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Catalytic C–F Activation and Hydrodefluorination of Fluoroalkyl Groups

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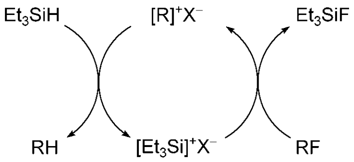
C–F activation · homogeneous catalysis · hydrodefluorination · Lewis acids · weakly coordinating anions

Dedicated to Professor Helmut Werner on the occasion of his 75th birthday

The catalytic functionalization of carbon–fluorine bonds is a major challenge in modern organometallic chemistry.[1] Not only can new compounds be prepared selectively in this way, but the coordination sphere of transition metals also enables unusual derivatization reactions. C–F bonds are characterized by their strength as well as the small size and the high electronegativity of the fluorine atom.[2] Because of these properties, and also because of the kinetic inertness of fluoroalkyl groups, fluorinated building blocks can be found in molecules with countless applications, for example, as refrigerants, anesthetics, polymers, solvents, ligands in catalysis, and even as blood substitutes.[2] On the other hand, the high persistence of perfluorocarbons is responsible for their contribution to global warming and their ability to destroy the ozone layer.[3] The catalytic replacement of C–F with C–H bonds in fluoroalkanes (hydrodefluorination) provides interesting opportunities to tackle this problem, as the resulting hydrofluoroalkanes are believed to have little or no ozone-depletion potential.

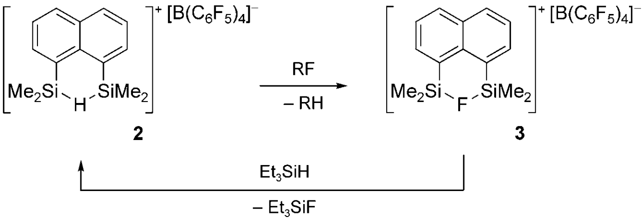
One strategy for hydrodefluorination consists of the activation of a carbon–fluorine bond in the coordination sphere of a transition metal. Activation in this way can lead to selective transformations; however, known catalytic homogeneous hydrodefluorination reactions of highly fluorinated alkyl groups are sparse.[1,4] As an alternative, extremely powerful Lewis acids have a remarkable affinity for fluoride and can be used for the abstraction of fluoride from fluoroalkanes.

Ozerov and co-workers demonstrated that the triethylsilyl cation in $[Et_3Si]^+[B(C_6F_5)_4]^-$ (**1**) reacts with fluoroorganic compounds, such as α,α,α-trifluorotoluene derivatives $ArCF_3$ ($Ar = C_6H_5$, p-C_6H_4F, p-C_6H_4Cl, p-C_6H_4Br, m-C_6H_4F, o,p-$C_6H_3Cl_2$) and 1-fluoropentane, at room temperature (Scheme 1).[5] A carbocation and Et_3SiF are formed in an initial reaction step, and C–H bond formation through reaction of the carbocation with the hydride source Et_3SiH completes the catalytic cycle. The overall conversion is thermodynamically favorable: Si–F bonds are stronger than C–F bonds in fluoroalkyl groups, and Si–H bonds are weaker than C–H bonds. Remarkably, the hydrodefluorination process tolerates aryl halide functionalities. The products of complete replacement of the aliphatic fluorine atoms with hydrogen atoms are obtained. However, perfluorinated substrates remained untouched. Originally, the weakly coordinating anion $[B(C_6F_5)_4]^-$ was chosen to stabilize the reactive cationic intermediates. Fairly high turnover numbers were observed with this anion.



Scheme 1. Reaction cycle for the catalytic hydrodefluorination of fluoroalkyl groups by $[Et_3Si]^+X^-$; for $X^- = [B(C_6F_5)_4]^-$ (reagent **1**): $RF = CH_3$-$(CH_2)_3CH_2F$, $ArCF_3$ ($Ar = C_6H_5$, p-C_6H_4F, p-C_6H_4Cl, p-C_6H_4Br, m-C_6H_4F, o,p-$C_6H_3Cl_2$); for $X^- = [CHB_{11}H_5Cl_6]^-$ (reagent **7**): $RF = C_6F_5CF_3$, $C_6H_5CH_2CH_2CF_3$, $F_3C(CF_2)_3CH_2CH_3$.

