6, 1a, 75%; n=8, 1d, 70%; n=10, 1e, 62%
$R^1 = C_6H_{13}$. $R^2 = H$	n=6, 2a, 77%; n=8, 2d, 63%; n=10, 2e, 59%
$R^1 = C_8H_{17}$, $R^2 = H$	n=6, 3a, 65%; n=8, 3d, 59%; n=10, 3e, 48%
R^1 = Ph, $R^2 = H$	n=6, 4a, 80%; n=8, 4d, 81%; n=10, 4e, 77%
R^1 = *p*-$CH_3C_6H_4$, R^2 =H	n=6, 5a, 66%; n=8, 5d, 55%; n=10, 5e, 46%
R^1 = CN, R^2 = H	n=6, 6a, 51%; n=8, 6d, 50%; n=10, 6e, 44%
R^1 = CHO, $R^2 = CH_3$	n=6, 7a, 62%; n=8, 7d, 60%; n=10, 7e, 55%
R^1 = COOMe, R^2 = H	n=6, 8a, 55%; n=8, 8d, 53%; n=10, 8e, 43%
R^1 = COMe, R^2 = H	n=6, 9a, 67%; n=8, 9d, 70%; n=10,9e, 66%

[a] 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.

yield (Scheme 2). The reaction of 1-hexene with 1,4-diiodo-1,1,2,2,3,3,4,4-octafluorobutane, *n*-IC_4F_8I, affords 1,1,2,2,-3,3,4,4-octafluoro-1-iododecane **1c**, obtained in 75% yield (Scheme 2), and 15% of reduced 1,1,2,2,3,3,4,4-octafluorodecane, as observed from the ^{19}F NMR spectrum, with the CF_2H peak at $\delta = -114.15$ ppm.

When *n*-1-bromoperfluorohexane, *n*-$C_6F_{13}Br$, is allowed to react with 1-hexene, product **1a**[25a] is obtained in poor yield (21%, Scheme 2, cf. with the same reaction carried out with *n*-$C_6F_{13}I$, Scheme 1). Analogously, the reaction of 1-hexene with *n*-1-bromoperfluorooctane, *n*-$C_8F_{17}Br$, progresses poorly to give product **1d**[25b] in 14% yield, while the same reaction employing *n*-$C_8F_{17}I$ affords **1d**[25b] in 72% yield (Scheme 2). In the same fashion, *n*-1-iodoperfluorodecane, *n*-$C_{10}F_{21}I$, reacts with 1-hexene to afford **1e**[25b] in 70% yield (Scheme 2), but with *n*-$C_{10}F_{21}Br$, product **1e**[25b] is obtained in 9% yield. This could be in agreement with a stronger BDE of the bond R_f-Br than that of R_f-I.

To cast some light into the efficiency of the chain reaction with dioxygen, and see whether the low yields obtained from 1-hexene and R_fBr and $(Me_3Si)_3SiH$/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 iodoperfluoroalkanes, we undertook the radical chain initiation with the azo compound ACCN, at 70 °C in water (see the Experimental Section).

When a series of alkenes are allowed to react with bromoperfluoroalkanes (*n*-1-bromoperfluorohexane, *n*-1-bromoperfluorooctane, and *n*-1-bromoperfluorodecane) in water as described for the thermal radical initiation reaction (see the Experimental Section), the respective perfluoroalkylated products are obtained in yields ranging from 50% to 77% (Scheme 3).

Thus, 1-hexene reacts with *n*-$C_6F_{13}Br$, *n*-$C_8F_{17}Br$, and *n*-$C_{10}F_{21}Br$ to afford the corresponding perfluoroalkylated hexanes **1a**,[25a] **1d**,[25b] and **1e**[25b] in 75%, 70%, and 62% yields, respectively (Scheme 3). 1-Octene and 1-decene also afford perfluoroalkylated alkanes in fairly good yields (50−77%). Styrene and 4-methylstyrene react with *n*-$C_6F_{13}Br$, *n*-$C_8F_{17}Br$, and *n*-$C_{10}F_{21}Br$ to afford the alkylated products in good yields, ranging from 46% to 81% (Scheme 3).

