C−F Activation

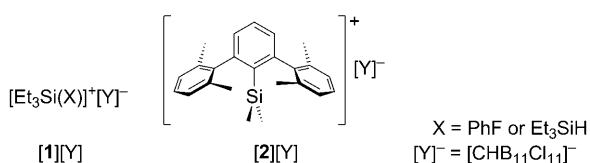# C−F Activation of Fluorobenzene by Silylium Carboranes: Evidence for Incipient Phenyl Cation Reactivity**

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Dedicated to Yitzhak Apeloig and Takaaki Sonoda

Silicon and fluorine are an unequal pair, and yet they form the strongest couple of all elements. The unmatched Si−F bond dissociation energy[1] of 662 kJ mol⁻¹ offers the possibility of abstracting fluoride from almost any fluorine-containing species, given a suitable silyl Lewis acid. In particular, fluoride abstraction from organofluorine compounds by a silylium ion R_3Si^+ is a thermodynamically favored process.[2] Silylium ion-based Lewis acids have been shown to effect C−F activation in aliphatic fluorocarbons, affording isolable carbocationic intermediates[3] or hydrocarbons $R_3C\text{-}H$ in the presence of a reducing agent.[4] The extension of such reactivity to the heterolytic activation of fluoroarenes, however, remains a fundamental challenge.[5] Herein we present the reactivity of silylium carboranes [**1**][CHB₁₁Cl₁₁] and [**2**][CHB₁₁Cl₁₁], both of which abstract fluoride from fluoroben-

zene at slightly elevated (**1**⁺) or even ambient temperatures (**2**⁺).

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The difficulty of bringing about heterolytic Ph−X bond cleavage (X = leaving group) analogous to the first step in classical S_N1 reactions is intrinsically tied to the instability of the phenyl cation.[6] In its ground state, $C_6H_5^+$ possesses the electronic configuration $(\pi)^6(sp^2)^0$ with all bonding π orbitals filled and a lower-lying orbital remaining vacant.[7,8] S_N1-like processes involving Ar−X substrates in solution are therefore rare and have only been accomplished with leaving groups such as N_2^+ in diazonium salts and/or highly activated aryl moieties.[9,10] Even in these cases, substitution reactions probably proceed via a loose S_N2 Ar path or radical intermediate rather than a purely dissociative cationic mechanism.[11] Recent investigations into photochemically generated $RC_6H_4^+$ intermediates have shed light on the reactivity and synthetic utility of aryl cations in the $(\pi)^5(sp^2)^1$ triplet state.[12] The fact that they have to be formed in solvents of high polarity and selectively react with π nucleophiles makes the development of a method for the controlled generation of singlet phenyl cations under weakly nucleophilic conditions an attractive goal.

Heating a solution of [**1**][CHB₁₁Cl₁₁][13] in fluorobenzene at 80 °C for several hours, followed by addition of *n*-hexane, afforded a colorless crystalline solid consisting of two Ph-CHB₁₁Cl₁₁ isomers, as inferred from ¹H, ¹³C, and ¹¹B NMR spectra (Scheme 1). X-ray rystallographic analysis of one of
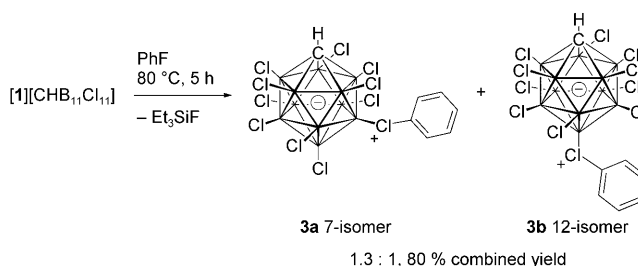
Scheme 1. C−F activation by **1**⁺ affording phenyl carboranes **3 a,b**.

the products and NMR studies of samples partially enriched in each isomer made it possible to identify them as 7- and 12-Ph-CHB₁₁Cl₁₁ (**3 a,b**, Table 1).[14] Full characterization was achieved by MS, IR, and 2D NMR experiments.

