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Hydrodefluorination of Perfluoroalkyl Groups Using Silylium-Carborane Catalysts

Christos Douvris and Oleg V. Ozerov*

Carbon-fluorine bonds are among the most unreactive functionalities in chemistry. Interest in their activation arises in part from the high global warming potentials of anthropogenic polyfluoroorganic compounds. Conversion to carbon-hydrogen bonds (hydrodefluorination) is the simplest modification of carbon-fluorine bonds, but efficient catalytic hydrodefluorination of perfluoroalkyl groups has been an unmet challenge. We report a class of carborane-supported, highly electrophilic silylium compounds that act as long-lived catalysts for hydrodefluorination of trifluoromethyl and nonafluorobutyl groups by widely accessible silanes under mild conditions. The reactions are completely selective for aliphatic carbon-fluorine bonds in preference to aromatic carbon-fluorine bonds.

Carbon-fluorine bonds are among the most passive functionalities in chemistry (*1*), and their selective activation and transformation under mild conditions remains a poorly realized challenge (*2*–*5*). The thermodynamic issues are considerable: C-F is the strongest single bond to carbon (*1*–*3*). The thermodynamic obstacles are compounded by the kinetic issues: Organic fluorides are poor ligands or Lewis bases, and poor substrates for nucleophilic substitution or oxidative addition to metals (*1*–*4*). In all of these regards, compounds containing fully fluorinated perfluoroalkyl groups prove even more inert than compounds containing a single C-F bond. With the increasing degree of fluorination at carbon, the strength of the C-F bond increases, and the C-F bond distances decrease, resulting in substantial steric shielding of the carbon site (*3*).

Perfluoroalkyl-containing organic compounds have beneficial uses in technology. Some applications include blood substitutes fostered by high O_2 solubility and inertness, (*1*, *6*) as well as solvent media for biphasic synthesis and purification (fostered by low miscibility with water and hydrocarbons) (*6*). On the other hand, perfluorooctanesulfonic acid derivatives (PFOS), used in surfactants and in fluorinated polymer production, have been recently shown to be toxic, widely spread in the biota, and highly persistent (*7*). Perfluoroalkyl-containing chlorofluorocarbons (freons or CFC), hydrofluorocarbons (partially fluorinated alkanes, HFC) and perfluorocarbons (perfluoroalkanes, PFC) are of increasing concern as anthropogenic "supergreenhouse gases" (*8*) of high global warming potential and exceedingly high atmospheric lifetimes. Development of efficient and economical chemical strategies for their disposal is thus of vital importance.

Transition-metal–mediated C-F activation has received substantial attention (*2*–*5*). The approach typically employs highly reducing, electron-rich metal reagents or catalysts. The critical cleavage of the C-F bond in this case is by definition of reductive nature, either through an oxidative addition or a single-electron transfer step. The simplest modification of the C-F bond is its conversion to the simplest functional group: a C-H bond (hydrodefluorination or HDF). The scope of the transition metal–catalyzed HDF has been largely limited to fluoroarenes (*2*–*5*). HDF of poly(tetrafluoroethylene) by stoichiometric Li metal in ammonia has been reported (*9*). Conversion of a C-F to a C-C bond is also of interest, but the progress so far has been limited (*10*). Recently, a Nb-mediated activation of trifluoromethylarene substrates with concomitant conversion of C-F bonds to C-H and C-C bonds was reported (*11*).

We were attracted to a conceptually different approach to C-F activation, in which the key C-F cleavage proceeds by a Lewis acid abstraction of fluoride rather than a redox event (Fig. 1A). Conventional acids, such as SiO_2 or concentrated H_2SO_4, require very high temperatures for cleavage of C-F bonds in perfluoroalkyl groups (*12*, *13*). In 2005, we reported an implementation of the nonredox approach under ambient conditions by using a silylium (R_3Si^+) Lewis acid (*14*). The proposed mechanism is depicted in Fig. 1A. Abstraction of fluoride by silylium from a C-F bond is complemented by the abstraction of hydride by the resultant carbocation from an Si-H bond. The overall process can be viewed as a Si-H/C-F metathesis (with conversion to Si-F/C-H). Given that Si-F is a stronger bond than C-F, and C-H is a stronger bond than Si-H, this metathesis is a very

