Activation of Carbon–Fluorine Bonds by Metal Complexes

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I. Introduction and Scope

An area of research that has recently attracted the attention of inorganic and organometallic chemists is the coordination and activation of fluorocarbons by transition-metal complexes.[1-3] Substantial progress was made in the 1970s and 1980s concerning the coordination and activation of halocarbons, and this vast body of work has been the subject of several reviews.[3-5] (In this review, the terms halo-, halogen, and halide refer to chlorine, bromine, and iodine.) The chemical and intellectual challenges of C–F bond activation rival those of C–H activation in hydrocarbons. Alkane coordination[6] and activation by transition-metal complexes has been achieved,[7-9] and as a result of heightened activity in recent years there are now comparable examples for fluorocarbons.

In general, fluorocarbons are reluctant to coordinate to metal centers and are resistant to chemical attack.[3,10] This is a consequence of the great strength of the C–F bond and the high electronegativity of fluorine. The chemical inertness and high thermal stability of fluorocarbons have increased public concerns over their impact on the upper atmosphere.[11] In fact, recent estimates place the atmospheric lifetime of perfluorocarbons at greater than 2000 years.[12] As such, the chemical modification and ultimate functionalization of these substrates provide a challenge for synthetic chemists. The organic chemistry of the C–F bond has been extensively studied.[13-16] Additionally, several books have reviewed the role of the C–F bond in bioorganic chemistry.[17-19] The use of transition-metal complexes offers another means with which to activate C–F bonds. Transition metals are employed as catalysts in several industrial processes involving the modification of hydrocarbons, such as olefin hydrogenations, hydroformylations, and polymerizations.[20] Analogous processes do not presently exist for fluorocarbons.

Interaction of a fluorocarbon with the metal center may ultimately lead to the cleavage of the robust carbon–fluorine bonds. C–F activation reactions that employ metal complexes, require comparatively mild conditions, are selective, and afford isolable products have recently been noted. Presumably, this is a thermodynamic consequence of the strong metal–carbon and metal–fluorine bonds formed in the products.[2,21] Unfortunately, examples of carbon–fluorine

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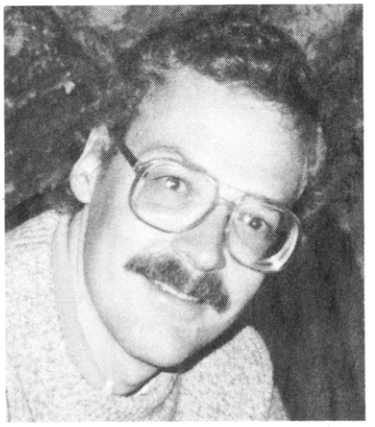
Jaqueline L. Kiplinger was born in Belleville, IL, in 1967. In 1990, she obtained her B.S. in chemistry, Summa Cum Laude, from the University of Colorado (Colorado Springs). She performed undergraduate research under the direction of Ronald R. Ruminski concerning the synthesis of polypyridyl bimetallic complexes of iron and ruthenium for use in photocatalyzed intramolecular energy-transfer processes. She is currently pursuing a Ph.D. at the University of Utah under the direction of Tom Richmond and is the recipient of a University of Utah Graduate Research Fellowship (1992–1994). Her present research interests concern synthetic and mechanistic studies of organometallic complexes directed toward carbon–fluorine bond formation, activation, and functionalization.



Tom Richmond was born in Buffalo, NY. He earned his Sc.B. in chemistry from Brown University where he did undergraduate research with John O. Edwards and Philip H. Rieger. He obtained his Ph.D. as an NSF Predoctoral Fellow at Northwestern University in 1983 under the direction of Fred Basolo and Duward F. Shriver. His thesis work dealt with the interactions of molecular Lewis acids with transition-metal carbonyl complexes as well as kinetic and mechanistic studies on vanadium hexacarbonyl. In the latter area, William C. Trogler played an important role. He spent 2 years as a Myron Bantrell Research Fellow at the California Institute of Technology working on high oxidation state transition-metal complexes with Terrence J. Collins. He joined the faculty at the University of Utah in 1985 and presently holds the rank of associate professor. His research interests are in the area of inorganic and organometallic synthesis with recent efforts directed toward developing the transition-metal chemistry of the carbon–fluorine bond. He is the recipient of a New Faculty Fellowship from the Camille and Henry Dreyfus Foundation, an NSF PYI Award, and an Alfred P. Sloan Research Fellowship (1991–1994). He also enjoys teaching chemistry and in 1993 received a campus-wide teaching award from the University of Utah student government.

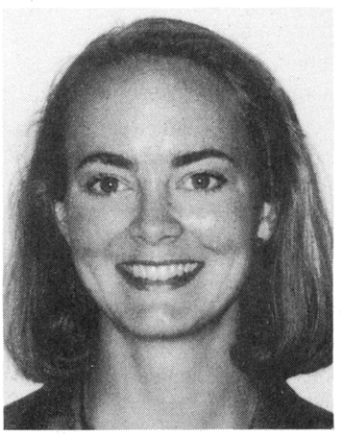
bond activation by metal complexes are rare and historically serendipitous.

Fluorinated alkenes and arenes are more reactive than are their saturated counterparts since π-frameworks are subject to nucleophillic attack and fluoride is a good leaving group.[1] Hence, it is not surprising that the bulk of the literature on carbon–fluorine bond activation by transition-metal complexes has dealt primarily with the activation of C–F bonds in unsaturated fluorocarbons. Only recently have reports of carbon–fluorine bond activation of saturated fluorocarbons using organometallic nucleophiles appeared.[22]

The focus of this review is the activation of carbon–fluorine bonds by metal centers. We will not specifically address the cleavage of carbon–fluorine bonds using main group metals, although the activation of C–F bonds by Lewis acids is important in the synthesis of difluorocarbenes[23] and in superacid systems.[24] We will briefly cover the properties of fluorocarbons pertinent to the topic of C–F activation. We will provide an update on the area of fluorocarbon coordination to transition metals by surveying the work reported since the review by Kulawiec and Crabtree in 1990.[3] C–F activation by metal complexes shall be addressed in the context of six subdisciplines: metalation by alkali and alkaline earth metals, defluorination by transition-metal anions, C–F activation by electron-deficient metal centers, C–F activation by electron-rich metal centers, reactions of coordinated fluorocarbon ligands that involve C–F bond cleavage, and C–F activation in biological systems. The literature up to December 1993 is covered.

II. Properties of Fluorocarbons and Transition-Metal Complexes with Perfluorinated Ligands

This section shall cover only those fluorocarbon properties pertinent to the carbon–fluorine bond activation issue since a significant number of papers addressing the structure, bonding, and reactivity of fluorinated hydrocarbons have been published.[13–15,25–28] The great strength of the carbon–fluorine bond is manifested in the general lack of reactivity associated with fluorocarbons. Fluorine is the most electronegative element and forms the strongest single bond with carbon. The C–F bond is 43% ionic from electronegativity considerations.[28] The C–F bond lengths are on the order of 1.3 Å versus 1.0 Å for C–H bonds.



Carolyn Osterberg grew up in Minneapolis, MN. She received a B.S. from the University of North Dakota in 1985 and an M.S. in chemistry from the University of California at Berkeley the following year. Her doctoral studies at the University of Utah were highlighted by the discovery of the first well-defined system for chelate-assisted carbon–fluorine bond activation and the use of transition-metal complexes as reagents for molecular recognition. She earned her Ph.D. in 1990 and was awarded the Graduate Research Prize by the department for her thesis work. Currently, she is an assistant professor of chemistry at Concordia College.

Furthermore, the van der Waals radius of fluorine (1.50 Å) is only slightly larger than that of hydrogen (1.20 Å).[29] As such, fluorine has the unusual ability to completely substitute for hydrogen in organic hydrocarbons without causing any gross geometrical distortions.

The replacement of hydrogen with fluorine results in a marked change in the physical and chemical properties of hydrocarbons versus fluorocarbons. Relative to hydrocarbons, fluorocarbons are resistant to chemical attack, demonstrate high thermal stability,[13,14,25–28] and are reluctant to coordinate to metal centers.[3,10] It is these properties of fluorocarbons which make them attractive to industry.[30] As such, high-value fluorocarbons have been used as refrigerants and pesticides. Unfortunately, these same features have resulted in their accumulation in the environment.[31–35]

The stability of fluorocarbons relative to their hydrocarbon counterparts is evidenced by the larger dissociation energies for C–F bonds compared to their C–H analogues.[36–40] The ability of the fluorine atom to function as both a σ-acceptor and a π-donor is what imparts the C–F bond with its great strength. The π-donor ability of fluorine arises via donation of the lone pair orbitals on the fluorine atom with the π-orbitals on the adjacent carbon atom.[41,42] Synergistically, fluorine can act as a σ-acceptor and pull electron density from the adjacent carbon atom as a result of its high electronegativity. It is this charge transfer from carbon to fluorine that is the cause for the observed progressive shortening of all bonds from a given carbon atom as the number of fluorines on this atom increases.[43]

Unsaturated fluorocarbons are more reactive than saturated fluorocarbons. Due to its high electronegativity, fluorine has a propensity to form bonds to carbon orbitals of low electronegativity and minimal s character. This combined with the destabilizing repulsive interactions of the fluorine lone pairs with filled π orbitals on adjacent carbon atoms generates a preference for fluorine to reside on sp^3 rather than sp^2 carbon centers.[44] This reactivity may arise from steric repulsions between fluorine atoms attached across the central C–C bond.[45] In fact, the propensity for fluorocarbons to achieve an sp^3 configuration on carbon is observed in many reactions involving transition-metal complexes containing perfluorinated ligands. These reactions usually proceed with C–F bond cleavage via fluoride migration (see section VIII).

Recently, this difference in reactivity between saturated and unsaturated fluorocarbons has been illustrated in the area of buckminsterfullerene chemistry.[46] The weaker bonds of the fluorofullerenes are exhibited with an average C–F bond length of 1.49 Å in $C_{60}F_n$ which is longer than the ca. 1.3 Å typical of perfluoroalkanes. $C_{60}F_n$ is quite reactive with nucleophiles and readily undergoes hydrolysis in solution.

Analogous to uncoordinated fluorocarbons, fluorocarbon–transition-metal complexes are extremely robust compared to hydrocarbon–transition-metal complexes.[47–49] There have been several reviews which summarize the synthesis and reactivity of fluorocarbon complexes of transition metals.[50–54] Fluorocarbon–metal complexes typically exhibit greater thermal stability compared to their hydrocarbon analogues.[55,56] In fact, in certain cases only the fluorinated analogue can be synthesized.[57] This improved stability is thought to be due, in part, to the contraction of the metal orbitals by the electronegative fluorocarbon group, thus allowing greater overlap with the carbon atomic orbital.[58] This is evidenced by the metal–carbon bond distance which is shorter in fluorocarbon–metal complexes than in the corresponding hydrocarbon–metal complexes.

In accordance with the Dewar–Chatt–Duncanson model describing transition metal–olefin bonding,[59,60] fluoroalkene complexes synergistically engage in an alkene π to metal d σ-bonding interaction and a metal d to alkene π^* bonding interaction. Due to electronegativity arguments, the bonding in fluoroalkene complexes also possesses a significant π-back-bonding component which leads to short metal–carbon$_{alkene}$ bond distances and increased pyramidalization at the carbon atoms.[47,61–65] Accordingly, higher barriers to propeller rotation are generally found in complexes bearing electronegative substituents on the olefin. Interestingly, Hughes and colleagues[66] recently reported an unprecedented low activation barrier to propeller rotation of η^2-tetrafluoroethylene ligands in a series of d^6 ruthenium complexes.

The reactivity of fluoroalkyl groups is dramatically changed by coordination to a transition metal. Upon coordination to a metal, the carbon–fluorine bonds α to the metal center are significantly weakened as evidenced by longer bond lengths[67] and reduced infrared stretching frequencies.[68,69] As we shall discuss later, this weakening of the C–F bond makes it more susceptible to electrophilic attack.[23,70]

In the case of σ-bonded fluoroaromatic groups there is the added possibility of interaction between the arene and metal d orbitals; the metal–carbon bond is quite robust.[57,71] The enhanced strength of the metal–carbon bond in perfluoroaromatic metal complexes is manifested in their unique ability to stabilize unusual bonding modes of ancillary ligands.[72] Reactions involving perfluoroaryl compounds tend to proceed to afford a product in which the metal is bonded preferentially to the perfluorophenyl moiety.[73] Migrations of the perfluorinated ligand are rather uncommon; however, several examples of perfluoroaryl migration at Pd(II)[74,75] and W(II)[76] centers have recently been reported.

III. Fluorocarbon Coordination to Metals

In order to develop metal-based catalysts capable of C–F bond activation it is necessary to understand the fundamental interactions of fluorocarbons with metal complexes. There are several examples of agostic C–H–M interactions short of oxidative addition.[77] Moreover, there is substantial evidence that alkane σ-complexes are intermediates in intermolecular C–H activation processes.[77] Accordingly, the very weak coordinating ability of fluorocarbons is one of the difficulties that must be overcome to achieve C–F activation. Examples of C–F–M complexes are quite rare; the bulk of the haloalkane coordination complexes prepared have involved the heavier halogens.[3]

It is well known that halocarbons oxidatively add to metal complexes to afford alkyl- or arylmetal halides. An attractive mechanism for oxidative addition involves the notion of precoordination of the halocarbon to the metal center. As a result of considerable activity in this area, there are now numerous examples of halocarbon coordination complexes, but none have yet been shown to directly lead to oxidative addition. However,

Winter and Gladysz[78] have shown that the dichloromethane complex $[(\eta^5\text{-}C_5Me_5)Re(ClCH_2Cl)(PPh_3)(NO)][BF_4]$ decomposes at −35 °C to give the oxidative addition product $[(\eta^5\text{-}C_5Me_5)Re(Cl)(CH_2Cl)(PPh_3)(NO)][BF_4]$. The authors were unable to conclude that the oxidative addition necessarily occurs via the dichloromethane complex.

In halocarbon coordination complexes, the weakly basic halocarbons coordinate via σ-donation of a halogen lone pair and retain their carbon–halogen bonds. The stability of these complexes follows the basicity of the coordinating halide.[3] Several complexes involving the coordination of primary,[78-84] secondary,[79,85] tertiary,[85] and aryl[79,81,86] halides have been prepared.[3]

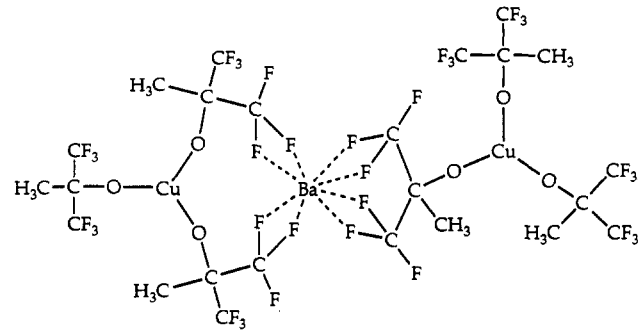
Recently, transition-metal complexes of alkyl and aryl iodides have realized increasing synthetic utility in several areas of chemistry. The groups of Gladysz[81,83,86] and Crabtree[3,79] have independently demonstrated that cationic rhenium(I) and ruthenium(II) iodoalkane complexes serve as excellent alkylating agents, respectively, since coordination activates the halocarbon toward nucleophilic attack. Importantly, reaction of these cationic iodoalkane and diiodoalkane complexes with fluoride ion affords fluorocarbons in moderate to good yields.[79,80,85] Furthermore, Zhou and Gladysz[84] have recently reported that rhenium(I) ω-haloalkane complexes are useful molecular building blocks for the construction of novel bimetallic bridging haloalkyl complexes.

A. Group 1 and Group 2 Fluorocarbon Complexes

The alkali and alkaline earth metals tend to form complexes with fluorocarbons by way of weak secondary bonding interactions.[3,87] This was previously illustrated in a biological context by Glusker and associates[87] who showed that close M–F–C interactions (Na···F–C in sodium fluoropyruvate = 2.470(1) Å and Rb···F–C in rubidium ammonium fluorocitrate = 2.979(5) and 3.095(4) Å) are present within the alkali metal salts of fluoro acids. These hard acid/hard base associations are well within the van der Waals contacts ($Na\text{–}F_{VDW}$ = 3.80 Å; $Rb\text{–}F_{VDW}$ = 3.70 Å)[29,88] and constitute significant interactions.

In the past few years there has been a surge in the interest in compounds with M–F–C interactions with Group 1 and Group 2 metals stemming from their use as precursors in chemical vapor deposition (CVD) studies. Importantly, Purdy[89] and others[90,91] have shown that using perfluorinated alkoxide and perfluorinated β-diketonate systems (which contain M–F–C interactions) as CVD precursors not only results in increased volatility but also results in the deposition of metal fluoride in the CVD product. The extensive M–F–C interactions may assist in carbon–fluorine bond cleavage in these types of compounds to afford metal fluorides. In particular, Purdy and co-workers[92] have demonstrated that there are close intramolecular Ba···F–C interactions in the barium–copper alkoxide $Ba\{Cu[OCCH_3(CF_3)_2]_3\}_2$ (1). The twelve-coordinate Ba^{2+} cation is environed by four oxygens (2.636–2.644 Å) and eight fluorines (2.94–3.14 Å).[92] The Ba···F–C interactions are rather significant considering that the sum of F (van der Waals' radius) and Ba (metallic radius) is 3.33 Å.[88,93]

Recently, Hubert-Pfalzgraf and co-workers[94] noted a similar environment for barium in the mixed-metal



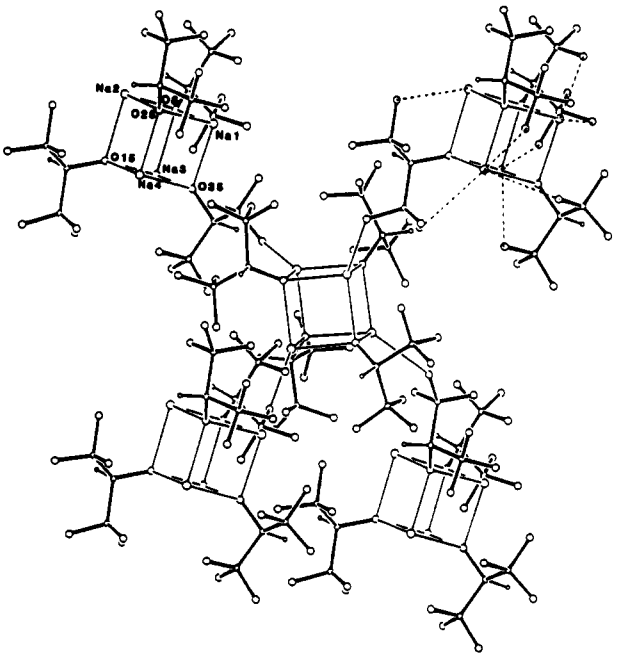
(1)

yttrium–barium compound $BaY_2[\mu\text{-}OCH(CF_3)_2]_4(thd)_4$ (thd = 2,2,6,6-tetramethylheptane-3,5-dionato). The twelve-coordinate barium atom interacts closely with four alkoxide oxygens (2.63(1)–2.68(1) Å) and eight fluorine atoms (2.9–3.2 Å).

In the related 1,1,1,5,5,5-hexafluoropentane-2,4-dionato (hfa) systems, Bradley et al.[95] have identified intermolecular Ca···F–C and Ba···F–C interactions in the dimeric $[Ca(hfa)_2(OH_2)_2]$ and polymeric $[Ba(hfa)_2(OH_2)]$, respectively. In the centrosymmetric dimer, $[Ca(hfa)_2(OH_2)_2]$, each eight-coordinate Ca^{2+} cation is bonded to one chelating hfa, two *cis* water molecules, and a second chelating hfa which bridges the two calciums through one of the oxygens. Importantly, in the complex there exist strong Ca···F–C bridging interactions (Ca···F interatomic distance = 2.52 Å; $Ca\text{–}F_{VDW}$ = 3.20 Å)[88,93] between the calcium and the CF_3 group on a neighboring hfa ligand. In the $[Ba(hfa)_2(OH_2)]$ polymer the ten-coordinate Ba^{2+} cations are linked by the oxygens of the hfa and water ligands. Each barium ion also interacts intimately with two hfa fluorine atoms displaying Ba···F–C distances of 2.92(2) Å and 2.97(2) Å.[95]

Caulton and associates[96] have observed organofluorine binding to sodium and thallium(I) in several fluoroalkoxide compounds. For instance, in the tetramer $[Na(OCH(CF_3)_2]_4$ (2), the coordination polyhedron of each sodium atom formed by the three alkoxide oxygens (Na···O = 2.250(4)–2.342(5) Å) is supplemented by several intramolecular and intermolecular interactions with fluorine atoms (Na···F–C = 2.635(2)–3.750(2) Å) (Figure 1). CVD of $[Na(OCH(CF_3)_2]_4$ (2) onto silica at 285 °C resulted in the deposition of crystalline NaF. Thus, these Na···F–C interactions appear to promote the rupture of strong C–F bonds.[96] Sodium–fluorine interactions have been previously seen by Purdy and co-workers[97] in the analogous alkoxide compound $Na_2Cu[OCH(CF_3)_2]_4$ in which the Na^+ ions are each coordinated to two oxygens (2.281(6) Å and 2.318(6) Å) and five fluorines (2.481(7)–2.791(7) Å).

Similarly, an X-ray crystallographic study showed evidence of secondary Na···F–C interactions in the fluoroalkoxide ("sandwich-type") compounds $[Na_2Zr(OCH(CF_3)_2)_6(C_6H_6)]$ (3) and $[Na_2Zr(OCH(CF_3)_2)_6(C_6H_6)_2]$ (4) (Figure 2).[96] $[Na_2Zr(OCH(CF_3)_2)_6(C_6H_6)]$ (3) forms an infinite chain of alternating benzene and $Na_2Zr(OCH(CF_3)_2)_6$ links. Each sodium atom forms identical bonds to three oxygen atoms (2.50 Å), a benzene molecule (Na···C = 3.13 Å), and three fluorine atoms (2.72 Å). The six Zr–O distances are 2.063(3) Å. In contrast, $[Na_2Zr(OCH(CF_3)_2)_6(C_6H_6)_2]$ (4) is a monomer in which each sodium atom is bound to two



(2)

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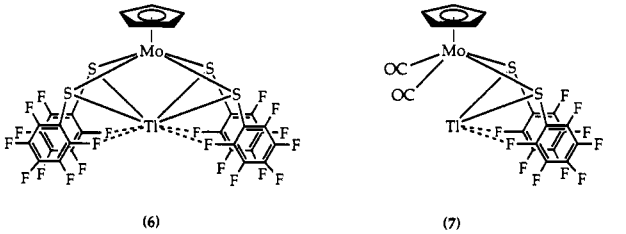
oxygen atoms (2.413(4) Å) and four fluorine atoms [2.673(3) Å (twice) and 2.810(3) Å (twice)]. The bonding at each sodium atom is supplemented via interaction with the π-cloud of a benzene molecule.

The related thallium(I) fluoroalkoxide compound $[Tl_2Zr(OCH(CF_3)_2)_6]$ (**5**) was shown to possess moderate intramolecular and intermolecular Tl···F–C interactions (Figure 3).[96] Each Tl^+ center is formally twelve-coordinate and is intramolecularly bound to three oxygen atoms (2.740(9)–2.831(11) Å) and six fluorine atoms (3.068(8)–3.287(11) Å).[98] These contacts are further supplemented with two intermolecular Tl···F–C interactions from one neighboring molecule (3.442(11) and 3.378(8) Å) and one Tl···F–C interaction from a second neighboring molecule (3.289(11) Å). These intermolecular interactions are impressive considering the van der Waals distance for Tl···F is 3.50 Å.[29,88] Furthermore, these interactions produce a two-dimensional lattice for $[Tl_2Zr(OCH(CF_3)_2)_6]$ in the solid state which is not retained in the solution NMR. However, the intramolecular Tl···F–C interactions were further supported by the fact that both ^{205}Tl and ^{19}F NMR spectra show Tl–F couplings consistent with direct bonding.[96]

Davidson, Lindsell, McCullough, and co-workers[99] observed close Tl···F–C contacts in the molybdenum–thallium complexes $[Tl(\eta^5\text{-}C_5H_5)Mo(SC_6F_5)_4]$ (**6**) and $[Tl(\eta^5\text{-}C_5H_5)Mo(SC_6F_5)_2(CO)_2]$ (**7**). In $[Tl(\eta^5\text{-}C_5H_5)Mo(SC_6F_5)_4]$ (**6**), the coordination polyhedron of Tl^+ formed by four sulfur atoms (3.200(8)–3.342(7) Å) is supplemented by contacts with four *ortho*-F atoms of each C_6F_5 ring (2.978(1)–3.144(1) Å). In contrast, $[Tl(\eta^5\text{-}C_5H_5)Mo(SC_6F_5)_2(CO)_2]$ (**7**) forms extensive chains in the solid state in which the six-coordinate Tl^+ forms two intramolecular sulfur atom contacts (2.998(4) and 3.032(4) Å) and two intermolecular sulfur atom contacts (3.333(3) and 3.772(3) Å), thus creating a tetrasulfur environment similar to that found for Tl^+ in compound **6**. This sulfur coordination sphere is supplemented by two intramolecular Tl···F–C interactions (3.090(10) and 3.099(9) Å).



