Reaction of Cp*Ir(CO)$_2$ with Activated Perfluoroaromatic Compounds: Formation of Metallocarboxylic Acids via Aromatic Nucleophilic Substitution

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The reaction of Cp*Ir(CO)$_2$ with activated perfluoroaromatic compounds such as pentafluoropyridine and -benzonitrile afforded the metallocarboxylic acids Cp*Ir(COOH)(L)(CO), L = C_5F_4N or C_6F_4CN, respectively. The reaction probably proceeds via aromatic nucleophilic substitution followed by nucleophilic attack by water at one of the carbonyl ligands.

Introduction

Activation of the strong C−F bond remains a very important goal, and several examples of cleavage of C−F bonds in fluoroaromatics and fluoropyridines by the platinum group metals are known.[1] For group 9 transition metal complexes, activation of C−F bonds in fluoroaromatics often involves photolytic or thermal conditions.[2] Thus the photolysis of Cp*Rh(PMe$_3$)(C$_2$H$_4$) in hexafluorobenzene affords Cp*Rh(PMe$_3$)(η^2-C$_6$F$_6$), which upon further irradiation results in C−F activation to form Cp*Rh(PMe$_3$)(C$_6$F$_5$)(F).[2a] Ru, Rh, and Ir dihydride complexes are also known to activate C−F bonds in fluoroaromatics.[1,3] For Cp*Rh(PMe$_3$)(H)$_2$, a mechanism that involves initial deprotonation and nucleophilic attack by the resultant anion [Cp*Rh(PMe$_3$)(H)]$^-$ on the fluoroaromatic compounds was proposed.

For the nickel triad, activation of C_5F_5N, for example, occurs predominantly at the 2-position for Ni and at the 4-position for Pt and Pd. The difference in regiochemistry has been accounted for with differing mechanisms.[4] For nickel complexes, the observed preference for C−F activation at the 2-position suggests that the reaction takes place via a three-center transition state in a concerted oxidative addition reaction. Reaction via a tight ion pair, or a Meisenheimer intermediate, would result in activation at the 4-position as observed for platinum[5] and palladium[4b] complexes, and in nucleophilic substitution by various transition metal anions.[6]

Cp*Ir(CO)$_2$, **1a**, and its related derivatives are known to undergo photochemical C−H activation with alkanes.[7] In an attempt to study its C−F activation potential, we have examined the reaction of **1a** with neat pentafluorobenzonitrile (C_6F_5CN). The reaction proceeded at room temperature to precipitate Cp*Ir(COOH)(*p*-C$_6$F$_4$CN)(CO), **2a**, as a white solid. In this paper, we present our study on the reaction of **1a** with C_6F_5CN and other fluoroaromatic compounds.

Results and Discussion

Reaction of 1a with Fluoroaromatic Compounds. The reaction of **1a** with C_6F_5CN proceeded at room temperature, leading to the slow precipitation of **2a** as a white powder. The ^{19}F NMR spectrum of the solid crude showed that C−F bond cleavage of C_6F_5CN occurred exclusively at the *para* position. The reaction is accelerated in the presence of a small amount of water, to afford **2a** in essentially quantitative yield (Scheme 1).

Compound **2a** has been completely characterized, including by a single-crystal X-ray crystallographic study; the ORTEP plot showing the molecular structure of **2a**, together with selected bond parameters, is given in Figure 1.

The most important structural feature of **2a** is probably the M-COOH moiety. The earliest reported example appears to be also an iridium species,[8] although there have since been a

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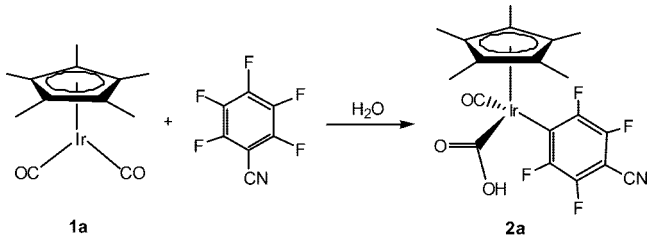
Scheme 1



1a **2a**

number of related examples; these were generally obtained via attack of a base, such as OH^-, on a carbonyl ligand.[9] Although there is no evidence of H-bonding in the solid-state structure of **2a**, the solid-state infrared spectrum, however, shows two broad ν_{OH} bands at 3447 and 2700 cm^{-1}, which suggest that both the monomeric and dimeric forms exist in the solid. The latter band is typical of organic carboxylic acids, which exist as H-bonded dimers in the solid state. The ^1H NMR spectrum of **2a** displayed one signal at δ 1.95 for the methyl protons of the Cp* ligand and a broad peak at δ 8.45 for the carboxylic group; the latter was confirmed by its disappearance when D_2O was added to the NMR sample. This signal is typical of a metallocarboxylic acid (7–11 ppm) and is upfield of that for organic carboxylic acids (10–13 ppm),[9e] suggesting that the iridium center is still relatively electron-rich despite the presence of an electron-withdrawing perfluorinated ligand.

A similar reaction occurred with some other fluoroaromatic compounds such as pentafluoropyridine (C_5F_5N), pentafluorobenzaldehyde (C_6F_5CHO), and 1-fluoro-4-nitrobenzene (p-$FC_6H_4NO_2$), to afford the corresponding metallocarboxylic acids Cp*Ir(COOH)(L)(CO) (where L = p-C_5F_4N (**2b**), p-C_6F_4CHO (**2c**), or p-$C_5H_4NO_2$ (**2d**)), although only for **2b** was the product isolated in analytically pure form. The spectroscopic data for **2b** confirm that substitution also occurred exclusively at the *para* position. Compound **2d** was obtained in low yield (7%), but the site of substitution of the arene at the *para* position was suggested on the basis of the absence of resonances in the ^{19}F NMR spectrum. The reaction with 1,3-$C_6F_4(CN)_2$ afforded the hydride species Cp*Ir(H){2,4-$C_6F_4(CN)_2$}(CO), **4**, instead, presumably via decarboxylation of the initially formed metallocarboxylic acid Cp*Ir(COOH){2,4-$C_6F_3(CN)_2$}(CO). Attempts at the reaction of **1a** with a number of other fluoroaromatics carrying a substituent less electron-withdrawing than CN, viz., C_6F_5X (where X = OMe, NH_2, H, Cl, F, COOMe, CH_2CN, CF_3, in order of increasing electron-withdrawing ability) under similar conditions failed.