In a comparable approach, Müller and co-workers synthesized the silylium compound **2**, which features a hydrogen-bridged disilyl cation with a 1,8-naphthalenediyl backbone (Scheme 2).[6] The cation is also stabilized by the $[B(C_6F_5)_4]^-$ anion and combines the strong electrophilic silylium functionality and the hydrogen source in one species. The treatment of **2** with alkyl fluorides, such as 1-fluorodecane ($C_{10}H_{21}F$) and trifluorotoluene ($C_6H_5CF_3$), yielded the hydrodefluorination products. Species **3** formed in the reaction can be transformed with excess Et_3SiH into **2**, which can initiate the next C–F activation step. Thus, the fluorinated substrates



Scheme 2. Hydrodefluorination with **2** as the catalyst ($RF = C_{10}H_{21}F$, $C_6H_5CF_3$).

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$C_{10}H_{21}F$ and $C_6H_5CF_3$ can be hydrodefluorinated with a catalytic amount of **2** and an equimolar amount of Et_3SiH. However, the catalytic experiments proceeded with fairly low turnover numbers. Compound **2** exhibits comparable selectivities to those observed with the trialkyl silylium compound **1** described by Ozerov and co-workers: Benzylic C–F bonds are more reactive than alkyl C–F bonds; no reaction was observed with C_6F_6.

Organoalumyl cations have also been applied in catalytic C–F activation reactions.[7] A system consisting of iBu$_2$AlH and $[Ph_3C]^+[B(C_6F_5)_4]^-$ (**4**), $[Ph_3C]^+[Al(C_6F_5)_4]^-$ (**5**), or $[Ph_3C]^+[Al\{OC(CF_3)_3\}_4]^-$ (**6**) promoted the hydrodefluorination of C–F bonds at room temperature. The electrophilic cation $[i\mathrm{Bu}_2\mathrm{Al}]^+$ was suggested as an intermediate species. Unlike the hydrodefluorination reactions with **1** and **2**, the conversion of trifluorotoluene ($C_6H_5CF_3$) with $[i\mathrm{Bu}_2\mathrm{Al}]^+$ was incomplete and led to mono- and dihydrodefluorination only. Fluorohexane was transformed into hexane in good yield. The highest turnover numbers were observed with **6**, probably because $[Al\{OC(CF_3)_3\}_4]^-$ is the anion with the weakest cation–anion interaction. In this context, note that Kambe and co-workers reported the conversion of 1-octylfluoride into octane with R_2AlH (R = Et, iBu).[8]

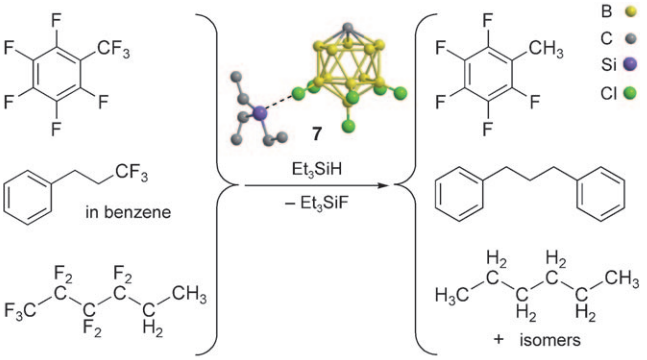
A rational approach to a more efficient, catalytic homogeneous hydrodefluorination of highly fluorinated alkyl groups involves the use of highly electrophilic trialkyl silyl cations, which exhibit even weaker interactions with the corresponding anions. Icosahedral carborane anions, such as $[CHB_{11}F_{11}]^-$, $[CHB_{11}Cl_{11}]^-$, $[CHB_{11}I_{11}]^-$, and $[CHB_{11}H_5Cl_6]^-$, are amongst the least coordinating, least basic, and chemically most inert anions known.[9] Reed and co-workers showed that the trialkyl silylium carborane $[Et_3Si]^+[CHB_{11}I_{11}]^-$ can abstract a fluoride substituent from the C(sp^3)–F bonds in both p-$FC_6H_4CF_3$ and CH_3CF_3 to yield Et_3SiF and the cation $[p\text{-}FC_6H_4CF_2]^+$ or $[CH_3CF_2]^+$ as intermediates.[10] The fluorobenzene solvent undergoes electrophilic attack by the cationic intermediates to form $[(p\text{-}FC_6H_4)_2CF]^+$ and $[(p\text{-}FC_6H_4)(CH_3)CF]^+$ as well as HF.

