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COMMUNICATION

Practical and scalable synthesis of bench-stable organofluorosilicate salts

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Silanes have enjoyed sigificant success as synthetic tools in the last few decades. In many of the reactions that use silanes, a pentacoordinate silicate is proposed as the reactive intermediate. Despite this, there is no general method to synthesize pentacoordinate fluorosilicates and use them as reagents instead of organo- or alkoxysilanes. Herein, we report the first practical synthesis of organotetrafluorosilicates. The method is tolerant of a number of different functional groups including electrophiles with preferential attack of the fluoride on the silane rather than the electrophile. This transformaton is generally high yielding, even at the mole scale. Furthermore, we demonstrate that organotetrafluorosilictes are both more reactive than the corresponding trialkoxysilanes and more stable under solvolytic conditions. Organotetrafluorosilicates can be used as substrates for a variety of coupling reactions, oxidations, and radical reactions. Overall, organotetrafluorosilicates represent a new platform on which to develop challenging transformations.

Introduction

Silanes have been used widely in a broad range of different reactions.[1-4] Activated silanes can be oxidized to form a number of different carbon-heteroatom bonds, most notably, alcohols can be produced by the Fleming-Tamao oxidation.[1] In the last three decades, silanes have experienced an influx of new reactivity since the introduction of the Hiyama coupling.[2] They have received much attention because of their ease of synthesis, mild reactivity, and high selectivity. However, because silanes tend to have low reactivity, they almost always need an activating agent in order for the reaction to proceed. Silicates have also been widely used as radical precursors for a number of photoredox transformations.[3] Because of this propensity to form radicals, silanes can also participate in radical reactions as radical mediators.[4]

In nearly every coupling reaction developed for silanes, a stoichiometric amount of either a fluoride or a base is necessary for the reaction to proceed.[1,2] This base or fluoride attacks the silane to form an oft-invoked pentacoordinate silicate, which is the reactive species. To our surprise, and in spite of the fact that these intermediates seem to be more reactive, there has been no general method to synthesize pentacoordinate fluorosilicates to be used as a starting material.[5]

Other 'ate' species have been synthesized, particularly organotrifluoroborates. Treatment of a boronic acid or ester with KHF_2 yields the corresponding trifluoroborate salt cleanly and in high yield.[6] Furthermore, not only do organotrifluoroborates have a wider range of reactivity than boronic acids, particularly in transition metal catalysed cross coupling reactions,[7] they tend to be more stable on the benchtop since they do not undergo self-condensation like boronic acids[8] and are less prone to hydrolysis than boronic esters.[9] Recently, effort has been made to synthesize and explore the reactivity of bis(catecholato)silicates for a number of different transformations, however, these transformations tend to suffer from poor atom economy.[3] Additionally, Kumada published a series of papers in the late 1970's and early 1980's which synthesized organopentafluorosilicates and demonstrated their reactivity (Figure 1, a).[10] Unfortunately, these coordinatively saturated species tended to suffer from low reactivity mainly due to the poor solubility. Since their initial report, the chemistry of pentafluorosilicates has only recently been explored further as alkyl radical precursors to form C(sp^3)-C(sp^3) bonds.[11] One of the first reported means of synthesizing

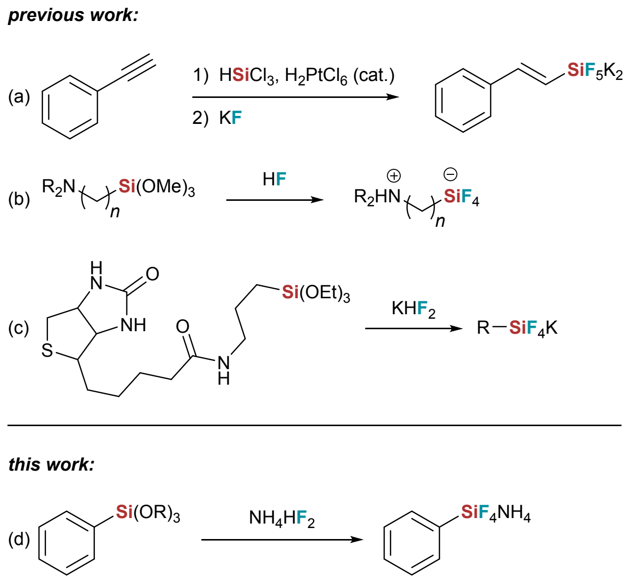

Figure 1: Methods to synthesize organofluorosilicate compounds.

