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Defluorosilylation of Industrially Relevant Fluoroolefins Using Nucleophilic Silicon Reagents

Greg Coates,^[a] Hui Yee Tan,^[a] Carolin Kalff,^[a] Andrew J. P. White,^[a] and Mark R. Crimmin^{[a]*}

Dedication ((optional))

Abstract: A number of new magnesium and lithium silyl reagents were prepared and shown to be outstanding nucleophiles in reactions with industrially relevant fluoroolefins. These reactions result in a net transformation of either sp^2 or sp^3 C–F bonds into C–Si bonds by two modes of nucleophilic attack (S_NV or S_N2'). The methods are mild, proceeding with high chemo- and regioselectivity. Mechanistic pathways are described that lead to new substitution patterns from HFO-1234yf, HFO-1234ze and HFO-1336mzz, previously inaccessible by transition metal catalysed defluorosilylation routes.

Over recent years there has been a push towards the development and implementation of more environmentally-friendly chemicals in the refrigeration industry. The so called '4th generation' of refrigerant gases consist mainly of hydrofluoroolefins (HFOs), as successors to widely employed hydrofluorocarbons (HFCs). HFOs possess much lower global warming potentials (GWPs) than HFCs. With the production of HFOs set to increase, the development of efficient protocols to re-use or recycle waste streams becomes ever more important. One potential approach that has been identified is the use of waste refrigerants as a synthetic entry point to organic molecules and materials.^[1,2] It is well documented that fluorine atoms act as isosteres for hydrogen atoms and can have a marked impact on the efficacy of pharmaceuticals and agrochemicals.^[3,4] In this context, the upgrading of low-cost fluorocarbons to form reactive fluorinated building blocks is an important and timely challenge.

Copper catalysts have been reported for the defluoroborylation and defluorosilylation of fluoroolefins, including industrially relevant refrigerants.^[5–7] The defluorosilylation procedure is proposed to proceed through the 1,2-addition of an intermediate copper silyl *e.g.* [LCu–SiR₃] to the alkene followed by β -fluoride elimination. Despite the importance of this work, the reactions have low efficiency, they rely on the combination of copper(I) catalyst at modest loading (5 mol%), high temperatures (100 °C) and employ stoichiometric quantities of main group reagents (R₃Si–Bpin or B₂pin₂; R = alkyl, pin = pinacolato).^[5–7] In contrast, *s*-block silyl anions (M–SiR₃; M = Li, Na, K) have been invoked as intermediates in highly efficient methods for the defluorosilylation of sp^2 C–F bonds of fluoroarenes and terminal sp^3 C–F bonds of fluoroalkanes.^[8–11] In related studies we, and others, have shown that main group nucleophiles are exceptional

reagents for the C–F functionalisation of fluoroarenes, fluoroalkenes and fluoroalkanes.^[12–17] Strong M---F interactions provide a large thermodynamic driving force for the reaction and can also play a role in determining the selectivity of which C–F bond reacts.^[13]

Herein, we extend our studies to nucleophilic magnesium and lithium silyl reagents and demonstrate a procedure for the selective sp^2 and sp^3 C–F bond functionalisation of industrially relevant fluoroolefins. The method is synthetically straightforward being free from additives or transition metals and in the case of the lithium-based nucleophiles proceeds with high yields, high selectivity and high atom-efficiency under mild conditions.^[5–7]

A number of lithium and magnesium silyls were synthesized.^[8,9] Magnesium silyl reagents (**1** – **4**) were prepared by a two-step procedure involving sequential deprotonation of the pro-ligand (β -diketiminato, iminoanilide or guanidine) with [Mgⁿ/sBu₂] followed by a metathesis reaction with R₃Si–Bpin (Figure 1).^[18] In an alternative approach, lithium silyls (**5**•THF, **5**•TMEDA, **5**•PMDETA) were synthesised by direct metalation of PhMe₂SiCl with Li metal (Figure 1). **5**•THF was isolated as a dark-red oil and based on ¹H NMR spectroscopic analysis contains 1.5 THF molecules per silicon atom. The remaining members of the series could be isolated as crystalline solids and have been characterised by multinuclear NMR spectroscopy and single crystal X-ray diffraction (Figure 2). In benzene-*d*₆ solution at 22 °C **2a** and **3b** demonstrate resonances at δ_{29Si} = –26.9 and 0.3 ppm respectively in the ²⁹Si NMR spectrum. The different solvates of **5** show a similar range of resonances to **2a**, δ_{29Si} = –27.5 to –29.8 ppm.

