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Conjugate Addition of Perfluoroarenes to *α,β*-Unsaturated Carbonyls Enabled by an Alkoxide-Hydrosilane System: Implication of a Radical Pathway

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KEYWORDS: conjugate addition • perfluoroarenes • sodium *tert*-butoxide • hydrosilanes • radical pathway

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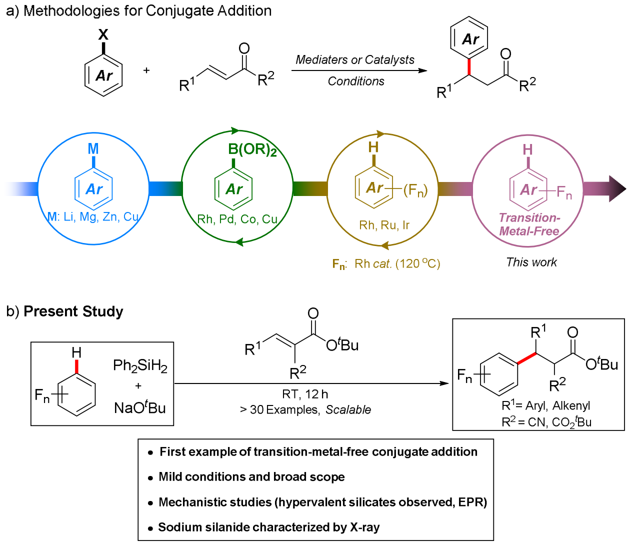
ABSTRACT: Conjugate addition of organometallic reagents to *α,β*-unsaturated carbonyls is a key strategy for the construction of carbon-carbon bond in organic synthesis. Although direct C–H addition to unsaturated bonds via transition metal catalysis is explored in recent years, electron-deficient arenes that do not bear directing groups continue to be challenging. Herein we disclose the first example of a conjugate addition of perfluoroarenes to *α,β*-unsaturated carbonyls enabled by an alkoxide-hydrosilane system. The reaction is convenient to carry out at room temperature over a broad range of substrates and reactants to furnish synthetically versatile products in high to excellent yields. Mechanistic experiments in combination with computational studies suggest that a radical pathway is most likely operative in this transformation. The hypervalent silicate and silanide species, which are relevant to the proposed mechanism, were observed experimentally by NMR and single crystal X-ray diffraction analyses.

■ INTRODUCTION

Construction of a carbon-carbon bond via a conjugate addition of organometallic reagents to *α,β*-unsaturated carbonyls is a well-established methodology in organic synthesis (Scheme 1a).[1] An array of organometallic reagents, including organomagnesiums (commonly referred to as Grignard reagents),[2] organolithiums,[3] and organozincs[4] either in the presence or absence of copper catalysts are employed in these reactions. Unfortunately, special precautions such as low temperature (i.e., –78 °C) and inert atmosphere are often required for stabilizing the highly reactive organometallic reagents to attain satisfactory yields and/or selectivity. In this context, transition metal catalyst systems based on rhodium, also palladium, cobalt or copper, in combination with organoboron reagents emerged as promising alternatives in the last decades.[5] Alkyl radical species generated *in situ* via several photoredox systems have also been utilized for the conjugate addition reactions.[6]

More recently, a strategy towards the direct C–H addition of hydrocarbons to *α,β*-unsaturated carbonyls has been of great interest, as it may offer a more straightforward alternative to the conventional approaches that rely on preactivated reagents.[7] In this context, metal catalysts again proved important for progress, mainly enabling a chelation-assisted C–H bond activation.[8] The scope of substrates amenable to these efficient methods has been extended to some extent, but remains a challenge in part due to the required presence of directing groups.[9] While some transition metal systems were successfully applied for non-directed C–H addition, electron-deficient arenes continue to be a problematic class of substrates even for precious metal catalysts at elevated temperatures (90 ~ 120 °C).[9]

Scheme 1. Conjugate Addition of Perfluoroarenes



Perfluoroarenes are an important class of molecules that are utilized widely in drugs, agrochemicals, functional materials such as liquid crystals (LCs), organic light-emitting diodes (OLEDs), and electron transport materials owing to the unique property of the fluorine group.[10] Thus, a mild, efficient and selective method for the facile functionalization of perfluoroarenes is highly sought after. Recently, transition metal catalysts, including palladium, nickel, copper and gold, have been successfully employed for this purpose.[11] Curiously, the conjugate addition of perfluoroarenes is an underexplored mechanistic possibility. For instance, Zhao *et al.* reported a rhodium catalyst for the conjugate addition of perfluoroarenes to acryl esters at 120 °C.[9b] Mainly because perfluoroarenes ligate to transition metals leading to relatively strong σ-bonds ($M–C_6F_5$),[12] harsh reaction conditions are accordingly required to achieve the subsequent transmetalations efficiently.

Stoltz, Grubbs *et al.* recently disclosed a novel and elegant strategy for the C–H silylation of heteroarenes employing KO^tBu as a catalyst.[13] A plausible mechanism was proposed where either trialkylsilyl radicals or pentavalent silicates are involved.[13c,d] Interestingly, electron-rich silicates were reported to undergo a single-electron transfer (SET) pathway to form radical species.[13g,14] Given that perfluoroarenes exhibit high electron affinities,[10b,i,15] we envisioned that an alkoxide-hydrosilane system could enable an electron transfer to perfluoroarene to generate an aryl radical anion that may subsequently add to α,β-unsaturated carbonyls, possibly in a selective manner. In fact, alkoxide-hydrosilane systems were utilized effectively in the C–X bond cleavage (X = O or S),[13e,f] C(*sp*)–H bond silylation[13b] and carbonyl reduction reactions.[16] The alkoxide-hydrosilane system has attracted much attention because it can provide notable advantages over transition metal-based procedures, such as practicability, sustainability and cost effectiveness. However, mechanistic details are not straightforward in the most known reactions mediated by alkoxide-hydrosilanes.[13] Moreover, the isolation of mechanistically relevant intermediates (i.e., ionic and/or radical silyl species) has remained elusive thus far.