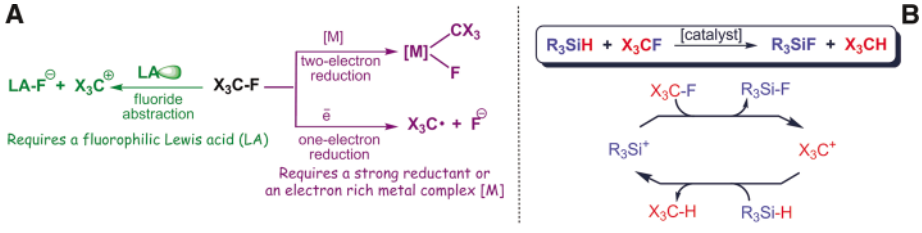

Fig. 1. (**A**) Representation of different approaches to C-F bond cleavage. X stands for an organic substituent, and the X_3 notation does not imply that the three substituents must be identical. (**B**) The stoichiometry of Si-mediated HDF and the proposed mechanism.

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thermodynamically favorable reaction (by ~190 kJ/mol) (*15*). The most relevant precedent for this chemistry is the work of Krause and Lampe, who observed Si-H/C-F redistribution by mass spectrometry (MS) in the gas phase upon collision of SiH_3^+ with CF_4 (*16*, *17*).

The catalytic process as depicted in Fig. 1B requires generation of carbo- and silylium cations; these are species of exceptionally high Lewis acidity. In addition, they may also possess or give rise to species of high Brønsted acidity. The key to harnessing this chemistry in solution is the choice of the counterion. A successful anion must not only be weakly coordinating (i.e., a very weak Lewis base) but also resist decomposition via transfer of an anionic group to a Lewis or Brønsted acid. We originally employed $[B(C_6F_5)_4]^-$ as a weakly coordinating anion because it was known to support a silylium cation (*18*). Two other groups have since reported related chemistry (*19*, *20*). However, the reactivity in all three cases was by and large limited to simple alkyl fluorides and trifluoromethylbenzene, and the turnover numbers were limited (<100).

The use of halogenated monocarboranes (Fig. 2) as supporting anions substantially improves the longevity of the catalysis, promoting facile activation of perfluoroalkyl groups. Our study benefits from the sophistication in the chemistry of carboranes (recently reviewed by Korbe *et al.*) (*21*) brought to the fore by others; studies by the Reed group are particularly relevant (*22*, *23*). Carborane anions have been shown to be compatible with the highest levels of Brønsted and Lewis (e.g., silylium and carbocations) acidity in the condensed phase even under harsh conditions (*21*–*24*). For instance, $H[HCB_{11}Cl_{11}]$, the strongest known Brønsted acid, can be sublimed at 200°C without decomposition (*22*). We selected three carborane anions for investigation: $[HCB_{11}H_5Cl_6]^-$, $[HCB_{11}Cl_{11}]^-$, and $[HCB_{11}H_5Br_6]^-$ (*22*–*25*). We used either triethyl- or tris(*n*-hexyl)silane as the Si-H reagent and the Ph_3C^+ salt of the corresponding anion as the precatalyst. The Ph_3C^+ salt is convenient to store and is readily converted to the corresponding trialkylsilylium by reaction with excess R_3SiH in the reaction mixture (*20*).