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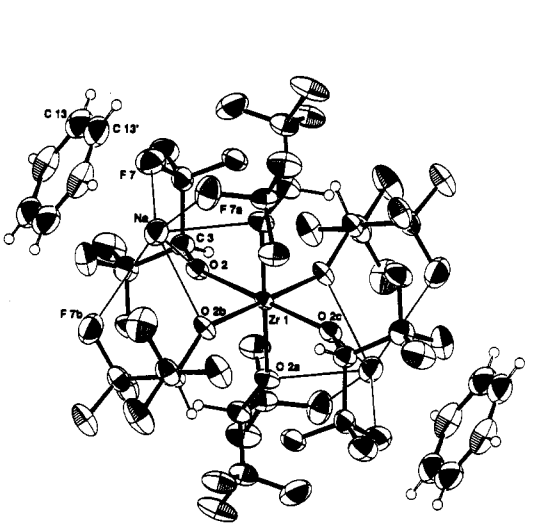
Although variable-temperature ^{19}F NMR studies established restricted rotation of the C_6F_5 groups, no Tl–F coupling was observed. The authors note that the close Tl···F–C contacts in these compounds may be the result of an electrostatic interaction between Tl^+ and $[(\eta^5\text{-}C_5H_5)Mo(SC_6F_5)_4]^-$.[99]

Klingebiel and associates[100] have observed an analogous Li···F–C interaction (2.273(10) Å) between Li^+ and the *ortho*-F atom of the C_6F_5 ring in lithium



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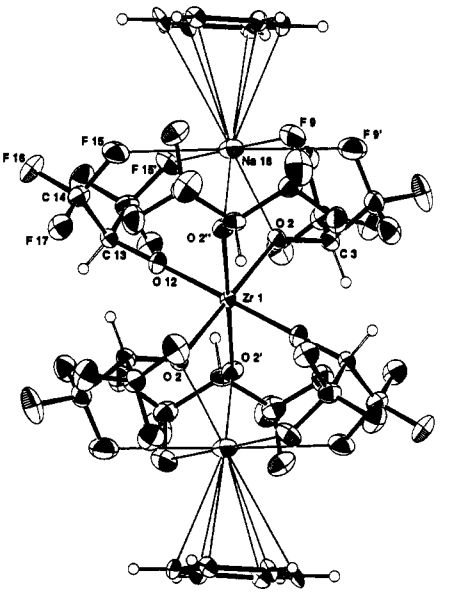

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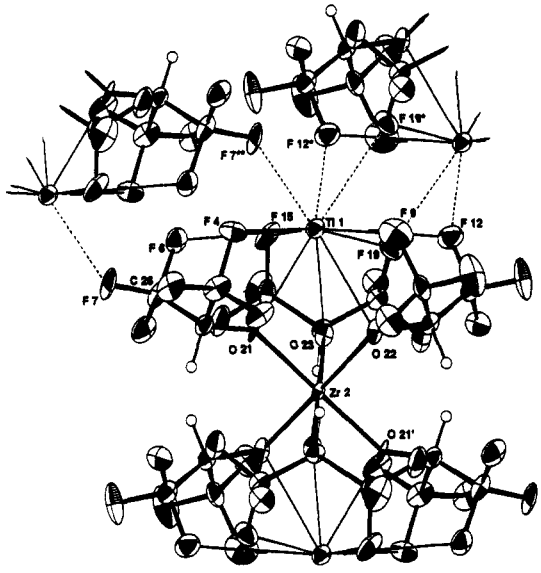

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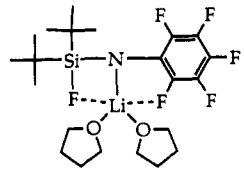
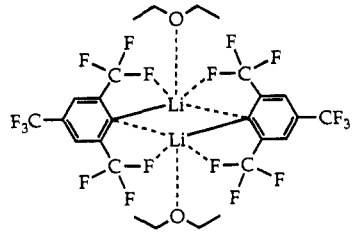
N-(fluorosilyl)pentafluoroaniline Li[$(CMe_3)_2SiFNHC_6F_5$] (**8**). The Li···F–C contact constitutes a significant interaction and is well within the van der Waals distance of 3.30 Å.[29,88]



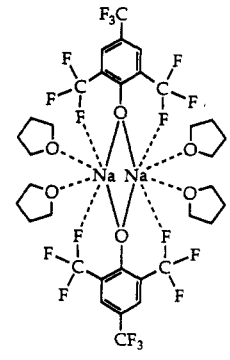
(8)

Stalke and Whitmire[101] observed that strong intermolecular Li···F–C contacts stabilize the dimer [2,4,6-$(CF_3)_3C_6H_2Li{\cdot}Et_2O]_2$ (**9**) in the solid state. Each five-coordinate, distorted trigonal bipyramidal Li^+ is bonded to two carbon atoms (2.223(9)–2.312(11) Å), an oxygen (1.964(10)–1.975(9) Å) of a diethyl ether molecule, and two fluorines (2.227(11)–2.293(12) Å) from *ortho*-CF_3 groups (one from each phenyl ring). ^7Li and ^{19}F NMR did not reveal any Li–F coupling in solution.



(9)

In related work, Brooker et al.[102] reported a series of monodentate sodium and potassium 2,4,6-tris(trifluoromethyl)phenoxides and 2,4,6-tris(trifluoromethyl)-benzenethiolates that contain secondary-bonded fluorocarbons. [$Na(2,4,6\text{-}(CF_3)_3C_6H_2O)(thf)_2]_2$ (**10**) is a dimeric structure which contains weak Na···F–C interactions between each six-coordinate Na^+ and two fluorine atoms (2.664(7) and 2.720(7) Å) from *ortho*-CF_3 groups. In contrast, the dimeric potassium salt [$K(2,4,6\text{-}(CF_3)_3C_6H_2O)(thf)_2(\mu\text{-}thf)]_2$ (**11**) has two strong K···F–C interactions (2.867(3) and 2.980(3) Å) which are well within the sum of the van der Waals radii (4.30 Å).[29,88] In contrast to the phenolates, the corresponding thiolates [$Na(2,4,6\text{-}(CF_3)_3C_6H_2S)(thf)_2(0.25thf)]_n$ and [$K(2,4,6\text{-}(CF_3)_3C_6H_2S)(thf)]_n$ are polymeric structures. Each six-coordinate Na^+ in the [$Na(2,4,6\text{-}(CF_3)_3C_6H_2S)(thf)_2(0.25thf)]_n$ polymer chain engages in two strong Na···F–C interactions (2.434(3)–2.486(3) Å) with the fluorine atoms from the *ortho*-CF_3 groups. [$K(2,4,6\text{-}(CF_3)_3C_6H_2S)(thf)]_n$ was also observed to contain several moderate K···F–C interactions (2.920(2)–3.094(2) Å) at each eight-coordinate potassium center.[102]



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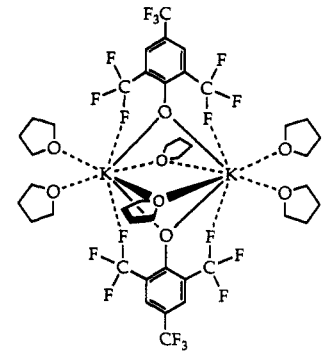
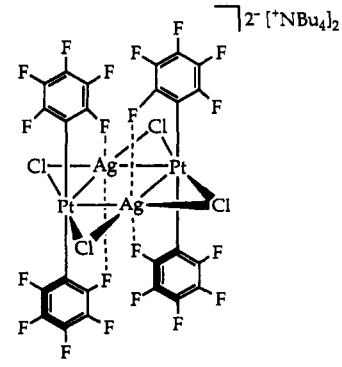


(11)

B. Transition-Metal–Fluorocarbon Complexes

Transition-metal fluorocarbon coordination compounds are rare compared to those of the heavier halocarbons.[3] Uson, Cotton, et al.[103] and Richards and associates[104] reported the first examples of fluorocarbon coordination to transition metals (**12** and **13**, respectively). However, it was Crabtree and co-workers[105] who provided the first spectroscopic evidence of fluorocarbon coordination in solution with the observation of a significant upfield shift in the ^{19}F NMR spectrum for the 8-fluoroquinoline–iridium complex **14**. This landmark discovery provided an important spectroscopic tool for seeking other examples of fluorocarbon coordination.



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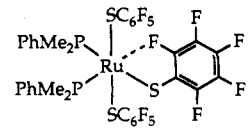

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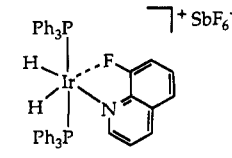
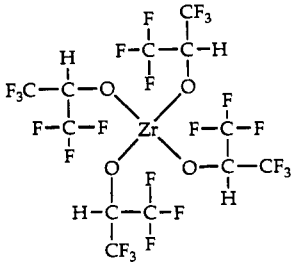


(14)

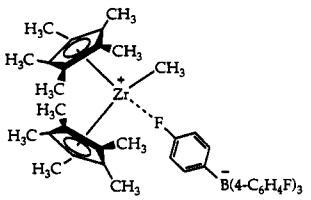
Recently, Caulton and co-workers[96] have detected intramolecular Zr···F–C interactions in the alkoxide compound $[Zr(OCH(CF_3)_2)_4]$ (**15**) using ^{19}F NMR spectroscopy. Although no changes in chemical shifts



(15)

were observed, there was evidence of fluxional processes which the authors speculated to arise via interaction of fluorine atoms with the Zr^{4+} metal center, thereby restricting the rotation of the CF_3 groups about the carbon–carbon single bond.[96]

Horton and Orpen[106] have observed intermolecular Zr···F–C interactions in the zirconocene complexes $[(\eta^5\text{-}C_5Me_5)_2Zr(CH_3)][B(4\text{-}C_6H_4F)_4]$ (**16**) and $[Cp'ZrC(Ph)=C(Ph)(CH_3)][B(4\text{-}C_6H_4F)_4]$ (**17**). Coordination



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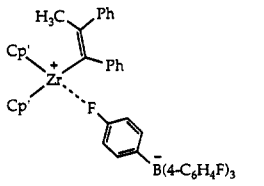
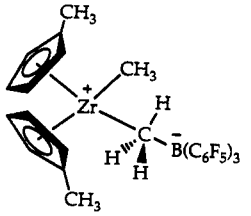


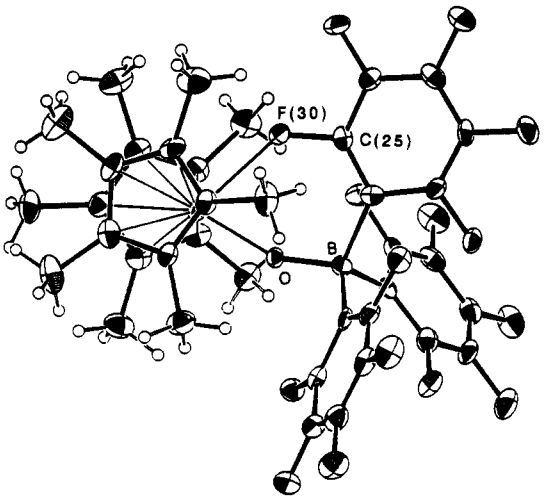
(17a) Cp' = $(\eta^5\text{-}C_5H_5)$
(17b) Cp' = $(\eta^5\text{-}C_5H_4(Me_3Si))$
(17c) Cp' = [*rac*-$C_2H_4(indenyl)_2$]

of the anion to zirconium in **16** via a single Zr···F–C bridge was evidenced by an upfield fluorine shift (δ −135.5 ppm versus δ −121.1 ppm for free $B(4\text{-}C_6H_4F)_4^-$, $C_2D_2Cl_4$, −30 °C) in the ^{19}F NMR spectrum. Similar upfield shifts in the ^{19}F NMR spectrum were observed for the complexes **17a–c**.[106] Interestingly, in the related zirconocene complex **18** prepared by Marks and associates[107] the anion is bonded through a methyl bridge and not a Zr···F–C bridge.



(18)

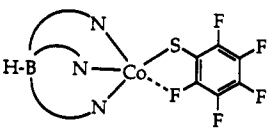
Siedle and co-workers[108] reported the structure of a zirconoxyborane complex that contains a Zr···F–C bridge. $[(\eta^5\text{-}C_5Me_5)_2ZrOB(C_6F_5)_3]$ (**19**) exhibits a close Zr···F–C contact of 2.346(3) Å ($Zr\text{–}F_{VDW}$ = 3.0 Å)[88,93] (Figure 4). Importantly, the Zr···F–C interaction in **19** was further verified by a significant upfield chemical shift for the shielded fluorine (δ −190.3 ppm versus δ −130 ppm (av) for an uncoordinated *ortho*-fluorine, toluene-d_8, −88 °C) in the ^{19}F NMR spectrum.[108]



(19)

Figure 4. Reprinted with permission from ref 108. Copyright 1993 American Chemical Society.

For comparative purposes, it is interesting that Marks, Ibers, and associates[109] did not consider the close Co···F–C contact (2.64(2) Å) in $[HB(3,5\text{-}Me_2pz)_3Co(SC_6F_5)]$ (**20**) a secondary interaction but rather a result of packing effects of the $C_6F_5S^-$ ligand.



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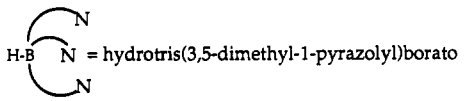
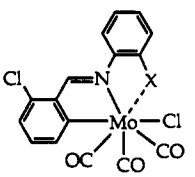
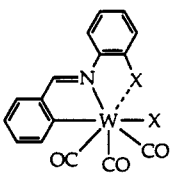


Recently, Harrison et al.[110] prepared the first series of seven-coordinate molybdenum– (**21**) and tungsten–aryl halide (**22**) complexes as illustrated below. Attempts to prepare the analogous fluorocarbon coordination complexes were unsuccessful. Interestingly, thermochemical measurements suggest that the structure of the chelate ring, rather than the identity of the halide (X = Cl, Br, I), controls the strength of the aryl halide binding in these complexes.[110,111]



(21a) X = Cl
(21b) X = Br
(21c) X = I



(22a) X = Br
(22b) X = I

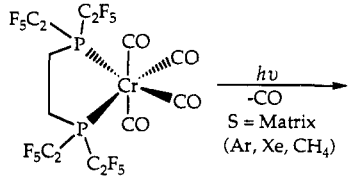
The unsaturated transition-metal carbonyl species $M(CO)_5$ (M = Cr, Mo, W), which are generated by photolysis of $M(CO)_6$, have been observed to weakly bind to a wide variety of fluorocarbons. For instance, early work by Perutz and Turner[112] provided evidence for the interaction of $Cr(CO)_5$ with CF_4 in low-temperature matrices using visible and infrared spec-

troscopy and comparing the spectrum of $Cr(CO)_5$ with respect to the spectra observed in rare-gas matrices.

Using visible absorption spectroscopy, Kelly and colleagues[113,114] have demonstrated that laser flash photolysis of $M(CO)_5$ (M = Cr, Mo, W) in perfluoromethylcyclohexane affords the weakly coordinated $(CO)_5M\cdots F-C_7F_{13}$ fluorocarbon complexes. Similarly, Nayak and Burkey[115] have observed the formation of a fluorocarbon complex using photoacoustic calorimetry and actinometry upon photolysis of $Cr(CO)_6$ in perfluorodecalin. The weak binding of the fluorocarbon results in anomolously fast ligand substitution reactions in these solvents.

Using time-resolved infrared spectroscopy, Hackett, Rayner and co-workers[116] have observed the CH_3F and CH_3CH_2F form complexes with $W(CO)_5$ in the gas phase with binding energies of ~11 and ~12 kcal/mol, respectively. Similarly, Weitz and co-workers[117] demonstrated that CF_2Cl_2 forms a complex with $W(CO)_5$ in the gas phase with a bond dissociation energy of 19.6 ± 0.6 kcal/mol. In both studies the authors were unable to rule out a W–F–C bonding interaction although interaction with C–H or C–Cl groups seems more likely.[116,117]

Recently, Brookhart, Perutz, and associates[118] reported that photolysis of $[(C_2F_5)_2PCH_2CH_2P(C_2F_5)_2Cr(CO)_4]$ (**23**) in rigid matrices at 12 K (Ar, Xe, CH_4) results in photodissociation of the *cis* carbonyl ligand to afford a mixture of **24** and **25** (eq 1). From infrared



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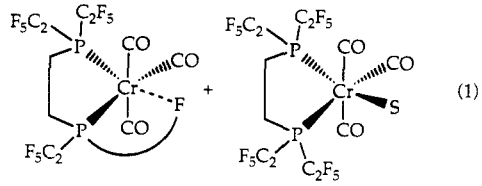


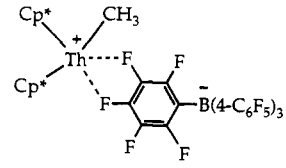
(24) (25) (1)

and UV–vis spectroscopy it was determined that **24** contains an intramolecularly coordinated fluorine atom donated from the perfluoroalkylphosphine ligand. Complex **25** contains a coordinated matrix host molecule in the site vacated by CO.

C. Lanthanide- and Actinide–Fluorocarbon Complexes

Similar to the alkali and alkaline earth metal alkoxide complexes discussed earlier, Bradley et al.[119] have observed Pr···F–C interactions in the trimeric lanthanide compound $[Pr(OCMe_2(CF_3))_3]_3$. In this structure, one praseodymium is eight-coordinate with no secondary fluorocarbon binding; the other two are five-coordinate with intramolecular Pr···F–C interactions (2.774 and 2.756 Å) with the fluorines from two CF_3 groups. These interactions are within the sum of the van der Waals radii (~3.10 Å) for a Pr···F interaction.[88,93]

A well-defined example of an actinide fluorocarbon complex has been reported by Marks and co-workers.[120] An X-ray crystallographic study revealed that the cationic thorium complex $[(\eta^5\text{-}C_5Me_5)Th(CH_3)][B(C_6F_5)_4]$ (**26**) contains two Th···F–C bridges (2.757(4) and 2.675(5) Å). The intimate Th···F–C contacts constitute



(26)

secondary interactions since they are considerably longer than the length assigned to a F → Th dative bond (2.28 Å),[120] yet shorter than the sum of the van der Waals radii (~3.10 Å).[88,93] These interactions clearly demonstrate that noncoordinating anions are capable of significant bonding interactions with metal centers via C–F bridges.[10,121]

IV. Metalation of Carbon–Fluorine Bonds

For clarity in this review, a metalation reaction is defined as the insertion of a Group 1 or a Group 2 metal into a carbon–fluorine bond. Specifically, we will be referring to the generation of alkyl-, alkenyl-, or aryllithium and -magnesium compounds consisting of C–Li–F and C–Mg–F bonds, respectively. Metalation reactions are well known for hydrocarbon compounds and have realized great synthetic utility in organic chemistry.[122] Lithium reagents as well as Grignard reagents are readily prepared by metal/halogen exchange. Both reagents are accessible by straightforward metalation; however, this route is dependent upon the acidity of the hydrocarbon since it is an acid–base reaction involving the insertion of a metal into a C–H bond. Insertion of either Li or Mg into a C–F bond is not trivial and generally entails long reaction times. Interestingly, recent ab initio studies of the insertion reaction of Mg into the C–F bond of fluoromethane reveal an activation energy of 31.2 kcal/mol and a substantially higher activation energy of 39.4 kcal/mol for the corresponding chloromethane reaction.[123] Aside from the intrinsic difficulty of inserting either a lithium or magnesium metal into a C–F bond, a severe problem is the rapid and sometimes explosive decomposition of the metalation product via β- or α-elimination of metal fluoride.[124] This has minimized the number of isolated and characterized fluorocarbon–lithium and fluorocarbon–magnesium complexes.

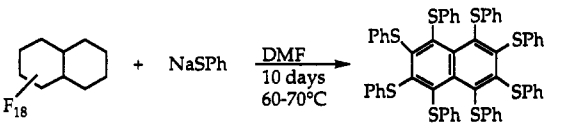
It is noteworthy that (pentafluorophenyl)lithium and pentafluorophenyl Grignard compounds demonstrate greater thermal stabilities than their perfluoroalkyl and perfluorovinyl counterparts.[48] This enhanced stability is manifest in their use as valuable synthetic precursors to other (pentafluorophenyl)–metal compounds.[58] Frequently, the decomposition of both (pentafluorophenyl)lithium and (pentafluorophenyl)magnesium bromide have been employed as means for generating the reactive intermediate tetrafluorobenzyne.[125,126] The most convenient method of preparation of (pentafluorophenyl)lithium involves the reaction between pentafluorobenzene and *n*-butyllithium at −70 °C in diethyl ether. Thus, C–H activation is favored over C–F

cleavage in this reaction. Similarly, bromopentafluorobenzene and pentafluoroiodobenzene readily form their respective Grignard reagents in ether solvents at low temperatures but become unstable at elevated temperatures.

A. Metalation of C–F Bonds via Group 1 Metals

The earliest report of a metalation of a C–F bond using a Group 1 metal was reported in 1947 by Miller and co-workers.[127] The technique employed sodium metal and was designed as an analytical method for the determination of fluorine in organic compounds. The fluorocarbon decomposed using sodium metal in liquid ammonia at −78 °C. The lithiation was effective for cleaving both C–F and C–Cl bonds. The fluorine content in all fluorinated alkanes was accurately determined. No comment was made on the decomposition product other than the fluoride ion and its analysis. In general, the C–F bond is highly susceptible to cleavage by lithium ammonia solutions, and under suitable conditions the cleavage can be quantitative. The reaction has been employed to quantitatively determine the fluorine contents of organic compounds.[128]

In related chemistry, MacNicol and Robertson[129] have recently shown that sodium arenethiolate slowly reacts with cyclic perfluoroalkanes that contain tertiary carbon centers to completely defluorinate and aromatize the molecules in 55% yield (eq 2). The authors proposed

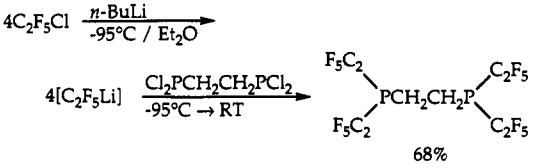


55% (2)

a mechanism with single electron transfer (SET) as the first step of the reductions.

In a gas-phase study, Kavan and Dousek[130] reported that hexafluorobenzene and perfluorohexane in the gas phase react spontaneously with ambient temperature lithium amalgam to give a solid composed of lithium fluoride and elemental polymeric carbon with a small amount of superstoichiometric lithium. The elemental carbon was determined to be electronically conducting, highly disordered, and reactive toward oxygen. The mechanism was described by an electrochemical corrosion model. The first step is a mild and quantitative chemical reduction of C_6F_n to a C–Li–F mixture in which ion conduction is the rate-determining step. The highly reactive carbon produced by this reaction then forms a polymeric network with widespread sp^2-hybridized C–C bonds which sustain the observed electronic conductivity. Similar electrochemical reductions with lithium amalgam have been reported for other fluorinated materials such as the sulfonated fluoropolymer Nafion 117[131,132] and poly(tetrafluoroethylene).[133,134]

Presumably due to the strength of the C–F bond, there have been no reports of generating lithium reagents via insertion of Li into a C–F bond. However, lithium reagents of fluorocarbons are readily prepared via metal/halogen exchange from the corresponding chlorofluoroalkanes and chlorofluoroalkenes, or metalation with the selective introduction of a lithium center into a hydrogen site of a hydrofluorocarbon.[135] Application of this methodology has been nicely illustrated by Ernst and Roddick[136] who generated C_2F_5Li in situ at −95 °C from C_2F_5Cl and *n*-BuLi in diethyl ether. Most impressive is that the lifetime of C_2F_5Li is 5–10 min at −95 °C. Subsequent addition of a solution of $Cl_2PCH_2CH_2PCl_2$ affords essentially pure $(C_2F_5)_2PCH_2CH_2P(C_2F_5)_2$ in 68% yield (eq 3).



(3)

Interestingly, chemical reduction of poly(tetrafluoroethylene) to poly(ethylene) was reported by Chakrabarti and Jacobus[137] employing the action of lithium metal in liquid ammonia. The complete reduction of a two-carbon poly(tetrafluoroethylene) segment requires 8 equiv of metal; each C–F bond requires 2 equiv of lithium for reduction (eq 4). A recent review

$$-(CF_2CF_2)- + 8Li + 4NH_3 \longrightarrow -(CH_2CH_2)- + 4LiF + 4LiNH_2 \quad (4)$$

summarizes the chemical and electrochemical techniques for carbonization of fluoropolymers.[138]

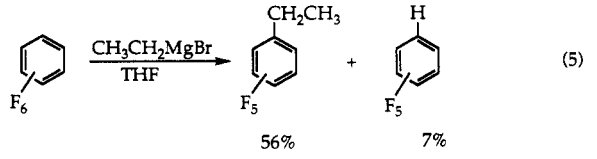
Pez and co-workers[139] recently reported the selective partial reduction of perfluorodecalin to perfluoronaphthalene upon treatment with sodium benzophenone ketyl in tetrahydrofuran. This is in contrast to the work discussed above where total reduction occurs or complete substitution of the carbon–fluorine bonds takes place. The authors note the importance of tertiary C–F bonds and postulate a mechanism with single electron-transfer (SET) as the first step of the reductions. The selective partial reduction and the mild conditions utilized in this work are noteworthy considering the strength of the C–F bond and intrinsic resistance of saturated perfluorocarbons to chemical attack.

B. Metalation of C–F Bonds via Group 2 Metals

Most attempts to isolate fluoro Grignard compounds have failed. The attempts to prepare fluoro Grignard reagents were frustrated by either a lack of reaction between the organo fluorides and magnesium or the formation of coupling products. However, reports of their existence have appeared in the literature, and proof of their generation is usually provided as derivatives of the organomagnesium fluoride.

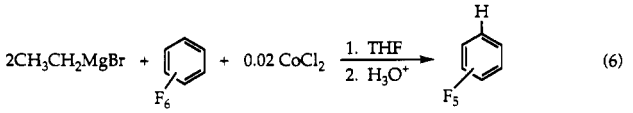
In 1964, Harper and co-workers[140] studied nucleophilic displacement reactions of Grignard reagents on hexafluorobenzene in tetrahydrofuran. A recurring theme that will be seen throughout this review is that the extensive fluorination of hexafluorobenzene renders it susceptible to nucleophilic attack. The authors report that the metalation of a C–F bond is a competing reaction occurring with nucleophilic substitution. This was shown not to occur by a halogen–metal interchange. Hexafluorobenzene was added to ethylmagnesium bromide in THF, and upon hydrolysis the authors noted a 56% yield of the expected ethyl-2,3,4,5,6-pentafluorobenzene as well as the formation of pentafluorobenzene in 7% yield (eq 5).