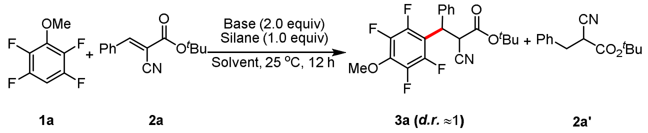
Herein, we report the first example of a C–H conjugate addition of perfluoroarenes to α,β-unsaturated carbonyls enabled by an alkoxide-hydrosilane system. The reaction was convenient to carry out under mild conditions (room temperature) over a broad range of substrates and reactants to furnish synthetically valuable products in high to excellent yields. Mechanistic studies revealed that a radical pathway is most likely involved based on the EPR and radical scavenger experiments. An *in situ* formed compound of sodium silanide was characterized by a single crystal X-ray diffraction study and its mechanistic role was contextualized.

RESULTS AND DISCUSSIONS

Reaction Optimization. Inspired by the single-electron transfer (SET) pathways of the alkoxide-silane systems,[13,14] we initially hypothesized that electron-deficient perfluoroarenes might be a plausible reagent to form an aryl radical anion that may react with α,β-unsaturated carbonyls to enable the desired conjugate addition. Based on this proposal, we commenced our study by allowing a model substrate, 2,3,5,6-tetrafluoroanisole (**1a**), to react with *tert*-butyl benzylidenecyanoacetate (**2a**, 1.0 equiv), a representative α,β-unsaturated carbonyl compound (Table 1).

While examining various combinations of alkoxides and hydrosilanes, we realized that an alkoxide-silane was previously employed for the reduction of unsaturated bonds.[16] Therefore, we were concerned initially that a simple reduction product (**2a'**) may also be formed in addition to the desired conjugation product (**3a**). No desired product was formed in the absence of hydrosilane (entry 1), and significantly tertiary silanes such as Et_3SiH, $PhMe_2SiH$, or Ph_2MeSiH were ineffective (entries 2–4). In contrast, the use of secondary hydrosilanes such as Et_2SiH_2 furnished the desired product in moderate yield (entry 5). Solvents other than THF gave low product yields (entries 5–10).

Table 1. Optimization for Conjugate Addition[a]



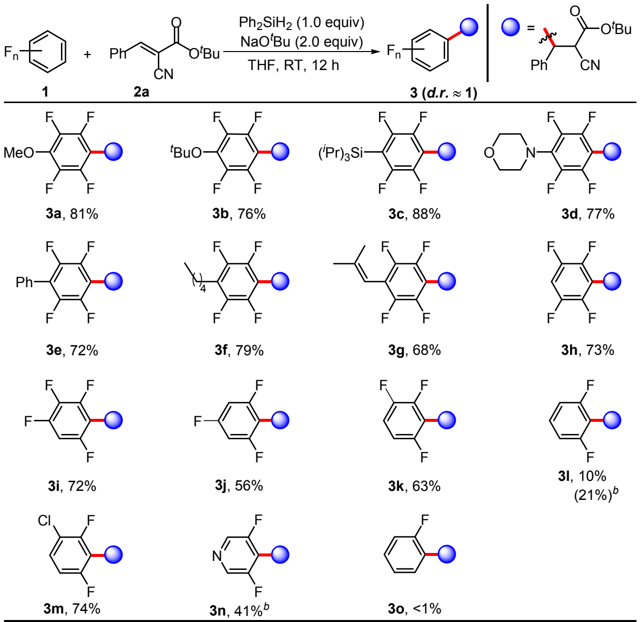
Entry	Base	Silane	Solvent	Conversion (%)[b]	Yield(%)[b]	
					3a	**2a'**
1	NaO^tBu	–	THF	37	<1	<1
2	NaO^tBu	Et_3SiH	THF	55	<1	<1
3	NaO^tBu	$PhMe_2SiH$	THF	62	<1	<1
4	NaO^tBu	Ph_2MeSiH	THF	88	3	<1
5	NaO^tBu	Et_2SiH_2	THF	90	68	<1
6	NaO^tBu	Et_2SiH_2	1,4-dioxane	89	12	<1
7	NaO^tBu	Et_2SiH_2	Et_2O	88	49	<1
8	NaO^tBu	Et_2SiH_2	toluene	70	38	11
9	NaO^tBu	Et_2SiH_2	pentane	57	29	7
10	NaO^tBu	Et_2SiH_2	1,2-DCE	31	<1	6
11	NaO^tBu	$^tBu_2SiH_2$	THF	33	<1	<1
12	NaO^tBu	$PhMeSiH_2$	THF	>99	78	<1
13	NaO^tBu	Ph_2SiH_2	THF	>99	91	<1
14	NaO^tBu	$Ph(Mes)SiH_2$	THF	>99	67	<1
15	NaO^tBu	$(Mes)_2SiH_2$	THF	81	<1	<1
16	NaO^tBu	$PhSiH_3$	THF	>99	56	7
17	LiO^tBu	Ph_2SiH_2	THF	>99	<1	<1
18	KO^tBu	Ph_2SiH_2	THF	82	18	6
19	NaOMe	Ph_2SiH_2	THF	>99	<1	<1
20[c]	NaO^tBu	Ph_2SiH_2	THF	52	<1	29
21[d]	NaO^tBu	Ph_2SiH_2	THF	>99	20	8
22[e]	NaO^tBu	Ph_2SiH_2	THF	>99	50	<1
23[f]	NaOH	Ph_2SiH_2	THF	>99	<1	<1

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (1.0 equiv), base (2.0 equiv) and silane (1.0 equiv) in THF (0.5 mL) at 25 °C for 12

h. [b]Conversions of **2a** and crude NMR yields were obtained after aqueous workup. [c]0.5 Equiv of NaO^{t}Bu. [d]1.0 Equiv of NaO^{t}Bu. [e]1.5 Equiv of NaO^{t}Bu. [f]25 or 60 °C.

The reduction product **2a'** was formed in certain solvents (entries 8–10), but remained a minor side product, in general. A subsequent study on the effect of secondary hydrosilanes for improving the reaction efficiency disclosed some interesting aspects. For instance, while $^t\mathrm{Bu}_2\mathrm{SiH}_2$ was totally ineffective (entry 11), the use of $\mathrm{PhMeSiH}_2$ or $\mathrm{Ph}_2\mathrm{SiH}_2$ gave higher yields (entries 12–13). Hydrosilanes bearing a sterically bulky Mes moiety (Mes = 2,4,6-trimethylphenyl) were much less effective (entries 14–15). Primary hydrosilane PhSiH_3 displayed lower efficiency (entry 16). In addition, both counter cations and alkoxides were found to have dramatic effects: $\mathrm{Na}^+ > \mathrm{K}^+ > \mathrm{Li}^+$ (entries 13 and 17–18); $^t\mathrm{BuO}^- > \mathrm{MeO}^-$ (entries 13 and 19). Finally, the amount of NaO^{t}Bu was critical with 2 equiv of alkoxide being optimal (entries 13 and 20–22).