We chose three representative substrates (Fig. 3A and Table 1): $C_6F_5CF_3$ [a perfluorocarbon that highlights the C(sp^2)-F versus C(sp^3)-F selectivity], $PhCH_2CH_2CF_3$, and $^nC_4F_9C_2H_5$ (both containing nonbenzylic perfluoroalkyl groups) (*26*). In particular, $^nC_4F_9C_2H_5$ is a reasonable and convenient (liquid) approximation of commercially used HFC coolants, such as tetrafluoroethane (R-134a). Our approach relies on the abstraction of fluoride and generation of a carbocation. Increased fluorination should make the generation of carbocations through fluoride abstraction ever more challenging. Because of the even greater instability of aryl cations, the process targets C(sp^3)-F bonds in preference to the aromatic C(sp^2)-F bonds. Thus, haloarenes are acceptable solvents and, although C_6F_6 is one of the most compliant substrates in transition metal–mediated C-F activation (*27*), here it is sufficiently inert that we use it (or C_6F_5Br) as a ^{19}F nuclear magnetic resonance (NMR) integration standard. In the process of the HDF reactions, fluorine is transferred from the C-F bonds of the substrate to Si, with the formation of R_3SiF and R_2SiF_2. R_2SiF_2 is formed presumably by redistribution of Si substituents (R_4Si is also formed) in the Lewis acidic medium. Discrepancies in the C-F/Si-F mass balance may be due to the leaching of F into the borosilicate glassware (*14*).

At first, we compared the activity of the three chosen carborane-supported catalysts to that of $[B(C_6F_5)_4]^-$ in the HDF reaction (all at 0.4 mol % catalyst) of Et_3SiH (~9 equivalents) and $C_6F_5CF_3$ in *o*-$C_6H_4Cl_2$ solvent (table S1) (*26*). The reaction with the $[B(C_6F_5)_4]^-$ catalyst stopped after only ~15 turnovers, whereas the reactions with all three carborane catalysts proceeded to >97% completion (240 turnovers). In a separate pair of similar reactions ($Et_3SiH/C_6F_5CF_3$ molar ratio of ~3.3) using higher catalyst loading for convenience of monitoring by NMR spectroscopy, we observed that the $[B(C_6F_5)_4]^-$ anion was degraded after 19 turnovers (^{19}F NMR evidence), whereas >95% (^{11}B NMR evidence) of the $[HCB_{11}H_5Cl_6]^-$ anion was intact after >97% conversion at 140 turnovers (figs. S1 and S2) (*26*).

In all likelihood, in our solution chemistry the silylium or carbocations are stabilized by weak interactions with the solvent, anion, substrates, or products (*18*–*20*). Nonetheless, these are highly electrophilic species that approximate the reactivity of true free cations. Although $[B(C_6F_5)_4]^-$ is experimentally compatible with triethylsilylium under ambient conditions (*18*), it is ostensibly not resistant to carbocations and high levels of Brønsted acidity (*28*). Thus, the advantage of the carboranes is in their incomparable robustness.

We next scrutinized the relative activity of the three carborane catalysts using the same HDF

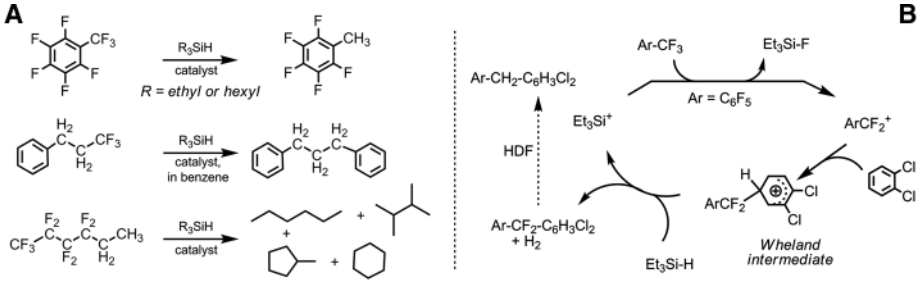

Fig. 3. (**A**) HDF reaction under study. (**B**) Proposed mechanism of formation of the Friedel-Crafts products.

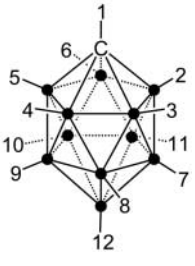

Fig. 2. Representation of the icosahedral carba-*closo*-dodecaborate(–) $[HCB_{11}H_{11}]^-$ anion, or carborane (dots at vertices represent boron atoms; each vertex is capped with a hydrogen atom). Hexahalogenation to give $[HCB_{11}H_5Br_6]^-$ and $[HCB_{11}H_5Cl_6]^-$ occurs in positions 7 to 12; undecachlorination to give $[HCB_{11}Cl_{11}]^-$ occurs in positions 2 to 12.