The C−F activation hinges upon the use of the extremely weakly coordinating CHB₁₁Cl₁₁⁻ counterion. Silylium-ion-like species Et₃Si-Y with more nucleophilic carboranes (Y = CHB₁₁H₅Cl₆⁻ and CHB₁₁H₅Br₆⁻)[13,15] did not abstract fluo-

Table 1: ^{1}H and $^{13}C\{^1H\}$ NMR data of **3 a,b**. CD$_2$Cl$_2$ solution, 500 MHz for ^{1}H, 300 K, CHDCl$_2$ = 5.32 ppm, CD$_2$Cl$_2$ = 54.00 ppm. Aromatic ^{1}H resonances are multiplets, br = broad signal.

	3 a		**3 b**	
	^{1}H	^{13}C	^{1}H	^{13}C
carb. CH	3.49 br	48.6 br	3.65 br	48.6 br
C$_{ipso}$	–	127.2	–	127.5
C$_{ortho}$	7.87–7.83	132.1	7.82–7.79	132.2
C$_{meta}$	7.72–7.67	133.3	7.67–7.63	133.1
C$_{para}$	7.83–7.78	135.1	7.79–7.75	134.9

ride from fluorobenzene under the conditions given in Scheme 1. The enhanced silyl Lewis acidity provided by the CHB$_{11}$Cl$_{11}$$^-$ anion seems to be crucial in terms of reaction kinetics. In the reaction mixture, small amounts of 2- and 4-fluorobiphenyl, probably stemming from attack of the incipient phenyl cation on fluorobenzene rather than the carborane, were detected by GC–MS analysis.

A colorless single crystal of **3 a**·0.5 C$_6$H$_5$F was obtained from fluorobenzene/n-hexane at room temperature. X-ray crystallography revealed that the phenyl ring is bound to one of the lower-belt chlorine atoms of the carborane anion (Figure 1). The Cl6–C1 and B6–Cl6 bond lengths are
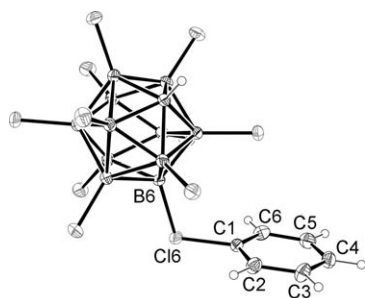

Figure 1. ORTEP plot of **3 a** (thermal ellipsoids set at 50% probability).

1.798(2) Å and 1.854(2) Å, respectively, and the B6-Cl6-C1 angle is 109.65(7)° (Table 2). These values can be compared to standard covalent C$_{aryl}$–Cl 1.74 Å,[16] and carborane B–Cl 1.77 Å bond lengths as well as angles recently observed in dicoordinate chloronium ions like Me$_2$Cl$^+$, Et$_2$Cl$^+$ and (Me$_3$Si)$_2$Cl$^+$ (central angles 102°, 106° and 119°, respectively).[17] The structural features in **3 a** are thus consistent with predominant covalent B6–Cl6 and Cl6–C1 interactions

Table 2: Selected bond lengths [Å] and angles [°] for the X-ray structure of **3 a** and the calculated (B98/TZVP) structure *syn*-**3 a**.

Parameter	Expt	Calcd	Parameter	Expt	Calcd
B6–Cl6	1.854(2)	1.884	C6–C1	1.375(2)	1.388
Cl6–C1	1.799(2)	1.798	B6-Cl6-C1	109.65(7)	112.18
C1–C2	1.372(2)	1.388	Cl6-C1-C2	117.3(1)	117.28
C2–C3	1.386(2)	1.398	Cl6-C1-C6	116.8(1)	117.28
C3–C4	1.387(3)	1.398	C2-C1-C6	125.9(2)	125.25
C4–C5	1.382(2)	1.398	$\Sigma\sphericalangle$ (C1)	360.0(1)	359.82
C5–C6	1.390(2)	1.398			

and pronounced chloronium ion character. The phenyl ring shows a slightly opened C2-C1-C6 angle, 125.9(2)°, but no significant distortions from planarity.