The reaction of **1a** with C_6F_5CN in alcoholic solvents, namely, methanol or 2-propanol, produced the corresponding esters, Cp*Ir(COOR)(p-C_6F_4CN)(CO) (R = Me (**3a**); ^{i}Pr, (**3b**)). These esters can also be formed by stirring a solution of **2a** in the respective alcohol. The carbonyl vibration of the ester group appears at 1661 and 1652 cm^{-1} for **3a** and **3b**, respectively, which is shifted to higher frequencies than that for the carboxylic acid group in **2a** (1630 cm^{-1}), consistent with the expected increase in carbonyl stretching frequency on going from a carboxylic acid to an ester. The reaction of **1a** with C_5F_5N in methanol similarly produced Cp*Ir(COOMe)(p-C_5F_4N)(CO), **3c**. All three complexes **3a**–**c** were isolated as white powders that were moderately air-stable in their solid state, but air-sensitive in solution. Compound **3a** has been completely characterized, including by single-crystal X-ray crystallographic study; the ORTEP plot showing the molecular structure of **3a**, together with selected bond parameters, are given in Figure 2. The bond parameters for **3a** are very similar to those in **2a**.

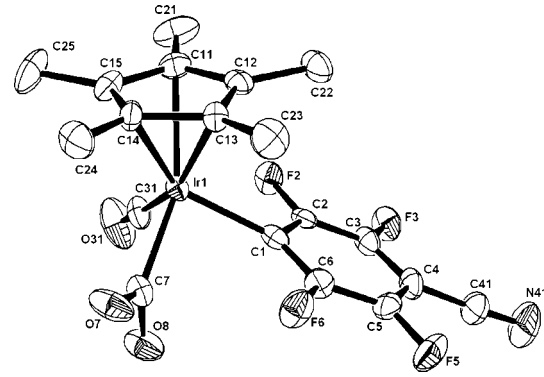


Figure 1. Molecular structure of **2a**. ORTEP plot with thermal ellipsoids drawn at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond distances [Å] and angles [deg]: Ir(1)–C(1), 2.090(8); Ir(1)–C(7), 2.040(6); Ir(1)–C(31), 1.906(10); C(7)–O(7), 1.227(9); C(7)–O(8), 1.330(10); C(7)–Ir(1)–C(1), 88.9(3); C(31)–Ir(1)–C(1), 89.8(4) C(31)–Ir(1)–C(7), 86.9(3); O(7)–C(7)–O(8), 118.8(6); O(7)–C(7)–Ir(1), 122.9(5); O(8)–C(7)–Ir(1), 118.3(5).

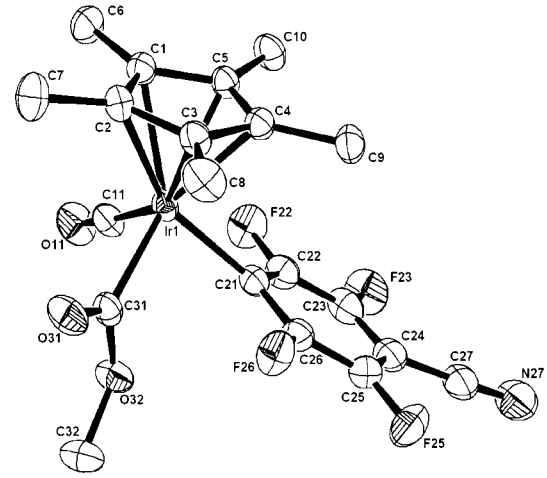


Figure 2. Molecular structure of **3a**. ORTEP plot with thermal ellipsoids drawn at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond distances [Å] and angles [deg]: Ir(1)–C(11), 1.873(3); Ir(1)–C(21), 2.068(3); Ir(1)–C(31), 2.047(3); O(31)–C(31), 1.200(4); O(32)–C(31), 1.369(4); O(32)–C(32), 1.441(4); C(11)–Ir(1)–C(21), 93.41(13); C(11)–Ir(1)–C(31), 89.09(12); C(31)–Ir(1)–C(21), 88.84(11) O(31)–C(31)–Ir(1), 126.3(2); O(32)–C(31)–Ir(1), 113.84(19); O(31)–C(31)–O(32), 119.9(3); C(31)–O(32)–C(32), 117.2(2).

Mechanistic Studies. As mentioned above, there are two principal reaction pathways leading from **1a** to **2a** that can be considered: (a) oxidative addition into a C–F bond or (b) nucleophilic aromatic substitution. These alternative pathways are depicted for C_6F_5CN in Scheme 2. There are a number of alternatives to the first intermediate **A** for the oxidative addition pathway, including prior CO dissociation followed either by

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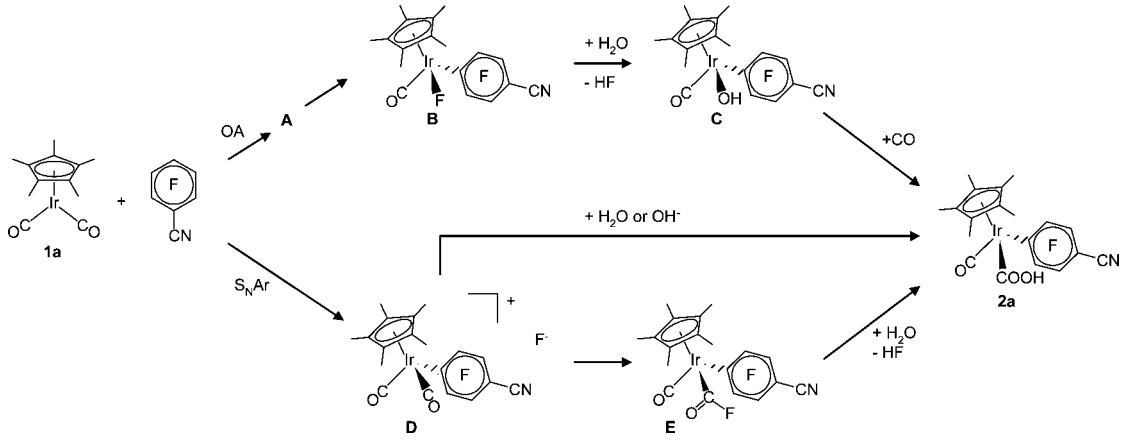
Scheme 2



direct insertion into a C−F bond or via formation of an Ir-(η^2-C_6F_6) intermediate (either with prior CO loss or via a 20-electron species such as Cp*Ir(CO)$_2$(η^2-C_6F_6), or a ring slippage complex (η^3-Cp*)Ir(CO)$_2$(η^2-C_6F_6)). The resultant intermediate **B**, which contains an Ir−F bond, may then undergo hydrolysis to form an Ir−OH bond followed by CO insertion; the last step has been reported for Ni, Pt, and Pd complexes,[9e,10] Although complexes such as LRh(PMe$_3$)(C_6F_5)(F) (where L = Cp or Cp*) may be obtained photochemically from the reaction of LRh(PMe$_3$)(C_2H_4) with C_6F_6,[2a] CO dissociation is not likely to be so facile at room temperature in the absence of photoactivation. UV irradiation should promote CO dissociation and hence increase the rate of reaction. However, UV irradiation of a solution of **1a** in C_6F_5CN did not give **2a** but a mixture of other products, suggesting that the oxidative addition pathway is unlikely.