Table 1. HDF reactions with $Ph_3C[HCB_{11}H_5Cl_6]$ as catalyst; catalyst loading is given per number of C(sp^3)-F bonds. Si-F conversion is calculated as fraction of F from the original aliphatic C-F bonds, found in the Si-F bonds of R_3SiF and R_2SiF_2 (by ^{19}F NMR spectroscopy). Turnover numbers (TON) are calculated based on the C-F conversion (disappearance of the starting material by ^{19}F NMR spectroscopy) and represent the number of consumed C-F bonds per molecule of catalyst. >97% C-F conversion corresponds to the absence of discernible ^{19}F NMR resonances of the starting material. The amount of Et_3Si-H used corresponded to ~1.1 Si-H bond per 1 C(sp^3)-F bond in the substrate.

No.	Substrate	Silane	T (°C)	Time (h)	Cat. mol (%)	Solvent	Si-F conv. (%)	C-F conv. (%)	TON
1	$C_6F_5CF_3$	Et_3SiH	25	24	0.080	*o*-$C_6H_4Cl_2$	84	>97	1250
2	$C_6F_5CF_3$	Et_3SiH	25	6	0.080	Neat	82	>97	1250
3	$C_6F_5CF_3$	Et_3SiH	25	72	0.036	*o*-$C_6H_4Cl_2$	76	>97	2700
4	$Ph(CH_2)_2CF_3$	Et_3SiH	25	24	0.13	Neat	79	>97	780
5	$Ph(CH_2)_2CF_3$	Et_3SiH	25	48	0.13	C_6H_6	75	>97	780
6	$^nC_4F_9C_2H_5$	Hex_3SiH	50	120	0.50	Neat	92	>97	200

reaction between Et_3SiH (3.3 equivalents) and $C_6F_5CF_3$ (table S2) (*26*). The results showed the activity increasing in the order $[HCB_{11}H_5Br_6]^- < [HCB_{11}Cl_{11}]^- < [HCB_{11}H_5Cl_6]^-$. Reed previously determined that the basicity decreases in the series $[HCB_{11}H_5Br_6]^- > [HCB_{11}H_5Cl_6]^- > [HCB_{11}Cl_{11}]^-$, albeit the differences are small (*22*). In that context, the lower activity of $[HCB_{11}H_5Br_6]^-$ is logical, but the higher activity of $[HCB_{11}H_5Cl_6]^-$ versus $[HCB_{11}Cl_{11}]^-$ is unexpected. The reasons behind this apparent anomaly remain unclear (*29*).

We concentrated our attention on $[HCB_{11}H_5Cl_6]^-$ because of its higher activity. Catalytic HDF of $C_6F_5CF_3$ was performed at ambient temperature in *o*-$C_6H_4Cl_2$ as solvent and also using neat reagents (Table 1, entries 1 to 3). Turnover numbers of up to 2650 were achieved. With 0.08% catalyst loading in *o*-$C_6H_4Cl_2$, $C_6F_5CF_3$ was >97% consumed within 24 hours. In addition to the 53% yield of $C_6F_5CH_3$, most of the balance (32%) was accounted for by the presence of two isomers of $C_6H_3Cl_2$-$CH_2C_6F_5$, an apparent product of a Friedel-Crafts attack on *o*-dichlorobenzene. The observation of the Friedel-Crafts products should not be surprising given the proposed generation of highly reactive carbocations. Figure 3B illustrates the proposed mechanism of the formation of $C_6H_3Cl_2$-$CH_2C_6F_5$. It assumes an attack on *o*-dichlorobenzene by $C_6F_5CF_2^+$, followed by proton transfer and HDF; however, it is possible that intermittently formed cations $C_6F_5CFH^+$ and $C_6F_5CH_2^+$ may attack *o*-dichlorobenzene, ultimately leading to the same product. The Friedel-Crafts products are generated catalytically; this requires that the Wheland intermediate in Fig. 3B react with Et_3SiH by proton transfer, evolution of H_2, and generation of Et_3Si^+. In corroboration of this proposition, H_2 was detected in the reaction mixture by ^1H NMR spectroscopy, and perceptible pressurization of a closed reaction vessel was obvious upon opening. Performing the HDF of $C_6F_5CF_3$ using neat reagents (Table 1, entry 3) obviated the Friedel-Crafts chemistry and led to the formation of $C_6F_5CH_3$ in 86% yield by gas chromatography MS (GC-MS) analysis (*26*).