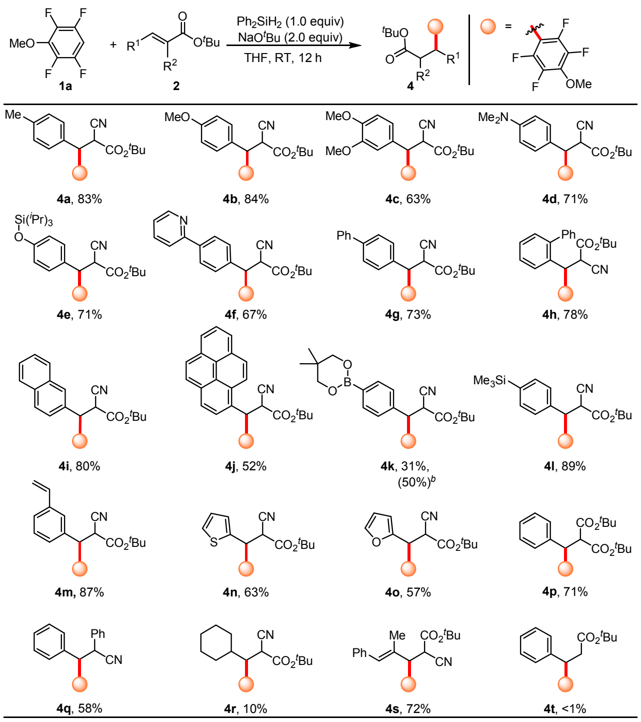
Table 2. Scope of Fluoroarenes[a]



[a]Reaction conditions: fluoroarenes (0.2 mmol), *tert*-butyl benzylidenecyanoacetate (1.0 equiv), NaO^{t}Bu (2.0 equiv) and $\mathrm{Ph}_2\mathrm{SiH}_2$ (1.0 equiv) in THF (0.5 mL) at 25 °C for 12 h; isolated product yields. [b]NaOCMe$_2$Et was used as a base.

Scope of Perfluroroarenes and Michael Acceptors. With the optimized reaction conditions in hand, we proceeded to evaluate the scope of perfluoroarene substrates engaging a model reactant **2a** (Table 2). Tetrafluorobenzenes with methoxy or *tert*-butoxy substituent at the 4-position underwent the desired reaction smoothly (**3a**–**3b**). Substrates bearing a silyl or amino group were compatible with the present conditions to afford the corresponding products in high yields (**3c**–**3d**). Tetrafluorobenzenes having phenyl, alkyl, or alkenyl substituents underwent the Michael addition also efficiently (**3e**–**3g**). Two isomeric products were obtained in similar efficiency from the individual isomeric tertaflurobenzenes (**3h**–**3i**). Trifluorobenzenes afforded the desired products in moderate yields (**3j**–**3k**), and that having more than one reactive C–H bonds showed reaction at the more acidic position. 1,3-Difluorobenzene provided the desired product (**3l**) in low yield (10%) that was slightly improved when using NaOCMe$_2$Et instead of NaO^{t}Bu. 1-Chloro-2,4-difluorobenzene and 3,5-difluoropyridine underwent the desired conjugate addition in varied yields (**3m**–**3n**) while monofluorobenzene did not react (**3o**).

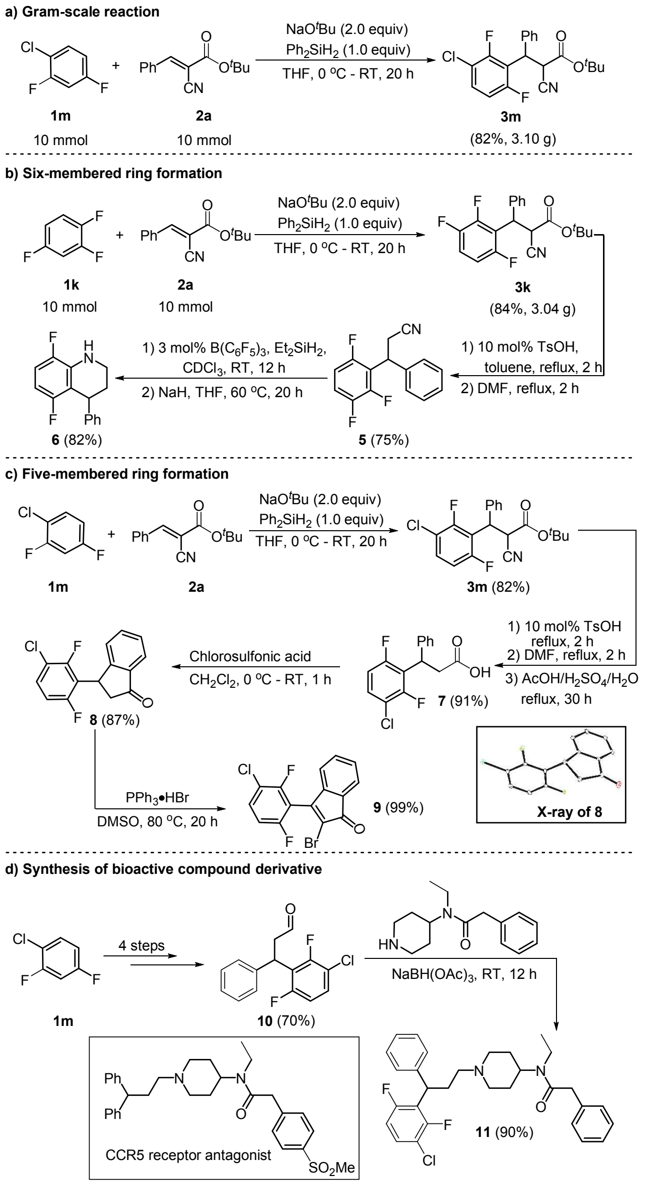
Table 3. Scope of *α*,*β*-Unsaturated Carbonyl Compounds[a]



[a]Reaction conditions: 2,3,5,6-tetrafluoroanisole (0.2 mmol), *α*,*β*-unsaturated carbonyl compounds (1.0 equiv), NaO^{t}Bu (2.0 equiv) and $\mathrm{Ph}_2\mathrm{SiH}_2$ (1.0 equiv) in THF (0.5 mL) at 25 °C for 12 h; isolated product yields. [b]3.0 Equiv of NaO^{t}Bu was used.

