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Room-Temperature Catalytic Hydrodefluorination of C(sp^3)−F Bonds

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Activation of carbon−fluorine bonds remains one of the major challenges of modern organometallic chemistry. C−F activation is both a fundamentally appealing task (C−F is the strongest single bond to carbon)[1] and one of practical relevance to the potential remediation of atmospheric pollutants. Freons (CFCs) are a proven hazard to the ozone layer,[2] while CF_4 and heavier perfluoroalkanes are extremely potent and long-lived greenhouse gases.[3] The simplest transformation of a C−F bond is conversion to a C−H bond (hydrodefluorination or HDF, eqs 1 and 2). Utilization of H_2 in HDF results in formation of the toxic and difficult-to-handle hydrogen fluoride. Replacement of H_2 with X_3SiH (X = alkyl, aryl) as the source of hydride leads to the more benign X_3SiF and makes the overall reaction more thermodynamically favorable.[4a]

$$\text{R−F} + \text{H−H} \xrightarrow{\text{catalyst}} \text{R−H} + \text{H−F} \qquad (1)$$

$$\text{R−F} + X_3\text{Si−H} \xrightarrow{\text{catalyst}} \text{R−H} + X_3\text{Si−F} \qquad (2)$$

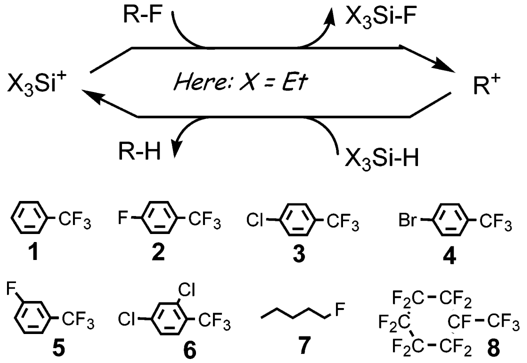
Transition metal-*catalyzed* HDF has so far been largely limited to select fluoroarene substrates,[4] although stoichiometric HDF reactions with aliphatic fluorides have been reported by Jones et al. with the $Cp^*{}_2ZrH_2$ reagent.[5] Most designs for C−F bond activation utilize electron-rich transition metal centers and depend on C−F oxidative addition or one-electron transfer followed by loss of fluoride as the key C−F bond-breaking steps.[6,7] In this work we present the first example of the room-temperature HDF of aliphatic C(sp^3)−F bonds.

We set out to explore a conceptually different approach to C−F activation wherein the crucial C−F cleavage step occurs via abstraction of F^- by a Lewis acid. This clearly requires a Lewis acid with exceptional affinity for F^-, and we surmised that an X_3Si^+ cation should be an appropriate choice (Scheme 1). The high affinity of Si for F is well-established. It is a matter of some debate what should be considered a "free" X_3Si^+ cation in the condensed phase.[8,9] Regardless, it is clear that X_3Si^+ "salts" of weakly coordinating anions (carboranes and tetrarylborates) are exceptionally electrophilic and approach the properties and the reactivity of the putative "free" X_3Si^+.[8,9] Abstraction of F^- from a C−F bond in R−F would generate a carbocation R^+. Conveniently, many X_3Si^+ "salts" are generated by abstraction of H^- from X_3SiH by Ph_3C^+.[8,9] It is reasonable to assume that a carbocation R^+ more reactive than the relatively stabilized Ph_3C^+ would be able to abstract H^- from X_3SiH as well. The overall process is designed to be a Si−H/C−F metathesis catalyzed by X_3Si^+ (Scheme 1).