Acrylonitrile, upon reaction with the series $C_nF_{2n+1}Br$ ($n = 6$, 8, and 10) affords the perfluoroalkylated-substituted propiononitriles **6a**,[28] **6d**,[32] and **6e**[28] in 51%, 50%, and 44% yields, respectively. Crotonaldehyde, upon reaction with *n*-$C_6F_{13}Br$, *n*-$C_8F_{17}Br$, and *n*-$C_{10}F_{21}Br$ under the reaction conditions described above, gives the perfluoroalkylated-substituted butyraldehydes **7a**, **7d**, and **7e** in 62%, 60%, and 55% yields, respectively (Scheme 3).

Methyl acrylate upon reaction with the series $C_nF_{2n+1}Br$ ($n = 6$, 8, and 10) affords the perfluoroalkylated-substituted methyl propionates **8a**, **8d**,[33] and **8e** in 55%, 53%, and 43% yields, respectively (Scheme 3), while vinyl methyl ketone when reacted with *n*-$C_6F_{13}Br$, *n*-$C_8F_{17}Br$, and *n*-$C_{10}F_{21}Br$ in water under ACCN/$(Me_3Si)_3SiH$ thermal initiation affords the 5-perfluoroalkylated-substituted 2-butanones **9a**,[28,29] **9d**,[34,28] and **9e**[34,28] in 67%, 70%, and 66% yields, respectively (Scheme 3).

We also undertook the ACCN-radical initiated perfluoroalkylation of 1-hexene with $C_nH_{2n+1}I$ ($n = 8$, and 10), and obtained compounds **1d**[25b] and **1e**,[25b] respectively, in yields ranging from 90% to 95%, while the same yields under dioxygen-radical initiation were in the 70% range (cf. O_2-initiated radical yields of **1d** and **1e** from Scheme 2).

These sets of experiments would reveal that the lower yields obtained with the bromoperfluoroalkanes 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 R_f-I and R_f-Br bonds; however, some involvement of the BDE of R_f-I versus R_f-Br should also be considered.

Given the optimal yields obtained from the radical reactions of 1-bromoperfluoroalkanes and alkenes in water initiated by $(Me_3Si)_3SiH$/ACCN, we undertook the reactions depicted in Scheme 1 (*n*-$C_6F_{13}I$ and different alkenes) this time under ACCN initiation. Table 1 summarizes the reaction yields of perfluoroalkyl-substituted compounds **1a**−**9a** obtained from *n*-$C_6F_{13}I$, an array of alkenes, and $(Me_3Si)_3SiH$/ACCN initiator.

It is observed that the yields of products **1a**−**9a** are much better under ACCN initiation (Table 1) than under dioxygen initiation (Scheme 1)

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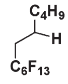
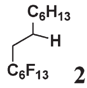
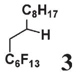
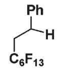
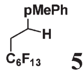
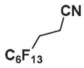
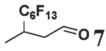
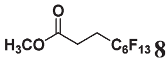
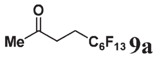
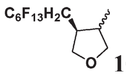
TABLE 1. Intermolecular Radical Carbon−Carbon Bond Reactions in Water: Reactions of Different Alkenes (20−25 mM) with n-$C_6F_{13}I$ (10 mM), Initiated by $(Me_3Si)_3SiH$ (5 mM)/ACCN (3 mM):

Entry	**Alkene**	**Product, (%)[a]**
1[ref.25a]	1-Hexene	 **1a, (81)**
2[ref..25b]	1-Octene	 **2a, (92)**
3[ref..25b]	1-Decene	 **3a, (84)**
4[ref.26]	Styrene	 **4a, (77)**
5[ref.27]	4-Methylstyrene	 **5a, (79)**
6[ref.28]	Acrylonitrile	 **6a, (80)**
7	Crotonaldehyde	 **7a, (71)**
8	Methylacrylate	 **8a, (75)**
9[ref.28]	Vinyl methyl ketone	 **9a, (76)**
10[ref.25c]	Diallyl ether	 **10a, (68)[b]**

[a] Isolated yield after purification. [b] Obtained in a 81:19 cis:trans ratio measured by ^1H NMR

We also subjected electron-rich diallyl ether (3-(allyloxy)-prop-1-ene) to the radical perfluoroalkylation reaction in water with n-$C_6F_{13}I$ (ACCN-initiation) and obtained the perfluoroalkylated tetrahydrofuran derivative **10a**[25c] in 68% yield, in a cis:trans ratio of ca. 80:20 (Table 1, entry 10). Exo-cyclization of the 6-hexenyl radical is a useful probe for the elucidation of the radical mechanism of the reaction in water, as has been observed for the cyclization of a 1-allyloxy-2-iodobenzene derivative in water as well.[21,25a]

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 $(Me_3Si)_3SiH$ and dioxygen.