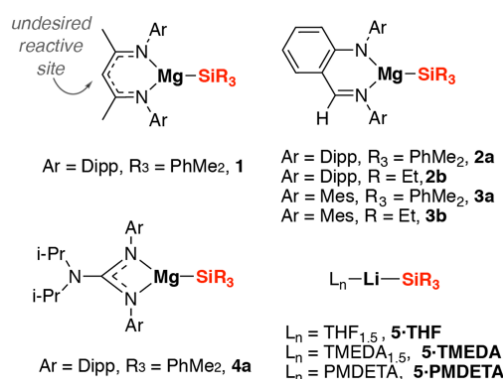


Figure 1. Li and Mg silyl nucleophiles. TMEDA = tetramethylethylenediamine, PMDETA = pentamethyldiethylenetriamine.

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Supporting information for this article is given via a link at the end of the document. Single crystal data has been deposited in the CCDC (1915213 to 1915217).

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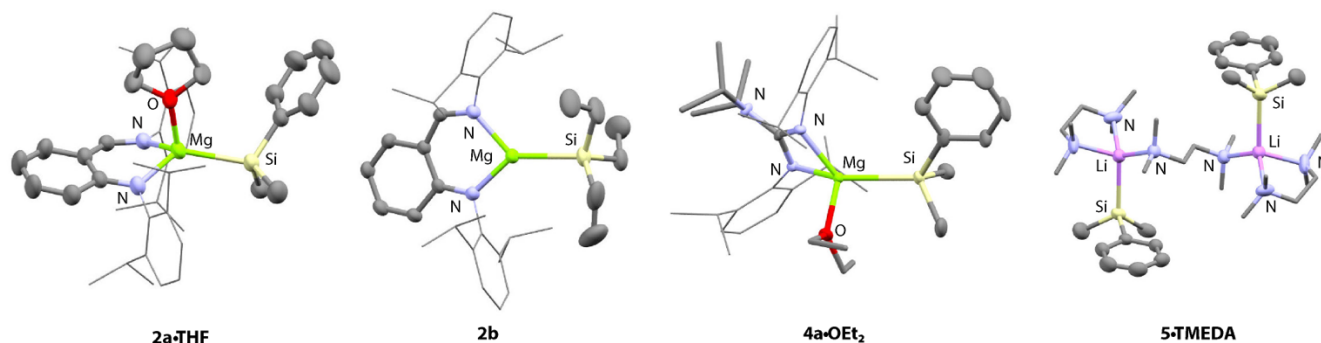


Figure 2. Structures of **2a**·THF, **2b**, **4a**·OEt₂ and **5**·TMEDA determined by single-crystal X-ray diffraction. Selected bond lengths (Å) and angles (°). **2a**·THF: Mg–N 2.041(2) and 2.096(3), Mg–O 2.077(13), Mg–Si 2.6144(12), N–Mg–N 90.04(10). **2b**: Mg–N 2.0040(15) and 2.0615(16), Mg–Si 2.6022(9), N–Mg–N 91.28(6). **4a**·OEt₂ (Molecule A, 1 of 2 in the asymmetric unit) Mg–N 2.089(5) and 2.102(5), Mg–O 2.078(4), Mg–Si 2.664(3), N–Mg–N 64.0(2). **5**·TMEDA: Li–Si 2.736(3).

Compound **2b** represents, to the best of our knowledge, only the second example of a three-coordinate magnesium silyl as characterised by single crystal X-ray diffraction.^[18–20] The Mg–Si interaction of 2.6022(9) Å is slightly longer than that reported for **1** of 2.5900(7) Å.^[18] Due to difficulty in isolation, a number of these species were isolated as solvates containing coordinating ethers. **2a**·THF and **4a**·OEt₂ exhibit longer Mg–Si bonds (2.614(1) and 2.664(3) Å respectively) than **1**, consistent with the higher coordination number at Mg. These values fall well within the range established for simple silicon analogues of Grignard reagents, e.g. [Mg(κ²-TMEDA)(Br)(SiMe₃)] for which Mg–Si = 2.651(6) Å.^[19,21] The Li–Si bond length in **5**·TMEDA is towards the upper end of the range established for lithium silyls for which Li–Si distances vary between 2.52 – 2.76 Å.^[21–24] The structure of **5**·PMDETA has been previously reported by Strohmman and co-workers.^[22]

A series of reactions between **1** – **5** and industrially relevant fluoroolefins were conducted. While **1** shows undesirably ligand-based reactivity due to the nucleophilic carbon of the β-diketiminato ligand, **2** – **5** are effective reagents for defluorosilylation of fluoroolefins.