In related work, Respess and colleagues demonstrated the intermediacy of (perfluoroaryl)magnesium fluorides via the reaction of perfluoroaryl compounds with



(5)

ethylmagnesium bromide and a catalytic amount of certain transition-metal halides ($CoCl_2$ was most effective) in tetrahydrofuran (eq 6)[141] and from the



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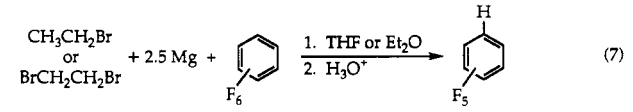
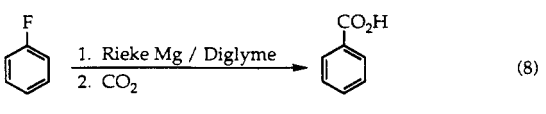


(7)

reaction of hexafluorobenzene with magnesium and an equal molar amount of an entrainer such as ethyl bromide or 1,2-dibromoethane in THF or diethyl ether (eq 7).[142] The intermediacy of a fluoro Grignard compound was indicated by hydrolysis of the reaction product to produce pentafluorobenzene in high yield and by the reaction of the product with an organosilane. However, no attempt was made to isolate the possible intermediate fluoro Grignard compound.

Ashby and co-workers[143,144] prepared for the first time alkylmagnesium fluorides in high yield by the reaction of alkyl fluorides with magnesium in ether solvents (tetrahydrofuran or 1,2-dimethoxyethane) at reflux in the presence of catalytic iodine. Most impressive is that the researchers were able to produce *n*-hexylmagnesium fluoride in 92% yield in 4 h in 1,2-dimethoxyethane using iodine as a catalyst. Ethylmagnesium fluoride was prepared in 36% yield.[145] Once the alkyl fluoro Grignard compound is formed in either diethyl ether or tetrahydrofuran the compound is stable indefinitely and in solution is present as discrete dimers bound by a double fluoride bridge as determined by low-temperature NMR, IR, fractional crystallization, and dioxane precipitation studies (Figure 5).[146]

In a paper on the preparation of highly reactive magnesium metal, Rieke and Hudnall[147] noted the first successful generation of phenylmagnesium fluoride from fluorobenzene and magnesium. Previous to this study (and mentioned above), the general procedures included the use of higher reaction temperatures, the use of more strongly coordinating solvents, and the activation of the magnesium metal by catalyst or entrainer. In this work, refluxing fluorobenzene was reacted with the highly activated Rieke magnesium metal ($MgCl_2$–K–THF) in diglyme for only 1 h to yield a modest 5% benzoic acid after treatment with carbon dioxide (eq 8).[147] Subsequent to this study, Rieke and Bales[148] reported that addition of potassium iodide to



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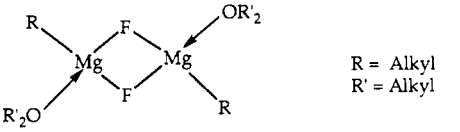
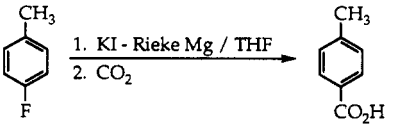


Figure 5.

the $MgCl_2$–K–THF mixture prior to reduction of the $MgCl_2$ results in enhanced reactivity of the Rieke magnesium metal. Treatment of *p*-fluorotoluene with potassium iodide-activated magnesium in refluxing tetrahydrofuran for 1 h affords the fluoro Grignard reagent in 70% yield. The Grignard reagent was identified by its hydrolysis to toluene and its reaction with CO_2 to give *p*-toluic acid in 65% yield (eq 9).



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V. Defluorination of Fluorocarbons

A. Displacement of Fluoride Ion via Transition-Metal Anions

It has long been known that transition-metal nucleophiles readily displace fluoride from highly fluorinated arenes and alkenes to afford metal–arene and metal–vinyl complexes, respectively.[149-166] These reactions are commonly viewed as simple nucleophilic substitution reactions. Accordingly, the nature of the product depends on whether the intermediate carbanion eliminates fluoride ion or abstracts a proton from the solvent.[22,151] The new complexes obtained have structures in which the metal has replaced (in a σ-fashion) one of the fluorine atoms attached to a carbon of the π-system.[149-164] Rearrangements are typically not observed.

Metal anions generally react to form monosubstitution products for both polyfluorinated alkenes and arenes.[149-164] Complex formation depends upon the nucleophilic behavior of the transition-metal anion and the susceptibility of the fluorocarbon to nucleophilic attack.[167] As such, polyfluorinated compounds are more susceptible to nucleophilic attack, compared with the corresponding hydrocarbons, due to withdrawal of electron density onto the fluorine atoms. Thus, hexafluorobenzene readily reacts with $[CpFe(CO)_2]^-$ to form $CpFe(CO)_2(C_6F_5)$; however, no reaction is observed between fluorobenzene and $[CpFe(CO)_2]^-$.

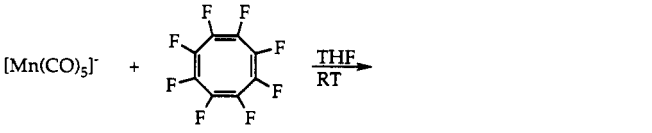
The nucleophilic displacement of fluoride ion from perfluorinated aromatics using organometallic nucleophiles is analogous to the classical nucleophilic aromatic substitution reactions found in organic chemistry; substitution of the arene system with an electron-rich metal deactivates the ring toward further reactivity.[22,150-152,154-156] For example, hexafluorobenzene undergoes nucleophilic attack by $[CpFe(CO)_2]^-$ to afford only $CpFe(CO)_2(C_6F_5)$; no polysubstituted aromatic complexes are formed.[150] If the arene system contains an electron-withdrawing substituent, nucleophiles substitute predominantly *para* to that functional group already present.[153,157-159]

The reactivity of the carbonyl metal anion depends markedly upon the nature of the coordinated ligands

and increases when carbonyl ligands are replaced by more basic ligands such as phosphines or a cyclopentadienyl group.[149–164] On the basis of the myriad studies[22,151,159] performed on the reaction of metal carbonyl anions with perfluorinated substrates the following sequence of decreasing nucleophilicity for the selected carbonyl anions has been established: $[CpFe(CO)_2]^- \geq [Re(CO)_5]^- \approx [Ni(PEt)_4] > [Mn(CO)_4PPh_3]^- \geq [Mn(CO)_5]^- > [Co(CO)_4]^- \approx [Fe(CO)_4]^{2-}$. The anions' strength as nucleophiles parallels their reactivity with a given substrate and correlates with the reduction potential of these reagents.[168] As we shall see in the next section this is important in the design of defluorinating agents for saturated perfluorocarbons.

In their early studies King and Bisnette[69] noted that fluoride as well as chloride displacement occurs upon treatment of trifluoroacetyl chloride with $[CpFe(CO)_2]^-$. This was evidenced by the production of large amounts of $[CpFe(CO)_2]_2$ during the preparation of trifluoroacetyl complex $CpFe(CO)_2(COCF_3)$, whereas very little $[CpFe(CO)_2]_2$ was formed during the corresponding preparations of the nonfluorinated acetyl derivative, $CpFe(CO)_2(COCH_3)$. The authors suggested that the formation of $[CpFe(CO)_2]_2$ resulted from the decomposition of the unstable $CpFe(CO)_2(CF_2COCl)$ intermediate.[69]

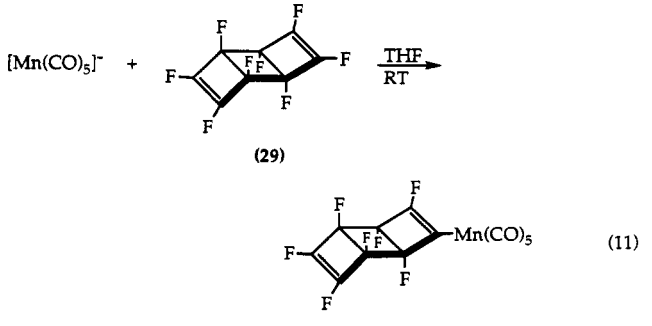
Recently, Hughes and co-workers[169–172] have reported that octafluorocyclooctatetraene (OFCOT) reacts with several metal carbonyl anions to afford monosubstitution products via net displacement of fluoride ion. Treatment of OFCOT with $Na[Mn(CO)_5]$ at room temperature in tetrahydrofuran affords an equilibrium mixture of the η^1-heptafluorocyclooctatetraene complex **27** and its valence isomer complex **28** (eq 10).[172] The



(10)

(27) (28)

η^1-heptafluorocyclooctatetraene complex **27** is the major product of the reaction as determined by ^{19}F NMR spectroscopy. Indirect confirmation of the structure of **28** was obtained by the room-temperature reaction of the tricyclic OFCOT valence isomer **29** with $Na[Mn(CO)_5]$ which gives the monosubstituted tricyclic complex **30** (eq 11).[172] The structure of **30** was confirmed



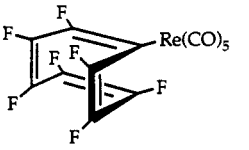
(29)

(11)

(30)

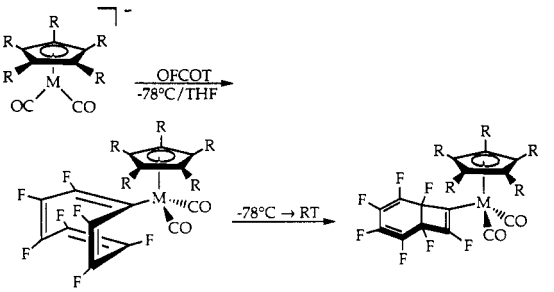
by a single-crystal X-ray diffraction study.

Interestingly, the room-temperature reaction of $Na[Re(CO)_5]$ with OFCOT afforded only the monocyclic complex **31**.[172]



(31)

Low-temperature reactions were achieved with the more nucleophilic carbonyl anions $[(\eta^5\text{-}C_5R_5)M(CO)_2]^-$ (M = Fe, R = H; M = Fe, R = CH_3; M = Ru, R = H). Reaction of $K[(\eta^5\text{-}C_5R_5)M(CO)_2]$ (M = Fe, R = H; M = Fe, R = CH_3; M = Ru, R = H) with OFCOT in tetrahydrofuran at −78 °C afforded exclusively the η^1-heptafluorocyclooctatetraene complexes **32**, **34**, and **36**. When the reaction mixture was warmed to room temperature, the corresponding bicyclic OFCOT valence isomer complexes **33**, **35**, and **37** were formed (eq 12).[172] Thus, it was concluded that formation of the



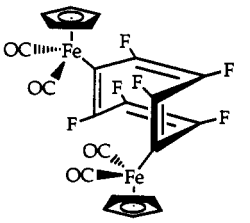
(12)

(32) M = Fe, R = H
(34) M = Fe, R = CH_3
(36) M = Ru, R = H

(33) M = Fe, R = H
(35) M = Fe, R = CH_3
(37) M = Ru, R = H

bicyclic complex occurs exclusively from valence isomerization of its initially formed monocyclic valence isomer and not from the nucleophilic attack of the carbonyl anion on the free bicyclic OFCOT valence isomer ligand.[172]

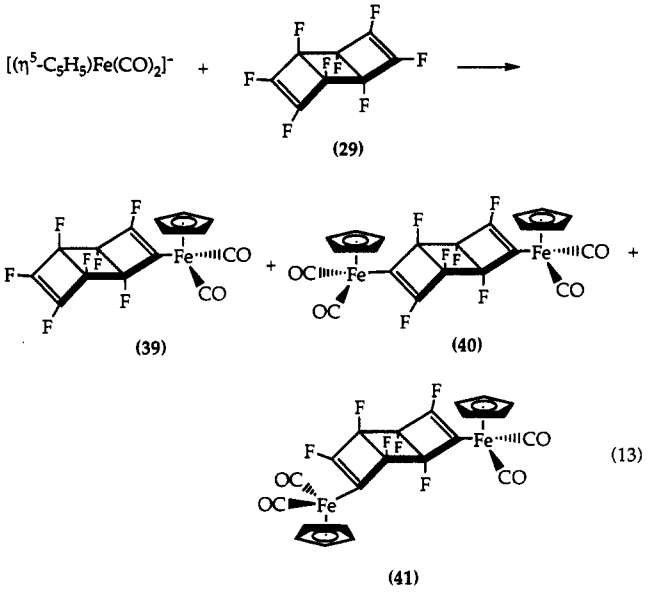
Surprisingly, the disubstituted complex **38** was produced along with an equilibrium mixture of **32** and **33** upon reaction of OFCOT with 2 equiv of $[(\eta^5\text{-}C_5H_5)Fe(CO)_2]^-$ in tetrahydrofuran at room temperature.[170,172]



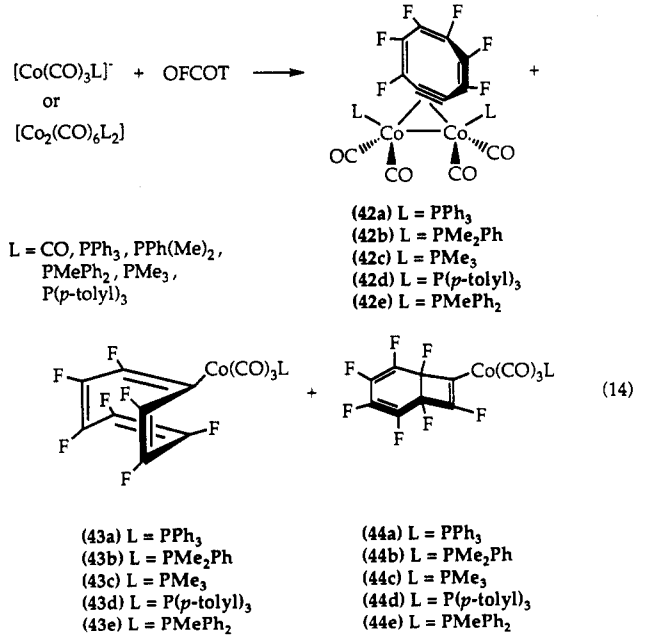
(38)

The structure of the 1,5-disubstituted complex (**38**) was determined by X-ray crystallography.

In contrast to the reaction with $Na[Mn(CO)_5]$, the reaction of $K[(\eta^5\text{-}C_5H_5)Fe(CO)_2]$ with the tricyclic OFCOT valence isomer **29** results in the formation of a mixture of monosubstituted (**39**) and disubstituted complexes (**40** and **41**) (eq 13).[172] The structures of the products were ascertained unambiguously through selective $^{19}F\{^{19}F\}$ decoupling experiments.



Particularly noteworthy is that the reactions of several cobalt carbonyl anions $[Co(CO)_3L]^-$ or the corresponding neutral dimers $[Co_2(CO)_6L_2]$ (L = PPh_3, PMe_2Ph, PMe_3, $P(p\text{-tolyl})_3$), $PMePh_2$) with OFCOT afford the dinuclear cobalt μ-hexafluorocyclooctatrienyne complexes **42** and the η^1-heptafluorocyclooctatetraene complexes **43**, which are in equilibrium with the monosubstituted bicyclic OFCOT valence isomer complexes **44** (eq 14).[169-171] The structures of the dicobalt



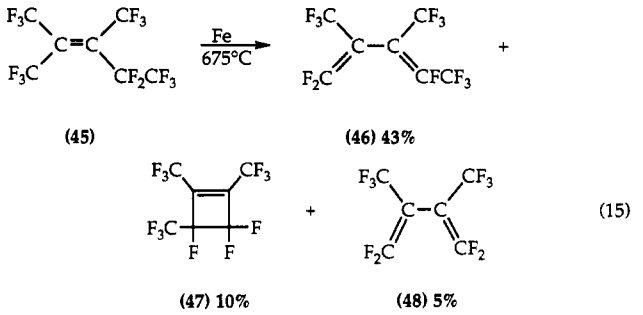
μ-hexafluorocyclooctatrienyne complexes **42a–d** have been determined through X-ray diffraction studies.[170,171] Interestingly, the conformation of the OFCOT ligand varies from puckered to planar as the steric bulk of the ancillary ligands on the adjacent cobalt atoms increases.

Clearly, the 1,2-disubstituted complexes **42** result from the net displacement of two fluorines. The exact mechanism for this transformation is unclear; however, it was demonstrated that **42a** is not produced by a consecutive displacement reaction since treatment of **43a** with a second equivalent of $[Co(CO)_3(PPh_3)]^-$ afforded only **43a**.[170,171] Indeed, this is in marked contrast to the formation of the 1,5-disubstituted complex **38** from the reaction of 2 equiv of $[(\eta^5\text{-}C_5H_5)\text{-}Fe(CO)_2]^-$ with OFCOT.[170,172]

B. Reductive Defluorination Using Organometallic Reagents

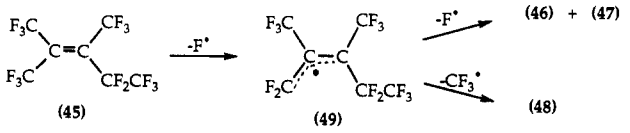
Tatlow and co-workers[173-175] provided the initial reports of high-temperature metal-catalyzed defluorination of cyclic perfluorocarbons to perfluoroaromatics. The authors prepared perfluorotoluene, perfluoroethylbenzene, perfluoro-*p*-xylene, perfluorobiphenyl, and perfluoronaphthalene from the appropriate saturated perfluorocarbons. The process typically consisted of passing the fluorocarbon in a stream of nitrogen through a metal tube packed with small pieces of iron gauze (or fresh nickel turnings[176]) and heated to a temperature of 400–600 °C. Iron fluoride was produced in the defluorination process and was reduced back to metal by passing hydrogen through the tube. This process was later used on an industrial scale for the preparation of fluorinated arenes from the readily available perfluoroalkanes.[30]

Cha and associates[177,178] later extended this metho toward the synthesis of perfluorocyclobutene and fluorinated dienes from the reductive defluorination of acyclic perfluoroalkenes (eq 15). The



authors offer a mechanism to explain the defluorination process involving the initial formation of the intermediate allylic radical **49** (Scheme 1). Preferential loss of

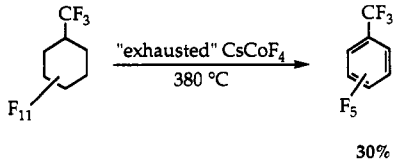
Scheme 1



a fluorine atom from **45** gives the radical **49** which can subsequently lose a second fluorine atom to yield **46** and **47**. Alternatively, loss of a trifluoromethyl radical from **49** would yield **48**.

More recently, Tatlow and colleagues[179] have reported related chemistry at slightly lower temperatures (380–400 °C) using "exhausted" $CsCoF_4$—presumably $CsCoF_3$. Perfluoromethylcyclohexane (eq 16) and perfluoro-1,4-dimethylcyclohexane (eq 17) were passed over this catalyst to yield octafluorotoluene in 30% yield and perfluoro-*p*-xylene in 45% yield, respectively. The authors offered no mechanism to account for the defluorination process.

Interestingly, a low-temperature (155 K and below) decomposition of oligomeric perfluoroalkyl ethers (PFAE) has been reported by Napier and Stair[180,181] on an atomically clean iron surface under ultrahigh vacuum conditions. The decomposition reaction involved the defluorination of the PFAE carbon–oxygen backbone



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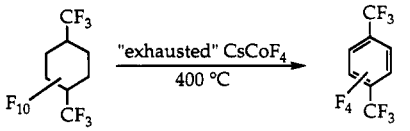


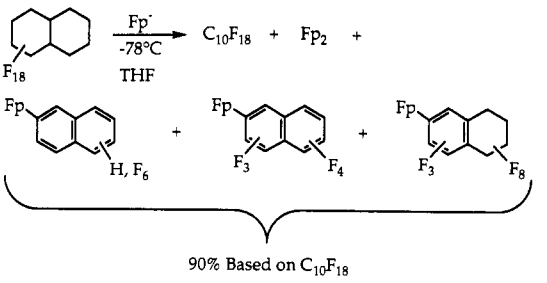
(17)

with formation of iron fluoride, followed by a dissociation of the entire molecule from the iron surface. As determined via X-ray photoelectron spectroscopy and secondary ion mass spectrometry, the decomposition for $CF_3OCF_2CF_2OCF_2CF_3$ and $CF_3OCF_2CF(CF_3)OCF_2CF_3$ was initiated at 140 K at the terminal fluoromethoxy group, and for $CF_3CF_2OCF_2CF_2CF_2OCF_2CF_3$, the decomposition was initiated at 155 K at either CF_3 or CF_2O. This increased reactivity of the terminal CF_3O group toward iron fluoride formation is attributed to the greater electrophilicity of the CF_3O versus CF_2O or CF_3. No detailed mechanistic explanation was presented. According to the authors, the low-temperature threshold for the decomposition reflects the low activation barrier for the C–F activation. Presumably, the driving force for the reaction is the formation of the strong iron–fluorine bonds. The iron fluoride, which exhibits Lewis acidic character, was further observed to catalyze the decomposition of the fluorinated ethers.

In related work, Rabalais and co-workers[182] communicated the decomposition of hexafluorobenzene on a polycrystalline platinum surface via a defluorination pathway affording the deposition of a carbide species, PtC, evolution of F_2, and the formation of platinum fluoride. The defluorination process occurs at room temperature. A detailed mechanism was not provided, although the migration of surface fluorine is thought to be the rate-limiting step for this decomposition reaction.

Smentkowski and Yates[183,184] reported that selective C–F bond activation occurs for CCl_2F_2 at 156 K on an Fe(110) surface. The C–F activation was observed at defect sites on the Fe(110) surface via selective interaction with the fluorines to form iron fluoride and $:CCl_2$. Interestingly, there was no evidence of any C–Cl cleavage processes.

The high reactivity of these clean metal surfaces suggests that appropriately activated metal powders might also react with saturated fluorocarbons. Recently, Harrison and Richmond[22] reported the first examples of reductive defluorination of saturated perfluorocarbons using organometallic nucleophiles. The defluorinations reported were selective, and iron-bound fluorinated aromatic products were isolated. Treatment of perfluorodecalin with Fp^- [Fp = $CpFe(CO)_2$] at −78 °C in tetrahydrofuran affords unreacted perfluorodecalin, Fp_2, and a minimum of three products in 90% yield (eq 18). Simpler organometallic products were obtained from the reaction of perfluoromethylcyclohexane with Fp^- at ambient temperature for 4 h to afford a mixture of unreacted perfluoromethylcyclohexane, Fp_2, and three products in 31% yield (eq 19). The reactions of a variety of other organometallic



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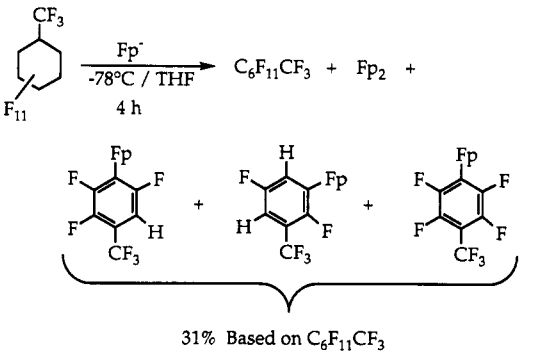
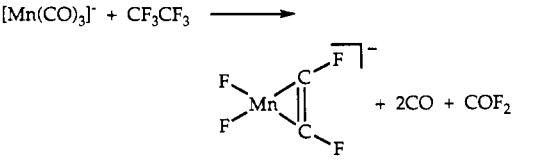
nucleophiles (see section V.A) and perfluorinated substrates were studied. A trend in reactivity which



(19)

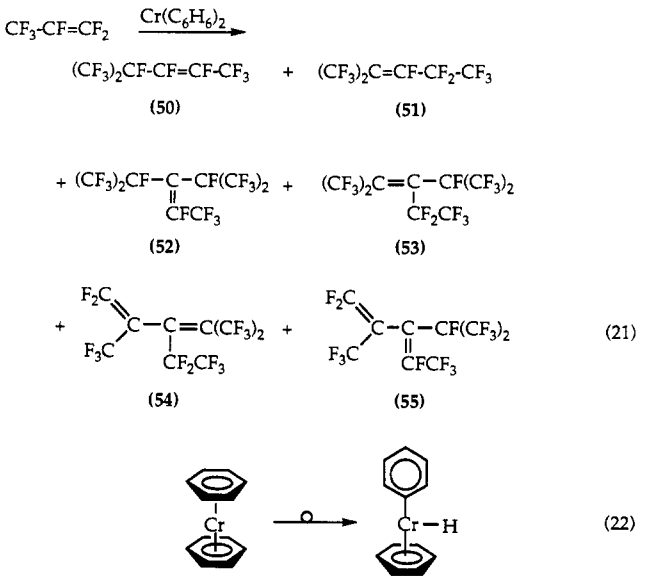
corresponds to the reducing power of the organometallic anion was observed. Consistent with these observations, the authors proposed a mechanism involving a single electron transfer to the fluorocarbon as the first step. In regard to these studies it is important to mention that comparable organic nucleophilic reagents have been technologically useful in the chemical modification of poly(vinylidene difluoride), PVDF.[185] Furthermore, photochemically generated organic radical reducing agents have even been employed to "etch" the surface of Teflon.[186]

Although not a synthetic technique, C–F activation of C_2F_6 by $[Mn(CO)_3]^-$ in the gas phase was reported by Jones and McDonald.[187] Using a flowing afterglow apparatus, $[Mn(CO)_3]^-$ was generated by dissociative electron attachment to $Mn_2(CO)_{10}$ and reacted with C_2F_6 to quantitatively afford the proposed π-bound complex, carbon monoxide, and COF_2 via neutral expulsion (eq 20). The authors did not elaborate on a mechanism for the vicinal defluorination of C_2F_6.