The scope of the Michael acceptors, i.e. the *α*,*β*-unsaturated carbonyls (all are in *E*-form except for the formation of product **4q** obtained from *Z*-olefin), was investigated against 2,3,5,6-tetrafluoroanisole (**1a**) at room temperature (Table 3). *tert*-Butyl benzylidenecyanoacetate derivatives having methyl, (bis)methoxy, and dimethylammino substituents at the phenyl moiety underwent the conjugate reaction with **1a** smoothly in good product yields (**4a**–**4d**). Functional groups such as silyloxy and pyridinyl were compatible with the current conditions (**4e**–**4f**). Modification of the aryl moiety to include biphenyl, naphthyl, and pyrenyl groups also gives the desired products without difficulty (**4g**–**4j**). While boronic ester was found to be less tolerant (**4k**), other functional groups including silyl and vinyl groups were completely compatible with the present conditions (**4l**–**4m**). Michael acceptors having heterocycles such as thiophene or furan instead of phenyl also underwent the desired reaction (**4n**–**4o**). Importantly, the presence of cyano or ester groups in the Michael acceptors was not required as demonstrated in the formation of products **4p** and **4q**. In contrast, a (hetero)aryl moiety was found to be essential as seen in the poor product yield from an alkyl-substituted Michael acceptor (**4r**). Notably, a conjugated dienyl carbonyl underwent the reaction in a selective manner with good yield (**4s**). On the other hand, a reaction of **1a** with *tert*-butyl cinnamate without bearing an *α*-substituent did not furnish the desired Michael addition product (**4t**).

Scheme 2. Synthetic Applications of Obtained Products



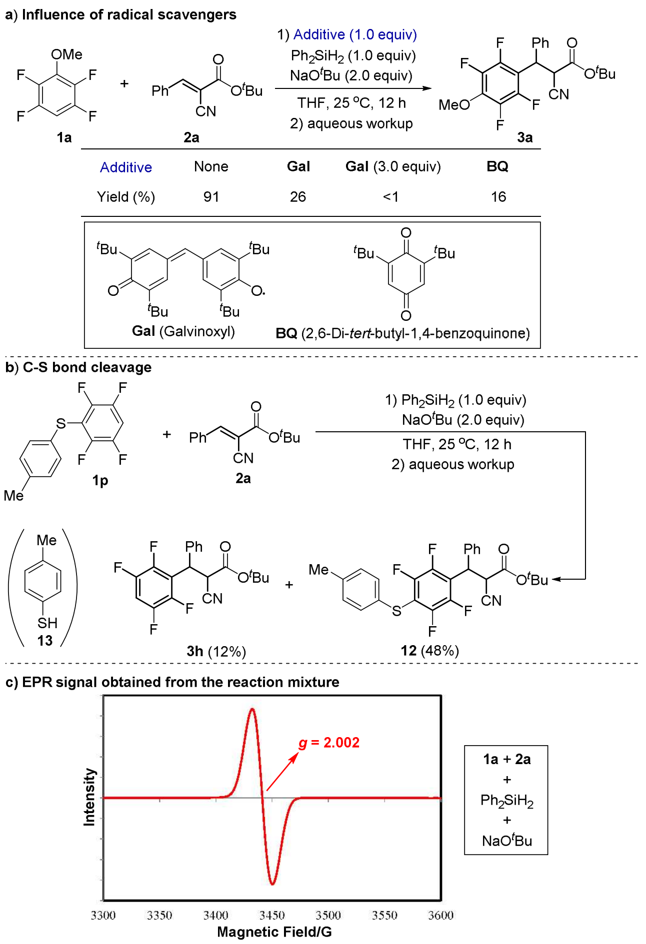
Synthetic Applications. The synthetic utility of this novel methodology was briefly examined, as summarize in Scheme 2. First, a gram scale reaction of 1-chloro-2,4-difluorobenzene (**1m**) with **2a** (1.0 equiv) afforded the desired product **3m** in 82% yield (3.10 g, Scheme 2a). Similarly, 1,2,4-trifluorobenzene (**1k**) efficiently underwent the conjugate addition to afford **3k** (84%, 3.04 g). Decarboxylation of **3k** was catalyzed by TsOH affording **5** (75%), which was subsequently cyclized to furnish a six-membered tetrahydroquinoline derivative **6** (82%) via a B(C_6F_5)$_3$-catalyzed silylative reduction of nitrile, which was recently developed in our research group,[17] and then followed by an intramolecular nucleophilic *ipso*-substitution (Scheme 2b).[10k] In addition, a product **3m** was easily converted to its carboxylic acid **7** (91%) via a tandem process of decarboxylation of ester and hydrolysis of nitrile. A Friedel-Crafts cyclization of **7** was found to be facile by the action of chlorosulfonic acid to form an indanone derivative **8** (87%), the structure of which was confirmed by an X-ray crystallographic analysis. Reductive bromination of **8** took place quantitatively to give **9** (Scheme 2c). Finally, a synthetic route to a bioactive compound was preliminarily examined on the basis of the currently developed approach (Scheme 2d). 3,3-Diphenylpropanal **10** could be readily obtained in 70% yield (4 steps; see the SI for details) starting from 1-chloro-2,4-difluorobenzene (**1m**). Reductive amination of **10** with a substituted piperidine compound afforded **11** in high yield, a fluoro-substituted analogue of CCR5 receptor antagonist.[18]

■ MECHANISTIC STUDIES

A number of alkoxide-hydrosilane systems were previously utilized to mediate different reactions, including carbonyl reduction, C–X bond cleavage (X = O, S), and C–H bond silylation.[13,14,16] Various mechanisms were proposed to rationalize these alkoxide/silane-based transformations. For instance, Stoltz, Grubbs and co-workers suggested that trialkylsilyl radicals and/or pentavalent silicates play a key role in the C–H silylation on the basis of experimental and computational studies.[13c,d] Despite this notable advance, more mechanistic data are needed to better understand the alkoxide-hydrosilane systems and establish it as a general platform in organic synthesis.