Krause and Lampe in the 1970s studied the reactions between CF_4 and SiH_3^+ (or between CF_3^+ and SiH_4) in the gas phase and found that redistribution favoring F on Si and H on C occurred readily.[10] Attempts at preparation of $Et_3Si[B(C_6H_3(CF_3)_2)_4]$ resulted in the formation of Et_3SiF, presumably via abstraction of F^- from the anion.[11] The mechanism in Scheme 1 is also related to the reduction of ethers and ketones, reported by Gevorgyan and Piers.[12]

We chose $Et_3Si[B(C_6F_5)_4]$ (**B**)[9b,c] as a synthetic equivalent of "X_3Si^+" and Et_3SiH as the H source. Isolation *and storage* of pure **B** have proven difficult. Our catalytic cycle calls for excess Et_3SiH, and **B** is made by abstraction of hydride from Et_3SiH by $Ph_3C[B(C_6F_5)_4]$ (**A**).[9b,c] We find that generation of **B** in situ via addition of a catalytic amount of **A** to the mixture of substrate and Et_3SiH is preferable.

Scheme 1



We selected a series of benzotrifluorides as well as 1-fluoropentane and perfluoromethylcyclohexane as our test substrates (Scheme 1).[13] We performed the reactions either "neat" (substrate + Et_3SiH + catalytic (1−4%) amount of **A** or **B**) or in a solvent, with monitoring by ^{19}F NMR and eventually by GC−MS. The results are summarized in Table 1. For substrates **1**−**7**, products resulting from complete replacement of aliphatic fluorines by hydrogens were identified. The relative activity of the substituted benzotrifluorides can be roughly correlated with standard substituent effects.[14] For the more reactive substrates **1**−**3** and **7**, complete consumption was observed in <2 h at 22 °C. The results are consistent with the more facile F^- abstraction from the more electron-rich substrates that would generate more stable carbocations. For the Ar−CF_3 substrates we did not observe $ArCHF_2$ or $ArCH_2F$ intermediates (^{19}F NMR in situ), which is consistent with the slow abstraction of first F^-. We have no evidence of the formation of *free* silylium or alkyl cations in our reactions. However, it is likely that highly electrophilic species approaching "free" cations are generated,[15] and qualitative considerations for the cations should be applicable. The HDF reactions are tolerant of the aryl halide functionality. Abstraction of Hal^- (halide) from Ar−Hal is expected to be more difficult because of the great instability of the aryl cations. Lectka et al. documented abstraction of F^- from Ar−CF_3 groups by aryl cations.[16] The inertness of **8** probably reflects the relative difficulty in generating a perfluoroalkyl cation under the employed conditions. The reactions proceed more slowly in $p\text{-}C_6H_4BrF$ and in some neat reactions, likely because of the lower polarity of the media. In the reactions in $o\text{-}C_6H_4Cl_2$, we also observed partial disproportionation of Et_3SiF into Et_4Si and Et_2SiF_2 (GC−MS and ^{19}F NMR evidence). This redistribution is undoubtedly catalyzed by one of the strong Lewis acids in solution and is probably boosted by the higher solvent polarity.

10.1021/ja0426138 CCC: $30.25

Table 1. HDF Results after 24 h at 22 °C ($Ar{-}CF_3 \rightarrow ArCH_3$)