(20)

Huang and colleagues[188–190] have shown that $Cr(C_6H_6)_2$ defluorinates perfluoroolefins as supported by the ambient temperature catalytic oligomerization of perfluoropropene producing two dimers (**50** and **51**), two trimers (**52** and **53**), and two defluorotrimers (**54** and **55**) (eq 21). The reductive defluorination is thought to proceed via the hydrogenation of the trimer **53** followed by the spontaneous elimination of two molecules of HF to yield **54** and **55**.[188,189] Interestingly, the hydrogen source is believed to be a chromium hydride intermediate arising from a η^6–η^1 rearrangement of the $Cr(C_6H_6)_2$ catalyst (eq 22). In contrast, Watson and coworkers[191] believe that the trimers **54** and **55** ensue from fluorine atom abstraction from the initially formed olefins **52** and **53** by low-valent chromium.



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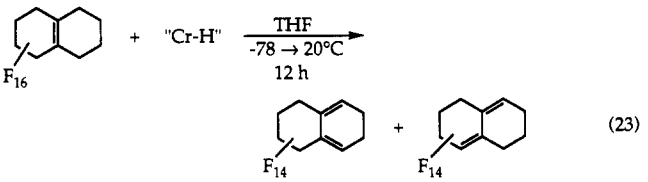
(22)

The intermediate Cr(II) moiety can be independently generated and exhibits the same chemistry with the perfluoroolefin **53** to yield the dienes **54** and **55** in 75% and 25% yields, respectively. A "Cr–H" reagent derived from n-$Bu_3Cr/LiAlH_4$ in THF defluorinates perfluorooctalin to afford two isomers of perfluorohexalin in 83% yield (eq 23).[190]



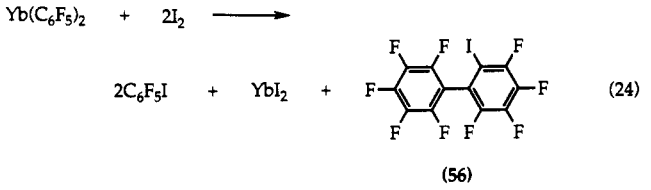
(23)

VI. Activation of C–F Bonds via Electron-Deficient Transition-Metal Reagents

Although relatively uncommon, C–F activation has been observed to occur in a number of reactions of electron-deficient (d^0f^n, or d^1f^n) metal complexes with fluorinated substrates. Due to the highly electrophilic nature of the metal center, these reactions typically involve the heterolytic cleavage of a C–F bond. Electron-transfer pathways are frequently proposed to trigger the C–F activation sequence in these systems. However, α-fluoride abstraction by a coordinatively unsaturated, electron-deficient metal center has also been noted. The high affinity for fluoride as a ligand is a common feature of these systems, and it appears that the great strength of the metal–fluorine bond is the primary driving force for these fluoride abstractions.[2,21] For clarity in this review, electron-deficient metals include lanthanides, actinides, and the transition metals in Groups 3–5. Herein, only well-defined examples of C–F activation promoted by electron-deficient metal complexes will be considered. There are undoubtedly other less well-defined examples of C–F activation in the chemistry of the early transition metals and lanthanide and actinide series because of the great strength of the metal–fluoride bond formed. This property also may limit the possibility of catalytic reactions for these complexes.

A. Lanthanides/Actinides

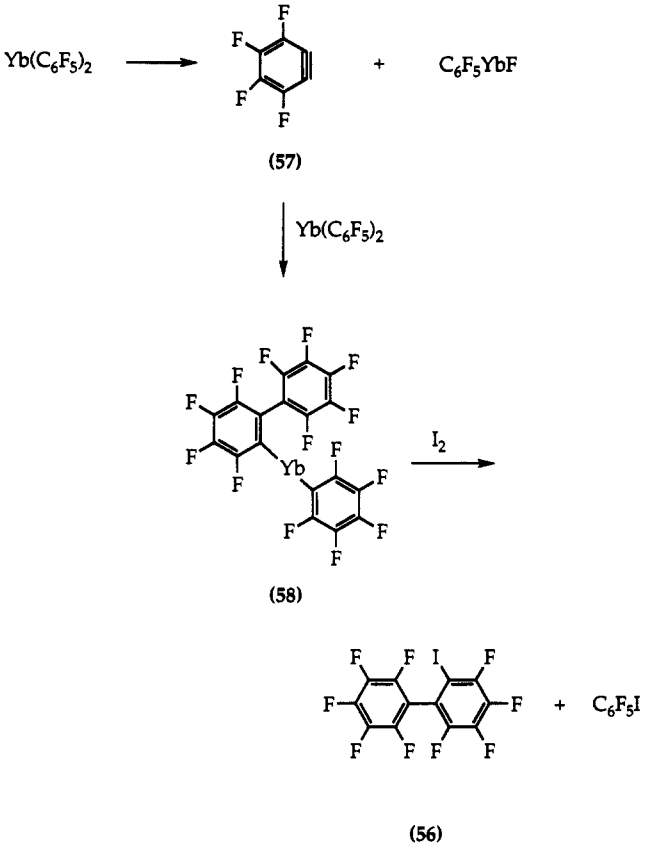
Deacon and co-workers[192] reported that $Yb(C_6F_5)_2$ reacts with I_2 under mild conditions to produce C_6F_5I and YbI_2 in addition to a small amount of unexpected $C_{12}F_9I$ (**56**) in which an *ortho* fluorine has been replaced by a much weaker C–I bond (eq 24). To account for the



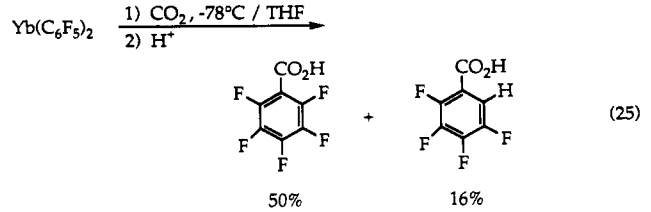
(24)

2-iodononafluorobiphenyl, the authors proposed the intermediacy of tetrafluorobenzyne (**57**) which adds to the starting material to form o-$C_6F_5C_6F_4YbC_6F_5$ (**58**). This complex then reacts with I_2 to form the observed products (Scheme 2). The formation of tetrafluorobenzyne derived products and nonafluorobiphenyl derivatives have similarly been observed in the thermal decomposition of $Yb(C_6F_5)_2$.[125]

Scheme 2



Interestingly, reaction of $Yb(C_6F_5)_2$ with acids resulted in the unexpected net replacement of an *ortho* C–F bond with a C–H bond. Treatment of $Yb(C_6F_5)_2$ with carbon dioxide in tetrahydrofuran at −78 °C for 30 min, followed by acidic workup, afforded pentafluorobenzoic acid in 50% yield and 2,3,4,5-tetrafluorobenzoic acid in 16% yield (eq 25). 2,3,4,5-Tetraflu-



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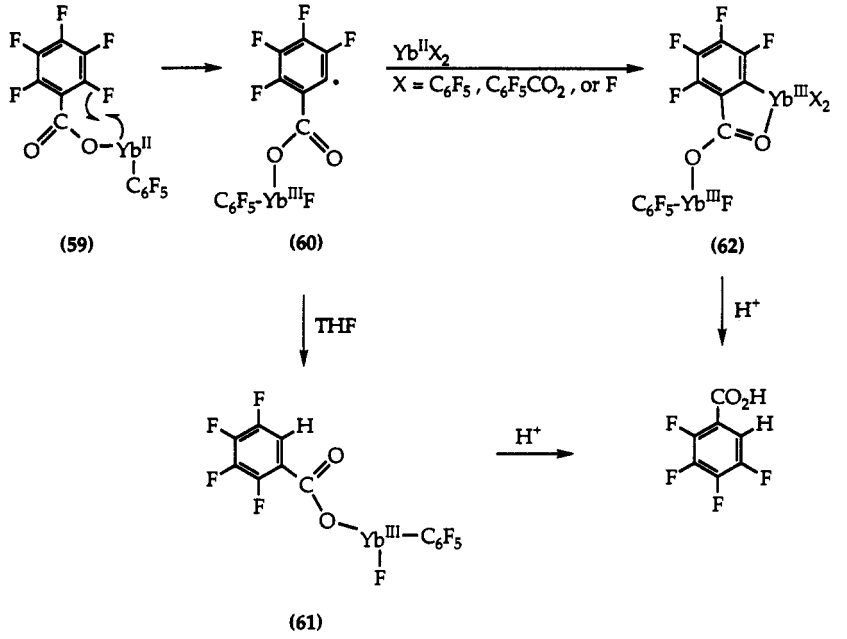
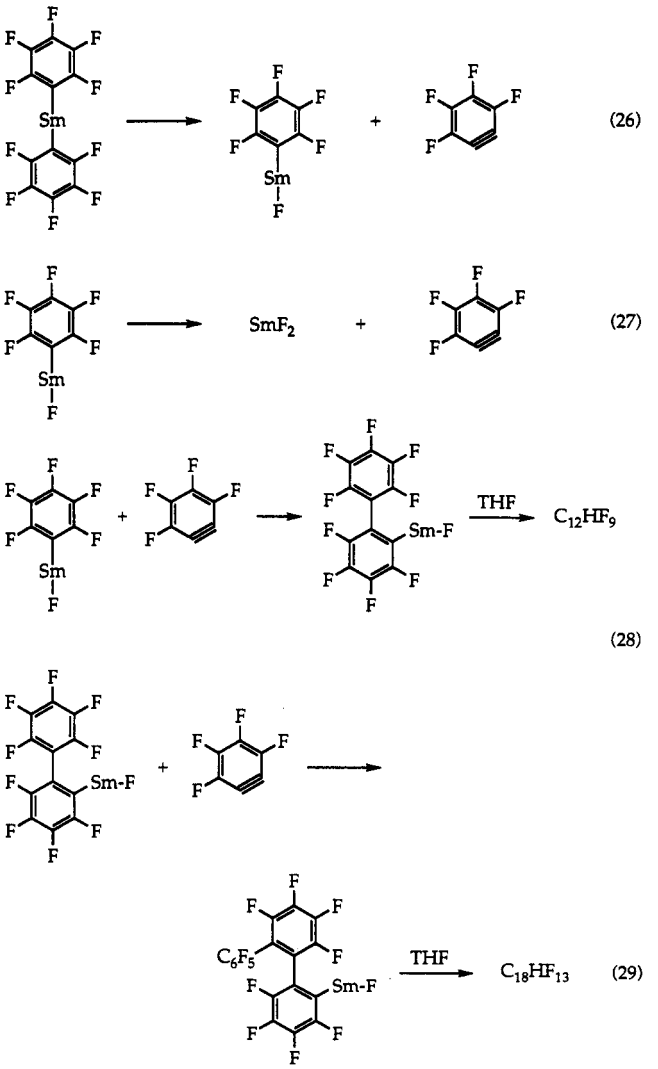
Scheme 3



orobenzoic acid was independently synthesized in 44% yield by reaction of $Yb(C_6F_5)_2$ with pentafluorobenzoic acid. It was determined that no fluoride elimination had occurred from either YbC_6F_5 or C_6F_5H. Consequently, these workers proposed a mechanism that invokes the initial formation of pentafluorobenzoato-(pentafluorophenyl)ytterbium(II) (**59**) from either monocarbonation or a cleavage of $Yb(C_6F_5)_2$ in the presence of $C_6F_5CO_2H$.[192] This compound then undergoes an intramolecular one-electron transfer from ytterbium-(II) to an *ortho* fluorine of the pentafluorobenzoate group as shown in Scheme 3. This results in fluoride elimination and formation of the ytterbium(III) radical complex **60** which can either abstract a hydrogen atom from tetrahydrofuran forming **61** or can undergo further reduction by a ytterbium(II) species giving **62**. Upon workup both **61** and **62** would afford 2,3,4,5-tetrafluorobenzoic acid.[192]

The substitution of *ortho* fluorines has also been observed with the analogous $Sm(C_6F_5)_2$ and $Yb(o\text{-}HC_6F_4)_2$ compounds. The decomposition of these compounds has been studied in detail by Deacon and colleagues,[192] and both tend to follow a path similar to that reported for $Yb(C_6F_5)_2$.[192] Since $Sm(C_6F_5)_2$ and $Yb(o\text{-}HC_6F_4)_2$ undergo identical decomposition processes, we will only discuss the decomposition process for $Sm(C_6F_5)_2$.

Unfortunately, the decomposition of $Sm(C_6F_5)_2$ proceeds with the generation of many complex organic and organometallic products including $C_6F_5SmF_2$, SmF_2, C_6F_5SmF, $C_{12}HF_9$, $C_{18}HF_{13}$, and $SmC_{12}F_9$. The observed products were explained through a series of fluoride elimination and tetrafluorobenzyne insertion reactions (eqs 26–29).[193] The initial products formed are C_6F_5SmF and tetrafluorobenzyne, C_6F_4 (eq 26). Subsequent reaction of C_6F_5SmF forms another molecule of tetrafluorobenzyne and SmF_2 (eq 27). The observation of $C_{12}HF_9$, $C_{18}HF_{13}$, and $SmC_{12}F_9$ is accountable via insertion reactions of tetrafluorobenzyne (from eqs 26 and 27) into perfluoroarylsamarium bonds (eqs 28 and 29).[193] The formation of tetrafluorobenzyne and analogous insertion reactions involving tetrafluorobenzyne has also been reported in the thermal decomposition of LiC_6F_5 (see section IV).[125]



An intriguing example of intermolecular C–F activation was communicated by Burns and Andersen[194] who observed that reaction of $Yb(C_5Me_5)_2$ with hexafluorobenzene in hexanes at 20 °C affords $(C_5Me_5)_2Yb(C_6F_5)$ (**63**) and $(C_5Me_5)_4Yb_2(\mu\text{-}F)$ (**64**) (eq 30). As

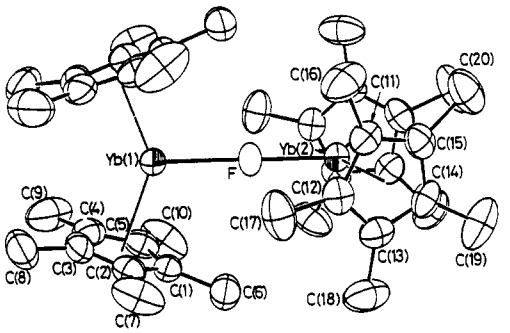
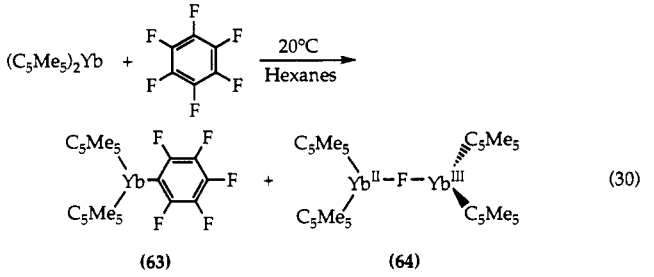


Figure 6. Reprinted with permission from ref 194. Copyright 1989 The Royal Society of Chemistry.

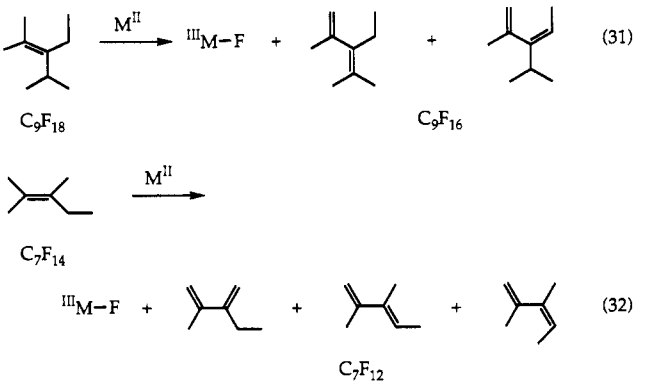
determined by NMR spectroscopy, the C–F bond cleavage was manifested in the formation of the new Yb–C bond in **63**. Additionally, the mixed-valence



binuclear $Yb^{II,III}$ complex with a bridging fluoride ligand was confirmed by X-ray diffraction studies (Figure 6). The Yb^{II}–F–Yb^{III} bond angle was found to be linear, and the bond lengths were 2.317(2) and 2.084(2) Å, respectively, consistent with a mixed-valence complex.

$Yb(C_5Me_5)_2$ was also observed to cleave C–F bonds in $CFHCH_2$, CF_2CH_2, C_2F_4 (84% yield in 4 h), $C_6H_5CF_3$ (67% yield in 14 h), and C_6H_5F (20% yield in 2 weeks) as evidenced by the formation of the dimer complex **64**. Interestingly, no reaction was observed with C_2F_6 or CF_3CH_3, despite their weaker C–F bond strengths versus C_6F_6. The authors remarked that in these systems C–F bond activation is promoted by polarizable functional groups on the fluorocarbons and noncoordinating solvents, implying that a vacant coordination site on the metal is necessary for C–F activation to occur.[194]

In related work, Watson and associates[191] have observed facile bimolecular fluoride abstraction upon reaction of the divalent lanthanoid complexes $(C_5Me_5)_2M{\cdot}OEt_2$ (M = Yb, Sm, Eu) and $(C_5H_4CH_3)_2Yb{\cdot}THF$ with perfluoro-2,4-dimethyl-3-ethylpent-2-ene, C_9F_{18}, or perfluoro-2,3-dimethylpent-2-ene, C_7F_{14}, in toluene or ether solutions to afford the corresponding trivalent lanthanoid fluorides and perfluorodienes, C_9F_{16} or C_7F_{12} (>95% yield) (eqs 31 and 32). The

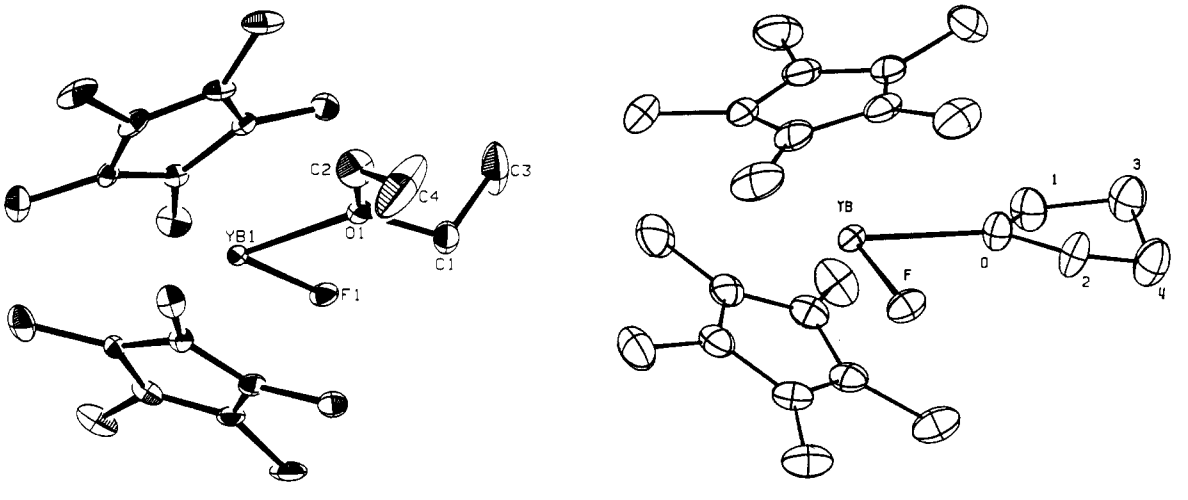


M = $M(C_5Me_5)_2$ (M=Yb, Eu, and Sm) and $Yb(C_5H_4Me)_2$

ytterbium complex $(C_5Me_5)_2YbF$, as both the ether and THF solvates, was characterized by X-ray diffraction. The Yb–F bond lengths were found to be 2.015(4) and 2.026(2) Å, respectively (Figure 7a,b).

As for a mechanism, the authors suggest a radical pathway which is triggered by fluorine abstraction from an allylic sp^3 carbon not unlike the heavier halide abstraction reactions which occur by fast inner-sphere "atom abstraction" processes.[195,196] Interestingly, the rate of fluorine abstraction from the sp^2 carbons in hexafluorobenzene was slower than from the perfluoroolefins. Both the tendency of the divalent species to be oxidized and the strength of the resulting metal–fluorine bond are thought to be the driving forces in these reactions. In analogy to the Burns and Andersen system,[194] these workers note that the reactions are more facile in less coordinating solvents and consequently postulate the existence of a transient fluorocarbon complex, $Cp^*_2M{\cdots}F{-}R$, prior to C–F cleavage.[191]

Watson and associates[191] also observed an increase in both the reaction rates and the yields upon exposure

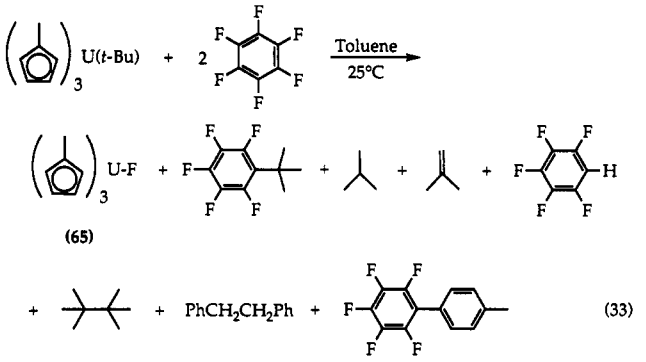


(a) (b)

Figure 7. Reprinted with permission from ref 191. Copyright 1990 American Chemical Society.

of the system to light from a tungsten light bulb ($\lambda >$ 560 nm). Lanthanide ions are well known for possessing long excited-state lifetimes.[197] Thus it was proposed that, in the excited state, the lanthanide metal complex has an enhanced reduction potential and a lifetime sufficiently long enough to react with the perfluoro substrates.[198] The authors suggest that this may be an example of an excited-state reaction with well-defined products.[191]

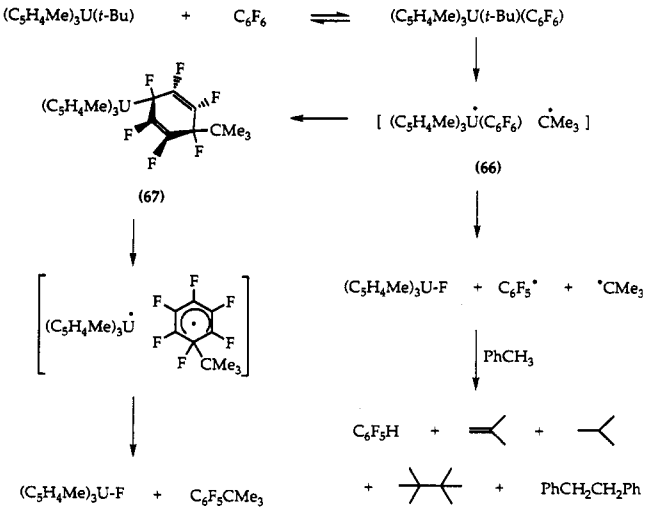
Most recently, Weydert et al.[199] reported that the complex $(C_5H_4Me)_3U(t\text{-Bu})$ engages in intermolecular C–F activation with hexafluorobenzene, benzotrifluoride, perfluoromethylcyclohexane, and perfluorocyclohexane to give $(C_5H_4Me)_3UF$ in high yield. Remarkably, this highly efficient system offers the first well-defined examples of C–F activation by an actinide metal complex. Treatment of the starting material with hexafluorobenzene in a 1:2 ratio in toluene solution at ambient temperature for 24 h affords the uranium(IV) fluoride $(C_5H_4Me)_3UF$ (**65**), in quantitative yield as determined by ^1H NMR (eq 33).[199] In addition to **65**,



(33)

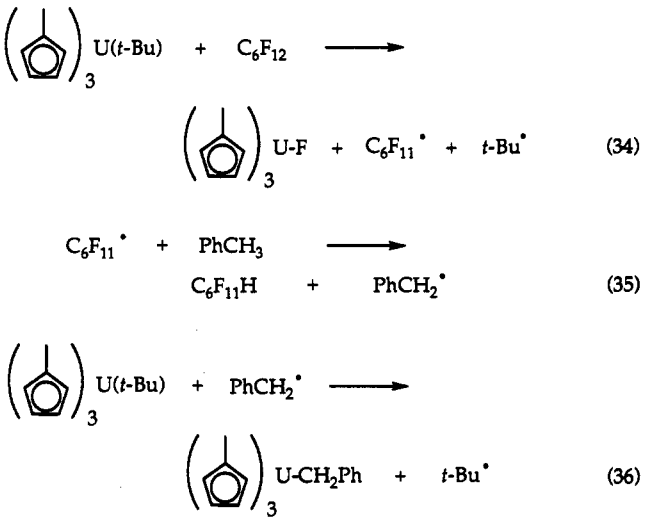
several organic products were formed including $C_6F_5(t\text{-Bu})$, isobutane, isobutene, and C_6F_5H as well as trace amounts of hexamethylethane, bibenzyl, and 2,3,4,5,6-pentafluoro-4′-methylbiphenyl. The organic products observed suggest a radical mechanism. The rate of reaction was determined to be dependent on C_6F_6 concentration, and the observed product distribution was determined to be dependent upon temperature. Accordingly, the authors postulate that an initial attack on $(C_5H_4Me)_3U(t\text{-Bu})$ by C_6F_6 leads to a caged radical pair, **66** (Scheme 4).[199] A *tert*-butyl radical can then

Scheme 4



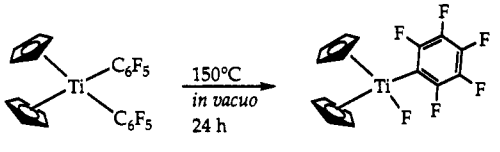
escape from this cage, leading to C_6F_5H and products arising from free *tert*-butyl radical coupling. Alternatively, the *tert*-butyl radical can recombine in the cage with pentafluorophenyl radical to afford **67** which could collapse leading to $C_6F_5(t\text{-Bu})$. A slightly different radical process was proposed for the bimolecular C–F activation reactions of saturated perfluorocarbons with $(C_5H_4Me)_3U(t\text{-Bu})$. Reaction of a 5-fold excess of perfluorocyclohexane and $(C_5H_4Me)_3U(t\text{-Bu})$ in toluene for 12 h at room temperature afforded $C_6F_{11}H$, isobutane, isobutene, and a 1:1 mixture of $(C_5H_4Me)_3U(F)$ and $(C_5H_4Me)_3U(CH_2Ph)$. In contrast to Harrison and Richmond's $[CpFe(CO)_2]^-$ chemistry (see section V.B), this system does not appear to require a tertiary C–F bond to initiate the defluorination sequence of the saturated perfluorocarbon. The products were rationalized by the radical reaction sequence shown in Scheme 5.[199]

Scheme 5



B. Groups 3 and 4: Sc, Y, La, Ac, Ti, Zr, Hf

One of the earliest examples of C–F activation in a d^0 complex came from Stone and co-workers[200,201] who observed that upon pyrolysis $(C_5H_5)_2Ti(C_6F_5)_2$ undergoes an intramolecular fluorine migration to produce $(C_5H_5)_2Ti(C_6F_5)F$ (**68**) in 8.5% yield (eq 37). Decom-



(37)

position of fluoroorganometallic compounds via fluorine migration has been observed in a number of systems[49] and will be discussed in detail later in this review (see section VIII).