Highly fluorinated aromatic compounds are susceptible to nucleophilic substitution because fluoride is a good leaving group, and the presence of electron-withdrawing substituent(s) favors the reaction by stabilizing the negative charge in the intermediate;[11] nucleophilic attack occurs predominantly at the position *para* to the functional group present.[12] That the reaction between **1a** and C_6F_5CN or C_5F_5N is highly regioselective is therefore consistent with a nucleophilic substitution pathway. Nucleophilic aromatic substitutions by organic and organometallic nucleophiles are known,[6] although the organometallic nucleophiles employed to date are metal anions. The order of nucleophilicity has previously been established on the basis of empirical observations: $[Re(CO_5)]^- \sim [CpFe(CO)_2]^- > [CpRu(CO)_2]^- [Mn(CO)_4(PPh_3)]^- > [Mn(CO_5)]^- > [CpMo(CO)_3]^- > [Fe(CO_4)]^{2-} > [Co(CO_4)]^-$.[6c] Strong nucleophiles react with hexafluorobenzene to afford stable complexes, while weaker nucleophiles are unreactive. Thus $[Mn(CO_5)]^-$ has been reported to react with C_6F_5CN and C_5F_5N, but $[Co(CO_4)]^-$ failed to react.[6f] Although neutral transition metal carbonyls have been known to act as nucleophiles in oxidative addition reactions with simple alkyl halides,[13] to our knowledge this is the first report on nucleophilic substitution in fluoroarenes by a neutral transition metal carbonyl.

The effects of different substituents and the position of substitution were also tested with a number of other ligands, including 2,3,5,6-tetrafluoropyridine, 2,4,5,6-tetrafluoropyridine, 2,3,5,6-tetrafluoro-4-pyridinecarbonitrile, and 4-fluorobenzonitrile, which showed no reaction. The observations may be summarized as follows: (i) Reaction only proceeded when there was one or more highly electron-withdrawing substituent(s). For fluoroarenes containing a substituent less electron-donating than CN, no reaction occurred at room temperature, while those carrying a substituent more electron-donating than CN gave rapid reaction. (ii) The reaction was highly regioselective. When the *para* position was not available, substitution at other positions did not occur even when there were highly electron-withdrawing substituents. (iii) Reaction occurred only for highly activated compounds. (iv) The reaction rate was enhanced if there was a second electron-withdrawing substituent that was not *para* to the first substituent. Such high regioselectivity and substituent dependence is again uncharacteristic of oxidative addition. For example, the reaction of CpRh(PMe$_3$)(C_2H_4) with pentafluoroanisole (*p*-C_6F_5OMe) was found to be nonregioselective and occurred under photoirradiation to give two isomeric η^2-arenes.[14]

Although C_6F_5CN and C_5F_5N are different ring systems and hence the electron-withdrawing ability of the substituents cannot be compared directly, the reaction of **1a** with a 1:1 molar ratio of C_6F_5CN and C_5F_5N at room temperature gave, after 16 h, a ^{19}F NMR spectrum that shows that **2a** and **2b** were formed in a 1.4:1 molar ratio, indicating that C_6F_5CN was more susceptible to nucleophilic attack compared to C_5F_5N. As mentioned earlier, a large number of other fluoroaromatic compounds failed to react with **1a**, while others with more electron-withdrawing groups than CN afforded mixtures, presumably from further substitution. Although it may appear surprising that **1a** did not react with octafluorotoluene ($C_6F_5CF_3$), this is, however, consistent with an earlier report that the rate of nucleophilic substitution on $C_6F_5CF_3$ by ammonia at 80 °C is 42 times slower than that on C_5F_5N.[6b]

There are suggestions from the literature that **1a** may be very nucleophilic. For instance, CpIr(CO)$_2$ is known to act as a two-electron donor in several iridium-osmium complexes;[15] thus the more electron-donating Cp* should therefore make the iridium

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center more electron-rich and hence nucleophilic. A nucleophilic iridium center was also proposed recently for the formation of an Ir(III) metallocarboxylic acid starting from Tp′Ir(CO)$_2$ [Tp′ = hydrotris(pyrazolyl)borate or hydrotris(3,5-dimethylpyrazolyl)borate], one proposed mechanism involving initial protonation of the iridium center by water. The reaction showed a kinetic isotope effect of $k_{H_2O}/k_{D_2O} = 1.4$ at 20 °C, indicating that an O−H or O−D bond cleavage was involved in the rate-determining step.[16] We have also attempted to test the nucleophilicity of **1a** by its reaction with $BF_3 \cdot OEt_2$. Thus we have found that immediate precipitation of a white solid occurred when an ether solution of $BF_3 \cdot OEt_2$ was added to a solution of **1a** in hexane. The white solid was soluble in dcm initially but decomposed to a yellow insoluble solid upon standing. This white solid showed two CO stretching vibrations, which were blue-shifted by ca. 100 cm^{-1} from that for **1a** (ν_{CO} 2118 (s), 2078 (s) cm^{-1} cf. ν_{CO} 2009, 1937 cm^{-1} for **1a**), consistent with formation of an adduct. The ^{1}H NMR spectrum also showed a downfield shift in the Cp* resonance from δ 2.18 to δ 2.26, and the ^{11}B NMR spectrum showed a resonance upfield of that of $BF_3 \cdot OEt_2$ by 1.18 ppm, consistent with adduct Cp*Ir(CO)$_2$→BF_3, **5**, formed being a slightly stronger coordination complex than $BF_3 \cdot OEt_2$. The MS (FAB$^+$) showed a low-intensity cluster of peaks around *m*/*z* 451, which corresponded to the formulation Cp*Ir(CO)$_2$(BF$_3$). In contrast, the rhodium analogue of **1a**, viz., Cp*Rh(CO)$_2$, **1b**, failed to react with C_6F_5CN. This is consistent with the fact that rhodium, being above iridium in the same group, should be less electron-rich and hence less nucleophilic.