The silyl lithium reagents proved highly reactive, effecting defluorosilylation at 22 °C (or below) within 15 minutes of mixing. A range of fluoroolefins react at 1 bar pressure with a degassed 0.2 M solution of **5**·THF in C₆D₆ (Figure 3). The defluorosilylation products **6a–e** were formed in high yields 64–88 % and high selectivity. For example, in the case of hexafluoropropene the product, **Z-6a** was formed with 92:8 Z:E. Choice of solvent is important and while most reactions with **5**·THF proceed readily at 22 °C in benzene-d₆, HFO-1234yf requires modification of the conditions to –78 °C in THF to avoid the formation of doubly silylated products (*vide infra*). Preparative reactions with **5**·THF were performed on modest scales (~ 1 mmol) and the resulting organosilanes isolated by distillation in 47–69% yield. Care should be taken during these preparative scale reactions due to the exothermic nature of the reaction due to formation of LiF.

The coordination environment around lithium influences the reaction. **5**·PMDETA and **5**·TMEDA displayed diminished reactivity towards fluoroolefins relative to **5**·THF. In toluene-d₈ at –78 °C, **6a** was generated from hexafluoropropene in 31% yield (86:14, Z:E) from **5**·PMDETA, while **5**·TMEDA failed to produce any of the desired product. When performing the reaction with

5·PMDETA at 22 °C, a slightly higher yield of 46 % (91:9, Z:E) was achieved.

substrate	product	nucleophile	conditions	yield* (selectivity Z:E)
		2a 3a 4a ·OEt ₂ 5 ·THF 5 ·TMEDA 5 ·PMDETA 5 ·PMDETA	C ₆ D ₆ , 100 °C, 3d C ₆ D ₆ , 60 °C, 3d C ₆ D ₆ , 60 °C, 6d C₆D₆, 22 °C, 0.25h toluene, –78 °C, 14h ^b toluene, –78 °C, 14h ^b C ₆ D ₆ , 22 °C, 0.25h toluene, –78 °C, 14h ^b	82% (87:13) 60% (90:10) 20% (84:16) 81% (92:8) 57% (97:3) ^c 0% 46% (91:9) 31% (86:4)
		3a 5 ·THF 5 ·THF	C ₆ D ₆ , 22 °C, 24h C₆D₆, 22 °C, 0.25h toluene, –78 °C, 14h^b	68% 64%^d 77%
		2a 3a 4a ·OEt ₂ 5 ·THF 5 ·THF	C ₆ D ₆ , 100 °C, 3d C ₆ D ₆ , 60 °C, 3d C ₆ D ₆ , 22 °C, 5d C₆D₆, 22 °C, 0.25h toluene, –78 °C, 14h ^b	44% 63% 55% 88% 47% ^c
		3a 5 ·THF 5 ·THF	C ₆ D ₆ , 22 °C, 3d C₆D₆, 22 °C, 0.25h toluene, –35 °C, 3h	62% 75% 47% ^c
		3a 5 ·THF 5 ·THF	C ₆ D ₆ , 60 °C, 24h C ₆ D ₆ , 22 °C, 0.25h THF, –78 °C, 3h	0% 24% 69%^c

a - unless stated otherwise NMR yield versus ferrocene, mesitylene or trifluorotoluene as an internal standard. b - the reaction was warmed from –78 °C to 22 °C slowly over 14 h. c - isolated yield following distillation. d - 18% of a double addition product was observed.

Figure 3. Scope of silylation of fluoroolefins with Magnesium and Lithium Silyls.

The magnesium silyls reagents **2** – **4** also showed diminished reactivity toward fluoroolefins. **2a** reacts with hexafluoropropene or trifluoropropene but only at high temperature (100 °C) over long reaction periods. **2b** did not react with hexafluoropropene despite heating for several days at 100 °C. We have previously shown that accessibility to the reactive metal–metal bond of Mg–Mg and

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Mg–Zn nucleophiles is the most important factor in determining reactivity with fluorocarbons.^[13] Consistent with this finding, the enlarged pocket around the Mg–Si bond in **3a-b** leads to improved reactivity relative to **2a-b**. Nucleophilic attack of **3a** on fluoroolefins at 1 bar was observed between 22 and 60 °C with NMR yields recorded between 60–68 %. No reaction was observed between **3a** and 1,1,1,2-tetrafluoropropene (HFO-1234yf). The low-coordinate geometry and associated vacant coordination site at Mg proved essential for reactivity as **3a-THF** did not react with hexafluoropropene even at 100 °C while **4a-OEt₂** gave products in only low yields.