More recently, Burk et al.[202] reported that tetrakis(trifluoromethyl)cyclopentadienone (**69**) undergoes rapid reaction at −20 °C with the d^0 bis(cyclopentadienyl)titanacyclobutanes **70a–c** to afford the thermally sensitive titanium fluoride product **71** in approximately 80% yield (eq 38). The products were fully characterized by multinuclear NMR spectroscopy. An X-ray crystallographic study confirmed that a sp^3 C–F bond was broken and a Ti–F bond and a C=C bond were formed (Figure 8). The Ti–F bond length was found

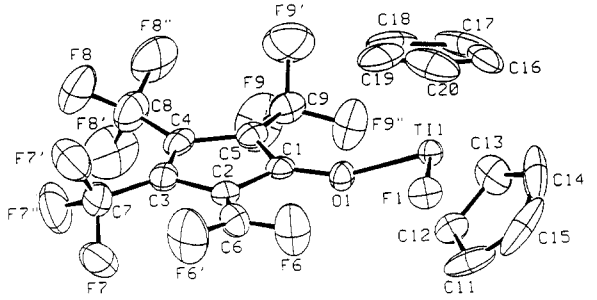
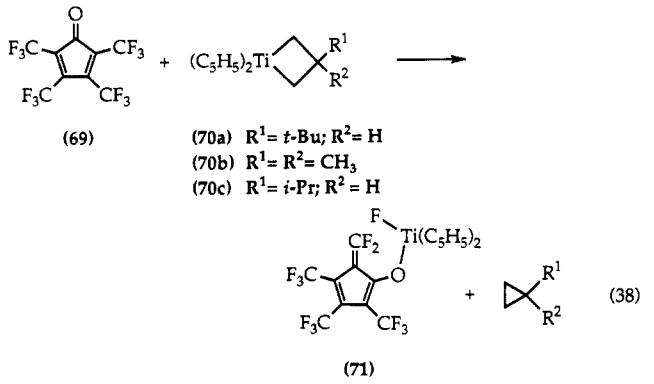
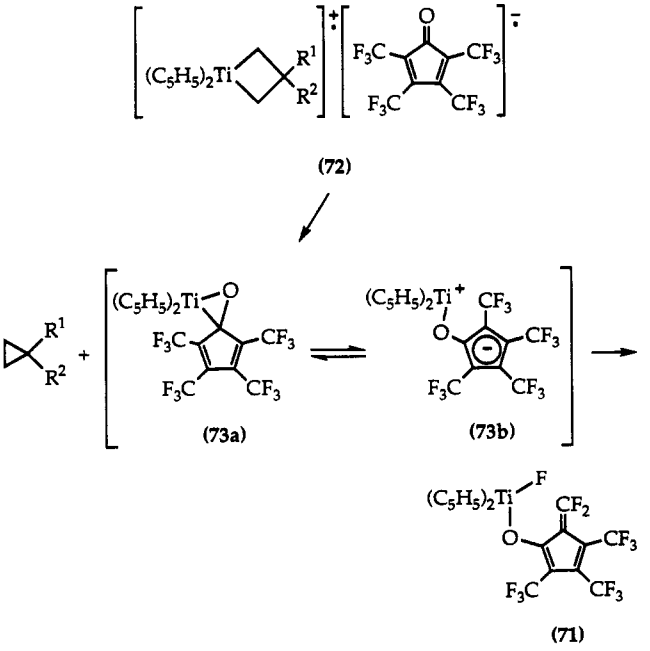


Figure 8. Reprinted with permission from ref 202. Copyright 1990 The Royal Society of Chemistry.



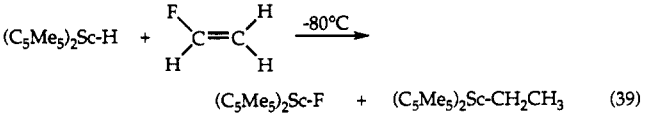
to be 1.838(3) Å with an O–Ti–F angle of 97.6°. Interestingly, the authors postulate a radical mechanism for the transformation involving an initial charge transfer to form the radical ion pair **72** followed by reductive elimination of cyclopropane with subsequent collapse of the ion pair producing a titanocene–dienone complex **73a–b** (Scheme 6).[202] This complex could

Scheme 6

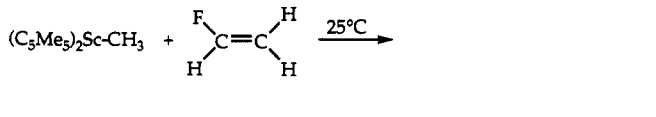


either be coordinated through the carbonyl π system (**73a**) or to the oxygen directly (**73b**). Coordination through the oxygen would put the titanium cation in close proximity to the CF_3 group adjacent to the oxygen, thereby providing a channel for facile fluoride transfer to the electrophilic titanium metal center.[202] Conceptually, this reaction is reminiscent of other Lewis acid-induced fluoride abstractions involving the intermediacy of cationic difluorocarbene complexes (see section VIII.F).[23,70,203–205]

Activation of C–F bonds has been observed in the reaction of permethylscandocene complexes with vinyl fluoride.[206] Treatment of permethylscandocene hydride with vinyl fluoride at −80 °C affords an equimolar mixture of $(C_5Me_5)_2ScF$ and $(C_5Me_5)_2ScCH_2CH_3$ (eq 39). Additionally, $(C_5Me_5)_2ScCH_3$ reacts with vinyl

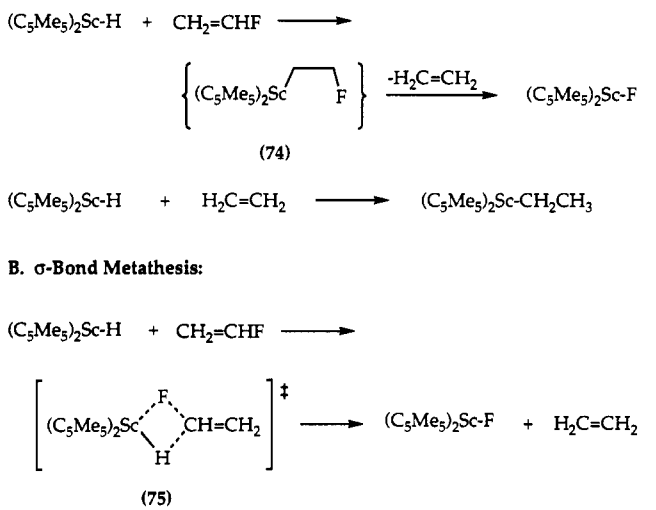


fluoride at 25 °C to form $(C_5Me_5)_2ScF$ and propene (eq 40). To account for the observed reactivity of the



permethylscandocene hydride complex with vinyl fluoride two possible mechanisms were proposed (Scheme 7).[206] Unfortunately, neither mechanism could be

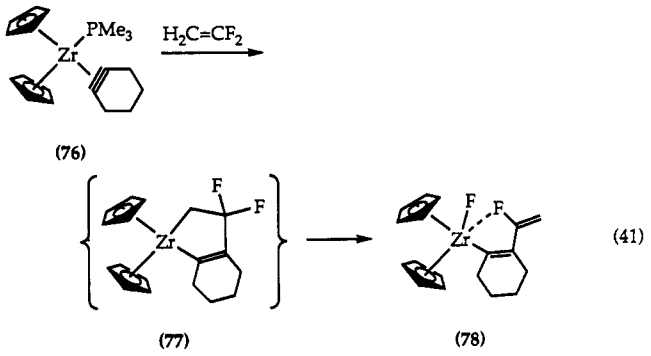
Scheme 7



discounted since no intermediates were observed. In the first mechanism, the vinyl fluoride can insert into the Sc–H bond to form a β-fluoroethyl permethylscandocene intermediate **74**, which then undergoes β-F elimination to form $(C_5Me_5)_2ScF$ and free ethylene.[206] This ethylene can then insert into the Sc–H bond of $(C_5Me_5)_2ScH$ to form the observed $(C_5Me_5)_2ScCH_2CH_3$. This mechanism also explains the reaction of $(C_5Me_5)_2ScCH_3$ with vinyl fluoride. Alternatively, $(C_5Me_5)_2ScH$ and vinyl fluoride can engage in a direct σ-bond metathesis to generate the intermediate **75** which subsequently affords $(C_5Me_5)_2ScF$ and free ethylene.[206] Again, the liberated ethylene could insert into the Sc–H bond of $(C_5Me_5)_2ScH$ to give $(C_5Me_5)_2ScCH_2CH_3$. The activation of carbon–halogen bonds has been previously reported for the reaction of permethylscandocene alkyl complexes with alkyl halides.[207]

An intriguing example of C–F activation involving a zirconium metal center has been noted by Buchwald.[208] Treatment of the zirconocene complex **76** with 1,1-

difluoroethylene affords the zirconocene complex 78 (eq 41). The C–F cleavage is the result of an apparent



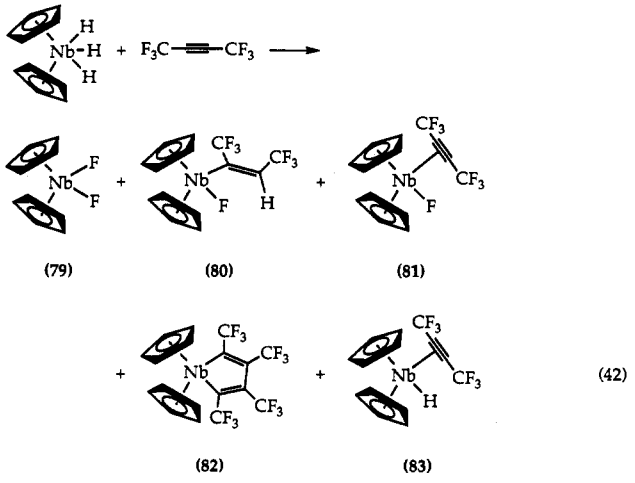
(76) (77) (78) (41)

β-fluoride elimination from the intermediate 77.[208] The major driving force of this reaction is the formation of the strong Zr–F bond.

Morrison[54] has mentioned a conceptually similar reaction involving intermolecular fluoride abstraction by $(C_5Me_5)_2ZrCl_2$ from $Cd(CF_3)_2(DME)$ (where DME is $CH_3OCH_2CH_2OCH_3$) in $CDCl_3$ at −25 °C to yield $(C_5Me_5)_2ZrF_2$. No details on this transformation were available; however, α-fluoride elimination from a $(C_5Me_5)_2Zr(CF_3)_2$ species seems likely. This system further illustrates the great fluoride affinity of the early transition metals.

C. Group 5: V, Nb, Ta

Surprisingly, only one example of C–F activation has been reported for the Group 5 metals. Sala-Pala et al.[209,210] observed that treatment of the d^0 niobium(V) complex $(\eta^5\text{-}C_5H_5)_2NbH_3$ with hexafluoro-2-butyne in toluene or benzene at room temperature affords a mixture of the complexes **79–83** in low to moderate yields (eq 42). The products were characterized using



(79) (80) (81) (82) (83) (42)

mass spectrometry and infrared spectroscopy, as well as ESR and NMR spectroscopy. In all five complexes, the niobium has been reduced. The authors comment that the Nb–F complexes **79–81** which result from C–F cleavage are extremely air sensitive, but compounds **82** and **83** are rather stable. Interestingly, this reaction was also effected by photolysis of a mixture of the niobium complex $(\eta^5\text{-}C_5H_5)_2NbH_3$ with hexafluoro-2-butyne in toluene. The mechanism for this complex transformation was not determined.[209,210]

VII. Activation of C–F Bonds via Electron-Rich Transition-Metal Reagents

Most of the reported C–F activation reactions by transition metals occur at electron-rich d^n ($n \geq 6$) metal centers via an oxidative addition process. Both one-electron and two-electron oxidative additions are known. Most common is the two-electron oxidative addition reaction in which the metal increases its formal oxidation state by two units. However, there are examples of one-electron oxidative additions whereby the metal increases its formal oxidation state by one unit; this is primarily seen for systems in which the metal has an odd number of electrons. In both cases, there is an *overall* two-electron change accompanied by an increase in coordination number at the metal center.

Although oxidative addition reactions are ubiquitous in organometallic chemistry, they are not mechanistically well understood.[211] The question as to whether or not oxidative addition is a concerted or electron-transfer process has been a subject of controversy. There are four fundamental mechanisms that have been proposed for the oxidative addition of aryl and alkyl carbon–halogen bonds to transition metals.[4,5] The first is a free-radical chain mechanism with a stepwise transfer of two electrons. The second and third mechanisms require a concerted transfer of two electrons and involve the direct insertion of the metal into the carbon–halogen bond. These reactions can either be a concerted nucleophilic displacement (S_N2) which is characterized by a two-centered transition state with significant charge separation or a concerted frontside displacement which is characterized by a three-centered displacement with little charge separation. The final mechanism is a radical chain or electron-transfer process which may be partially or completely concerted. It involves variable transition states, making it difficult to distinguish as either a one or two electron-transfer process.

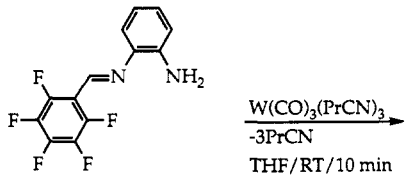
The intramolecular C–X oxidative addition reaction, also known as cyclometalation, is also quite common.[212–215] It is often referred to as *ortho*-metalation when an *ortho* aromatic C–H bond is activated.[216,217] However, there are several examples of aliphatic C–H metalation.[218–222] In these types of reactions a coordinated ligand undergoes an intramolecular metalation forming a chelate ring containing a metal–carbon σ bond.[214] A primary driving force for these reactions is the formation of an unstrained five-membered metallacycle.[223]

Recall that the nucleophilic displacement of fluoride ion from perfluorinated aromatics using organometallic anions is comparable to the classical nucleophilic aromatic substitution reactions found in organic chemistry; substitution of the arene system with a metal deactivates the ring towards further reactivity (see section V. A). Similarly, cyclometalation resulting from a net fluoride abstraction involves nucleophilic substitution when electron-rich transition-metal complexes are employed.[214,224,225] Interestingly, the cyclometalation of *para*-substituted azobenzenes is akin to an electrophilic substitution reaction when electron-deficient palladium(II) metal complexes are used, and the presence of one metalated site on the arene ring actually seems to activate it toward further substitution.[212,214]

For clarity in this review the C–F activation reactions by electron-rich transition-metal complexes will be organized by periodic group.

A. Group 6: Cr, Mo, W

In 1987, Richmond and co-workers[226] reported the first mild high-yield oxidative addition of a C–F bond to a transition-metal center by treating the Schiff base ligand **84** with $W(CO)_3(PrCN)_3$ in tetrahydrofuran for 10 min at room temperature to afford the air-stable seven-coordinate tungsten(II) fluoride (**85**) in 69% yield (eq 43).[226] Likewise, treatment of the unsymmetrical



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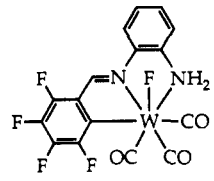
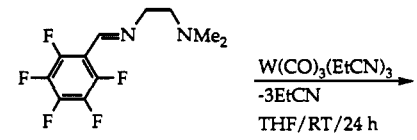


(85) (43)

Schiff base ligand **86** with $W(CO)_3(EtCN)_3$ in tetrahydrofuran for 24 h at room temperature affords **87** in 66% yield (eq 44).[227] These transformations involve chelate-assisted intramolecular C–F activation and provided the first well-defined examples of net insertion of a transition metal into an aromatic C–F bond.[228] Although these ligand-based systems are limited with respect to catalytic chemistry, they do serve as model compounds for systematic studies of structure and reactivity. Both **85** and **87** are air and water stable and have been fully characterized by spectroscopic and crystallographic techniques (Figure 9a, and b, respectively). The geometry of both seven-coordinate structures can be approximated as a capped octahedron with C4 as the capping atom. For compound **85·THF**, a W–F bond length of 2.032(4) Å and a W–C4 bond length of 2.232(6) Å were found with a F1–W–C4 bond angle



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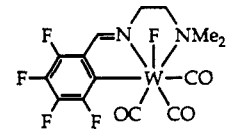
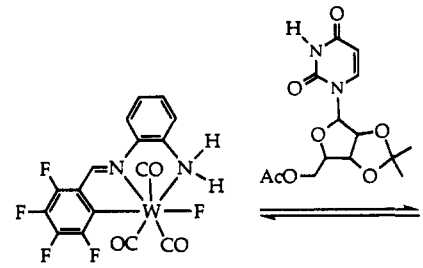
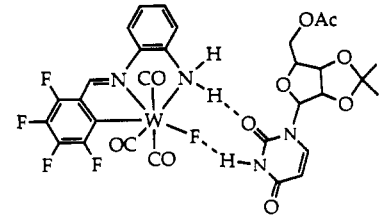


(87) (44)

of 125.5(2)°.[226] For compound **87**, a W–F bond length of 2.029(3) Å and a W–C4 bond length of 2.226(5) Å were determined with a F1–W–C4 bond angle of 131.4-(2)°.[229] Interestingly, **85·THF** formed head-to-tail dimers in the solid state suggesting that these *cis*-amino halide tungsten(II) complexes could function as ditopic molecular receptors for biologically relevant molecules.[230] The proposed interaction of **85** with 2′,3′-*O*-isopropylideneuridine-5′-monoacetate, consistent with the formation of a 1:1 adduct, is shown below (eq 45).[230]

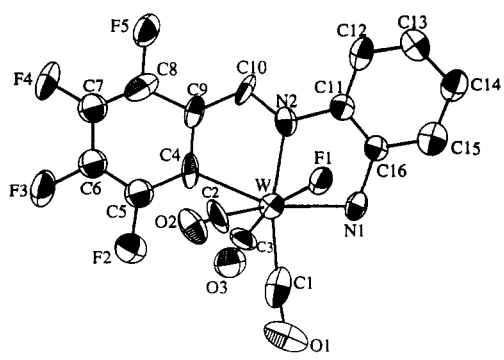


(85)

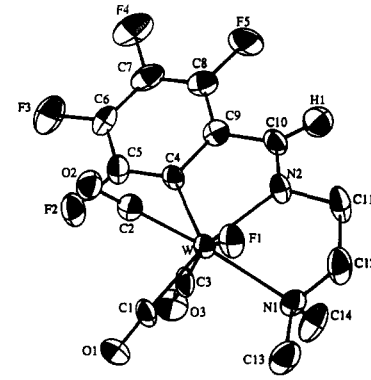


(45)

The fluoride in **87** also forms hydrogen bonds to weak protonic acids such as 4-chlorophenol or water as evidenced by an upfield shift in the ^{19}F NMR signal



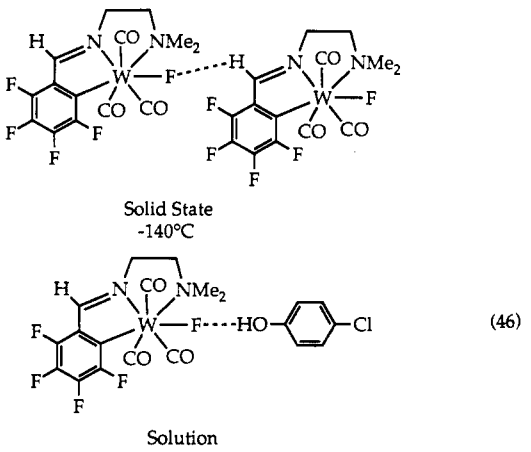
(a)



(b)

Figure 9. (a) Reprinted with permission from ref 226. Copyright 1987 American Chemical Society.

upon complex formation.[227,231] Not surprisingly, the basicity of the fluoride in **87** increases if the aromatic C–F bonds are replaced by C–H bonds and the hydrogen bonding ability approaches that of pyridine. The basicity of these systems has been attributed to the inability of the electronically saturated 18-electron metal center to accept π-donation from the fluoride. Additional evidence for the basicity of the fluoride in **87** is provided by the solid-state packing of the molecules linked by weak sp^2-C–H···F–W hydrogen bonds which were also detected by a reduced C–H stretching frequency in the solid state relative to solution measurements (eq 46).[227]

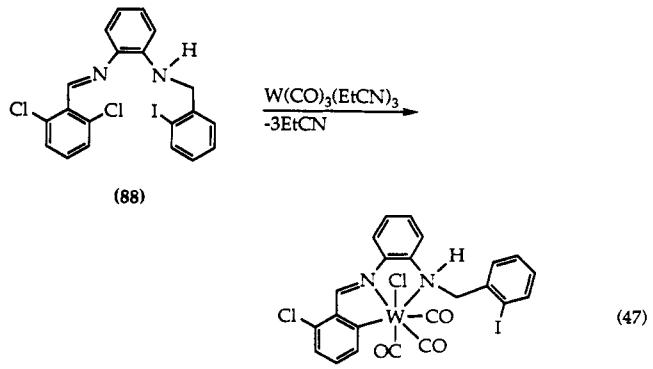


Solid State
-140°C

Solution

(46)

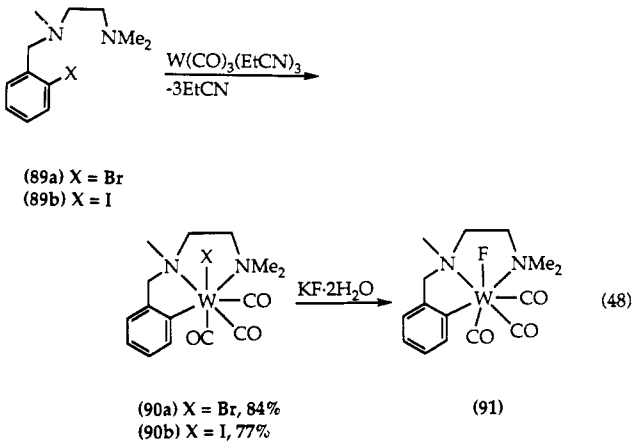
The remarkable ability of these systems to engage in facile C–F oxidative addition processes has been attributed to several factors associated with ligand design. The nitrogen donor ligand supports a very basic metal center which is required for oxidative addition. The chelating nature of the ligand is crucial since it reduces the entropic barrier to reaction by placing the C–F bond in close proximity to the W(0) metal center. No evidence of bimolecular C–F activation of C_6F_6 with $W(CO)_3(PrCN)_3$ has been observed. Finally, the restricted conformation as well as the extended conjugation imparted by the imine moiety in the resulting metallacycle seem to be most important for promoting C–F activation. This has been nicely demonstrated in a competition experiment using the unsymmetrical ligand **88** in which exclusive C–Cl bond (94 kcal/mol)[37] activation on the imine arm of the ligand is observed in the presence of a much weaker C–I bond (63 kcal/mol)[37] on the saturated arm of the ligand (eq 47).[232]



(88)

(47)

Furthermore, unlike the Schiff base ligand system, activation of C–F bonds does not take place using the saturated η^3-[C,N,N'] aryl halide ligand **89**.[233] Treatment of the ligand **89** with $W(CO)_3(EtCN)_3$ results in the facile oxidative addition of the C–X bond (X = Br, I) to afford the W(II) bromide **90a** or iodide **90b** in 84% and 77% yield, respectively (eq 48).[233] Although the



(89a) X = Br
(89b) X = I

(90a) X = Br, 84%
(90b) X = I, 77%

(91)

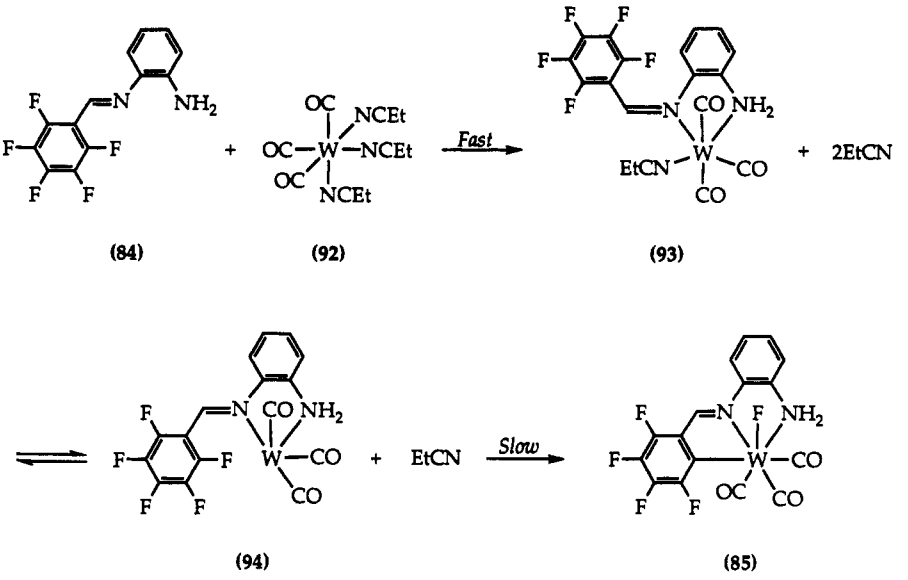
(48)

fluoride complex **91** cannot be formed by oxidative addition, it is readily prepared by metathesis with $KF{\cdot}2H_2O$.[233] It is interesting to note that even with the pentafluorophenyl derivative of ligand **89** C–F activation was not observed.[234]

Similar to other nucleophilic aromatic substitution processes, including the nucleophilic displacement of fluoride by organometallic anions, increasing the fluorination on the pendant aromatic ring enhances the rate of C–F oxidative addition.[235] The most facile reactions occur with pentafluorinated aryl rings. As the number of fluorine atoms is increased, the aryl carbon atoms become more susceptible to nucleophilic attack.[236] Additionally, there is increased thermodynamic stability of M–C bonds with increasing fluorination of the organic unit.[43,45,48,49,237] However, both mono- and difluoro-substituted aromatic rings have undergone oxidative addition of a C–F bond at tungsten(0).[238] The resulting tungsten(II) fluorides are stable, indicating that these C–F activation reactions are governed by kinetic rather than thermodynamic factors.