Nucleophilic aromatic substitution by **1a** would lead to a cationic intermediate **D**, similar to the reaction of CpIr(CO)(PPh$_3$) with alkyl halides (RX) to form the stable ionic species [CpIr(CO)(PPh$_3$)(R)]$^+$[X]$^-$ via a bimolecular mechanism.[13a] We found that the reaction of **1a** with C_6F_5CN at room temperature, in the presence of molecular sieves to remove water, gave an off-white precipitate. The IR spectrum of the crude mixture (taken in C_6F_5CN) showed only weak IR bands for **2a**, presumably resulting from trace amounts of moisture. The residue obtained after removal of solvent and other volatiles was not soluble in C_6D_6 or $CDCl_3$, but dissolved in methanol to give **3a**, suggesting that it was ionic and may possibly be the ionic intermediate [Cp*Ir(CO)$_2$(*p*-C_6F_4CN)]$^+$[F]$^-$, **D**. Unfortunately, attempts to stabilize this putative intermediate by salt exchange with $AgBF_4$ were unsuccessful, although the reaction of **2a** with HBF_4 yielded a compound that analyzed as [Cp*Ir(CO)$_2$(C_6F_4CN)]$^+$[BF_4]$^-$, **6**. We also attempted to stabilize the intermediate by reducing the electrophilicity of the remaining CO ligand toward nucleophilic attack by water or hydroxide ion via phosphine substitution.[16] Thus the reaction of the phosphine-substituted complex Cp*Ir(CO)(PPh$_3$), **7**, with C_6F_5CN afforded a brown oil, which still contained a CO (by IR spectrum) and a phosphine ligand (from the ^{1}H NMR spectrum). The FAB-MS spectrum showed a molecular ion peak corresponding to the formulation [Cp*Ir(CO)(PPh$_3$)(C_6F_4CN)]$^+$, and the ^{19}F NMR spectrum showed three resonances in a 2:2:1 relative integration ratio; the chemical shift for the fluoride ion is known to vary over a wide range.[17] The data are thus consistent with the formulation [Cp*Ir(CO)(PPh$_3$)(C_6F_4CN)]$^+$[F]$^-$, **8**, suggesting that species such as **D** can indeed be formed in the reaction leading to **2a**.

The cationic intermediate **D** may undergo attack by water or OH$^-$ on one of the carbonyl carbons to form the COOH moiety,[9] or a nucleophilic attack by fluoride ion may occur to form a fluoroacyl species such as Cp*Ir(L)(COF)(CO), **E**, which would then be expected to undergo hydrolysis of the COF moiety to COOH.[18] In contrast to a number of precedents for the formation of metallocarboxylic acid via nucleophilic attack of water or hydroxide ions on cationic metal–carbonyl complexes,[9,19] there is no precedent for a fluoroacyl intermediate. A similar pathway is proposed for the formation of the iridium alkoxycarbonyls **3a** and **3b**, and we believe that the transformation from **D** to **2** or **3** is the rate-determining step. The latter is supported by the observation that the rate of formation of the acid **2a** is faster than for the methyl ester **3a**, followed by the isopropyl ester **3b**: the reaction of **1a** with C_6F_5CN in the presence of water to form **2a** took 8 h to complete, while the same reaction in the presence of methanol or 2-propanol to form their corresponding esters **3a** and **3b** gave a 98% and 82% conversion, respectively, after 22 h of stirring at room temperature; complete conversion was obtained after approximately 2 days. Similarly, the reaction of **1a** with C_6F_5CN in a 1:1 molar ratio of MeOH to ^{i}PrOH under anhydrous condition gave a 7:1 ratio of **3a** to **3b** (from ^{19}F NMR integration). Thus the rate followed the acidicity of the nucleophile;[20] if the rate-determining step (rds) involved nucleophilic attack by F$^-$, the reaction time required for all the alcohols would have been similar.

We attempted to obtain more information on this step by making a rough measure of the kinetic isotope effect (k_{H_2O}/k_{D_2O}); if the rds was a general base-catalyzed attack by H_2O, the reaction in H_2O would have been expected to be faster than in D_2O. In contrast, an rds involving nucleophilic attack by OH$^-$ would give a k_{H_2O}/k_{D_2O} generally close to unity or even the inverse because OD$^-$ is a better nucleophile that OH$^-$.[21] If the rds involved nucleophilic attack by F$^-$, no kinetic isotope effect would be expected. We observed a kinetic isotope effect of ∼1.2 at room temperature. The observed value was thus relatively small compared to the generally observed value of 2 or above for general base catalysis,[21b,22] although there have been reports of a kinetic isotope effect much smaller than 2 for reactions that proceeded via general base catalysis. For example, a kinetic isotope effect of 1.38 was observed in the transesterification (ethanolysis) of 2′/3′-*O*-peptidyl adenosine where the molecule acted as a general base in its own external peptidyl transfer, and it was interpreted to suggest significant movement of a proton toward the base concurrent with the attack of the neutral ethanol molecule.[23] In our case, there may be strong hydrogen