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organofluorosilicates involves treating aminosilanes with dry HF.[12] There are a few methods that synthesize organotetrafluorosilicates, but none of them represent a general procedure that can be used in a number of different contexts. Trialkoxysilanes with appended amines have been treated with HF to generate a zwitterion (Figure 1, b).[13] Organotetrafluorosilicates have also been synthesized by treating ArylSiF_3 with KF and 18-crown-6 for an early study of the structure of an organotetrafluorosilicate.[14] Lastly, a biotin derivative with an appended trialkoxysilane was treated with KHF_2 to make an organotetrafluorosilicate for potential use in ^{18}F PET imaging Figure 1, c).[15] However, we were not able to reproduce their results using a model substrate (see below, Table 1, entry 2). In fact, their characterization data seems to indicate a mixture of fluorosilicates rather than a homogenous organotetrafluorosilicate. Thus, we set out to develop a general method that would synthesize this potentially useful class of compounds.

While synthesis of organofluorosilicates should be straightforward, their synthesis exhibits challenges not present with organotrifluoroborates. For instance, either the tetra- or pentafluorosilicate could be formed in the presence of a nucleophilic fluoride source, so mixtures of products are likely, whereas there is only one possible product from fluoroborate formation. Additionally, fluorosilicate polymers and/or oligomers could form.[16] Ideal reaction conditions would form one product selectively without the presence of the others.

Herein, we report a convenient synthesis of organotetrafluorosilicates from readily available starting materials (Figure 1, d). We demonstrate that organotetrafluorosilicates are both more stable under solvolytic conditions and more reactive in couplings and oxidations than a trialkoxysilane. Furthermore, because we want this reaction to enjoy wide use, this transformation has been performed on the mole scale without loss of yield.

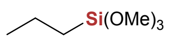
Results and discussion

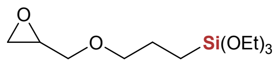
Given its success with generating trifluoroborates and the previous report using a biotin derivative as the substrate, initial optimization was performed with potassium bifluoride (Table 1). The identity of the solvent proved to be essential as alcohols and DMSO produced mixtures of products rather than the desired tetra- or pentaflurosilicate (entries 1-2). Excesses of the fluoride source still produced mixtures which indicated that the tetrafluorosilicate might be preferred over the pentafluosilicate. Indeed, when the stoichiometry was reduced to 2.0 equivalents of potassium bifluoride, the tetrafluorosilicate was produced cleanly and in high yield (entry 3). The method was also tolerant of ammonium counter ions, though some re-optimization was necessary. At more dilute concentrations, the product did not precipitate. Higher concentrations with short reaction times did not allow the silane to fully dissolve, and therefore minimal product was formed, but using a more concentrated solution with longer

$$\underset{\mathbf{1}}{R{-}Si(OR)_3} \xrightarrow[\text{2h, } \textit{solvent}]{MHF_2\text{ (2 equiv)}} \underset{\mathbf{T}}{R{-}SiF_4M} \quad \underset{\mathbf{P}}{R{-}SiF_5M_2}$$

entry	substrate	fluoride	solvent	conc.	T	P
1[a]	**1a**	KHF_2	1:1 H_2O:MeOH	0.25 M	*mixture*	
2	**1a**	KHF_2	1:1 H_2O:DMSO	0.25 M	*mixture*	
3	**1a**	KHF_2	1:1 H_2O:acetone	0.25 M	89%	0
4[b]	**1b**	NH_4HF_2	H_2O	4 M	91%	0

1a





1b

[a]10 equiv of KHF_2 was used. [b]The reaction was stirred for 16 h.