The lithium and magnesium nucleophiles show similar reactivity patterns to one another. Product distributions are consistent with two established mechanisms: S_NV (nucleophilic vinylic substitution) and S_N2' pathways. These nucleophilic pathways of silyl anions are complementary to the C–F activation of fluorocarbons by silylium cations, which are typically selective for sp³ C–F bonds over sp² C–F bonds and involve fluoride abstraction by highly electrophilic R₃Si⁺ species.^[25–27]

The new methodology offers important advantages over literature approaches to the silylation and borylation of fluoroalkenes. For the silyl lithium reagents **5**, all reactions proceed rapidly under ambient conditions and can operate as low as –78 °C (cf. 100 °C for Cu-catalysed methods).^[5] The reaction proceeds with very high atom economy (LiF and THF solvent as byproducts), in a single step from simple starting materials, while avoiding transition metals or additives. Furthermore, high selectivity of >9:1 (Z:E) can be achieved for the silylation of hexafluoropropene on a preparative scale (cf. 5:1 from Cu-catalysed methods).^[5] Both Li and Mg nucleophiles demonstrate S_N2' reactivity in reactions with HFO-1234yf and HFO-1336-mzz giving access to new fluorinated organosilane building blocks **6d** and **6e** yet to be observed in transition metal catalysed protocols.

Re-exposing **6e** to the reaction conditions results in an additional defluorosilylation step. Hence, an NMR titration of **6e** with **5-THF** cleanly produces the double silylation product **7e**. This reaction is remarkably selective and provides a fluorinated building block with potential dual points of reactivity from HFO-1234yf (Figure 4).

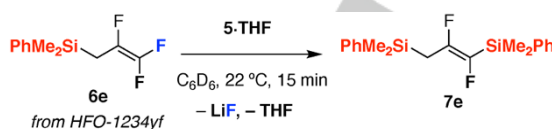


Figure 4. Reaction of **6e** with silyl lithium **5-THF**

To gain a deeper mechanistic understanding of the reactivity, a series of calculations were undertaken on the reactions of fluoroolefins with **2a** and **3a**. While these magnesium silyl reagents showed diminished reactivity toward fluoroolefins relative to their lithium counterparts, the defined coordination sphere at magnesium makes them ideal candidates to probe the mechanism of C–F bond activation. These calculations capture both modes of reactivity described herein along with the ligand

effects.^[28] The B3PW91 functional and a hybrid basis set was used (6-31G**/SDDALL), incorporating single point energy calculations to account for dispersion (GD3) and solvation (PCM, benzene). These computational methods have been previously benchmarked against experimentally determined activation parameters.^[13]

The calculations support the proposed S_NV and S_N2' pathways and account for the experimentally observed products (Figure 5). For example, reaction of **3a** with hexafluoropropene is calculated to proceed by a concerted S_NV pathway from encounter complex **Int-1-Z** via a low energy four-membered transition state, **TS-1-Z** ($\Delta G^\ddagger = +13.6 \text{ kcal mol}^{-1}$) to yield **Z-6a** in an exergonic process ($\Delta G^\circ = -58.9 \text{ kcal mol}^{-1}$). The reaction product was modelled as a weak encounter complex with association occurring through coordination of the π -system of the organosilane to the metal atom of the magnesium fluoride moiety (see supporting information).

The lowest energy transition state, **TS-1-Z**, corresponds to the major stereoisomer **Z-6a** observed in experiments. In **TS-1-Z**, C–Si bond formation is accompanied by C–F bond breaking. Both the Mg---Si and C---F distances lengthen significantly from the starting materials stretching from 2.616 to 2.780 Å and 1.323 to 1.439 Å respectively. A similar S_NV pathway via an alternative transition state **TS-1-E** ($\Delta G^\ddagger = +15.5 \text{ kcal mol}^{-1}$) leads to the minor isomer **E-6a**. An even higher S_NV pathway was located for the activation of the internal C–F bond of HFP ($\Delta G^\ddagger = +19.0 \text{ kcal mol}^{-1}$), the product of which was not observed experimentally. Analogous transition states for the more sterically encumbered nucleophile **2a** are expectedly higher in energy than those derived from **3a** (see supporting information).

While the S_NV pathway was calculated to be the most favourable mechanism for hexafluoropropene or *E*-1,3,3,3-tetrafluoropropene (HFO-1234ze), upon modification of the substrate to 3,3,3-trifluoropropene, 1,1,1,3,3,3-hexafluorobut-2-ene (HFO-1336-mzz) or 1,1,1,2-tetrafluoropropene (HFO-1234yf) the S_N2' pathway becomes dominant. For example, addition of **3a** to 1,1,1,2-tetrafluoropropene occurs via the 6-membered transition state **TS-2** ($\Delta G^\ddagger = 22.5 \text{ kcal mol}^{-1}$). The fluoroolefins studied herein all behave like Michael-acceptors and are susceptible to nucleophilic attack at terminal position. When this position bears a fluorine leaving group S_NV occurs, when it does not the S_N2' mechanism can take over. Due to the substrate polarisation, nucleophilic attack at the internal carbon is disfavoured.