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Scheme 3

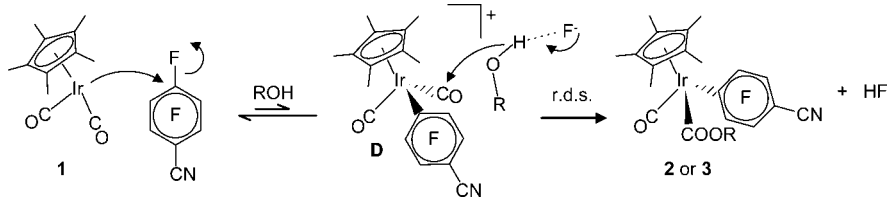

Table 1. Crystal and Refinement Data for 2a and 3a

	2a	3a
empirical formula	$C_{19}H_{16}F_4IrNO_3$	$C_{20}H_{18}F_4IrNO_3$
fw	574.53	588.55
temperature	213(2)	223(2)
cryst syst	monoclinic	triclinic
space group	*C*2/*m*	$P\bar{1}$
a, Å	13.3143(8)	8.2139(5)
b, Å	8.8432(6)	9.1750(6)
c, Å	16.7447(10)	14.0581(9)
α, deg	90	73.4480(10)
β, deg	108.601(3)	84.5460(10)
γ, deg	90	75.8680(10)
volume, Å^3	1868.5(2)	984.45(11)
Z	4	2
density calc, Mg m^{-3}	2.042	1.986
absorp coeff, mm^{-1}	7.204	6.839
F(000)	1096	564
cryst size, mm^3	0.17 × 0.10 × 0.06	0.42 × 0.32 × 0.24
θ range for data collection, deg	2.57 to 30.50	2.38 to 26.37
no. of reflns collected	8728	15 037
no. of indep reflns	2879 [*R*(int) = 0.0358]	4034 [*R*(int) = 0.0231]
max. and min. transmn	0.6718 and 0.3739	0.2906 and 0.1613
no. of data/restraints/params	2879/0/256	4034/0/268
goodness-of-fit on F^2	1.076	1.063
final *R* indices [$I > 2\sigma(I)$]	R1 = 0.0346, wR2 = 0.0719	R1 = 0.0171, wR2 = 0.0422
R indices (all data)	R1 = 0.0386, wR2 = 0.0737	R1 = 0.0177, wR2 = 0.0424
largest diff peak and hole (e Å^{-3})	1.800 and −1.355	1.001 and −0.439

bonding and significant H−F bond formation in the transition state, leading to the small kinetic isotope effect.

The effect of fluoride ions on the rate of reaction was also studied. Reaction of **1a** with C_6F_5CN in the presence of water and tetrabutylammonium fluoride (Bu_4NF) or tetramethylammonium fluoride (Me_4NF), which will be reported elsewhere, resulted in the formation of the decarboxylated product Cp*Ir(H)(*p*-C_6F_4CN)(CO). However, the reaction of **1a** with C_6F_5CN in methanol to give **3a** proceeded to completion in 8 h in the presence of 5 equiv of $[Me_4N]F$, but failed to complete even after 22 h in the absence of $[Me_4N]F$. This result suggested that the formation of **D** from **1a** and C_6F_5CN was reversible, with the equilibrium lying to the left; the addition of F^- promoted the second step (nucleophilic attack on carbonyl carbon) by partial abstraction of proton from H_2O or ROH (Scheme 3).

Conclusion

We have reported here that the reaction of **1a** with C_6F_5CN proceeded with high regioselectivity in the presence of water or alcohols to produce the metallocarboxylic acid or esters Cp*Ir(COOR)(*p*-C_6F_4CN)(CO), **2** or **3**, where the substituent in the arene ring was in the *para* position. Similar reactions with perfluoroarenes carrying one or more highly electron-withdrawing groups and with pentafluoropyridine also yielded *para*-substituted products. Experimental evidence suggested that the formation of **2** or **3** occurred via aromatic nucleophilic substitution by **1a** on the fluoroarene followed by nucleophilic attack by water or alcohol, probably via a general base-catalyzed route, on one of the carbonyl ligands to form the carboxylic group.

Experimental Section

General Procedures. All manipulations of air-sensitive materials were carried out with rigorous exclusion of oxygen and moisture in Schlenk-type glassware or Carius tubes on a dual-manifold Schlenk line under an atmosphere of argon. Solvents were purified, dried, distilled, and stored under argon prior to use. NMR spectra were measured on a Bruker 300 MHz FT NMR spectrometer. ^{1}H chemical shifts were referenced to residual $CHCl_3$ proton signal (δ 7.26) in $CDCl_3$. ^{19}F chemical shifts were referenced to external CF_3COOH (δ 0.00). Elemental analyses were carried out by the elemental analysis laboratory in the department. Solvents were purified, dried over the appropriate drying agents, distilled, and stored under argon in flasks fitted with Teflon valves prior to use. Pentafluorobenzonitrile and pentafluoropyridine (Aldrich) were stored as degassed solutions in Carius tubes and used without further purification. All other reagents were also purchased commercially and used as supplied. Compounds **1a** and **7** were synthesized by the literature methods;[24,25] the former was purified by column chromatography (neutral alumina, 50–200 μm, hexane as eluant).

Reaction of 1 with Fluoroarenes and Fluoropyridines in the Presence of Water. In a typical reaction, to a Carius tube containing **1a** (10 mg, 26 μmol) was added the fluoroarene or fluoropyridine (0.5 mL) and deionized H_2O (0.1 mol). The reaction mixture was degassed by three cycles of freeze–pump–thaw and stirred at room temperature. Details on the amount of substrates used are given in Table S1.

With Pentafluorobenzonitrile, C_6F_5CN. Cp*Ir(CO)(COOH)(*p*-C_6F_4CN), **2a**, precipitated out of solution as a white solid. The

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mixture was filtered via a cannula, and the solvent was removed from the supernatant under reduced pressure. Additional product was recovered from the supernatant by addition of a hexane−dichloromethane solution followed by slow evaporation. Combined yield: 76.6 mg (99%). X-ray diffraction quality crystals of **2a** were obtained by slow evaporation from a C_6F_5CN solution. IR (KBr): ν_{OH} 3447 (br), 2700 (br, w), ν_{CN} 2237 (w), ν_{CO} 2036 (s), 1624 (m) cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.45 (brs, 1H, IrCOO*H*), 1.96 (s, 15H, Cp*C*H*$_3$). ^{19}F NMR ($CDCl_3$): δ −34.27 (m, 2F, F_{meta}), −59.17 (m, 2F, F_{ortho}). MS FAB$^+$ (*m*/*z*): 576 $[M + H]^+$, 558 $[M - OH]^+$, 530 $[M - OH - CO]^+$, 502 $[M - OH - 2CO]^+$. Anal. Calcd for $C_{19}H_{16}F_4NO_3Ir$: C, 39.72; H, 2.81; F, 13.23; N, 2.44. Found: C, 39.84; H, 2.60; F, 13.20; N, 2.68. HR-MS FAB$^+$ (*m*/*z*): calcd for $C_{19}H_{17}F_4NO_3Ir$ $[M + H]^+$ 576.0774, found 576.0757.