Table 1: Optimization of reaction conditions.

conditions A $\underset{\mathbf{1a,b,c,g}}{R{-}Si(OR)_3} \xrightarrow[\text{acetone/}H_2O]{0.25\text{ M }KHF_2} \underset{\mathbf{2a,b,c,g}}{R{-}SiF_4K}$

conditions B $\underset{\mathbf{1a\text{-}n}}{R{-}Si(OR)_3} \xrightarrow[H_2O]{4\text{ M }NH_4HF_2} \underset{\mathbf{3a\text{-}n}}{R{-}SiF_4NH_4}$

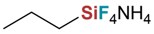
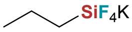
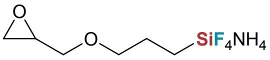
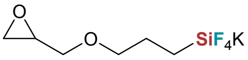
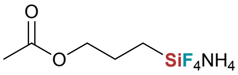
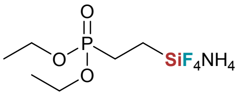
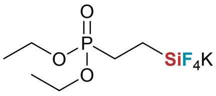
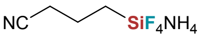
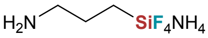
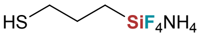
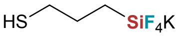
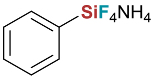
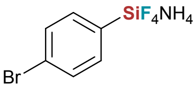
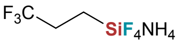
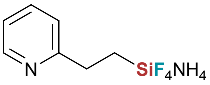
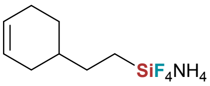
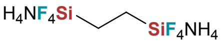
entry	substrate	conditions		product	yield
1	**1a**	**B**	**3a**		67%
2	**1a**	**A**	**2a**		89%
3	**1b**	**B**	**3b**		91%
4	**1b**	**A**	**2b**		74%
5	**1c**	**B**	**3c**		80%
6	**1d**	**B**	**3d**		99%
7	**1d**	**A**	**2d**		77%
8	**1e**	**B**	**3e**		>99%
9	**1f**	**B**	**3f**		98%
10	**1g**	**B**	**3g**		91%
11	**1g**	**A**	**2g**		96%
12	**1h**	**B**	**3h**		80%
13	**1i**	**B**	**3i**		93%
14	**1j**	**B**	**3j**		85%
15	**1k**	**B**	**3k**		75%
16	**1l**	**B**	**3l**		85%
17	**1m**	**B**	**3m**		64%
18	**1n**	**B**	**3n**		81%

Table 2: Substrate scope.

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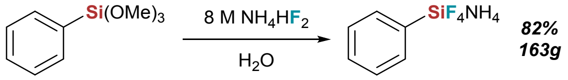
reaction times produced the product in excellent yield (Table 1, entry 4).

However, when the substrate scope was explored (Table 2), we found that the method which formed potassium salts (conditions A) was not robust and produced varying results depending on the substrate. A few potassium tetrafluorosilicates were able to be formed in good yield (Table 2, entries 2, 4, 7, and 11). However, many substrates produced mixtures of products and none of them were more than slightly soluble in a small number of solvents. In fact, they could not be detected by NMR at all in most solvents. Additionally, the potassium salts tended to hydrolyse appreciably in 1-2 hours, whereas the ammonium salts were highly resistant to hydrolysis (see below).

With a reliable procedure in hand that produced ammonium salts rather than potassium salts, the substrate scope was explored further (Table 2). Moreover, ammonium salts were at least moderately soluble in a wide number of polar, aprotic organic solvents. A number of different functional groups were tolerated including electrophiles such as epoxides, esters, nitriles, and phosphonates (entries 3-8). Notably, the fluoride preferred to attack the silicon rather than the appended electrophile in all cases. No competing fluoride attack on any electrophile was detected. Substrates with labile protons, such as amines and thiols, were also tolerated (entries 9-11). Synthetically useful products, such as vinyl and phenyl tetrafluorosilicates, were formed in high yield as well (entries 12-14). Even (bis)silanes were tolerated in the reaction conditions when 4.0 equiv of NH_4HF_2 was used (entry 18). Overall, the method seems to be general and is highly tolerant of a number of different functional groups.

With a substrate scope established, the scalability of the method was explored (eq. 1). On larger scales, more concentrated NH_4HF_2 (8 M) performed better than lower concentrations (see Electronic Supplementary Information for more details). Since the product is slightly soluble in water, this increase in yield was likely due to reduced loss of material that was still dissolved in the water. At smaller scales, loss of material from filtration is less of a concern since the reactions experience significant evaporation which aids in precipitating the product. Overall, the reaction was able to be scaled up to one mole of starting material with 163g of product isolated. Even at this significantly larger scale, the yield was not affected appreciably.

eq. 1 

To test the stability of the organotetrafluorosilicates under solvolytic conditions, their decomposition in water was studied and compared to the trimethoxysilane starting material. Saturated solutions of $4\text{-}BrC_6H_4Si(OMe)_3$ and $4\text{-}BrC_6H_4SiF_4NH_4$ were prepared and the concentration of the corresponding silanol was measured by NMR (Figure 2). The trialkoxysilane hydrolysed slowly over the course of 10 hours, however, the tetrafluorosilicate did not hydrolyse at all in the same timeframe. This clearly indicates that tetrafluorosilicates are more stable under solvolytic conditions than trialkoxysilanes.