On the basis of kinetic studies, Richmond and coworkers have proposed a two-step mechanism for the chelate-assisted C–F activation reactions in these Schiff base systems (Scheme 8).[231,235] The first step involves the substitution of two labile nitrile ligands in **92** by the chelate backbone of the ligand **84** to afford the isolable mononitrile complex **93**. This 18-electron complex subsequently loses the remaining nitrile ligand to yield a proposed 16-electron intermediate complex **94** which can oxidatively add the aromatic C–F bond to afford the observed product **85**.[229,231] Unfortunately, the coordinatively unsaturated intermediate has not been detected by either NMR or IR spectroscopy. The insertion of the metal into the C–F bond of the 16-electron intermediate is believed to be the rate-determining step.[235] It was determined that the rate of oxidative addition increases in the series F $\ll$ Cl < Br < I and that electron-withdrawing groups enhance the rate of C–F activation as evidenced by a faster relative rate of reaction for the perfluorinated versus the difluorinated ligand systems.[235] Furthermore, for the related chloro ligand system, a Hammett plot gave ρ = 2.8.[235] Arguably a nucleophilic process, it was suggested that these observations are consistent with

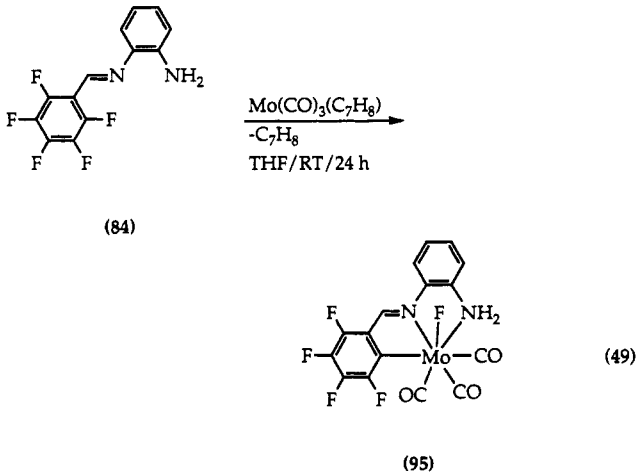
Scheme 8



(84) (92) (93) (94) (85)

a concerted three-centered pathway for the oxidative addition.[235]

Richmond and associates[229,239] successfully extended the carbon–fluorine activation in fluorinated Schiff base ligands to include reactions at molybdenum(0). Treatment of $Mo(CO)_3(THF)_3$, generated in situ from either $Mo(CO)_3$(diglyme) or $Mo(CO)_3(C_7H_8)$, with the Schiff base ligand **84** at ambient temperature for 24 h affords the molybdenum(II) fluoride complex **95** in 40% yield (eq 49).[239] Surprisingly, the major side product in the



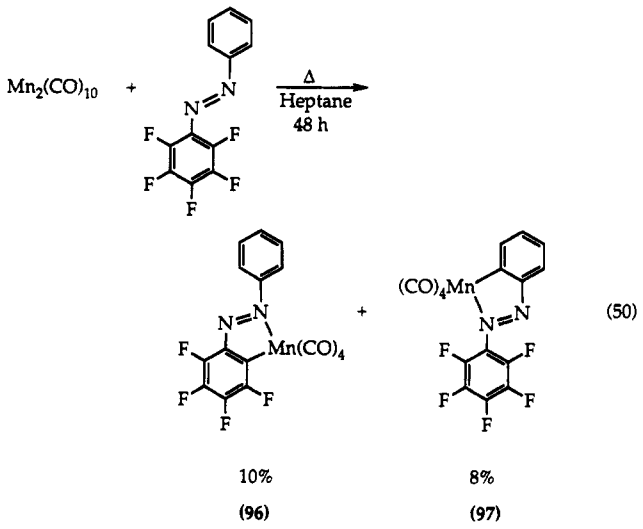
(84) (95) (49)

reaction was $Mo(CO)_6$.[229] Coordinatively unsaturated W(0) complexes have been known to scavenge free carbon monoxide in solution.[228,231,238] However, in the tungsten systems the inert $W(CO)_4$(Schiff base ligand) complexes were isolated. Spectroscopic and physical parameters of **95** are quite similar to **85**, but the molybdenum complex is slightly air sensitive.[239]

B. Group 7: Mn, Tc, Re

Early work by Bruce and co-workers[224,225,236] showed that low-valent metal centers react with fluorinated azobenzenes to afford cyclometalated products via fluorine abstraction. These reactions are typified by forcing conditions and low yields. Specifically, reaction of $Mn_2(CO)_{10}$ with pentafluoroazobenzene for 48 h in refluxing heptane affords the cyclometalated products **96** and **97** in 10% and 8% yields, respectively (eq 50).

Although **96** is clearly formed via metalation by nucleophilic displacement of fluoride, the exact fate of the fluorine was not determined. However, to account



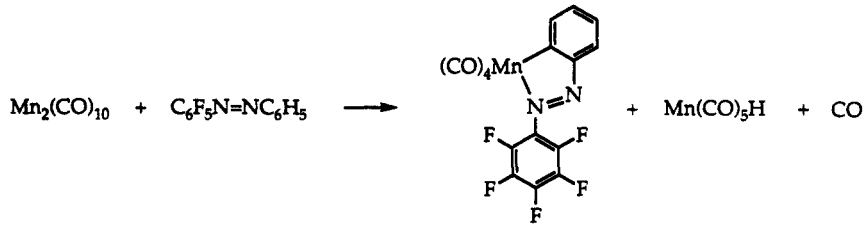
10% 8% (50)

(96) (97)

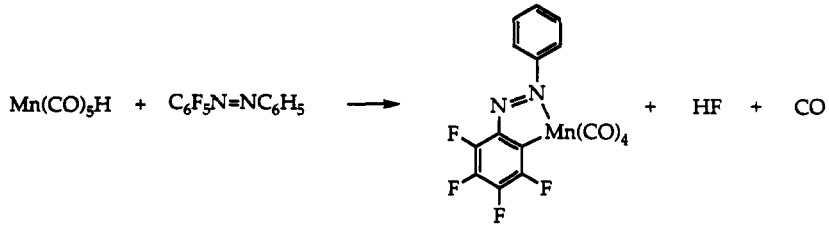
for the observed products, the authors postulated a mechanism which involves the initial formation of the metalated product **97** and $Mn(CO)_5H$ (Scheme 9). This manganese pentacarbonyl hydride undergoes a subsequent reaction with pentafluoroazobenzene to form the cyclometalated product **96** with elimination of the *ortho*-fluorine as hydrogen fluoride. This circuitous route helps to explain the low yield of **97**.[224] It was later noted that reaction of $Mn_2(CO)_{10}$ with decafluoroazobenzene produces the fully fluorinated *ortho*-metalated complex. Unfortunately, no details for this reaction were supplied by the author.[214]

Interestingly, the thermal reaction of pentafluoroazobenzene with $Mn(CO)_5CH_3$ did not result in any C–F activation nor did the reaction with $Re_2(CO)_{10}$.[224] While the reaction of $Re(CO)_5CH_3$ with pentafluoroazobenzene afforded the *ortho*-metalated species **98** with metalation of the nonfluorinated aromatic ring as the major product, a minor product resulting from C–F bond cleavage was observed, **99** (eq 51).[224] It was speculated that the minor product was formed by the dimerization of the *ortho*-metalated product and that

Scheme 9

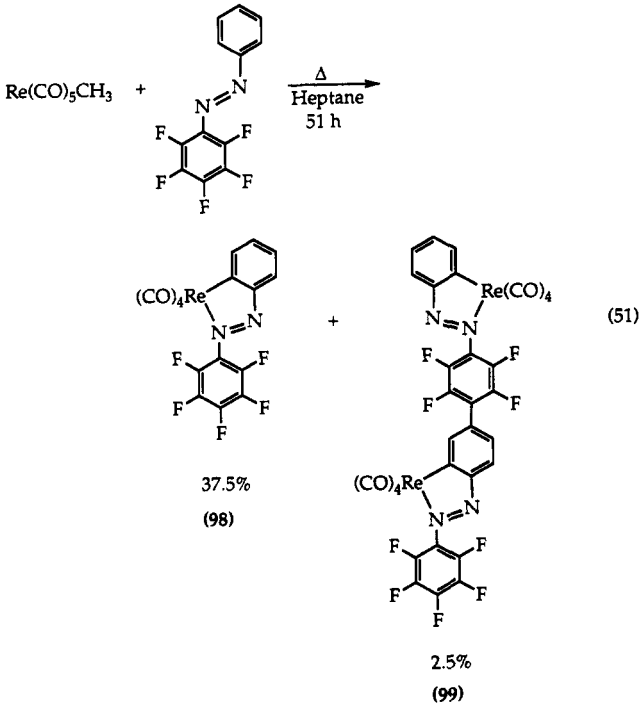


(97)



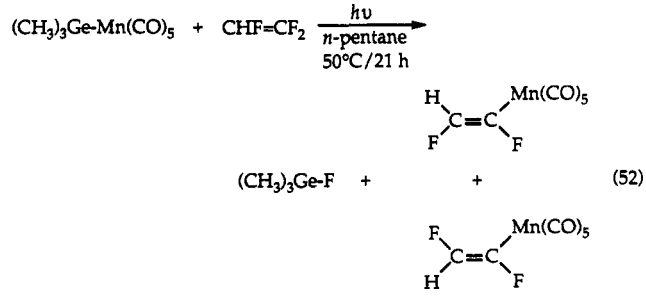
(96)

coupling occurred by the loss of an aromatic fluorine atom. The structure was proposed on the basis of mass spectrometry and infrared spectroscopy.[224]



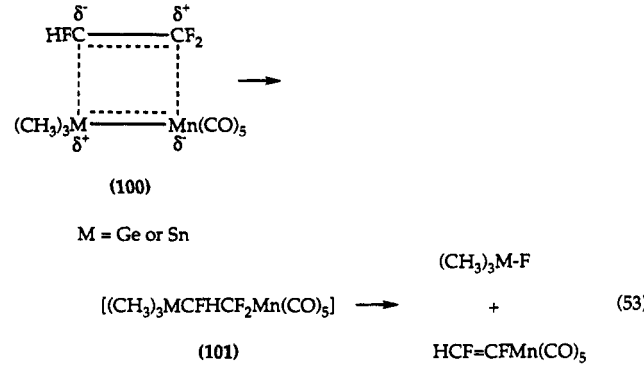
(51)

Clark and co-workers exploited the ionic character of Mn–Sn[240] and Mn–Ge[241] bonds to promote C–F activation in fluoroolefins. Photolysis of $(CH_3)_3GeMn(CO)_5$ with trifluoroethylene in *n*-pentane at 50 °C for 21 h afforded trimethylfluorogermane and a mixture of (*cis*- and *trans*-1,2-difluorovinyl)pentacarbonylmanganese (eq 52). The analogous products were also produced in the reaction of trifluoroethylene with $(CH_3)_3SnMn(CO)_5$. The driving force for the fluorine abstraction in these reactions appears to be the stability and high lattice energy of $(CH_3)_3SnF$ and $(CH_3)_3GeF$. The authors suggested a mechanism that involves the initial insertion of the olefin into the ionic M–Mn bond (M = Ge or Sn) to generate **101** (eq 53). This was explained via a highly polarized four-centered transition state (**100**). Subsequent fluorine atom migration would



(52)

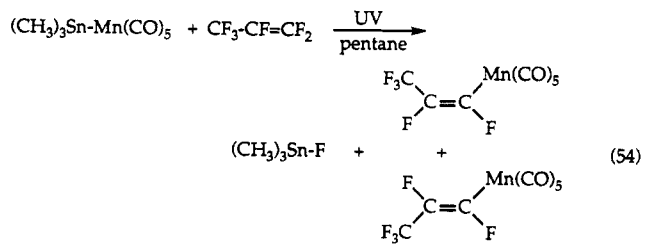
afford the observed products. Alternatively, one could view these reactions as essentially involving an attack of the $Mn(CO)_5^-$ anion on the olefin.



(53)

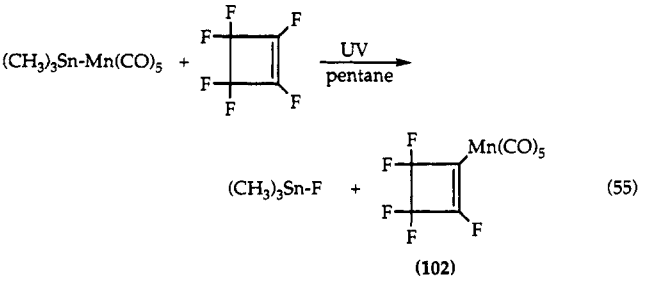
In support of the proposed mechanism, reaction of either $(CH_3)_3SnMn(CO)_5$ or $(CH_3)_3GeMn(CO)_5$ with tetrafluoroethylene primarily gives the insertion products $(CH_3)_3SnCF_2CF_2Mn(CO)_5$ and $(CH_3)_3GeCF_2CF_2Mn(CO)_5$, respectively. However, the Sn–Mn derivative is rather unstable and decomposes. Interestingly, thermal reaction with ethylene generates the coordination complexes $(CH_3)_3SnMn(CO)_4(C_2H_4)$ and $(CH_3)_3GeMn(CO)_4(C_2H_4)$ by displacement of carbon monoxide.

In related work, Clark and associates[242] reported that reaction of perfluoropropene with $(CH_3)_3SnMn(CO)_5$ at 25 °C in pentane under ultraviolet irradiation affords trimethyltin fluoride and a mixture of *cis*- and *trans*-$CF_3CF{=}CFMn(CO)_5$ (eq 54). Not surprising, a similar product mixture was observed from the reaction of



(54)

$(CH_3)_3GeMn(CO)_5$ with perfluoropropene.[241] Furthermore, the reaction of $(CH_3)_3SnMn(CO)_5$ with perfluorocyclobutene at 25 °C under ultraviolet irradiation gives trimethyltin fluoride and perfluorocyclobutenylmanganese pentacarbonyl **102** (eq 55).[242,243] Again, the



(55)

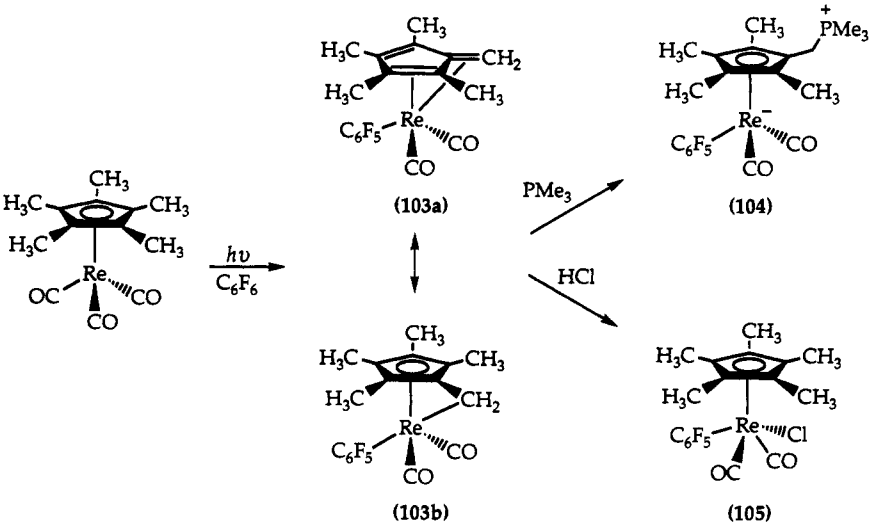
(102)

mechanisms of these reactions were believed to proceed via a four-centered-type transition state analogous to **100** as shown in eq 53.[241-243]

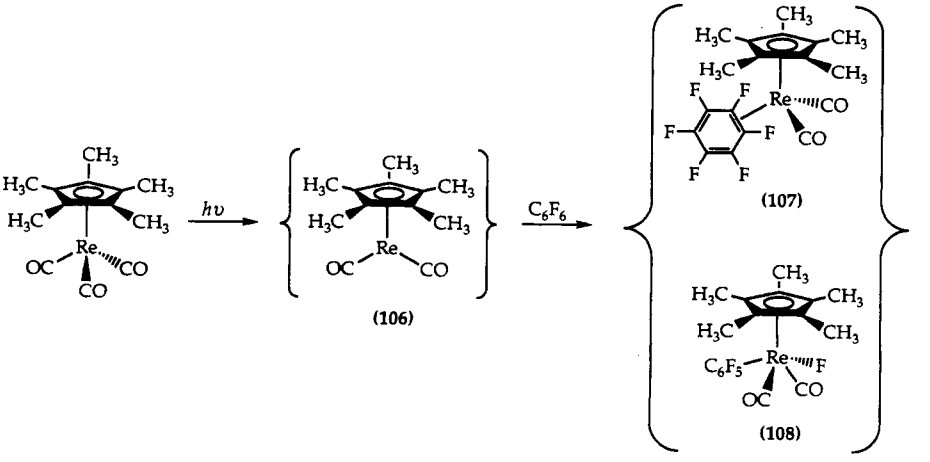
A rare example of intermolecular C–F activation employing a rhenium metal center was communicated by Perutz and co-workers.[244] Ambient temperature photolysis ($\lambda > 285$ nm) of $[Re(\eta^5\text{-}C_5Me_5)(CO)_3]$ in neat hexafluorobenzene for 8 h afforded $[Re(\eta^6\text{-}C_5Me_4CH_2)(CO)_2(C_6F_5)]$ (**103**) in 60% yield (Scheme 10). The product **103**, verified by X-ray crystallographic analysis, is the result of an intermolecular C–F bond activation followed by an intramolecular C–H bond activation and loss of HF. The bonding of the $(\eta^6\text{-}C_5Me_4CH_2)$ ligand in **103** can be represented by two canonical forms, η^6-conjugated triene (tetramethylfulvene) **103a** or η^5-tetramethylcyclopentadienyl σ-alkyl ("tucked-in") **103b**.[244] There is spectroscopic support for both isomers. Adding to the uncertainty, reactions of **103** with PMe_3 and with HCl show that the $(\eta^6\text{-}C_5Me_4CH_2)$ ligand is subject to both nucleophilic and electrophilic attack to give the complexes **104** and **105**, respectively.

With respect to the C–F bond activation reaction, the authors postulate that, upon irradiation, $[Re(\eta^5\text{-}C_5Me_5)(CO)_3]$ expels carbon monoxide to generate an unsaturated 16-electron fragment $[Re(\eta^5\text{-}C_5Me_5)(CO)_2]$ (**106**) which reacts with hexafluorobenzene to form $[Re(\eta^5\text{-}C_5Me_5)(CO)_2(\eta^2\text{-}C_6F_6)]$ (**107**) or a C–F oxidative addition product $[Re(\eta^5\text{-}C_5Me_5)(CO)_2(C_6F_5)(F)]$ (**108**) (Scheme 11).[244] No intermediates were detected. Perutz and co-workers proposed that **107** is an intermediate prior to C–F oxidative addition.[244] This is

Scheme 10



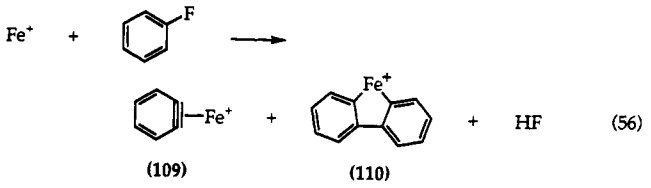
Scheme 11



supported by the isolation and characterization of the analogous $[Re(\eta^5\text{-}C_5H_5)(CO)_2(\eta^2\text{-}C_6F_6)]$.[245] As will be discussed shortly, Perutz and colleagues[246,247] have demonstrated similar reactivity with rhodium and iridium complexes and have elegantly shown that hexafluorobenzene reacts in two sequential photochemical steps to yield first the η^2-arene coordination product and then the C–F oxidative addition product.

C. Group 8: Fe, Ru, Os

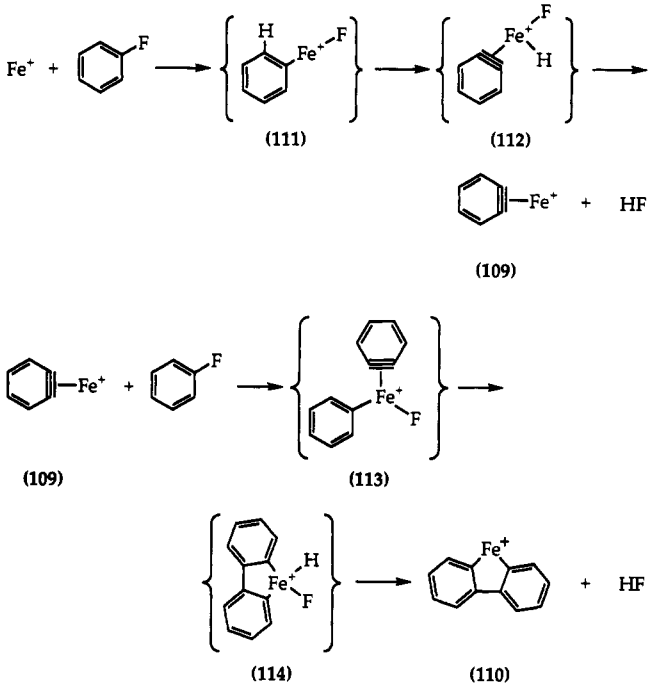
Examples of iron metal centers engaging in C–F activation have essentially been limited to gas-phase reactions. Independent studies by Ridge and coworkers[248] and Bjarnason and Taylor[249] have shown that iron ions react with fluorobenzene to afford a mixture of $Fe(C_6H_4)^+$ (**109**), $Fe(C_6H_4)_2^+$ (**110**), and HF (eq 56).



(109) (110) (56)

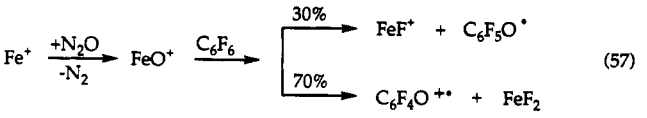
Both groups suggest insertion of the metal into the C–F bond to yield **111** as the initial step (Scheme 12).

Scheme 12



Subsequent dehydrohalogenation via **112** would afford the observed iron benzyne complex ion (**109**) and hydrogen fluoride. This complex ion can then react with another molecule of fluorobenzene in an identical fashion to afford the observed iron diphenylene complex ion (**110**) and another equivalent of hydrogen fluoride. Analogous reactivity has been reported for the reaction of iron ions with chlorobenzene and bromobenzene.[248,249] Upon examination of the gas-phase reactions of $Fe(C_6H_4)^+$ with alkyl halides, Freiser and associates[250] observed similar metal insertions into carbon–halogen bonds followed by dehydrohalogenation. However, only the formation of the condensation product, $FeC_7H_7F^+$, was observed with CH_3F.