With Pentafluoropyridine, C_5F_4N. Cp*Ir(COOH)(*p*-C_5F_4N)(CO), **2b**, precipitated out of solution as a white solid. The mixture was filtered through a cannula, the solvent removed under reduced pressure, and the residue washed with hexane (3 × 1 mL) to remove unreacted **1a** (7.9 mg, 35%). Combined yield of **2b**: 19.4 mg (59%). IR (KBr): ν_{OH} 3448 (br), 2705 (br, w), ν_{CO} 2040 (s), 1628 (m) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.98 (s, 15H, Cp*C*H*$_3$). ^{19}F NMR ($CDCl_3$): δ −20.60 (m, 2F, F_{meta}), −42.88 (m, 2F, F_{ortho}). MS FAB$^+$ (*m*/*z*): 552 $[M + H]^+$, 534 $[M - OH]^+$, 506 $[M - OH - CO]^+$, 478 $[M - OH - 2CO]^+$. Anal. Calcd for $C_{17}H_{16}F_4NO_3Ir$: C, 37.09; H, 2.93; F, 13.80; N, 2.54. Found: C, 37.20; H, 2.83; F, 13.62; N, 2.82. HR-MS FAB$^+$ (*m*/*z*): calcd for $C_{17}H_{17}F_4NO_3Ir$ $[M + H]^+$ 552.0774, found 552.0777.

With 2,3,4,5,6-Pentafluorobenzaldehyde, C_6F_5CHO. The reaction mixture turned from yellow to pale brown. Removal of volatiles under reduced pressure yielded a brown oil, which contained Cp*Ir(COOH)(C_6F_4CHO)(CO), **2c**, as the major product and a mixture of unknown compounds in minor quantities. IR (dcm): ν_{CO} 2046 (s), 1719 (m), 1700 (m), 1652 (s), 1627 (m) cm^{-1}. ^1H NMR ($CDCl_3$): 10.27 (s, 1H, C*H*O), 1.98 (s, 15H, Cp*C*H*$_3$). ^{19}F NMR ($CDCl_3$): δ −37.16 (m, 2F, F_{meta}), −71.13 (m, 2F, F_{ortho}). MS FAB$^+$ (*m*/*z*): 561 $[M - (OH)]^+$, 533 $[M - (COOH)]^+$, 505 $[M - (COOH) - (CO)]^+$. HR-MS FAB$^+$ (*m*/*z*): calcd for $C_{19}H_{16}O_3F_4{}^{193}Ir$ $[M - (OH)]^+$ 561.0683, found 561.066.

With 1-Fluoro-4-nitrobenzene, *p*-$FC_6H_4(NO_2)$. The reaction mixture turned slightly brown. Removal of volatiles under reduced pressure gave yellow solids. The integration ratio of the methyl resonance of the Cp* ligand in Cp*Ir(COOH)(*p*-$C_5H_4NO_2$)(CO), **2d**, to **1a** in the ^1H NMR spectrum was 1:14 (7% conversion). ^1H NMR ($CDCl_3$): 1.94 (s, 15H, Cp*C*H*$_3$) and other small peaks.

With Tetrafluoroisophthalonitrile 1,3-$C_6F_4(CN)_2$. To a Carius tube containing **1a** (10.0 mg, 26.1 μmol) and 1,3-$C_6F_4(CN)_2$ (7.0 mg, 35.0 μmol) was added C_6D_6 (1 mL) and deionized H_2O (0.1 mL). The reaction mixture was degassed by three cycles of freeze–pump–thaw, sonicated, and stirred for 40 h at room temperature. Half the solution was syringed into an NMR tube containing 1,3,5-triphenylbenzene (6.0 mg, 19.5 μmol) as internal standard. NMR yield of Cp*Ir(H){2,4-$C_6F_4(CN)_2$}(CO), **4**, was 92%. IR (dcm): ν_{CN} 2252, 2242(w), ν_{CO} 2052 (s) cm^{-1}. ^1H NMR (C_6D_6): 1.53 (s, 15H, Cp*C*H*$_3$), −14.39 (s, 1H, Ir-*H*). ^{19}F NMR (C_6D_6): δ −28.72 (d, $^3J_{FF}$ = 14.4, 1F, 3-F), −31.65 (dd, $^3J_{FF}$ = 15.5, $^2J_{FF}$ = 26.8, 1F, 5-F), −48.68 (d, $^3J_{FF}$ = 28.9, 1F, 6-F). MS FAB$^-$ (*m*/*z*): 537 $[M - H]$.

Competitive Reaction in C_6F_5CN/C_5F_5N. To a Carius tube containing **1a** (5.4 mg, 14.1 μmol) was added C_5F_5N (0.250 mL), C_6F_5CN (0.274 mL) (1:1 molar ratio), and deionized H_2O (0.2 mL). The reaction mixture was degassed by three cycles of freeze–pump–thaw and stirred at room temperature for 16 h. The volatiles were removed under reduced pressure, and the ^1H NMR spectrum of the residue was taken in $CDCl_3$. The integration ratio of the fluorine resonances of **2a**:**2b** in the ^{19}F NMR spectrum was 1.4:1.

Reaction of 1 with C_6F_5CN in Methanol. To a Carius tube containing **1a** (19.1 mg, 49.8 μmol) was added methanol (1.0 mL) and C_6F_5CN (0.5 mL). The resultant mixture was degassed by three cycles of freeze–pump–thaw and left to stand at room temperature for 2 days. The volatiles were removed under reduced pressure, and the residual solid was recrystallized from methanol to give white crystals of Cp*Ir($COOCH_3$)(*p*-C_6F_4CN)(CO), **3a**. Yield: 27.4 mg (93%). X-ray diffraction quality crystals of **3a** were grown from a concentrated methanol solution at 5 °C.

A similar procedure was followed for a reaction using **1a** (19.5 mg, 50.9 μmol) with 2-propanol (1.0 mL) and C_6F_5CN (0.5 mL) to afford white crystals of Cp*Ir(COO^iPr)(*p*-C_6F_4CN)(CO), **3b**. Yield: 20.5 mg (65%).

A similar reaction using **1a** (19.6 mg, 51.1 μmol) in methanol (1.0 mL) and C_5F_5N (0.5 mL) afforded unreacted **1a** (0.9 mg, 5%), which was recovered by washing the residue with hexane and a white crystalline solid of Cp*Ir($COOCH_3$)(*p*-C_5F_4N)(CO), **3c**, by recrystallization of the residue from methanol. Yield: 25.7 mg (89%).