In the current conjugate addition of perfluoroarenes to *α*,*β*-unsaturated carbonyls, a series of mechanistic experiments were performed with the hope to identify common features and highlight the differences to the originally proposed behavior of the alkoxide-hydrosilane system. The impact of radical scavengers on the reaction progress was first examined (Scheme 3a). Galvinoxyl (**Gal**) showed an apparent inhibition of the reaction, and no desired product was obtained when 3 equiv of **Gal** was added. With 2,6-di-*tert*-butyl-1,4-benzoquinone (**BQ**), known as an effective silyl radical trapping reagent,[19] the reaction was also largely suppressed. It was previously shown that the homolytic cleavage of a carbon–sulfur bond is accompanied in a radical pathway.[20,13f] In this context, when tetrafluorobenzene bearing an arylthiol substituent (**1p**) was subjected to the standard conditions, we obtained not only the desired product **12** (48%) but also observed its dethiolated derivative **3h** (12%) along with *p*-toluenethiol **13** by a GC-MS analysis (Scheme 3b). When an isolated compound **12** was subjected to the current alkoxide-hydrosilane system, the C–S bond of **12** was found to be significantly cleaved (see the SI for details). Likewise, an alkyl bromide bond was cleaved, and anthracene was partially reduced under the current reaction conditions (see the SI for details). In addition, a sharp EPR signal was detected from the reaction mixture (Scheme 3c), which strongly suggests that radical species are formed. Based on the above preliminary mechanistic data, we concluded that the present alkoxide/hydrosilane-mediated conjugate addition of perfluoroarenes to α,β-unsaturated carbonyls proceeds via a radical pathway.

Scheme 3. Preliminary Mechanistic Studies



Additive	None	Gal	Gal (3.0 equiv)	BQ
Yield (%)	91	26	<1	16

Next, we attempted to identify a plausible activation mode of hydrosilanes in interaction with sodium *tert*-butoxide. As explained above, the reaction efficiency was found to be closely connected to the structure of hydrosilanes and alkoxides examined (Table 1). Because of the vacant 3d orbitals available on the silicon atom, hypervalent silicates are commonly proposed to form *in situ* upon interaction with ligands such as fluoride or oxygen or nitrogen-containing Lewis bases.[21] Whereas a number of organosilicates are characterized by NMR and/or X-ray analyses,[22] no compelling spectroscopic analysis has been reported in case of a *tert*-butoxide-hydrosilane system.[13c,d,g] Stoltz and Grubbs *et al.* used *in situ* ATR-FTIR spectroscopy to trace the activation mode of Si–H bond in their C–H silylation reactions under the KO^{t}Bu-Et$_3$SiH system.[13c]

In our current system, when Ph$_2$SiH$_2$ was treated with NaO^{t}Bu at 213 K, a new resonance peak appeared at $\delta = -82.2$ ppm in ^{29}Si NMR, which can be attributed to hypervalent silicon species. However, five new Si–H peaks appeared in ^{1}H NMR with only 17% yield of the presumed silicate species (see the SI for details). Considering that the pentavalent silicate species tend to adopt the trigonal-bipyramidal geometries, they can undergo a facile and rapid intramolecular permutation between substituents via Berry pseudorotation, thus, making a precise spectroscopic observation of the silicates a difficult task.[22a] The poor conversion of Ph$_2$SiH$_2$ to its silicates as seen above was another critical issue in an attempt to isolate any mechanistically relevant silyl species. On the other hand, it is well known that silole rings have the C–Si–C angle at around 90°,[23] thereby likely positioning the silole rings of their resultant silicate species at the axial and equatorial positions. Consequently, this geometric arrangement will allow the presumed silole-derived pentavalent silicates to have only two isomers (Figure 1, **15-I** and **15-II**). Moreover, these putative silole silicates are expected to be stabilized by the delocalization of the negative charge over the silole ring, thus making the spectroscopic characterization more convenient when compared to

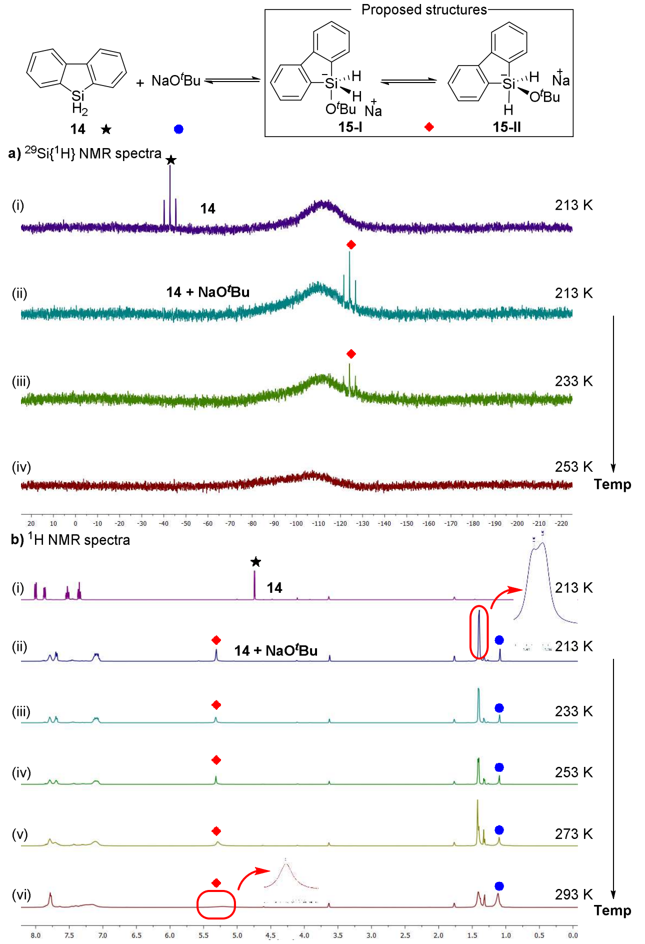


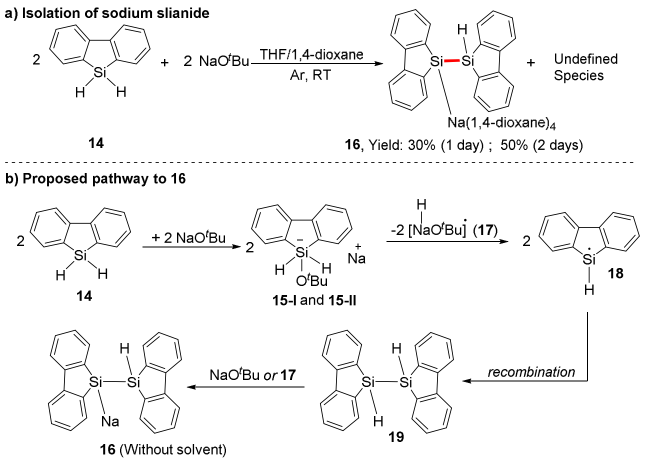
Figure 1. NMR spectra of silole (**14**) at 213 K [^{29}Si{^{1}H} NMR: Figure 1a-i, ^{1}H NMR: Figure 1b-i], variable-temperature (VT) NMR spectra for the interaction of silole (**14**) with NaO^{t}Bu (213 to 293 K) [^{29}Si{^{1}H} NMR: Figure 1a-ii ~ 1a-iv, ^{1}H NMR: Figure 1b-ii ~ 1b-vi].

the fluxional behavior of Ph_2SiH_2 that was employed in the current conjugate addition.