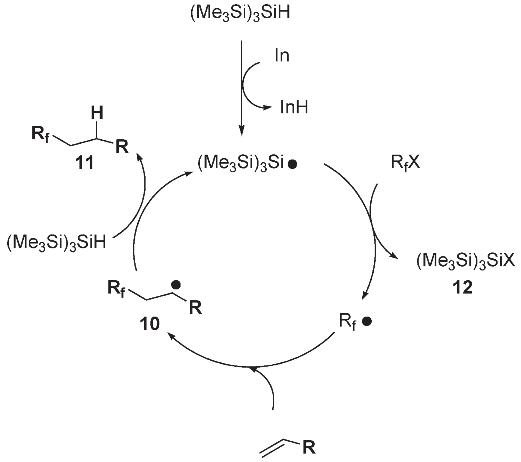
It is worth mentioning that under our experimental procedure, initiation with oxygen does not take place under O_2-purging of the solution, nor with slow, continuous bubbling of O_2 or air. Oxygen or air introduced slowly by syringe-pump techniques resulted in a less efficient initiation of the chain 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 1.34×10^{-3} M at 22 °C; taking into account that the substrate and $(Me_3Si)_3SiH$ concentrations are ca. 10 times higher, limiting working initiator concentrations could be reached by the methodology).

The mechanism of the $(Me_3Si)_3SiH$-mediated intermolecular perfluoroalkylation of alkenes in water is depicted in Scheme 4.

The $(Me_3Si)_3Si^\bullet$ radical (produced either by dioxygen or thermal decomposition of ACCN initiator) in water abstracts the halogen atom (iodine or bromine) from R_fX. This $R_f^\bullet$ radical reacts faster with the alkene than with the silicon hydride, affording the perfluoroalkylated radical adduct **10**. The perfluoroalkylated radical adduct **10** abstracts hydrogen from the silane, affording the perfluoroalkyl-substituted alkane **11**, and regenerating the silyl radical, thus propagating the chain.

According to what has been observed and measured by Dolbier et al.,[24] in benzene-d_6, the ratio of products [**3**]/[**2**] (eq 2) should equal the ratio of rate constants for addition

SCHEME 4. Mechanism for Radical Carbon−Carbon Bond Formation Reactions from Alkenes and Perfluoroalkyl Iodides in Water, Mediated by $(Me_3Si)_3SiH$



(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. According to our experimental conditions, employing the equation in ref 37, we would obtain a theoretical ratio of perfluoroalkylated alkane over reduced perfluoroalkane of ca. 1.3, which is not completely in agreement with the unobserved reduced perfluoroalkanes in our reaction systems (i.e., $CHF_2(CF_2)_4CF_3$, when iodoperfluorohexane is employed).

The electrophilicity of $R_f^\bullet$ radicals is the dominant factor giving rise to their high reactivity. The stronger carbon−carbon bond that 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).[35] 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).[31] 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 our results, however, it becomes apparent that in water the reactivity for both electron rich and electron deficient alkenes toward $R_f^\bullet$ radical addition could be comparable (cf. in Scheme 1, substrates **1a**−**3a** and **6a**−**9a**). To clarify this subtle aspect of the reaction in water, we undertook a set of experiments designed to compare the ratios of $(k_H/k_{add})_{1\text{-hexene}}$ and $(k_H/k_{add})_{acrylonitrile}$ for the addition reaction of n-$C_6F_{13}I$ to the electron rich 1-hexene and electron deficient acrylonitrile, respectively. These ratios of rate constants are obtained by plotting [n-$C_6F_{13}H$]/[**1a**] vs [$(Me_3Si)_3SiH$]/[1-hexene] and [n-$C_6F_{13}H$]/[**6a**] vs [$(Me_3Si)_3SiH$]/[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. We obtained slopes for both plots equal to 1.55 ± 0.09 ($r^2 = 0.998$) and 1.88 ± 0.19 ($r^2 = 0.989$) for $(k_H/k_{add})_{1\text{-hexene}}$ and $(k_H/k_{add})_{acrylonitrile}$, respectively. This seems to indicate that the reactivities of electron rich and electron deficient alkenes toward $R_f^\bullet$ radicals in water level off.