Calculations on **3 a** and **3 b** at the (B98/TZVP) level of theory are in agreement with the experimental findings and indicate a small energy difference between the two regioisomers. The two lowest-energy conformers of **3 a** are of C_s symmetry, differing in the orientation of the phenyl moiety with respect to the carborane CH apex (*syn*-**3 a**, *anti*-**3 a**).[18] The *syn* conformer, corresponding to the structure found in the crystal, is only $\Delta E_{ZPE} = 2.45$ kJ mol^{-1} ($\Delta H = 0.11$ kJ mol^{-1}) higher in energy than *anti*-**3 a**. On the basis of this small difference, it seems likely that packing forces determine the geometry that is adopted in the crystal. There is a good agreement between the observed and calculated structure, in particular with regard to the distances and angles around Cl6 (Table 2). For **3 b**, two low-energy conformers of C_s symmetry were found that differ in the conformation of the phenyl ring with respect to the lower-belt chlorine atoms (staggered-**3 b**, eclipsed-**3 b**). The staggered geometry is slightly higher in energy ($\Delta E_{ZPE} = 3.06$ kJ mol^{-1}, $\Delta H = 0.60$ kJ mol^{-1}) than the eclipsed conformer, but again the difference is small. The regio-isomers **3 a** and **3 b** are close in energy, with *anti*-**3 a** being $\Delta E_{ZPE} = 8.44$ kJ mol^{-1} ($\Delta H = 8.45$ kJ mol^{-1}) less stable than eclipsed-**3 b**.

Reactivity studies showed that the Ph-CHB$_{11}$Cl$_{11}$ isomers are inert in solution, but can act as phenylating agents towards nucleophiles. NMR spectra of CD$_2$Cl$_2$ and CDCl$_3$ solutions with varying ratios of **3 a** and **3 b** remained unchanged over more than two weeks, thus indicating neither isomerization nor dissociation into ions at room temperature. These findings are consistent with an electrophilicity which is lower than that of alkyl carboranes and comparable to that of the diphenylchloronium ion.[19, 20] In the presence of stronger nucleophiles such as pyridine, Et$_3$N or PPh$_3$, mass and NMR spectra indicated the formation of [Nu-Ph]$^+$ and free CHB$_{11}$Cl$_{11}$$^-$ within 1 h at 50°C in a toluene solution. Thus **3 a,b** have the potential to serve as a pacified Ph$^+$ source.[21]

An extreme fluorophilicity was found for silylium carborane [**2**][CHB$_{11}$Cl$_{11}$].[22] Fluoride transfer from fluorobenzene to silicon takes place within hours at room temperature to give silanes **4** and **5** (Scheme 2). Several unidentified minor by-products were observed as well, probably because equimolar amounts of highly reactive, Brønsted-acidic Wheland intermediates are formed. Addition of the sterically hindered base P(o-tol)$_3$ as a proton sponge leads to much cleaner reactions that afford **4** and **5** in 27% and 30% yield based on ^{1}H NMR integrals. Pure samples of these compounds were obtained by preparative HPLC and fully characterized (see
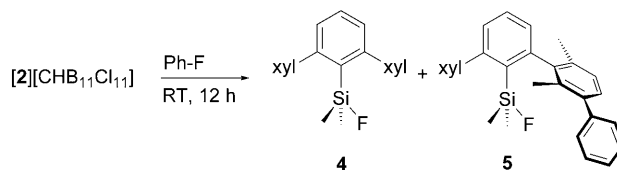
Scheme 2. C–F activation of fluorobenzene by **2**$^+$ to give fluorosilanes **4** and **5**.

the Supporting Information). As opposed to the fluorobenzene activation by [**1**][CHB$_{11}$Cl$_{11}$], only the xylyl rings or solvent molecules are phenylated in the case of [**2**][CHB$_{11}$Cl$_{11}$]; the carborane anion remains unchanged and the phosphine base is isolated only as [HP(*o*-tol)$_3$]$^+$, not [PhP(*o*-tol)$_3$]$^+$.