Ozerov and Douvris have now developed an inspiring catalytic system consisting of Et_3SiH and $[Ph_3C]^+[CHB_{11}H_5Cl_6]^-$ as precursors to $[Et_3Si]^+[CHB_{11}H_5Cl_6]^-$ (**7**) for an efficient catalytic hydrodefluorination of fluoroalkyl groups (Schemes 1 and 3).[11] In the presence of excess Et_3SiH, C(sp^3)–F bonds are activated catalytically and transformed into C–H bonds at room temperature with high turnover numbers. The catalyst **7** can be used for the hydrodefluorination of benzylic and non-benzylic alkyl groups in highly fluorinated compounds; however, so far, the transformation of perfluorinated alkanes has not been successful.

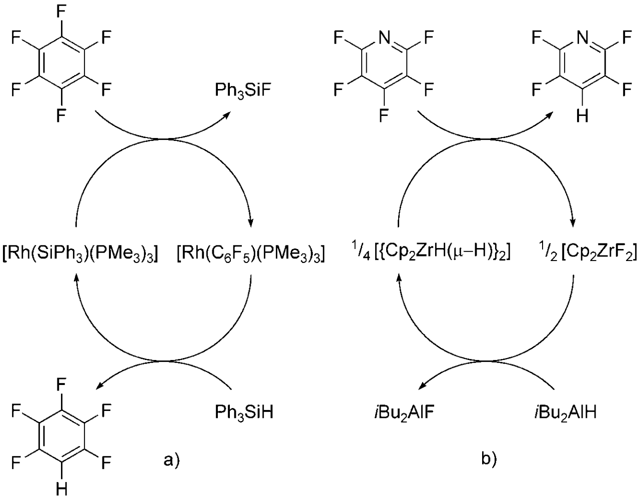
The reactions are chemoselective: Aromatic C–F bonds remain intact, whereas C(sp^3)–F bonds are converted into C–H bonds. Thus, $C_6F_5CH_3$ was synthesized from $C_6F_5CF_3$. Complete hydrodefluorination was observed with $C_6H_5(CH_2)_2CF_3$, and products derived from intra- and intermolecular Friedel–Crafts reactions were generated. For example, a reaction in benzene yielded 1,3-diphenylpropane. Complete hydrodefluorination of the nonafluorohexane $CF_3(CF_2)_3CH_2CH_3$ occurred with the formation of several hexane isomers. In this case, an excess of (hexyl)$_3$SiH was used to generate the catalytically active species to improve its solubility in nonpolar solvents.

These studies are complemented by hydrodefluorination reactions catalyzed by transition-metal complexes with silanes as the hydrogen source.[1,12–14] Thus, a cationic iridium pincer complex stabilized by the weakly coordinating anion $[B(C_6F_5)_4]^-$ catalyzed the transformation of 1-fluoropentane into pentane in the presence of Et_3SiH.[12] Silyl complexes such as $[Rh(SiRR'_2)(PMe_3)_3]$ (R,R′ = Ph or R = Ph, R′ = Me) have been used successfully for the catalytic C–F activation and hydrodefluorination of highly fluorinated arenes and alkenes.[15,16] Thus, a catalytic conversion of hexafluorobenzene into pentafluorobenzene with Ph_3SiH or $(EtO)_3SiH$ was developed. The transition metal mediates the transfer of the fluoride substituent from the fluorocarbon to the silyl fragment (Scheme 4a). Organometallic species are generated as intermediates.

In alternative reaction sequences, C–F bond activation occurs at transition-metal hydrides to yield fluorido complexes (Scheme 4b).[16–18] The fluorido ligand is then replaced by a hydrido ligand upon reaction with silanes or organo-



Scheme 3. Catalytic hydrodefluorination of highly fluorinated substrates.



Scheme 4. Transition-metal-mediated catalytic hydrodefluorination reactions with a) a silane or b) an alumane as the hydrogen source.

alumanes. For example, Rosenthal and co-workers showed that $i\mathrm{Bu_2AlH}$ serves as an activator for the precatalyst $[\mathrm{Cp'_2ZrF_2}]$ ($\mathrm{Cp'_2} = (\eta^5\text{-}\mathrm{C_5H_5})_2$ or *rac*-[ethylenebis(η^5-tetrahydroindenyl)]).[17] The system catalyzes the transformation of pentafluoropyridine into 1,2,4,5-tetrafluoropyridine and $i\mathrm{Bu_2AlF}$. A silane-assisted hydrodefluorination in the presence of a catalytic amount of an iron(II) diketiminate fluoro complex was also reported; however, the turnover numbers were low.[18] With this catalytic system, hexafluorobenzene, pentafluoropyridine, and octafluorotoluene were converted into products of monohydrodefluorination. Finally, highly fluorinated organic substrates do not only undergo hydrodefluorination under transition-metal catalysis, but other C−F functionalization reactions, such as cross-coupling reactions, are also possible.[1,16,19]

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