The ratio of rates constants $(k_H/k_{add})_{1\text{-hexene}}$ obtained in benzotrifluoride as solvent[24] for the reaction of n-$C_7F_{15}I$ and 1-hexene with $(Me_3Si)_3SiH$ as the hydrogen donor (eq 2) is 6.32, while that same ratio of rate constants for the reaction of n-$C_6F_{13}I$ with 1-hexene in water is 1.55 (vide supra). The unavailability of the rate constant for $R_f^\bullet$ radical addition onto double bonds *in water* makes comparisons difficult; however, our results would seem to imply that the rate for hydrogen donation from $(Me_3Si)_3SiH$ to the $R_f^\bullet$ radical relative to the addition reaction is four times slower in *water* than in benzotrifluoride as solvent (i.e., $(k_H/k_{add})_{water}/(k_H/k_{add})_{benzotrifluoride} = 0.25$). Indeed, it is likely that water does influence the H-transfer step from the silane to the C-radical. This is well established and important for phenols; however, for silanes this is not known. In the phenol series H-bonding of the phenol with the solvent leads to a stabilization and consequently to less efficient H-transfer.[36] H-bonding from the silane to water might have a similar effect, as we report on slower H-transfer in water. It can also be hypothesized that given the known hypervalency of silicon, coordination of a water molecule can diminish the hydrogen atom donation of the silicon hydride.

The intermolecular radical carbon−carbon bond formation reactions presented herein in water take advantage of the halophilicity of silyl radicals toward iodine and bromine atoms. In our case, the halogen atom transfer reaction from **12** toward the perfluoroalkylated radical adduct **10** (Scheme 4) is slower than the hydrogen atom abstraction from the $(Me_3Si)_3SiH$, thus providing the reduced perfluoroalkylated product **11**. As a support to the mechanism proposed (Scheme 4), 2-iodo-1,1,1,3,3,3-hexamethyl-2-(trimethyl)-trisilane (**12**, X = I, Scheme 4) was isolated and characterized[18] from the reaction mixtures described in Scheme 1. In the same fashion, from reactions described in Scheme 3, 2-bromo-1,1,1,3,3,3-hexamethyl-2-(trimethyl)trisilane (**12**, X = Br, Scheme 4) was detected by gas chromatography, isolated, and compared with an authentic sample.

As mentioned above, by plotting [n-$C_6F_{13}H$]/[**1a**] vs [$(Me_3Si)_3SiH$]/[1-hexene], a straight line, whose slope represents $(k_H/k_{add})_{1\text{-hexene}}$, is obtained (with a value of 1.55 ± 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-$C_6F_{13}^\bullet$ radical reduction (i.e., n-$C_6F_{13}H$) is the silane, and not the solvent or the alkene.[31]

3. Conclusions

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

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(37) [**3**]/[**2**] = k_{add}[1-hexene]/k_H[$(Me_3Si)_3SiH$], where k_{add} is the rate constant for of addition of perfluorinated radical to 1-hexene, k_H is the rate constant for H atom abstraction from the silane, and **2** and **3** are the reduced perfluorinated alkane and the addition product, respectively, shown in eq 2.

multiple bonds[19,22] to the intermolecular radical carbon−carbon bond formation.

From results obtained in Schemes 1−3 and Table 1, 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.[19,22]Also, 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 toward alkenes and silicon hydrides, respectively, as opposed to those found in benzene, where the latter rates are ca. 6 times faster at equal concentrations of silanes and alkenes.

Our account also provides 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. We are currently studying competition reactions between radical additions and H abstraction processes in water.