The reactions of **1**$^+$ and **2**$^+$ are carried out in an environment of exceptional low nucleophilicity, where one could imagine that they exhibit higher S$_N$1 character than previously studied systems. To address this important question regarding the dissociative S$_N$1-like nature of silylium-mediated C$_{aryl}$–F activations, the decay of **2**$^+$ in different fluoroarene solvents was monitored by ^{1}H NMR spectroscopy at 300 K. In fluorobenzene, the disappearance of the cation followed pseudo first-order kinetics with a half-life of $t_{1/2} = 88$ min that is independent of the amount of phosphine added (0–12 equivalents) and the carborane counterion (CHB$_{11}$Cl$_{11}$$^-$, CHB$_{11}H_5Br_6$$^-$). In 4-fluorotoluene, [**2**][CHB$_{11}$Cl$_{11}$] decayed with $t_{1/2} = 52$ min. In 1,4-difluorobenzene, no reaction took place; the concentration of the cation remained constant over 10 hours. The reactivity order 4-MeC$_6$H$_4$F > C$_6$H$_5$F > 4-FC$_6$H$_4$F suggests that fluoride abstraction proceeds via a transition state that is lowered by electron-donating substituents; that is, in which the initial fluoroarene possesses at least some aryl cationic character.[23]

In the calculated transition state for **2**$^+$ + PhF→**5**, fluoride transfer to silicon is accompanied by nucleophilic attack on C$_{ipso}$ by the xylyl π system (Figure 2). While the C$_6$H$_5$ moiety shows angle distortions typical of aryl cationic species[7] (C$_{ortho}$-C$_{ipso}$-C$_{ortho}$ 139°), it can not be regarded as a free
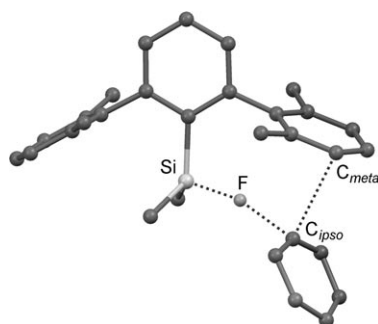

Figure 2. Calculated transition state for **2**$^+$ + PhF→**5** (B98/DZ-(2df,pd)). Si–F 1.680 Å, F–C$_{ipso}$ 2.189 Å, C$_{ipso}$–C$_{meta}$ 2.849 Å. H atoms omitted for clarity.

phenyl cation. Computational analysis of this reaction process at the MP2/DZ(2df,pd)//B98/DZ(2df,pd) level of theory predicts $\Delta H^{\ddagger}_{calc} = 85.77$ kJ mol^{-1} (100.17 kJ mol^{-1}, B98/DZ-(2df,pd)), which matches well with the experimental values, $\Delta H^{\ddagger} = 82$ kJ mol^{-1} and $\Delta S^{\ddagger} = -24$ J mol^{-1} K^{-1}, determined with an Eyring plot. These numbers reflect the strong C$_{aryl}$–F bond that has to be broken and are in line with a reaction in which two or more molecules combine to form a transition state.

The activation of fluoroarenes by [**1**][CHB$_{11}$Cl$_{11}$] and [**2**][CHB$_{11}$Cl$_{11}$] demonstrates the extreme fluorophilicity of silyl Lewis acids and paves the way for the development of a

phenylation prcedure using Ph-CHB$_{11}$Cl$_{11}$ and a novel Friedel–Crafts arylation method. With improvements in the preparation of CHB$_{11}$Cl$_{11}$$^-$,[24] silylium carboranes can be expected to become more common reagents in synthetic chemistry than they are at present.[25]

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