Thus, we prepared a silole **14** in 4 steps[24] and treated it with NaO^{t}Bu (1.0 equiv) at 213 K. As anticipated, a silicate species was observed to form, evidenced by an upfield shifted $^{29}Si\{^1H\}$ NMR signal at δ = –124.1 ppm [t, J(H,Si) = 210.5 Hz],[22] which was distinctive to the signature of **14**, which appeared at –42.8 ppm [t, J(H,Si) = 209.2 Hz] (Figure 1a-i and 1a-ii).

In the same line, ^1H NMR spectroscopy showed that the resonance peak of Si–H of **14** [δ = 4.70 (s, 2H)] was shifted downfield to δ = 5.27 (s, 2H) upon treatment with NaO^{t}Bu (Figure 1b-i and 1b-ii). Furthermore, the silole arene C–H peaks of the putative silicates were shifted upfield, implying that the negative charge of the silole silicate is delocalized over the arene rings, as predicted. Two new proton peaks were observed in the *tert*-butyl region of the presumed silicates (shown in the inset of Figure 1b-ii), suggesting the existence of two silicate isomers in the **14**-NaO^{t}Bu system. We also performed variable-temperature (VT) NMR experiments to monitor the interaction behavior of silole with NaO^{t}Bu. The Si–H peak of the assumed silicates became broadended from a sharp singlet upon a gradual increase of temperature from 213 to 293 K (Figure 1b-ii ~ 1b-vi), indicating that the silicate is in fast equilibrium with the individual silole and NaO^{t}Bu at higher temperatures. This interpretation was further substantiated by the silicon peak becoming similarly broadened at higher temperatures likely for the same reason.[25]

Scheme 4. Formation of Sodium Silanide



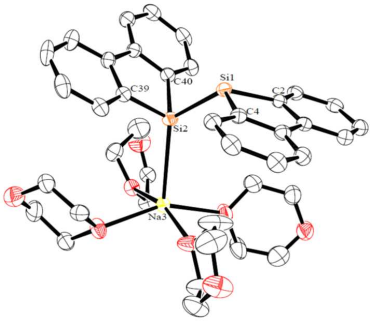


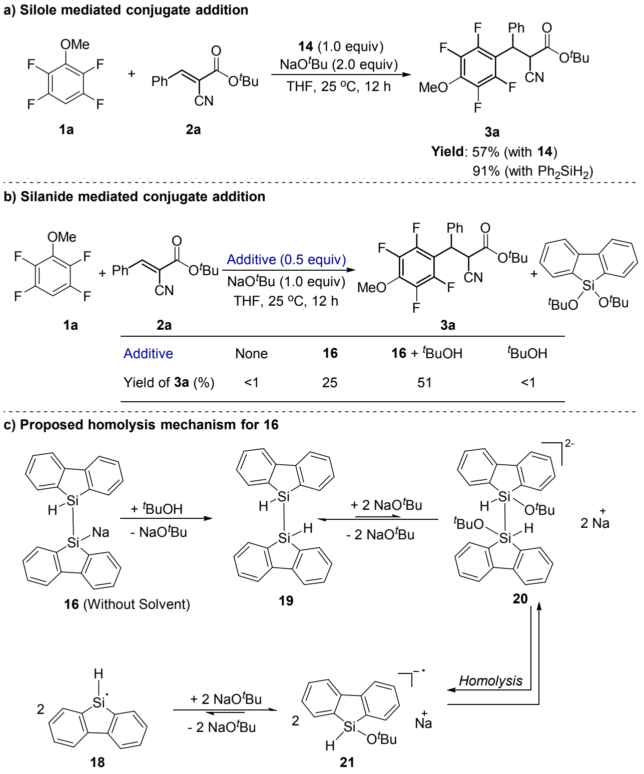
Figure 2. X-ray structure of **16** with minor parts of disordered solvent omitted for clarity. Selected bond lengths (Å) and angles (deg): Si1−Si2, 2.337(2); Si2−Na3, 3.090(2); C2−Si1−C4, 89.8(2); C2−Si1−Si2, 115.57(15); C4−Si1−Si2, 117.06(16); Si1−Si2−Na, 127.96(8).

Encouraged by the aforementioned spectroscopic observations of the putative hypervalent silicates of silole (**14**), we attempted to isolate this mechanistically relevant silyl species. When silole **14** was treated with NaO^{t}Bu (1.0 equiv) in anhydrous THF/1,4-dioxane, the initially colorless solution slowly turned yellow over time, and an air- and moisture-sensitive yellow solid (**16**) was isolated in 30% after one day (50% after 2 days, Scheme 4a). $^{29}Si\{^1H\}$ NMR spectrum displayed two silicon peaks at δ = –28.6 ppm (doublet, $J_{Si\text{-}H}$ = 180.1 Hz) and at δ = –71.5 ppm (singlet). In addition, a sharp peak was observed in ^{23}Na NMR at δ = 1.74 ppm. Pleasingly, we were able to obtain the solid state structure of **16** by X-ray crystallographic analysis to reveal a sodium silanide species with two silole moieties forming a new Si–Si bond (Figure 2). The bond length of Si1–Si2 is 2.337(2) Å, being slightly shorter than the known value (~2.36 Å) of a reported disilicate,[22c] and the bond angles of C2–Si1–Si2 and C4–Si1–Si2 are 115.57(15)^o and 117.06(16)^o, respectively. A sodium cation is ion-paired to the anionic silicon center with 3.090(2) Å, being slightly longer than the reported one (3.02 Å) for the trimethoxyhypersilanide.[26] To our best knowledge, silanide **16** represents the first silyl species isolated from the alkoxide/hydrosilane systems.