no.	substrate	catalyst	solvent	Si–F conv, %^{a}	C–F conv, %^{b}	TON^c
1	**1**	**A**	neat	75^d		126
2	**1**	**A**	o-$C_6H_4Cl_2$	65^e	100	60
3	**1**	**A**	p-C_6H_4BrF	38		35
4	**1**	**A**	p-ClC_6H_4Me	70	100	61
5	**1**	**A**	C_6H_5F	61	100	53
6	**1**	**A**	C_6D_5Br	75	100	65
7	**1**	**B**	o-$C_6H_4Cl_2$	73^e	100	63
8	**1**	**B**	p-C_6H_4BrF	22		19
9	**1**	**A**	o-$C_6H_4Cl_2{}^f$	81^e	100	71
10	**2**	**A**	neat	47^d		87
11	**2**	**A**	o-$C_6H_4Cl_2$	>95^e	100	97
12	**2**	**A**	p-C_6H_4BrF	>95		87
13	**2**	**A**	p-ClC_6H_4Me	53	100	46
14	**2**	**A**	C_6H_5F	77	100	67
15	**2**	**A**	C_6D_5Br	>95	100	94
16	**2**	**B**	o-$C_6H_4Cl_2$	>95^e	100	95
17	**2**	**B**	p-C_6H_4BrF	31		27
18	**2**	**A**	o-$C_6H_4Cl_2{}^f$	93^e	100	81
19	**3**	**A**	neat	19^d		31
20	**3**	**A**	o-$C_6H_4Cl_2$	82	100	75
21	**3**	**A**	o-$C_6H_4Cl_2{}^f$	>95^e	100	84
22	**4**	**A**	neat	15^d		26
23	**4**	**A**	o-$C_6H_4Cl_2$	31^e	60	28
24	**5**	**A**	neat	3^d		6
25	**5**	**A**	o-$C_6H_4Cl_2$	9^e	18	8
26	**6**	**A**	neat	11^d		21
27	**6**	**A**	o-$C_6H_4Cl_2$	70^e	86	64
28	**6**	**A**	p-C_6H_4BrF	29		26
29	**6**^{g}	**A**	p-ClC_6H_4Me	83	100	72
30	**6**^{g}	**A**	C_6H_5F	85	100	74
31	**6**	**B**	o-$C_6H_4Cl_2$	33^e	56	29
32	**6**	**B**	p-C_6H_4BrF	10		8.6
33	**7**^{h}	**A**	neat	31^d		48
34	**7**^{h}	**A**	o-$C_6H_4Cl_2$	92^e	100	28
35	**8**	**A**	neat	0^d		0
36	**8**	**A**	o-$C_6H_4Cl_2$	0	0	0

^{a} Fraction of F from the original aliphatic C−F bonds found in the Si−F bonds of Et_3SiF. ^{b} The number in this column = 100% − fraction of C−F bonds remaining in the starting material. ^{c} Number of Si−F bonds made per molecule of catalyst. ^{d} Conversion of Et_3SiH (substrate in excess). ^{e} Sum of the Si−F bonds in Et_3SiF and Et_2SiF_2. ^{f} Reactions were run in a plastic vial. ^{g} After 45 h. ^{h} The product is pentane.

Although fairly high turnover numbers were achieved, the catalyst employed in this study is not living. Its decomposition is evident by the decrease in the intensity of the $B(C_6F_5)_4{}^-$ signals in the ^{19}F NMR spectra during the reaction and appearance of $B(C_6F_5)_3$ and other, unidentified C_6F_5-containing products. This also prevented us from conducting kinetic studies. Ostensibly, attack on the anion is a competitive pathway for the highly electrophilic species (possibly including H^+)[17] generated in the HDF reactions, and the inertness of $B(C_6F_5)_4{}^-$ is critical. Even at 110 °C, Et_3SiOTf was not competent as catalyst at all, while $B(C_6F_5)_3$ (shown to reversibly abstract H^- from Et_3SiH)[12b] gave only ca. 1% conversion (substrate **1** or **2**).

The conversions (by ^{19}F NMR vs an internal C_6F_6 standard) were calculated on the basis of either (a) the disappearance of the C−F signals of the product or (b) the appearance of the Si−F signals. In nearly all cases, we discovered that there appeared to be fewer Si−F bonds produced (by ca. 10−20%) than C−F bonds consumed. We surmised that some of the F in the Si−F bonds is lost over time to the Si of the glass of the reaction vessels. In support of this hypothesis, performing the reactions in polypropylene vials resulted in higher observed Si−F conversions.

In summary, we have demonstrated the first room-temperature catalytic hydrodefluorination of aliphatic C−F bonds. Our process utilizes an unconventional method of C−F bond activation that relies on the abstraction of F^- by an electrophilic silylium species. Although activation of C−F bonds in perfluoroalkanes by this method remains elusive, it may yet be achieved via utilization of more robust counterions, such as halogenated carboranes,[8,9] and silanes other than Et_3SiH.

Acknowledgment. This research was supported by Brandeis University (start-up funds), Research Corporation (Research Innovation Award to O.V.O.), and the Nathan and Bertha Richter & Ernest Grunwald Undergraduate Award to V.J.S.

Supporting Information Available: Experimental details and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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JA0426138