4. Experimental Section

General Methods. The internal standard method was used for quantitative GC analysis with use of authentic samples, and one of the following capillary columns was employed: HP-1 (5 m × 0.53 mm i.d.) or HP-1 (30 m × 0.32 mm i.d.). Oven program: starting at 50 °C for 5 min, followed by an increase of 5 deg/min up to 250 °C. NMR spectra were recorded at 400 (for ^1H) or 100.6 MHz (for ^{13}C) in $CDCl_3$ as deuterated solvent and referenced with the residual solvent peak at 7.26 ppm in the ^1H NMR spectra and 77.0 ppm ($CDCl_3$) in the ^{13}C NMR spectra. Hydrogen multiplicity (CH, CH_2, CH_3) information was obtained from carbon DEPT-135 experiments for compounds **1c**, **7a**, **7d**, and **8d**. Some NMR spectral connectivity data were confirmed by $^1H-^{13}C$ HSQC and HMBC 2-D experiments. Reduced pressure distillation employed a bulb-to-bulb distillation apparatus with four glass bulbs. When necessary, compounds were isolated by flash chromatography performed on silica gel. High-resolution mass spectrometry measurements were performed with a resolution of 1−5 ppm.

Water was obtained from a milli-pore system, and extraction and chromatographic solvents were HPLC-grade. Products from Schemes 1−4 and Table 1 were characterized by standard spectroscopic techniques and compared with spectral data from the literature when available.

Materials. Perfluoroalkyl iodides and bromides were commercially available and used as received from the supplier. Alkene substrates were also commercially available and used as received from the supplier, except for styrene, 4-methylstyrene, acrylonitrile, crotonaldehyde, methyl acrylate, and vinyl methyl ketone, which were previously distilled and stored over molecular sieves (4 Å) prior to use.

Methods of Radical Initiation in Water: Study of the Reaction Stoichiometry. 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[22] in our initial studies and this trend has been confirmed by the present results.

A preliminary set of experiments were conducted 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 **3** and **2**, eq 2). For this preliminary experiment, we used 1-hexene as the alkene 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 are 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.

The procedure is the following: In a 5 mL conical vial, provided with a conical stir bar, a heterogeneous aqueous (5 mL) mixture of the alkene ($20-25 \times 10^{-5}$ mol), $(Me_3Si)_3SiH$ (2.5×10^{-5} mol), the perfluoroalkyl halide (5×10^{-5} mol), and ACCN (1.5×10^{-5} mol) is flushed with Ar for 10 min before heating at 70 °C for 2−4 h unless otherwise indicated. After the reaction time elapsed, addition of pentane, and extraction, the organic phase is analyzed. Perfluoroalkylated products are isolated and purified by distillation under reduced pressure with use of a short path distillation apparatus, and characterized by standard spectroscopic techniques. The purity of products is checked by gas chromatography, and in some cases redistilled or silica gel chromatographed.

Dioxygen Initiation[19]**.** A balloon filled with pure oxygen connected to the vessel where no apparent bubbling resulted allowed dioxygen to be introduced, in the reaction vessel, up to its solubility limits in water.

The dioxygen-initiated radical-induced reactions of alkenes with perfluoroalkyl halides in Ar-degassed water are carried out by adding subsequently $(Me_3Si)_3SiH$ (2.5×10^{-5} mol), the alkene ($20-25 \times 10^{-5}$ mol), and the perfluoroalkyl halide[37] (5×10^{-5} mol) in a conical vial provided with a conical stir bar, filled with 5 mL of Milli-Q water previously deoxygenated with a stream of Ar for 10 min. The vessel is tight-sealed, connected with a balloon filled with 99.99% dioxygen, and vigorously stirred at 20 °C (36 h). As a slight positive oxygen pressure is exerted on the reaction vessel, air does not leak in the system.

The mechanism for the unusual reaction of $(Me_3Si)_3SiH$ with oxygen has been investigated before[38a] and applied successfully in water.[19,22]

Spectroscopic Characterization of Known Compounds 1a−6a,[25−28] **9a,**[28] **10a,**[25c] **1b,**[31] **1d,**[25b] **2d,**[25b] **3d, 4d,**[39,40,41a] **5d,**[40,41] **6d,**[28,32] **8d,**[33] **9d,**[28] **1e,**[25b,42c] **2e,**[25b,42c,] **3e,**[42c] **4e,**[26] **6e,**[28] **9e**[28,34]**.** These compounds were characterized from comparison of their ^1H and ^{13}C NMR data with those found in the literature (references of compounds throughout the text).