Although mechanistic details on the formation of silanide **16** are not fully elucidated at the moment, recent studies showed that alkali metal-alkoxides can serve as an electron donor in ^{t}BuO-mediated arylation of arenes with aryl halides.[27] In addition, pentavalent silicates were shown to undergo a single-electron transfer (SET) to produce radical species.[14] On the other hand, hydrosilanes are known to accept an electron into vacant d orbitals to form silyl radicals.[28] Moreover, it was reported previously that a Si–Si bond can be formed via a recombination of two silyl radical species.[29] Based on our above mechanistic studies and literature precedents,[13,14,27-29] we propose a plausible pathway for the formation of silanide **16**, as illustrated in Scheme 4b. First, silole **14** interacts with NaO^{t}Bu to form hypervalent silicates (**15**), the two isomeric structures of which are shown in Figure 1. The release of the [Na(H)O^{t}Bu]$^•$ radical species (**17**) will lead to a silole radical **18**, which can dimerize to give **19** that being a precursor of **16**.

Considering that silanides are versatile and synthetically useful moieties in organic chemistry and that they are prepared mainly from the reduction of silicon halides or disilanes with alkali metals,[30] this unexpected result in our current procedure suggests that this new methodology may serve as an alternative route to silanides. Significantly, the silole **14** was also shown to mediate the desired conjugate addition between **1a** and **2a**, although the efficiency became expectedly lower when compared to Ph_2SiH_2 (Scheme 5a). More importantly, the isolated sodium silanide **16** enabled the desired conjugate addition albeit in only 25% NMR yield, which could be a bit improved to 51% by adding ^{t}BuOH (no desired product was formed in the absence of **16**). We rationalized this result by assuming that while silanide **16** can serve as a precursor of a silyl radical species **18** under the reaction conditions although this process is not fully understood at the moment. Since the reaction efficiency with **16** was improved by the presence of ^{t}BuOH (Scheme 5b), a dianionic silicate **20** is proposed to form more effectively via a disilane **19** with NaO^{t}Bu to generate **21** that is assumed to be a precursor of **18**.

Scheme 5. Silanide Mediated Conjugate Addition


a) Silole mediated conjugate addition

b) Silanide mediated conjugate addition

c) Proposed homolysis mechanism for 16

Additive	None	16	16 + ^{t}BuOH	^{t}BuOH
Yield of **3a** (%)	<1	25	51	<1

■ COMPUTATIONAL STUDIES

We sought to understand the mechanism by constructing a computer model based on density functional theory (DFT)[31] considering two mechanistic scenarios illustrated in Scheme 6. The B3LYP-D3[32] functional with 6-31G**[33] basis set was used for the geometry optimizations and the energies were re-evaluated with a larger basis set, cc-pVTZ(-f),[34] and solvation energies for THF (ε = 7.6) were obtained from a continuum model,[35] following a modeling protocol that were used in numerous previous studies.

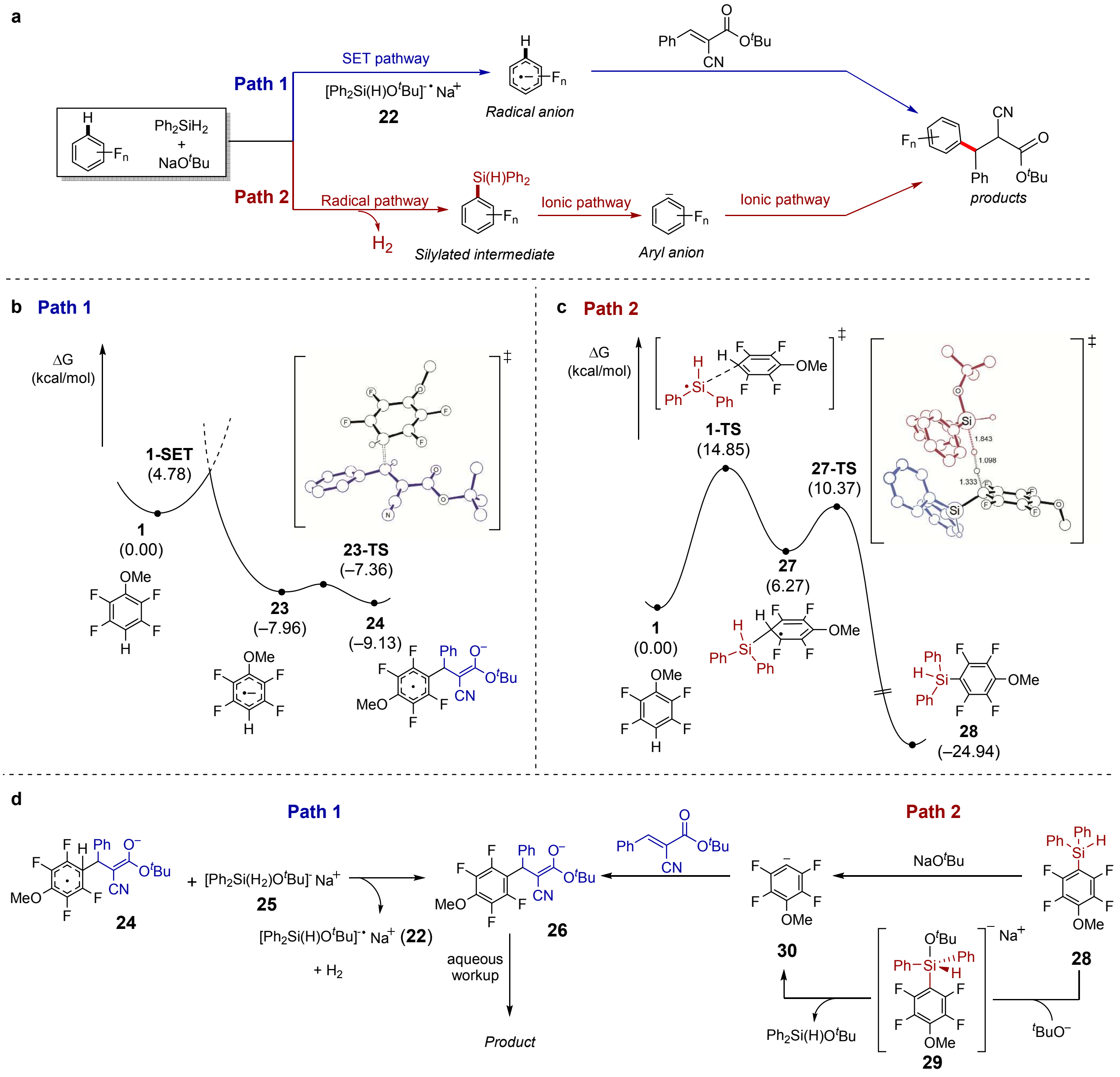
The first mechanistic scenario marked as **Path 1** in Scheme 6a invokes a single-electron transfer (SET) event to produce a radical anion, whereas in **Path 2** a radical-ionic process is proposed to furnish an aryl anion. In both pathways, the reactive intermediates can act as nucleophiles to attack the *α*,*β*-unsaturated carbonyls to form the desired products. In Scheme 5c, employing the silole substrate as a mechanistic probe, we suggested that a silyl radical species (**18**) can participate in the conjugate addition reaction. In the real system where Ph$_2$SiH$_2$ is used, it is reasonable to propose that an analogous radical anion (**22**) or a diphenylhydrosilyl radical [Ph$_2$(H)Si$^\bullet$] species is generated *in situ*.[36] The radical anion may undergo a single-electron transfer (SET),[13g] and trisubstituted silyl radicals may lead a radical chain pathway.[13c]