The HDF reaction between $C_6H_5CH_2CH_2CF_3$ and Et_3SiH and 0.13% catalyst in neat substrates resulted in complete consumption of C-F bonds in 24 hours (Table 1, entry 4). However, GC-MS analysis revealed a 5% yield of indane as the only volatile product. It is likely that extensive intra- and intermolecular Friedel-Crafts chemistry leads to the formation of oligomeric products. Indane itself is a product of intramolecular Friedel-Crafts reaction. In support of this hypothesis, ^{13}C NMR analysis of the reaction mixture revealed the presence of multiple resonances in the region expected for Ar-(CH_2)-Ar linkages (δ 32 to 36 parts per million). When an analogous HDF reaction was performed in the presence of benzene, intermolecular Friedel-Crafts reaction was favored, giving 1,3-diphenylpropane as the major product (76% yield) (Table 1, entry 5).

Hydrodefluorination of nonafluorohexane was carried out with 0.5% of $Ph_3C[HCB_{11}H_5Cl_6]$ and excess tris(*n*-hexyl)silane (Table 1, entry 6, and Fig. 4). Tris(*n*-hexyl)silane was chosen for reasons of higher solubility of the tris(*n*-hexyl)silylium derivative in a nonpolar medium. The reaction was conducted at 50°C, and complete consumption of nonafluorohexane was observed after 120 hours. Upon completion, GC-MS analysis revealed the formation of n-hexane (28%), 2,3-dimethylbutane (13%), methylcyclopentane (10%), and cyclohexane (<3%). The origin of methylcyclopentane and cyclohexane is unclear; one possibility is proton transfer from a carbocation (see Wheland intermediate in Fig. 3B), followed by isomerization. The ratio of methylcyclopentane to cyclohexane that we observed is not an equilibrium ratio (*30*). The presence of 2,3-dimethylbutane can be viewed as a consequence of the carbon skeleton rearrangements in the carbocation-like species that must be generated in the HDF process.

The high efficiency of this process may lend itself toward large-scale remediative applications. Success may depend on the viability of cheaper silanes as sources of Si-H and on the ability to remove Lewis-basic impurities from the substrate.

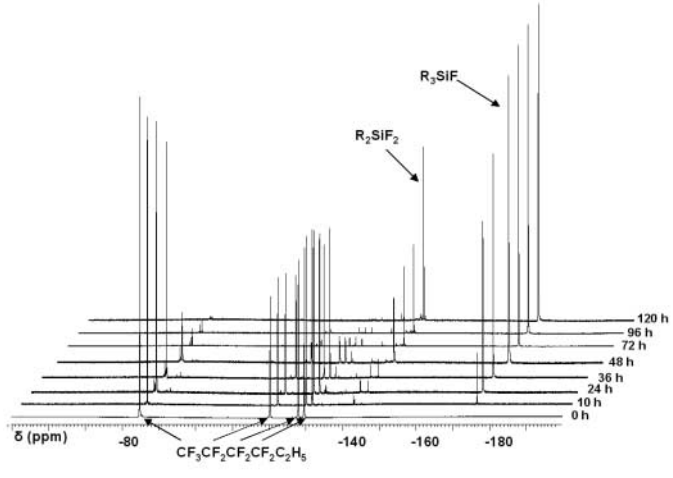

Fig. 4. ^{19}F NMR spectra showing the conversion of C-F into Si-F bonds over time in the HDF reaction of $^nC_4F_9C_2H_5$.

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