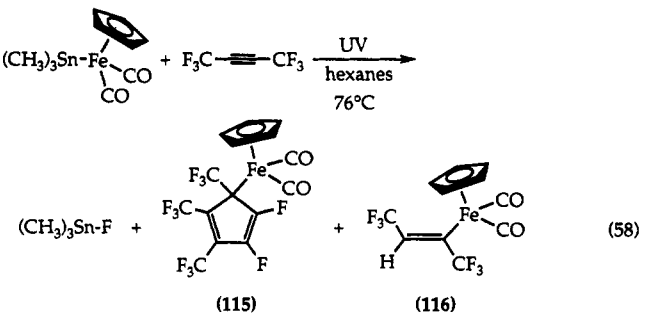
In related work, Schwarz and colleagues[251] noted that C–F activation takes place in the gas phase upon reaction of FeO^+ with hexafluorobenzene as evidenced by the generation of "bare" FeF^+ and $C_6F_5O^\bullet$ in 30% yield and FeF_2 and $C_6F_4O^{\bullet+}$ in 70% yield (eq 57). The



(57)

cationic metal–oxo species FeO^+ was generated from thermalized Fe^+ in the presence of N_2O. No mechanism for these transformations was presented.[251]

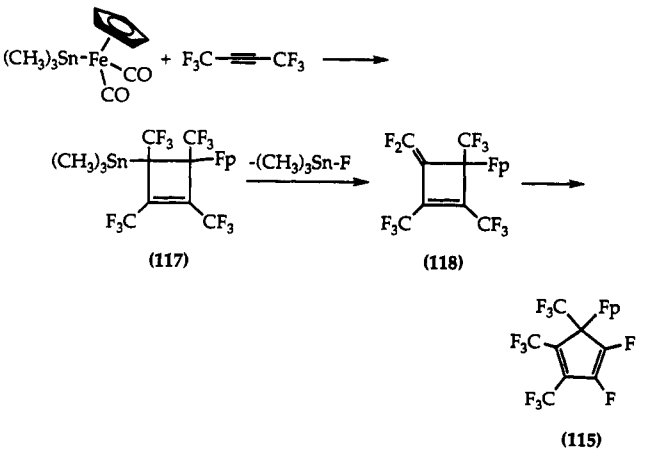
As a supplement to their studies on the reactivity of metal–metal bonds, Clark and associates[242] reported that reaction of $(CH_3)_3Sn\text{–}Fe(CO)_2(\eta^5\text{-}C_5H_5)$ with hexafluoro-2-butyne in hexanes at 76 °C under ultraviolet irradiation affords trimethyltin fluoride and the cyclopentadienyl iron complex **115** as the major product with small amounts of the *trans*-butenyl iron compound **116** (eq 58). Interestingly, no reaction was observed at



(115) (116) (58)

ambient temperatures under ultraviolet irradiation. In accord with the Mn–Sn and Mn–Ge chemistry discussed earlier, the authors rationalized the formation of **115** via the initial generation of the unstable cyclobutenyl iron complex **117** which rapidly undergoes β-elimination of $(CH_3)_3Sn\text{–}F$ to yield the exocyclic complex **118** (Scheme 13).[242] Subsequent rearrangement would then

Scheme 13

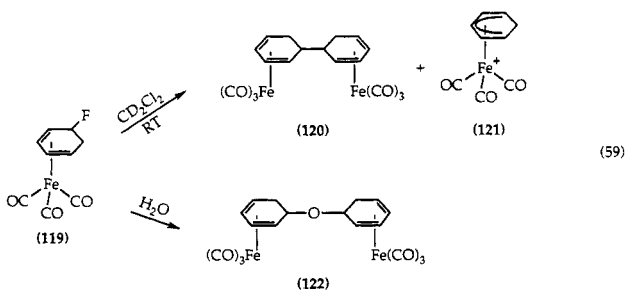


(117) (118) (115)

afford the observed product **115**. The authors invoke an ill-defined radical process to account for the production of the minor product **116**.[242]

Recently, Powell and Horvath[252] reported that the fluoro complex $(\eta^4\text{-}C_6H_7F)Fe(CO)_3$ (**119**) decomposes on standing at room temperature for 22 h to give the carbon–carbon linked dimer $(\eta^4\text{-}C_6H_7)_2Fe_2(CO)_6$ (**120**) as the major product along with small amounts of the

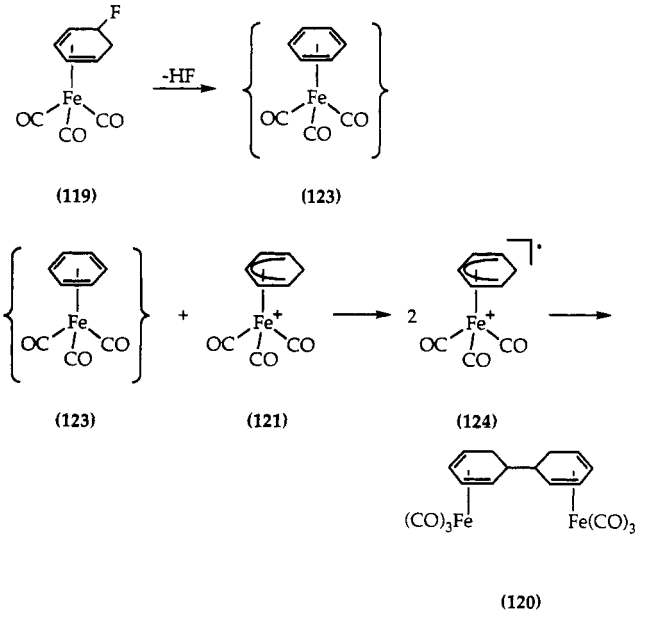
cation $[(\eta^5\text{-}C_6H_7)Fe(CO)_3][BF_4]$ (**121**) (eq 59). The fluoro complex **119** is also hydrolytically unstable and in the presence of water reacts to give the oxygen-linked dimer $[(\eta^4\text{-}C_6H_7)_2O]Fe_2(CO)_6$ (**122**).



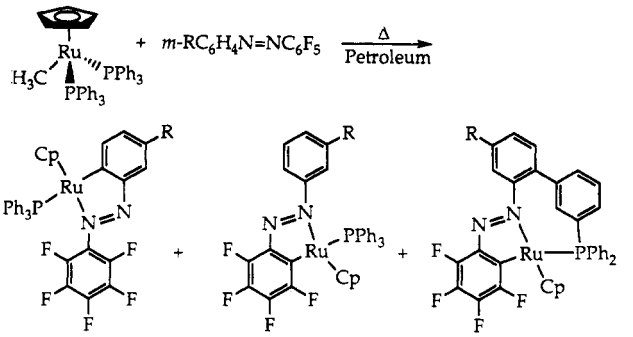
(59)

The C–F bond cleavage is realized upon elimination of HF from the 18-electron fluoro complex **119** to generate the kinetically unstable 20-electron species $(\eta^6\text{-}C_6H_6)Fe(CO)_3$ (**123**). Electron transfer from this intermediate to the cation **121** produces the 19-electron radicals $[(\eta^5\text{-}C_6H_7)Fe(CO)_3]^\bullet$ (**124**) which can couple to afford the observed C–C dimer product **120** (Scheme 14).[252]

Scheme 14



In 1976, Bruce and co-workers[225,236] reported the formation of metalated azobenzene derivatives by fluorine abstraction using the nucleophilic ruthenium complex $(\eta^5\text{-}C_5H_5)Ru(PPh_3)_2(CH_3)$. In all the reactions examined the fate of the abstracted fluorine was not determined. Treatment of the pentafluoroazobenzene $m\text{-}RC_6H_4N{=}NC_6F_5$ (R = H, CH_3, CF_3) with $(\eta^5\text{-}C_5H_5)$-$Ru(PPh_3)_2(CH_3)$ in refluxing petroleum produces the metalated complexes **125**, **126**, and **127** (eq 60). Although the major product **125** was from the metalation of the C_6H_5 ring, the two minor products, **126** and **127**, resulted from C–F activation or metalation of the C_6F_5 ring. Complex **127** underwent an unusual intramolecular reaction in which one of the phenyl groups on a PPh_3 ligand coupled to the phenyl group on the chelating azobenzene ligand. Interestingly, although two isomers are possible for R = CH_3 and CF_3, only one isomer was observed with R *para* to the ruthenium metal center. The mechanism for these reactions is

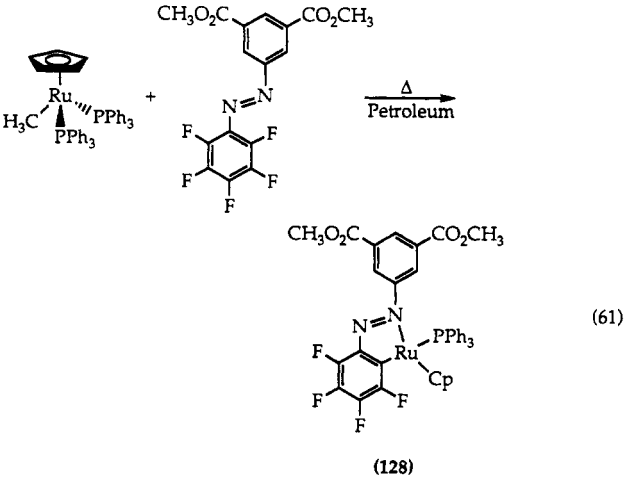


(125a) R = H, 19% **(126a)** R = H, 15.5% **(127a)** R = H, 9%
(125b) R = CH_3, 11.5% **(126b)** R = CH_3, 9% **(127b)** R = CH_3, 6%
(125c) R = CF_3, 16% **(126c)** R = CF_3, 9% **(127c)** R = CF_3, 6%

(60)

unknown. However, $(\eta^5\text{-}C_5H_5)RuF(PPh_3)_2$ was isolated from an independent synthesis. As such, one plausible mechanism involves the oxidative addition of C–F to the ruthenium center followed by the reductive elimination of CH_3F.[225]

Only one complex (**128**) was isolated (21% yield) from the reaction of $3,5\text{-}(CH_3OCO)_2C_6H_3N{=}NC_6F_5$ with $(\eta^5\text{-}C_5H_5)Ru(PPh_3)_2(CH_3)$ and is formed by metalation of the C_6F_5 ring (eq 61).[225] The lack of C–H activation was

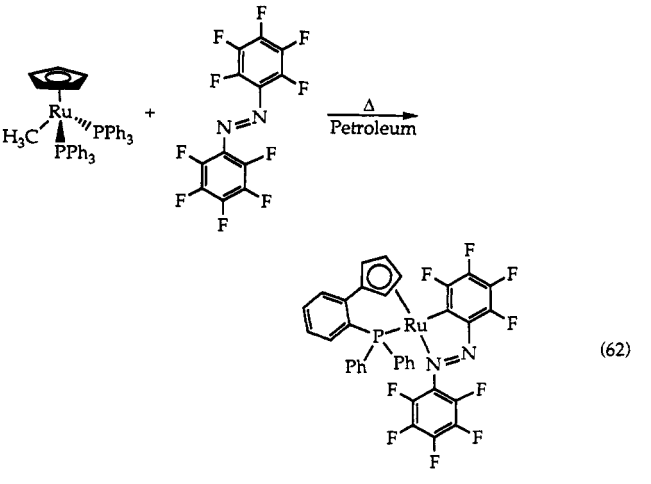


(128)

(61)

attributed to severe steric hinderance from the carbomethoxy substituents.

An unusual ligand coupling was also observed in the reaction of $(\eta^5\text{-}C_5H_5)Ru(PPh_3)_2(CH_3)$ with decafluoroazobenzene, which formed only one product, **129**, in



(129)

(62)

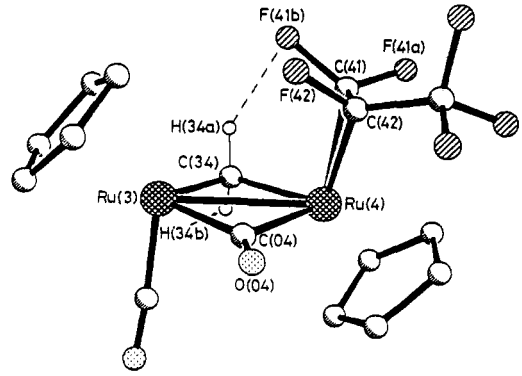
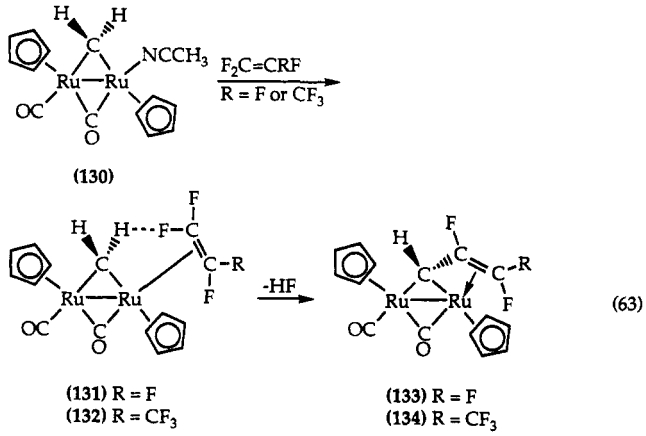


Figure 10. Reprinted with permission from ref 253. Copyright 1989 The Royal Society of Chemistry.

54% yield (eq 62).[225,236] The *ortho*-metalation of the fluorinated aromatic ring occurs with additional linking of the cyclopentadienyl ligand with a phenyl group on one of the PPh_3 ligands.

An intriguing example of intramolecular C–F activation at a dinuclear ruthenium center that results in the formation of a new carbon–carbon bond was noted by Knox and associates.[253] In this system, the acetonitrile complex $[Ru_2(CO)(CH_3CN)(\mu\text{-}CH_2)(\mu\text{-}CO)(\eta^5\text{-}C_5H_5)_2]$ (**130**) reacts under very mild conditions (<40 °C) with either perfluoroethylene or perfluoropropene in dichloromethane to afford the corresponding alkene derivatives $[Ru_2(CO)(F_2C{=}CFR)(\mu\text{-}CH_2)(\mu\text{-}CO)(\eta^5\text{-}C_5H_5)_2]$ (R = F (**131**); R = CF_3 (**132**)). Subsequent reflux of **131** or **132** in dichloromethane results in loss of HF and formation of complexes **133** and **134**, respectively (eq 63). The structure of **133** was confirmed by X-ray

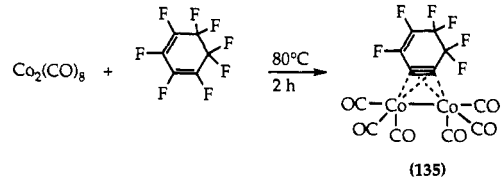


(63)

diffraction. It is believed that the HF elimination arises from incipient H···F hydrogen bonding between the methylene and the alkene ligands in compounds **131** and **132**.[253] In fact, X-ray crystallographic studies reveal a H(34a)···F(41b) separation of 2.23 Å for complex **132** which provides evidence for a weakly attractive intramolecular hydrogen–fluorine interaction (Figure 10).

D. Group 9: Co, Rh, Ir

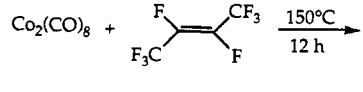
Early studies by Hunt and Wilkinson[254] illustrated that $Co_2(CO)_8$ engages in vicinal C–F bond activation with octafluorocyclohexa-1,3-diene to afford the air-stable dicobalt μ-alkyne complex **135** in a modest 15% yield (eq 64). The structure of **135** was confirmed by X-ray diffraction.[255] The mechanism of the transformation was not known.[254] However, vicinal defluorination was more recently demonstrated by Hughes and

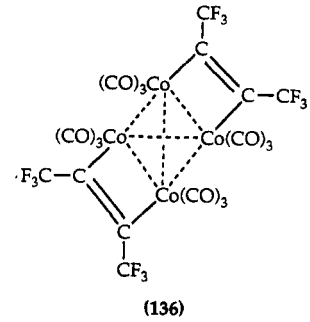


(64)

co-workers[169–171] using organometallic cobalt anions to generate analogous dicobalt–μ-alkyne complexes (see section V.A).

In related studies, Roundhill and Wilkinson[256] reported that reaction of $Co_2(CO)_8$ with an isomeric mixture of perfluoro-2-butene produced the air-stable bridged acetylene complex $Co_4(CO)_{12}(C_4F_6)_2$ (**136**) in 70% yield in which four C–F bonds have been ruptured (eq 65). Although no conclusive structural evidence



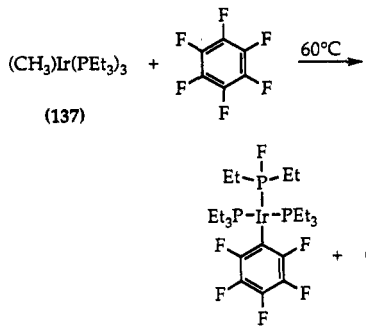


(65)

(136)

was obtained, C–F activation was confirmed upon detection of fluoride and Co^{2+} ions in solution.[256] The authors did not speculate on a mechanism for this reaction.

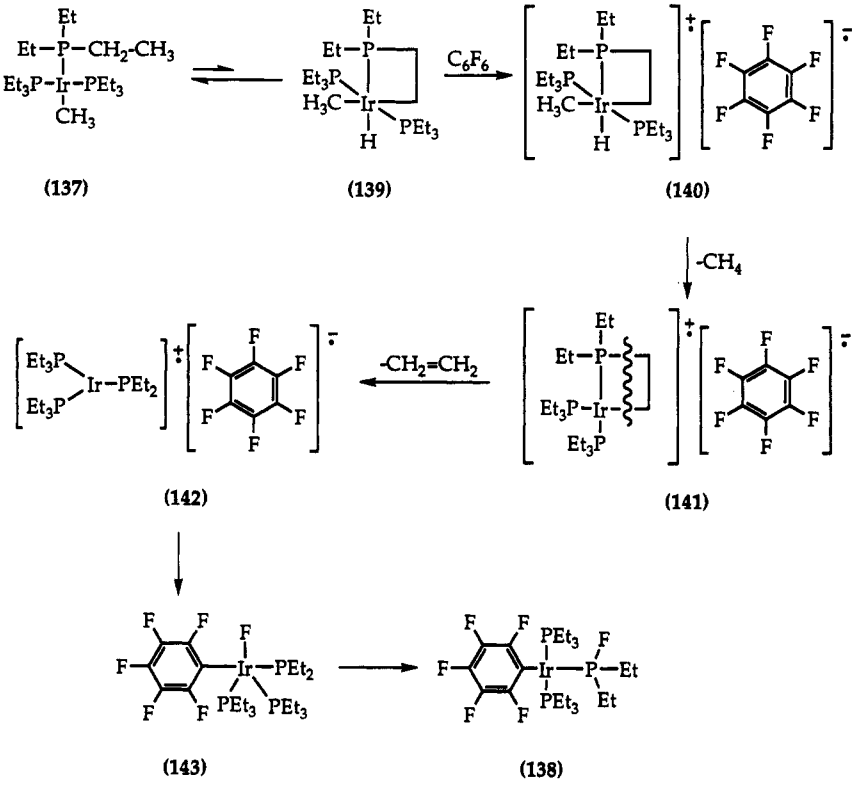
Milstein and co-workers[257] reported that thermolysis of $(CH_3)Ir(PEt_3)_3$ (**137**) in hexafluorobenzene at 60 °C affords $Ir(PEt_3)_2(PEt_2F)(C_6F_5)$ (**138**) with concomitant elimination of CH_4 and C_2H_4 (eq 66). In this unique



+ CH_4 + $CH_2{=}CH_2$ (66)

transformation, a P–F bond is formed at the expense of a strong C–F bond and a P–C bond. The complex **138** was crystallographically characterized. Since benzene was unreactive toward $(CH_3)Ir(PEt_3)_3$, a mechanism was proposed that assumes an initial equilibrium between the electron-rich **137** and the four-membered metallacycle **139** (Scheme 15).[257] **139** can then transfer an electron to hexafluorobenzene to afford the radical ion pair **140**. Reductive elimination of CH_4 from **140** followed by the expulsion of C_2H_4 from **141** would generate a highly unsaturated, low-valent radical complex **142**. This complex could subsequently undergo an oxidative addition of C_6F_6 followed by fluoride

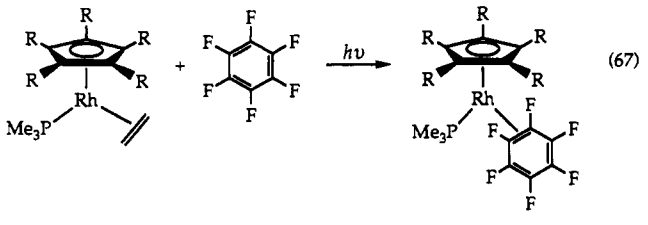
Scheme 15



migration to the phosphorous in **143** to give the observed iridium complex **138**.[257]

Several excellent studies have been reported by Jones, Perutz, and co-workers.[246,247,258-261] on the photochemically promoted η^2-coordination and C–F activation of hexafluorobenzene by d^8 cyclopentadienylrhodium and -iridium complexes. The rhodium and iridium reactions proceed by different pathways to initially yield an isolable η^2-coordinated arene complex, followed by metal insertion into the C–F bond to afford the oxidative addition product.

Photochemical reaction ($\lambda > 285$ nm) of $(\eta^5\text{-}C_5R_5)Rh(PMe_3)(C_2H_4)$ (R = H (**144a**); R = CH_3 (**144b**)) with hexafluorobenzene yields $(\eta^5\text{-}C_5R_5)Rh(PMe_3)(\eta^2\text{-}C_6F_6)$ (R = H (**145a**); R = CH_3 (**145b**)) (eq 67).[246,247,258] The

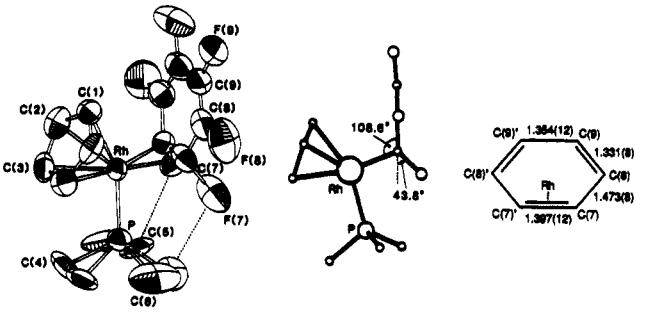


(67)

(144a) R = H
(144b) R = CH_3

(145a) R = H
(145b) R = CH_3

structure of the moderately stable η^2-arene complex **145a** has been elucidated through solution NMR spectroscopic data and confirmed by X-ray crystallography (Figure 11).[247,258] The hexafluorobenzene ligand is bonded to the rhodium via two adjacent carbon atoms in a symmetrical fashion with the center of the coordinated C=C bond of the C_6F_6 1.935 Å from Rh (Figure 11a). The fluorines at the site of η^2-coordination are bent out of the C_6F_4 plane by 43.8° (Figure 11b). Interestingly, the length of the coordinated C=C bond (1.397(12) Å) is not significantly different from that

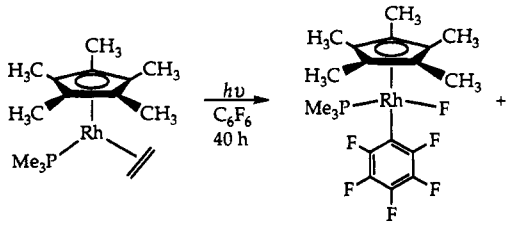


(a) (b) (c)

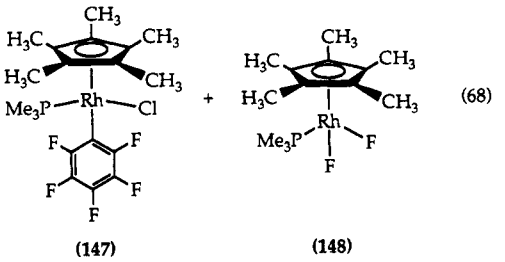
Figure 11. Reprinted with permission from ref 247. Copyright 1993 American Chemical Society.

found in free C_6F_6 (1.394(7) Å); however, the remaining C–C bond lengths of the C_6F_6 ring are perturbed from the free arene value and form a diene-type configuration with C(8)=C(9) of 1.331(8) Å, C(7)–C(8) of 1.473(8) Å, and C(9)–C(9′) of 1.354(12) Å (Figure 11c). The crystallographic studies revealed an intramolecular C–H···F interaction between the PMe_3 methyl protons and the fluorine atoms on the hexafluorobenzene ligand C···F = 2.773(17) Å); apparently, this interaction persists in solution as evidenced by coupling between the fluorines and the methyl protons in the ^{19}F NMR spectrum of **145a**.[247]

Extended photolysis ($\lambda > 285$ nm) of **144b** with hexafluorobenzene affords a mixture of $(\eta^5\text{-}C_5Me_5)Rh(PMe_3)(C_6F_5)(F)$ (**146**), $(\eta^5\text{-}C_5Me_5)Rh(PMe_3)(C_6F_5)(Cl)$ (**147**), and $(\eta^5\text{-}C_5Me_5)Rh(PMe_3)F_2$ (**148**) in 65%, 9.2%, and 7.8% yields, respectively (eq 68).[246,247] The major product $(\eta^5\text{-}C_5Me_5)Rh(PMe_3)(C_6F_5)(F)$ (**146**) arises from a formal oxidative addition of the coordinated η^2-arene and was determined through ^1H, ^{19}F, and $^{31}P\{^1H\}$ NMR studies. Surprisingly, the Rh–F resonance was not observed in the ^{19}F NMR spectrum but was inferred from coupling patterns in the $^{31}P\{^1H\}$ NMR spectrum.