Starting with the fluorobenzene substrate **1**, a single-electron transfer (SET) from [Ph$_2$Si(H)O^{t}Bu]$^{-\bullet}$Na$^+$ **22**, an analogue of **21**, to substrate **1** was modeled. The barrier of this electron transfer event was estimated using the computed energies of the reactant and product states and employing the Marcus theory.[13g,37] These calculations suggested a free energy barrier for the electron transfer to be only 4.8 kcal/mol. Thus, the aryl radial anion intermediate **23** may be generated readily, as illustrated in Scheme 6b. This radical anion intermediate **23** can attack the Michael acceptor to generate an intermediate **24** practically in a barrierless fashion to form the C–C bond, as our calculations found a transition state **23-TS** that is only 0.6 kcal/mol higher in energy than **23**. Next, the pentavalent silicate species (**25**) can abstract an *ipso*-hydrogen atom to evolve H$_2$ and afford the conjugate addition adduct **26** with a barrier of 26.5 kcal/mol, as shown in Scheme 6d (see the SI for details). The resulting radical species [Ph$_2$Si(H)O^{t}Bu]$^{-\bullet}$ (**22**) may participate in the next single-electron transfer process.

Alternatively, a mechanism similar to what was proposed by Stoltz, Grubbs *et al.* for the ^{t}BuOK-Et$_3$SiH-mediated C–H silyation[13c,d] may be operative. Accordingly, the conjugate addition may involve an arylsilane species as a key intermediate, as highlighted in Scheme 6c and marked **Path 2** in Scheme 6d. This mechanism starts with a diphenylhydrosilyl radical [Ph$_2$(H)Si$^\bullet$] that reacts with fluorobenzene traversing the transition state **1-TS** with barrier of 14.9 kcal/mol. The *ipso*-hydrogen of the radical adduct (**27)** may be detached by silicate **25** with a barrier of 4.1 kcal/mol to furnish a silylbenzene species **28**. This intermediate **28** may then be activated by ^{t}BuO$^-$ anion to transiently form a pentacoordinated species **29**, which will then lead to an aryl anion (**30**) with a negligible barrier of 3.4 kcal/mol upon cleavage of the C–Si bond. In this pathway, the Michael addition is proposed to occur via the aryl anion species (see the SI for full energy profiles).

Unfortunately, it is not possible to use these computed profiles to definitively conclude which of these two possible and plausible pathways are operative. The first pathway involves a single-electron transfer (SET), which is reasoned to occur readily upon collision of the reactants due to the low barrier for the key electron transfer event. The *ipso*-hydrogen abstraction, however, requires a barrier of 26.5 kcal/mol, which is a bit too high to explain the reaction at ambient conditions. But, since the SET is likely irreversible with the back transfer being associated with a much higher barrier, it can be argued that **Path 1** will be followed once the radical anion is produced. This reasoning is consistent with our experimental results summarized in Table 2, where the fluoroarene substrates become more reactive when they have multiple fluorine substituents. The fluorine atoms decrease the LUMO level of arene substrates with concomitant increase of electron acceptability, thereby making the key SET event more feasible.

Scheme 6. Proposed Mechanistic Pathways and Computational Studies



Whereas **Path 1** is plausible and is supported by experimental data, the alternative **Path 2** cannot be ruled out at the present stage because the barriers in each of the proposed steps are low and consistent with a facile reaction under the present conditions. The highest barrier in this pathway is 14.9 kcal/mol and is associated with the initial silyl radical [$Ph_2(H)Si\bullet$] attack on the fluorobenzene substrate. Considering the fact that we could not isolate or detect a silylaryl species (e.g. **28**),[38] an essential intermediate according to the **Path 2**, more definitive experimental evidence will be needed to support this pathway. Taken together, the EPR, radical scavenger experiments, and DFT calculations suggest that a radical pathway is mainly operative in the current reaction system while we cannot fully exclude other possibilities of ionic or neutral paths at the present stage.[13c,d]

■ CONCLUSION

We have developed for the first time a procedure for the conjugate addition of perfluoroarenes to *α*,*β*-unsaturated carbonyls by a system of NaO**^{t}Bu-hydrosilanes. The reaction is convenient to carry out at room temperature over a broad range of substrates and reactants to furnish synthetically useful products in high to excellent yields. Mechanistic studies suggested that a single-electron transfer (SET) process is most likely involved on the basis of EPR and radical scavenger experiments. Significantly, key hypervalent silicates were observed by NMR and a silanide species could be characterized by an X-ray crystallographic analysis, representing the first example of a mechanistically relevant silyl species from the alkoxide-hydrosilane systems. Computational studies also support our proposal of radical intermediacy, but an alternative radical-ionic pathway proposed for the related silylation intermediacy could not be ruled out at the moment. This transition metal-free method should be useful for various applications in synthetic and medicinal chemistry as a practical tool for forming carbon-carbon bonds of fluoroarenes.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures, characterization data, spectroscopic data, crystallographic data, Cartesian coordinates of all computed structures and energy components. The Supporting Information is available free of charge on the ACS Publications website at DOI:

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Notes

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Table of Contents