3a: IR (KBr): ν_{CN} 2236 (w), ν_{CO} 2038 (s), 1650 (m) cm^{-1}. IR (dcm): ν_{CN} 2239 (w), ν_{CO} 2041, 1659 (s) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.44 (s, 3H, OC*H*$_3$), 1.95 (s, 15H, Cp*C*H*$_3$). ^1H NMR (CH_2Cl_2): δ 3.36 (s, 3H, OC*H*$_3$), 1.91 (s, 15H, Cp*C*H*$_3$). ^{19}F NMR ($CDCl_3$): δ −35.07 (m, 2F, F_{meta}), −59.35 (m, 2F, F_{ortho}). ^{19}F NMR (CH_2Cl_2): δ −36.32 (m, 2F, F_{meta}), −62.53 (m, 2F, F_{ortho}). Anal. Calcd for $C_{20}H_{19}F_4NO_3Ir$: C, 40.81; H, 3.08; N, 2.38. Found: C, 41.29; H, 3.22; N, 2.19. MS FAB$^+$ (*m*/*z*): 590 $[M + H]^+$, 558 $[M - (OCH_3)]^+$, 530 $[M - (OCH_3) - (CO)]^+$. HR-MS FAB$^+$ (*m*/*z*): calcd for $C_{20}H_{19}F_4NO_3Ir$ $[M + H]^+$ 590.0930, found 590.0926.

3b: IR (dcm): ν_{CN} 2238 (w), ν_{CO} 2040 (s), 1652 (m). ^1H NMR ($CDCl_3$): δ 5.02 {sep, $^3J_{HH}$ = 6.2, 1H, OC*H*$(CH_3)_2$} 1.95 (s, 15H, Cp*C*H*$_3$), 1.05, 0.95 (dd, 6H, OCH(CH_3)$_2$. ^{19}F NMR ($CDCl_3$): δ −34.58 (m, 2F, F_{meta}), −59.81 (m, 2F, F_{ortho}). Anal. Calcd for $C_{22}H_{22}F_4NO_3Ir \cdot ½IPA$: C, 43.65; H, 4.05; N, 2.17. Found: C, 43.81; H, 3.87; N, 2.30. MS FAB$^+$ (*m*/*z*): 618 $[M + H]^+$, 558 $[M - (OC_3H_7)]^+$, 530 $[M - (COOC_3H_7)]^+$, 502 $[M - (COOC_3H_7) - (CO)]^+$. HR-MS FAB$^+$ (*m*/*z*): calcd for $C_{22}H_{23}F_4NO_3Ir$ $[M + H]^+$ 618.1244, found 618.1255.

3c: IR (dcm): ν_{CN} 2236 (w), ν_{CO} 2042 (s), 1661(m) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.45 (s, 3H, OC*H*$_3$), 1.96 (s, 15H, Cp*C*H*$_3$). ^{19}F NMR ($CDCl_3$): δ −20.88 (m, 2F, F_{meta}), −43.64 (m, 2F, F_{ortho}). Anal. Calcd for $C_{18}H_{18}F_4NO_3Ir$: C, 38.29; H,3.21; 2.48. Found: C, 38.54; H, 3.33; N, 2.43. MS FAB$^+$ (*m*/*z*): 566 $[M + H]^+$, 534 $[M - (OCH_3)]^+$, 506 $[M - (OCH_3) - (CO)]^+$. HR-MS FAB$^+$ (*m*/*z*): calcd for $C_{18}H_{19}F_4NO_3Ir$ $[M + H]^+$ 566.0925, found 566.0936.

Formation of 3a from 2a. Complex **2a** (5.0 mg, 13.0 μmol) was dissolved in methanol and stirred at room temperature for 16 h. The ^1H NMR spectrum showed partial conversion to **3a** (82%). Continued stirring of the solution at room temperature for 3 days did not increase the amount of **3a**.

Reaction of 1a with $BF_3 \cdot OEt_2$. To a dcm solution (2 mL) of **1a** (10.0 mg, 26.1 μmol) was added $BF_3 \cdot OEt_2$ dropwise until the solution turned colorless. Attempts to crystallize out the product from dcm/cyclopentane or dcm/hexane solutions were unsuccessful. The solution slowly turned yellow upon standing. A similar reaction using a hexane solution (2 mL) of **1a** (10.0 mg, 26.1 μmol) resulted in the formation of a fine white precipitate. The solid was soluble in dcm and slowly turned into an insoluble yellow solid upon standing.

An NMR scale reaction was carried out as follows: Complex **1a** (7.0 mg, 18.3 μmol) was dissolved in $CDCl_3$ (0.4 mL) in an NMR tube fitted with a rubber septum. BF_3OEt_2 (0.1 mL, 8.1 μmol withdrawn from a 10 μg/mL BF_3OEt_2 solution in $CDCl_3$) was added immediately prior to NMR analysis. An IR spectrum taken after NMR analysis showed a mixture of unreacted **1a** and Cp*Ir$(CO)_2(BF_3)$, **5**. IR (dcm): ν_{CO} 2118 (s), 2078 (s) cm^{-1}. IR ($CDCl_3$): ν_{CO} 2106 (s), 2065 (s) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.26

(s, Cp*). ^{19}F NMR ($CDCl_3$): δ −77.12 (s. 4F, BF_4). ^{1}H NMR (dcm, no-d)*: δ 2.35 (s, Cp*). ^{11}B NMR ($CDCl_3$): δ −1.18. MS FAB$^+$ (*m*/*z*): 451 [M]$^+$. *A reference NMR tube containing the same volume of $CDCl_3$ was locked and shimmed in the usual manner and then replaced with the "no-d" sample (crude aliquot in CH_2Cl_2).[26] ^{1}H chemical shifts were referenced with the resonance of CH_2Cl_2 set to δ 5.30.

Reaction of 1b with C_6F_5CN. Compound **1b** (6.0 mg, 20.4 μmol) was dissolved in C_6F_5CN (0.5 mL) and stirred at room temperature for 16 h. The IR spectrum shows only peaks due to unreacted **1b**.