Spectroscopic Characterization of Unknown Compounds 7a, 8a, 1c, 7d, 5e, 7e, and 8e. 7a (4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-3-methylnonanal): yellowish oil. GC/MS EI, m/z (%) 390 (32), 375 (21), 373 (12), 362 (29), 320 (39), 273 (100). EI-HRMS Anal. Calcd for $C_{10}H_7F_{13}O$ 390.0289, found 390.0296. Elemental analyses: Found: C (30.05%), H (1.71%), O (4.21%). Calcd for $C_{11}H_7F_{13}O$: C (30.79%), H (1.81%), F (63.31%), O (4.10%). FT-IR (ν, cm^{-1}) 1795 (C═O), 1204, 1140. ^1H NMR δ_H

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ppm (400.13 MHz, $CDCl_3$) 1.34 (d, 3H, Me), 2.69 (complex m, 3 H, CH and CH_2), 9.51 (s, 1 H, CHO). ^{13}C NMR $\delta_{^{13}C}$ ppm (100.6 MHz, $CDCl_3$) 11.3, 39.7, 43.0, 100−130 ($^{13}C-^{19}F$ coupling from $(CF_2)_6$), 203.4.

8a (methyl 4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononanoate): colorless oil. GC/MS EI, *m*/*z* (%) 406 (2), 391 (15), 373 (11), 354 (21), 347 (25), 319 (100), 87 (67). EI-HRMS Anal. Calcd for $C_{10}H_7F_{13}O_2$ 406.0238, found 406.0240. Elemental analyses. Found: C (29.54), H (1.75%), O (7.81%). Calcd for $C_9H_5F_{13}O_2$: C (29.57%), H (1.74%), F (60.81%), O (7.88%). FT-IR (ν, cm^{-1}) 1800 (C=O), 1527, 1302, 1209, 1143. ^1H NMR δ_H ppm (400.13 MHz, $CDCl_3$) 2.24 (complex m, 2 H, CH_2-R_f), 2.61 (complex m, 2 H, CH_2−COOMe), 3.62 (s, 3 H, CH_3). ^{13}C NMR $\delta_{^{13}C}$ ppm (100.6 MHz, $CDCl_3$) 26.2 (br. s, **C**H_2−COOMe), 27.5 (m, **C**H_2-R_f), 51.0, 100−130 ($^{13}C-^{19}F$ coupling from $(CF_2)_6$), 176.0 (**C**O).

1c (1,1,2,2,3,3,4,4-octafluoro-1-iododecane): pinkish oil. GC/MS EI, *m*/*z* (%) 413 (10), 412 (4), 335 (58), 327 (43), 285 (100), 185 (45). EI-HRMS Anal. Calcd for $C_{10}H_{13}F_8I$ 411.9934, found 411.9940. Elemental analyses. Found: C (29.24%), H (3.92%). Calcd for $C_{10}H_{13}F_8I$: C (29.14%), H (3.81%), F (36.86%), I (30.79%). ^1H NMR δ_H ppm (400.13 MHz, $CDCl_3$) 0.79 (t, 3 H, *J* = 7 Hz, CH_3), 1.32 (complex m, 2 H, CH_2-CH_3), 1.39 (complex m, 2 H), 1.60 (complex m, 1 H, $CH-HR_f$), 1.90 (complex m, 1 H, $CH-HR_f$). ^{13}C NMR $\delta_{^{13}C}$ ppm (100.6 MHz, $CDCl_3$) 13.9, 20.6, 22.1, 28.9, 30.3, 31.7, 80−120 ($^{13}C-^{19}F$ coupling from $(CF_2)_4$).

7d (4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-3-methylundecanal): yellowish oil. GC/MS EI, *m*/*z* (%) 490 (12), 471 (23), 462 (100), 420 (100), 371 (55), 271 (87). EI-HRMS Anal. Calcd for $C_{12}H_7F_{17}O$ 490.0225, found 490.0220. Elemental analyses. Found: C (29.10%), H (1.49%), O (3.33%). Calcd for $C_{12}H_7F_{17}O$: C (29.40%), H (1.44%), F (65.89%), O (3.26%). FT-IR (ν, cm^{-1}) 1798 (C=O), 1689, 1209, 1145. ^1H NMR δ_H ppm (400.13 MHz, $CDCl_3$) 1.30 (t, 3 H, *J* = 6.7 Hz, CH_3), 2.80 (complex m, 3 H, $CH-R_f$ and CH_2−CHO), 9.61 (s, *CHO*). ^{13}C NMR $\delta_{^{13}C}$ ppm (100.6 MHz, $CDCl_3$) 12.0, 40.3, 41.6, 100−135 ($^{13}C-^{19}F$ coupling from $(CF_2)_8$), 200.5 (CHO).