The concerted S_N2' pathway bears some resemblance to the stepwise addition-elimination pathway known to operate for copper(I) silyl nucleophiles. Under catalytic conditions copper(I) silyl complexes are proposed to achieve the silylation of fluoroalkenes by the silyl-cupration of the C=C π -bond to form an organocopper(I) intermediated followed β -fluoride elimination.^[5] The two pathways appear to be related aspects of a continuum differing only by the generation of a reaction intermediate as the result of formation and breaking of a Mg–C bond.^[29]

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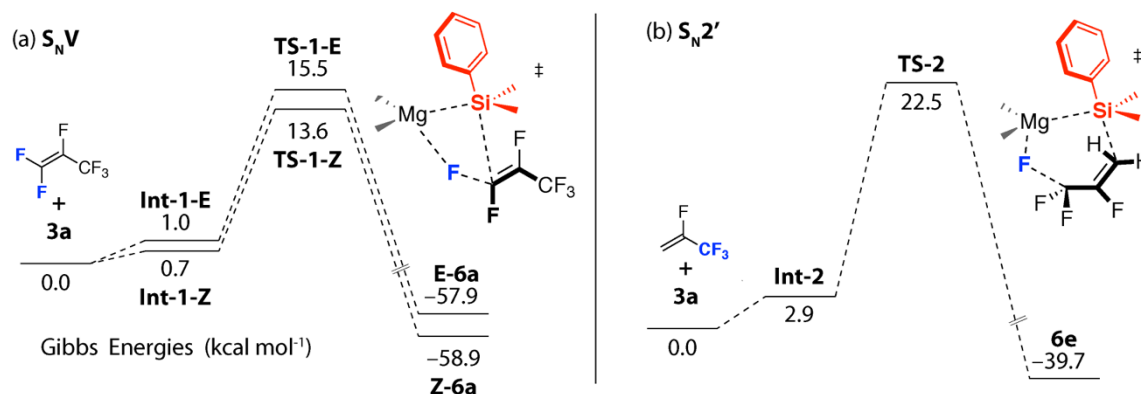


Figure 5. Calculated potential energy surfaces for the addition of **3a** to (a) hexafluoropropene and (b) HFO-1234yf. B3PW91 functional and a hybrid basis set was utilised (6-31G**/SDDALL), incorporating single point energy calculations to account for dispersion (GD3) and solvation (PCM, benzene). Product energies are those of a weak encounter complex between **6** and the magnesium fluoride side product.

In summary, we report a mild transition metal free method to generate fluorinated organosilanes from industrially relevant HFOs. Nucleophilic attack of s-block silyls on fluoroolefins was shown to occur by either S_NV or S_N2' type mechanisms leading to a diverse range of products. The route holds promise as a means to upgrade and recycle 4th generation refrigerants and we are currently studying the applications of the new building blocks in synthesis.

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Keywords: HFO-1234yf • HFO-1234ze • HFO-1336mzz • Fluorine • C–F Bond Activation • Silicon

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- [28] The coordination chemistry of the magnesium silyls is precisely understood. We are reluctant to conduct DFT calculations on the related lithium silyl species due to ambiguity in the nuclearity of the complexes and number of coordinated solvent molecules...
- [29] The resemblance between this mechanism and the S_N2' pathway is further underpinned by calculations on the addition of **3a** to 3,3,3-trifluoropropene. A defined intermediate associated with the 1,2-addition of magnesium silyl across the alkene moiety could be identified. This intermediate is calculated to be highly unstable and undergoes facile β -fluoride elimination (local barrier: $\Delta G^\ddagger = 0.8 \text{ kcal mol}^{-1}$).

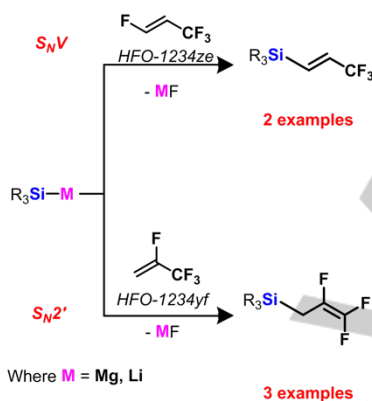
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Magnesium and lithium silyl reagents are outstanding nucleophiles for upgrading industrially relevant fluoroolefins to fluorinated organosilanes.



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