Reaction of 2a with HBF_4. To a Carius tube containing **2a** (10.0 mg, 17.4 μmol) in dcm (4 mL) was added HBF_4 (3 drops). The reaction mixture was stirred at room temperature for 16 h, and the volatiles were then removed under reduced pressure. The oily residue obtained was sparingly soluble in dcm and completely soluble in acetone and was identified to be [Cp*Ir(CO)$_2$(*p*-C_6F_4CN)]$^+$[BF_4]$^-$, **6**. IR (dcm): ν_{CN} 2246 (w), ν_{CO} 2124 (s), 2090 (s) cm^{-1}. ^{1}H NMR (d_6-acetone): δ 2.27 (s, 15H, Cp*CH_3). ^{19}F NMR (d_6-acetone): δ −33.92 (m, 2F, F_{meta}), −58.88 (m, 2F, F_{ortho}), −74.02 (s, 4F, BF_4). MS FAB$^+$ (*m*/*z*): 558 [M]$^+$, 530 [M − (CO)]$^+$, 502 [M − 2(CO)]$^+$. HR-MS FAB$^+$ (*m*/*z*): calcd for $C_{19}H_{15}O_2F_4N^{[193]}Ir$ [M]$^+$: 558.0663, found 558.0662.

Attempted Salt Exchange Reactions with $AgBF_4$. (i) To a Carius tube containing **1a** (20.0 mg, 52.2 μmol) was added anhydrous C_6F_5CN (1.0 mL). The solution was degassed by three cycles of freeze–pump–thaw and stirred at room temperature for 2 days. To half the solution, anhydrous $AgBF_4$ (10.0 mg, 51.3 μmol) was added under an argon atmosphere and the mixture was stirred for 3 h. Immediate precipitation of a tan solid was observed. Volatiles were removed under reduced pressure to afford a residue that was soluble in methanol but did not convert to **3a**. (ii) To a Carius tube containing **1a** (10.0 mg, 26.1 μmol) and anhydrous $AgBF_4$ (8.0 mg, 41.1 μmol) was added anhydrous C_6F_5CN (0.5 mL). The solution was degassed by three cycles of freeze–pump–thaw and stirred at room temperature for 16 h. A tan precipitate in an orange solution was obtained. The ^{1}H and ^{19}F NMR spectra showed complicated mixtures. The expected cationic dicarbonyl species [Cp*Ir(CO)$_2$(*p*-C_6F_4CN)]$^+$[BF_4]$^-$, **5**, was not detected (^{1}H NMR, ^{19}F NMR, and IR).

Reaction of 7 with C_6F_5CN. To a Carius tube containing **7** (5.0 mg, 8.09 μmol) was added C_6F_5CN (0.5 mL) and distilled H_2O (0.1 mL). The reaction mixture was degassed by three cycles of freeze–pump–thaw and stirred for 40 h. The volatiles were removed under reduced pressure to give **7** as a pale brown oil. IR (dcm): ν_{CN} 2248 (w), 2210 (w), ν_{CO} 2062 (s), 2019 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.8–7.3 (m, 15H, aromatic), 1.87 (s, 15H, Cp*CH_3). ^{19}F NMR ($CDCl_3$): δ − 31.7 (m, 2F), − 58.0 (m, 2F), −64.4 (s, 1F). MS FAB$^+$ (*m*/*z*): 792 [M]$^+$. HR-MS FAB$^+$ (*m*/*z*): calcd for $C_{36}H_{30}F_4NOP^{193}Ir$ 792.1625, found 792.1649.

Rate of Reaction in D_2O vs H_2O. (i) To a Carius tube containing **1a** (10.3 mg, 26.9 μmol) was added C_6F_5CN (0.5 mL) and D_2O (0.2 mL). The reaction mixture was degassed by three cycles of freeze–pump–thaw and stirred at room temperature for 2¾ h. The volatiles were removed under reduced pressure and the integration ratio of the Cp* resonance of **1a** against that of deuterated **2a** in the ^{1}H NMR spectrum was ∼1:1.5. (ii) To a Carius tube containing **1** (10.0 mg, 26.1 μmol) were added C_6F_5CN (0.5 mL) and deionized H_2O (0.2 mL). The reaction mixture was degassed by three cycles of freeze–pump–thaw and stirred at room temperature for 2¾ h. The volatiles were removed under reduced pressure, and a ^{1}H NMR spectrum of the residue taken in $CDCl_3$ showed that the integration ratio of the Cp* resonance of **1a**:**2a** was ∼1:1.8.

Rate of Formation of Methyl vs Isopropyl Ester. (i) To a Carius tube containing **1a** (10.0 mg, 26.1 μmol) were added C_6F_5CN (0.25 mL) and methanol (0.5 mL). The reaction mixture was degassed by three cycles of freeze–pump–thaw and stirred at room temperature. Aliquots (0.3 mL) for ^{1}H NMR analyses ($CDCl_3$ solutions) taken out after 8 and 22 h reaction time showed that the percentage conversion of **1a** to **3a** was 63% and 98%, respectively (from integration ratio of the Cp* resonance). (ii) A similar procedure with 2-propanol showed that the percentage conversion of **1a** to **3b** after 8 and 22 h was 57% and 82%, respectively.

Competitive Reaction in Methanol/2-Propanol. A mixture of methanol (0.500 mL), 2-propanol (0.945 mL), and C_6F_5CN (0.500 mL) was predried with molecular sieves and syringed into a Carius tube containing **1a** (10.0 mg, 26.1 μmol). The reaction mixture was degassed by three cycles of freeze–pump–thaw and stirred at room temperature for 22 h. ^{19}F NMR analysis of the residue ($CDCl_3$ solutions) showed that the ratio **3b**:**3a** was ∼1:7.

Reaction of 1a with C_6F_5CN in the Presence of 5 equiv of Me_4NF. To a Carius tube containing **1a** (10.0 mg, 26.1 μmol) and Me_4NF (25.0 mg, 269 μmol) was added anhydrous C_6F_5CN (0.25 mL) and methanol (0.5 mL). The mixture was degassed by three cycles of freeze–pump–thaw and stirred at room temperature for 8 h. The volatiles were removed under reduced pressure, and ^{1}H NMR analysis ($CDCl_3$ solution) of the residue showed complete conversion of **1a** to **3a**.

Crystal Structure Determinations. The crystals were mounted on quartz fibers. X-ray data were collected on a Bruker AXS APEX system, using Mo Kα radiation, with the SMART suite of programs.[27] Data were processed and corrected for Lorentz and polarization effects with SAINT,[28] and for absorption effects with the program SADABS.[29] Structural solution and refinement were carried out with the SHELXTL suite of programs.[30] The structures were solved by direct methods to locate the heavy atoms, followed by difference maps for the light, non-hydrogen atoms. Organic hydrogen atoms were placed in calculated positions. Crystal and refinement data are summarized in Table 1.

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Supporting Information Available: Crystallographic data in CIF format for **2a** and **3a**, and ^{19}F NMR spectra of **2a**, **2b**, and **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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