5e (1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-henicosafluorododecyl)-4-methylbenzene): colorless oil. GC/MS EI, *m*/*z* (%) 638 (5), 623 (41), 619 (21), 519 (100), 419 (23), 319 (33), 92 (54), 77 (51), 65 (11). EI-HRMS Anal. Calcd for $C_{19}H_{11}F_{21}$ 638.0525, found 638.0534. Elemental analyses. Found: C (35.55%), H (1.88%). Calcd for $C_{19}H_{11}F_{21}$: C (35.75%), H (1.74%), F (62.51%). ^1H NMR δ_H ppm (400.13 MHz, $CDCl_3$) 2.07 (s, 3 H, CH_3−Ph), 2.40 (complex m, 2 H, CH_2), 2.96 (complex m, 2 H, CH_2-R_f), 7.01 (m, 2 H, Ph), 7.23 (m, 2 H, Ph). ^{13}C NMR $\delta_{^{13}C}$ ppm (100.6 MHz, $CDCl_3$) 21.1, 27.0, 33.1, 100−120 ($^{13}C-^{19}F$ coupling from $(CF_2)_{10}$), 128.45, 128.11, 135.11, 137.51.

7e (4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-henicosafluoro-3-methyltridecanal): yellowish oil. GC/MS EI, *m*/*z* (%) 590 (5), 575 (32), 571 (12), 562 (59), 519 (55), 471 (100). EI-HRMS Anal. Calcd for $C_{14}H_7F_{21}O$ 590.0162, found 590.0156. Elemental analyses. Found: C (27.29%), H (1.29%), O (2.65%). Calcd for $C_{14}H_7F_{21}O$: C (28.49%), H (1.20%), F (67.60%), O (2.71%). FT-IR (ν, cm^{-1}) 1800 (C=O), 1206, 1143. ^1H NMR δ_H ppm (400.13 MHz, $CDCl_3$) 1.33 (d, 3 H, *J* = 7 Hz, CH_3), 2.65 (complex m, 3 H, $CH-R_f$ and CH_2−CHO), 9.11 (s, *CHO*). ^{13}C NMR $\delta_{^{13}C}$ ppm (100.6 MHz, $CDCl_3$) 11.2, 40.4, 44.5, 95−135 ($^{13}C-^{19}F$ coupling from $(CF_2)_{10}$), 200.21 (*CHO*).

8e (methyl 4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-henicosafluorotridecanoate): colorless oil. GC/MS EI, *m*/*z* (%) 606 (5), 591 (35), 587 (13), 578 (54), 575 (12), 519 (51), 487 (100), 387 (21). EI-HRMS Anal. Calcd for $C_{14}H_7F_{21}O_2$ 606.0111, found 606.0103. Elemental analyses. Found: C (26.94%), H (1.07%), O (5.39%). Calcd for $C_{14}H_7F_{21}O_2$: C (27.74%), H (1.16%), F (65,82%), O (5.28%). FT-IR (ν, cm^{-1}) 1798 (C=O), 1717, 1446, 1209, 1143. ^1H NMR δ_H ppm (400.13 MHz, $CDCl_3$) 2.15 (complex m, 2 H, CH_2-R_f), 2.55 (complex m, 2 H, CH_2−COOMe), 3.56 (s, 3 H, CH_3−COO). ^{13}C NMR $\delta_{^{13}C}$ ppm (100.6 MHz, $CDCl_3$) 26.2, 27.2, 52.6, 100−130 ($^{13}C-^{19}F$ coupling from $(CF_2)_{10}$), 176.55.

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra of compounds **1a** through **9a**, as well as spectral characterization of **1b**, **1c**, compounds **1d** through **9d**, and compounds **1e** through **9e**. This material is available free of charge via the Internet at http://pubs.acs.org.