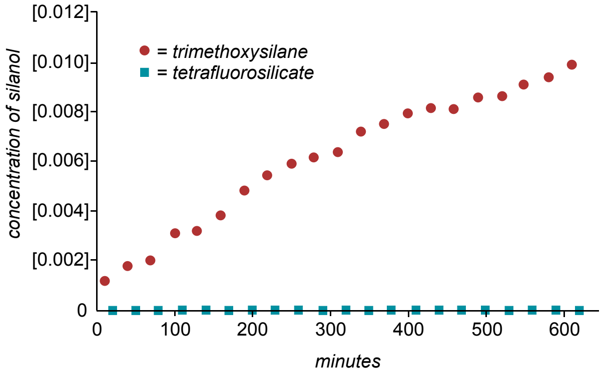


Figure 2: Hydrolysis of trimethoxysilane vs. tetrafluorosilicate.

Next, the difference in reactivity was studied in popular reactions that use silane starting materials (Figure 3). For both the Hiyama Coupling and Fleming-Tamao Oxidation, almost no reaction occurred with the trialkoxysilanes as starting materials. Conversely, the yields were substantially increased when the tetrafluorosilicates were used instead. This is not surprising as these reactions usually require the formation of a transient pentacoordinate silicate species for the reaction to proceed. Notably, the Hiyama coupling with the tetrafluorosilicate is a rare example of a coupling reaction occurring under acidic (due to the ammonium counter ion) rather than basic conditions. However, this shows that the organotetrafluorosilicates are much more reactive than their trialkoxysilane counterparts in spite of their increased stability.

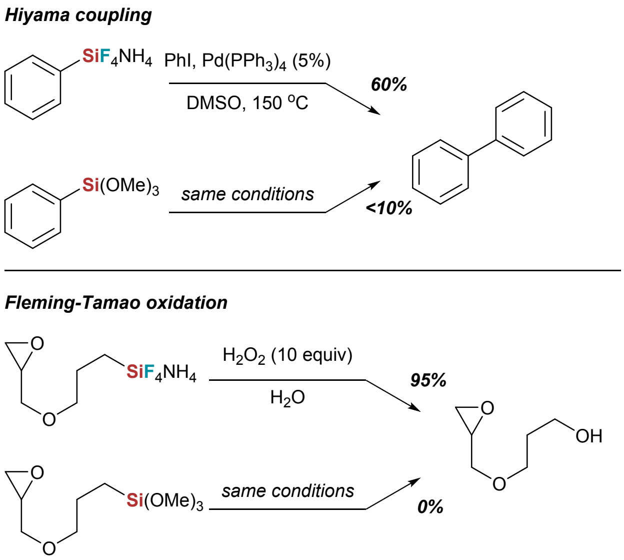


Figure 3: Comparison of the reactivity of trialkoxysilanes and tetrafluorosilicates.

Conclusions

In conclusion, organotetrafluorosilicates can be synthesized selectively over organopentafluorosilicates and in high yield.

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This procedure tolerates a large number of different functional groups and can be scaled without degradation of yield. Additionally, organotetrafluorosilicates seem to be both more stable under solvolytic conditions than their trialkoxysilane counterparts as well as more reactive. We hope that access to this uncommon silicon functional group will be a platform to develop new reactivity and new couplings.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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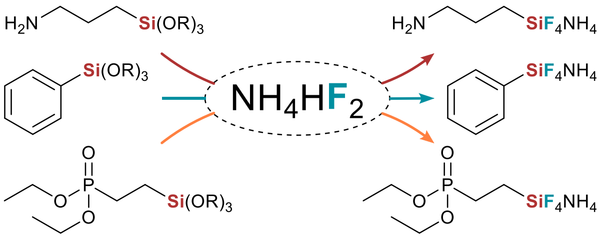
Ammonium organotetrafluorosilicates were synthesized in high yield for a wide range of substrates from readily available starting materials.



high yielding • scalable • resistant to hydrolysis