(144b) (146)



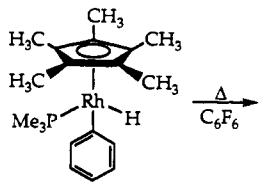
(147) (148)

(68)

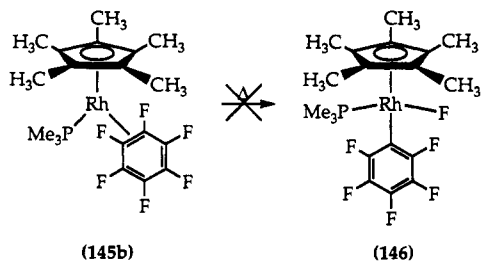
Importantly, it was shown that photolysis of **145b** yields **146**, thus demonstrating the significance of precoordination of the arene, and that **145b** is indeed an intermediate in the formation of the C–F activation product **146**.[246,247]

$(\eta^5\text{-}C_5Me_5)Rh(PMe_3)(C_6F_5)(Cl)$ (**147**) is a result of halide exchange of **146** with C_6F_5Cl impurities present in nominally 99.9% pure C_6F_6.[246,247] The oxidative addition product **146** is not stable and serves as a potent chloride scavenger as evidenced by reaction of **146** with $CHCl_3$ to yield **147**. This compound was isolated and characterized through X-ray diffraction studies, confirming that C–F cleavage had indeed occurred at the rhodium metal center.[246,247]

Interestingly, the $(\eta^5\text{-}C_5Me_5)Rh(PMe_3)(\eta^2\text{-}C_6F_6)$ (**145b**) coordination complex can be formed thermally from $(\eta^5\text{-}C_5Me_5)Rh(PMe_3)(C_6H_5)(H)$ (**149**); however, C–F activation cannot be effected thermally even after heating **145b** to 110 °C for 30 h (eq 69). Thus, the C–F



(149)

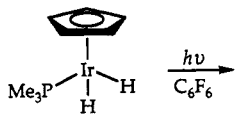


(145b) (146)

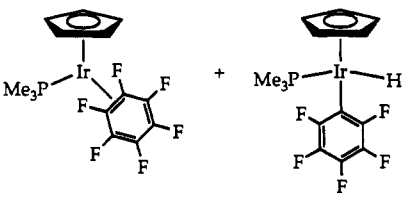
(69)

activation step has only been realized photochemically.[246,247] Furthermore, although the η^2-arene coordination complex can be formed and isolated using the less basic system $(\eta^5\text{-}C_5H_5)Rh(PMe_3)(C_2H_4)$ (**144a**) no C–F activation was achieved either photochemically or thermally.[247,258] It is interesting that photochemical reaction of **144a** with partially fluorinated $C_6F_{6-n}H_n$ arenes results in exclusive C–H oxidative addition to yield only hydride complexes.[262] However, photolysis of **144a** with $C_6F_5CH_3$ does yield an η^2-arene complex.[262]

Intermolecular C–F activation was also observed upon photolysis ($\lambda > 285$ nm) of $(\eta^5\text{-}C_5H_5)Ir(PMe_3)H_2$ (**150**) in C_6F_6 to generate $(\eta^5\text{-}C_5H_5)Ir(PMe_3)(\eta^2\text{-}C_6F_6)$ (**151**) and $(\eta^5\text{-}C_5H_5)Ir(PMe_3)(C_6F_5)(H)$ (**152**) concurrently (eq 70).[247] Deuterium labeling studies revealed that the



(150)

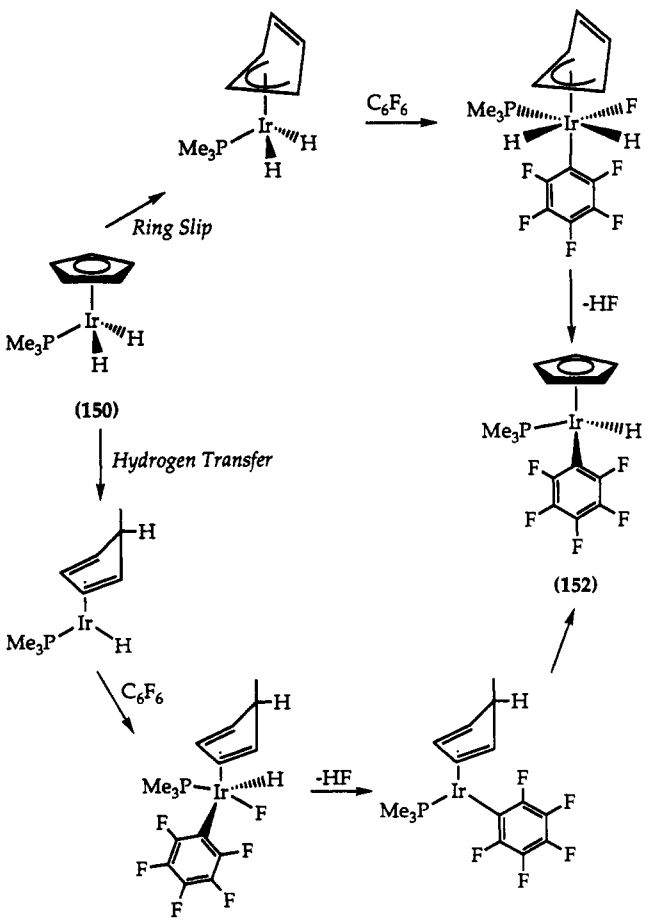


(151) (152)

(70)

hydride ligand of the product **152** originates from the hydride of the starting material **150**. This C–F insertion reaction was postulated to proceed via either a ring slip or a hydrogen-transfer mechanism, independently of the formation of $(\eta^5\text{-}C_5H_5)Ir(PMe_3)(\eta^2\text{-}C_6F_6)$ (**151**) as shown in Scheme 16.[247] The authors were unable to

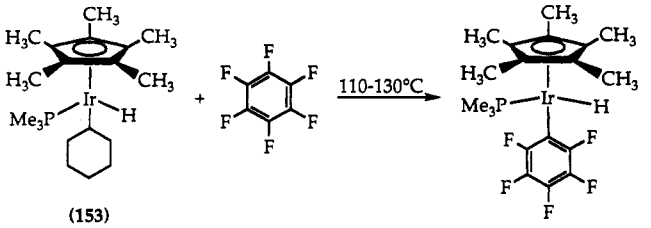
Scheme 16



differentiate between either mechanism, and they could not exclude the possibility of a radical process.[247]

In related work, Bergman[263] has noted that reaction of $(\eta^5\text{-}C_5Me_5)Ir(PMe_3)(C_6H_{11})(H)$ (**153**) with hexaflu-

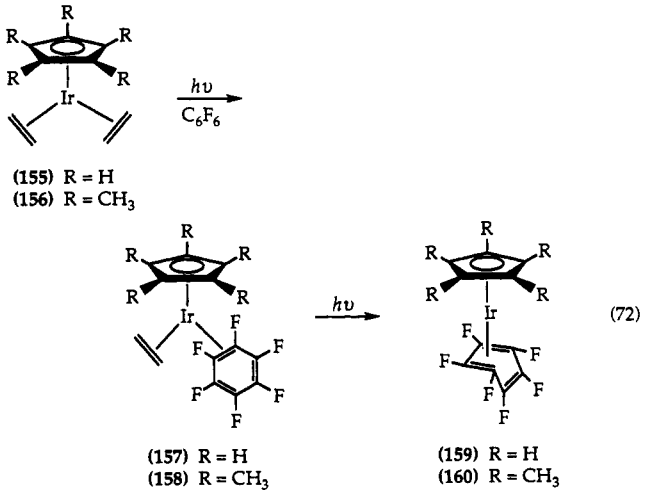
orobenzene at 110–130 °C affords a mixture of products in which the major constituents is $(\eta^5\text{-}C_5Me_5)Ir(PMe_3)(C_6F_5)(H)$ (**154**) (eq 71). The source of the hydride



(153) (154) (71)

ligand as well as the fate of the fluoride has not been established.

Of particular relevance is that Perutz and associates[260] demonstrated that $(\eta^5\text{-}C_5R_5)Ir(C_2H_4)_2$ (R = H (**155**); R = CH_3 (**156**)) reacts photochemically with hexafluorobenzene in two sequential steps to displace one ethylene and then another, yielding $(\eta^5\text{-}C_5R_5)Ir(C_2H_4)(\eta^2\text{-}C_6F_6)$ (R = H (**157**); R = CH_3 (**158**) and $(\eta^5\text{-}C_5R_5)Ir(\eta^4\text{-}C_6F_6)$ (R = H (**159**); R = CH_3 (**160**)) complexes, respectively (eq 72). The structures of both $(\eta^5\text{-}C_5H_5)Ir(C_2H_4)(\eta^2\text{-}C_6F_6)$ (**157**) and $(\eta^5\text{-}C_5H_5)Ir(\eta^4\text{-}C_6F_6)$ (**159**) have been ascertained by NMR and crystallographic studies (Figure 12a and b, respectively).[260] The most prominent feature in the structure of **157** is that the C_6F_4 moiety is planar, bonded through C(3) and C(4), and is tipped up toward the cyclopentadienyl group



(155) R = H
(156) R = CH_3

(157) R = H
(158) R = CH_3

(159) R = H
(160) R = CH_3

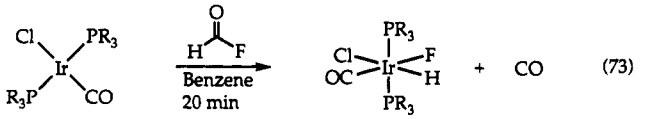
(72)

(see Figure 12a). Accordingly, the fluorines F(3) and F(4) are tipped out of the plane such that the dihedral angle between the C(3)F(3)C(4)F(4) plane and the C_6 plane is 47.9°. The proximity of these two fluorines and the ethylene carbons (C(1)···F(4) = 2.87(2) Å and C(2)···F(3) = 2.83(2) Å, well within the sum of the carbon and fluorine van der Waals radii of 3.17 Å) support the existence of an intramolecular sp^2-C–H···F interaction.

The crystal structure for **159** reveals that the iridium is coordinated to a diene unit with the remaining C_2F_2 folded away from the metal (see Figure 12b). No intramolecular interactions were observed for **159**. The behavior of C_6F_6 in an η^2-coordination mode resembles that of a fluoroalkene, and the behavior of C_6F_6 in an η^4-coordination mode resembles that of a fluorodiene.

Collectively, these studies by Jones, Perutz, and coworkers have clearly shown that C–F oxidative addition of hexafluorobenzene can be promoted with proper choice of ancillary ligand (C_5Me_5 versus C_5H_5) and metal (rhodium versus iridium). Similar studies have determined the thermodynamic preferences for η^2-arene coordination versus C–H bond activation.[259,261,262]

An intriguing transformation is the oxidative addition of the C–F bond (versus the C–H bond) of formyl fluoride at coordinatively unsaturated iridium and rhodium metal centers. In an attempt to prepare neutral formyl transition-metal complexes, Doyle[264] reported that facile C–F bond cleavage occurs upon reaction of formyl fluoride with either $Ir(PMe_3)_2(CO)(Cl)$ (**161**) or $Ir(PPh_3)_2(CO)(Cl)$ (**162**) at room temperature to afford the six-coordinate HF adducts $Ir(H)(F)(PMe_3)_2(CO)(Cl)$ (**163**) and $Ir(H)(F)(PPh_3)_2(CO)(Cl)$ (**164**) and CO, respectively (eq 73).[264] The products

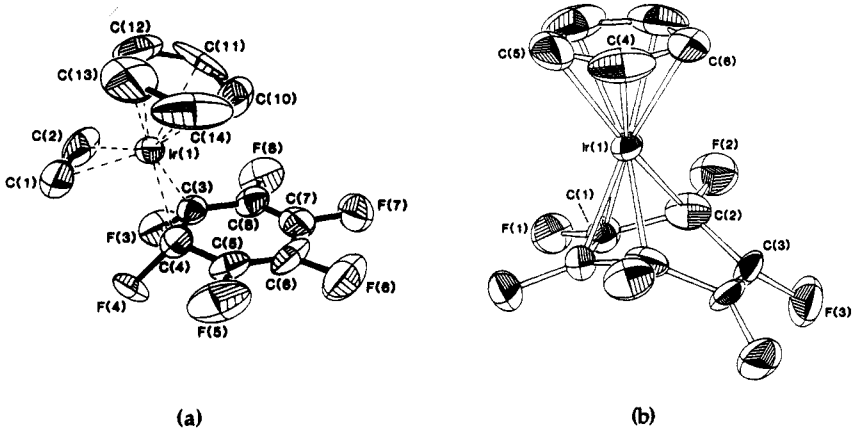


(161) R = CH_3
(162) R = Ph

(163) R = CH_3
(164) R = Ph

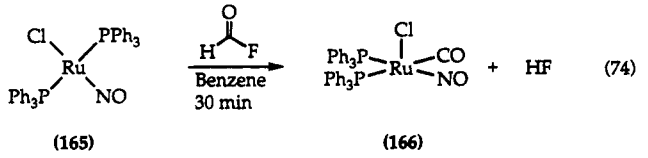
(73)

are the result of a formal *cis*-oxidative addition of HF at the metal center. Interestingly, the isoelectronic compound $Ru(NO)(PPh_3)_2(Cl)$ (**165**) reacts readily with formyl fluoride to yield the carbonyl complex $Ru(NO)(CO)(PPh_3)_2(Cl)$ (**166**) and HF (eq 74). To account for these apparently disparate reactivities Doyle proposed a mechanism that involves initial generation of a fluoroformyl intermediate (**167**) via the oxidative ad-



(a) (b)

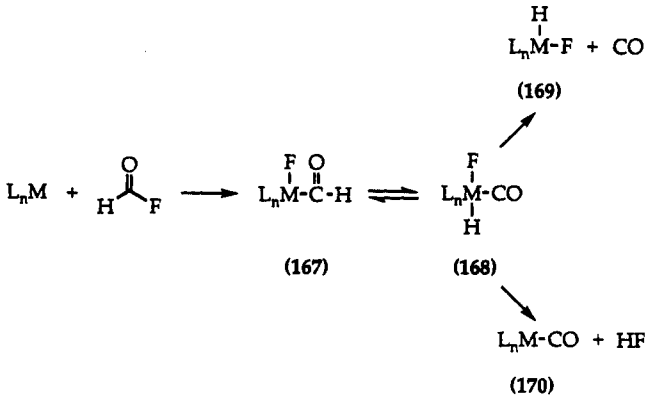
Figure 12. Reprinted with permission from ref 260. Copyright 1992 American Chemical Society.



(165) (166)

dition of formyl fluoride at the metal center (Scheme 17). This intermediate would then form the CO–H–F

Scheme 17

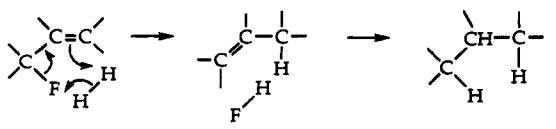


complex **168**. **168** would then either dissociate a CO ligand to yield the HF adduct **169** or reductively eliminate HF to afford the carbonyl complex **170**. Rh(PPh$_3$)$_3$(Cl) also forms a carbonyl complex upon reaction with formyl fluoride in addition to the production of PPh$_3$ and HF. This is explained by the speculative formation of the intermediate Rh(CO)(H)(PPh$_3$)$_2$(Cl)(F) which would rapidly decompose to Rh(CO)(PPh$_3$)$_2$(Cl) and HF.[264]

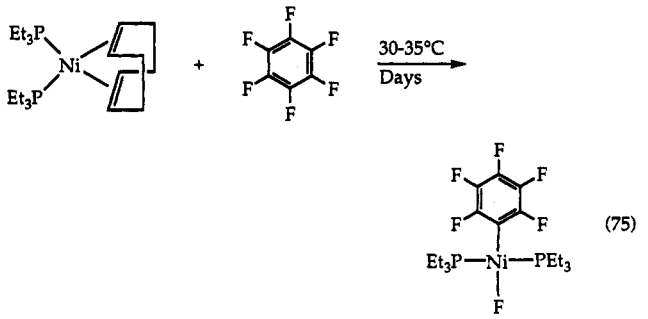
E. Group 10: Ni, Pd, Pt

The Group 10 metals, Ni, Pd, and Pt, are routinely used as solid-phase catalysts in several hydrogenation processes in organic chemistry. One intriguing process is the catalytic hydrogenolysis of carbon–fluorine bonds which involves the facile replacement of fluorine by hydrogen and utilizes either Ni, Pd, or Pt metal as catalyst. This reaction has been recently reviewed by Hudlicky.[265] The mild (room temperature and atmospheric pressure) exchange of fluorine for hydrogen has been observed for allylic, vinylic, benzylic, and aromatic fluorine atoms. The hydrogenolysis of the carbon–fluorine bond does not take place without concomitant saturation of the double bond. Since all of these fluorinated substrates contain π bonds, Hudlicky has accordingly postulated a π bond participation mechanism as generically illustrated in Scheme 18.[265] The exact role of the metal in this process is unknown.

Scheme 18

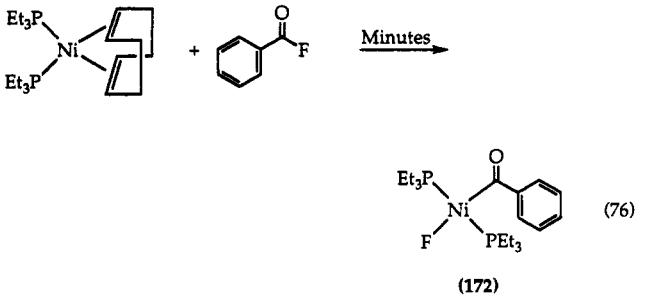


In 1977 Fahey and Mahan[266] reported the intermolecular oxidative addition of aryl and acyl C–F bonds to a low-valent nickel metal center. The mild thermal reaction (30–35 °C) between Ni(PEt$_3$)$_2$(COD) and C$_6$F$_6$ produced (PEt$_3$)$_2$Ni(C$_6$F$_5$)(F) (**171**) in 7% yield over a period of days (eq 75). The product decomposes at 30



(171)

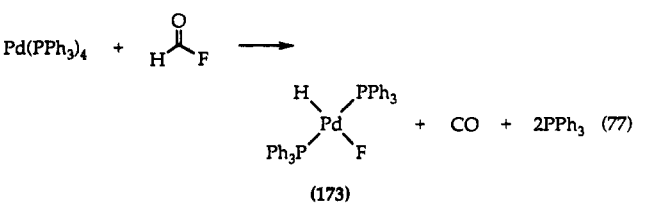
°C under an argon atmosphere. The mechanism is thought to be analogous to an aromatic nucleophilic substitution reaction. Similarly, the addition of (PEt$_3$)$_2$Ni(COD) to C$_6$H$_5$COF in hexane resulted in a rapid and exothermic oxidative addition forming (Et$_3$P)$_2$Ni(COC$_6$H$_5$)(F) (**172**) in 69% yield (eq 76).[266] Acid fluo-



(172)

rides, in particular benzoyl fluoride, have been noted for their unreactive behavior with several transition-metal complexes.[267] The nickel fluoride compound **172** is also unstable and decomposes on standing. This C–F activation is thought to occur via a template route in which the carbonyl π bond initially coordinates to the metal prior to the insertion reaction giving the final product.[266]

Doyle[264] has reported that both Pd(PPh$_3$)$_4$ and Pt(PPh$_3$)$_4$ react with formyl fluoride and proceed with C–F bond activation to afford the corresponding complexes Pd(H)(F)(PPh$_3$)$_2$ (**173**) and Pt(H)(F)(PPh$_3$)$_2$ (**174**) with loss of PPh$_3$ and CO (eqs 77 and 78, respectively). It is believed that these reactions proceed



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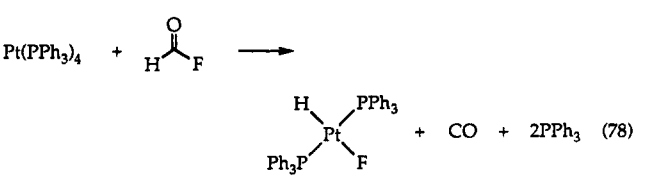
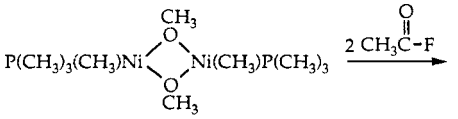


(174)

by the mechanism illustrated in Scheme 17. Initial dissociation of PPh$_3$ generates a 16-electron coordinatively unsaturated complex which then oxidatively adds the formyl fluoride to afford the five-coordinate fluoroformyl intermediate **167**. Subsequent dissociation

of CO and a second molecule of PPh_3 would account for the observed products.

In chemistry related to these formyl fluoride studies, Klein and Karsch[268] noted the preparation of an organometallic nickel(II) fluoride using acetyl fluoride as the fluoride source. The dimer, $[Ni(P(CH_3)_3)(CH_3)(\mu\text{-}OCH_3)]_2$ (**175**), reacts with 2 equiv of CH_3COF to give the fluoride-bridged dimer $[Ni(P(CH_3)_3)(CH_3)(\mu\text{-}F)]_2$ (**176**) and $CH_3CO_2CH_3$ (eq 79).



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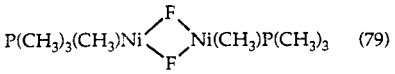
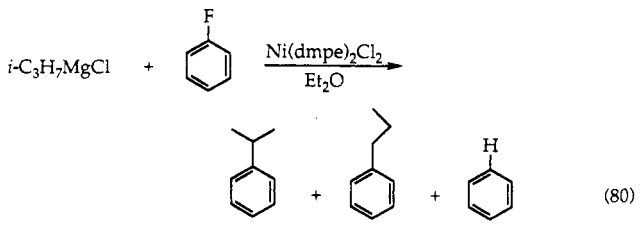


(176) (79)

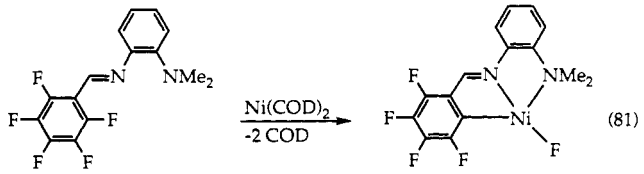
Intermolecular C–F activation at nickel(0) has realized synthetic utility as evidenced by the nickel-catalyzed cross-coupling reactions of secondary alkyl Grignard reagents with organic halides.[269] Treatment of an ether solution of $i\text{-}C_3H_7MgCl$ with fluorobenzene in the presence of $Ni(Me_2PCH_2CH_2PMe_2)Cl_2$ affords a mixture of three cross-coupling products, $i\text{-}C_3H_7C_6H_5$, $n\text{-}C_3H_7C_6H_5$, and HC_6H_5 in 62% overall yield (eq 80).



(80)

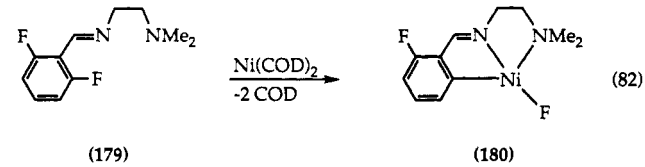
The pivotal step in this transformation is the oxidative addition of the C–F bond in fluorobenzene at Ni(0) prior to the cross-coupling step and isomerization. It is noteworthy that chlorobenzene and bromobenzene display comparable reactivities at Ni(0) in this process.[269]

As a logical extension of the chelate-assisted intramolecular C–F oxidative addition chemistry observed at tungsten(0), Richmond and co-workers[229,239] have similarly investigated the C–F activation process at a nickel(0) metal center. Reaction of ligand **177** with bis(cyclooctadiene)nickel(0) in tetrahydrofuran results in room-temperature C–F activation to afford **178** in 86% yield (eq 81). The air-stable square planar nickel-

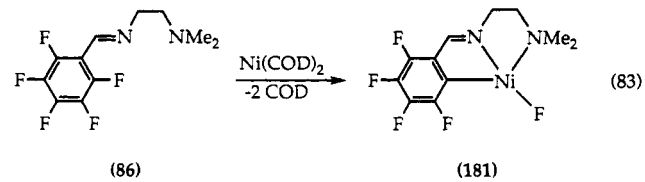


(177) (178) (81)

(II) fluoride was fully characterized by ^1H, ^{19}F, and $^{13}C\{^1H\}$ NMR spectroscopy as well as mass spectrometry. Related chemistry using the saturated ligand systems **179** and **86** provides an unusual case where higher yields were obtained for the 2,6-difluorinated ligand than for the pentafluorinated ligand (eqs 82 and 83, respectively).[270] The Ni–F bond in both **180** and **181** is sensitive to hydrolysis, presumably forming the hydroxide complex.

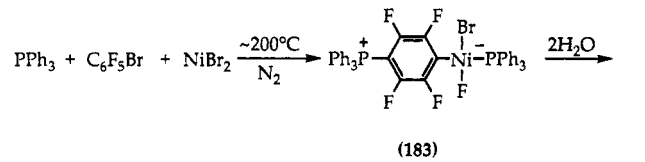


(179) (180) (82)



(86) (181) (83)

During an attempt to synthesize the phosphonium cation $[Ph_3(C_6F_5)P]^+$ an unexpected C–F activation reaction was discovered by Roundhill and co-workers.[271,272] A mixture of PPh_3, C_6F_5Br, and $NiBr_2$ was refluxed in an open vessel at 200 °C under a nitrogen flow. Treatment of this fusion product with water results in the formation of uncharacterized nickel-containing products, and the compound $[Ph_3(4\text{-}C_6F_4H)P]Br$ (**182**) in which the fluorine in the 4-position has been replaced by hydrogen (eq 84). As an explanation for this unusual cleavage reaction, the authors postulate that the melt contains an organonickel phosphonium salt **183** that has a nickel–carbon bond at the 4-position of the pentafluorophenyl ring.[271,272] Hydrolysis of this complex results in the selective cleavage of the Ni–C bond whereby hydrogen transfers to carbon and hydroxyl to the nickel. The reverse regioselectivity was not detected.



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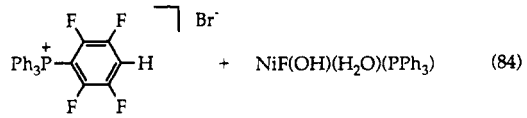
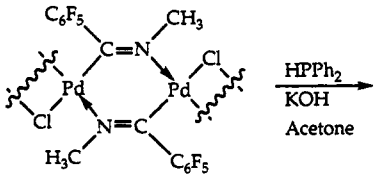


(182) (84)

Usón and associates[273] reported the base-promoted nucleophilic C–F activation on a Pd-bound ligand. Addition of $HPPh_2$ and KOH in acetone to the chloro-bridged dimer *cis*-$[\{Pd_2(\mu\text{-}Cl_2)[\mu\text{-}C(C_6F_5)=N(CH_3)]_2\}_n]$ (**184**) results in the cleavage of the chlorine bridges and formation of the imidoyl-bridged dimer **185** in 45% yield (eq 85). This intriguing reaction involves the formation of a C–P bond at the expense of a much stronger C–F bond. Undoubtedly, the favorable generation of the C,P-chelate ring in **185** is possible via internal nucleophilic displacement of an *ortho*-fluorine by the chelated phosphine. The metal acts to direct the Ph_2P^- substitution process since C–F activation was not observed by Bruce and colleagues upon reaction of $PdCl_2$ with $C_6F_5N{=}NC_6H_5$.[224,236]

Roundhill and associates[272,274] have reported several interesting cyclometalation reactions involving intramolecular C–F activation at a platinum(II) metal



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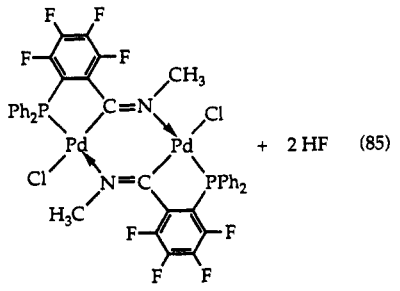
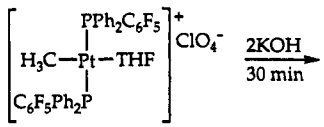
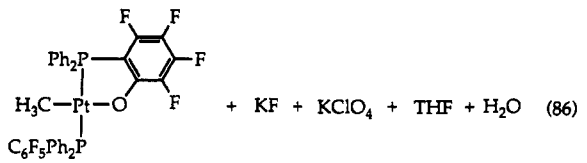


(185)

center. The reaction of *trans*-$[Pt(CH_3)(THF)(PPh_2C_6F_5)_2]ClO_4$ (**186**) with aqueous KOH (2-fold excess) at room temperature affords the oxoplatinacycle *trans*-$[Pt(CH_3)(2\text{-}OC_6F_4PPh_2)(PPh_2C_6F_5)]$ (**187**) in 68% yield (eq 86). The product has been characterized by X-ray



(186)



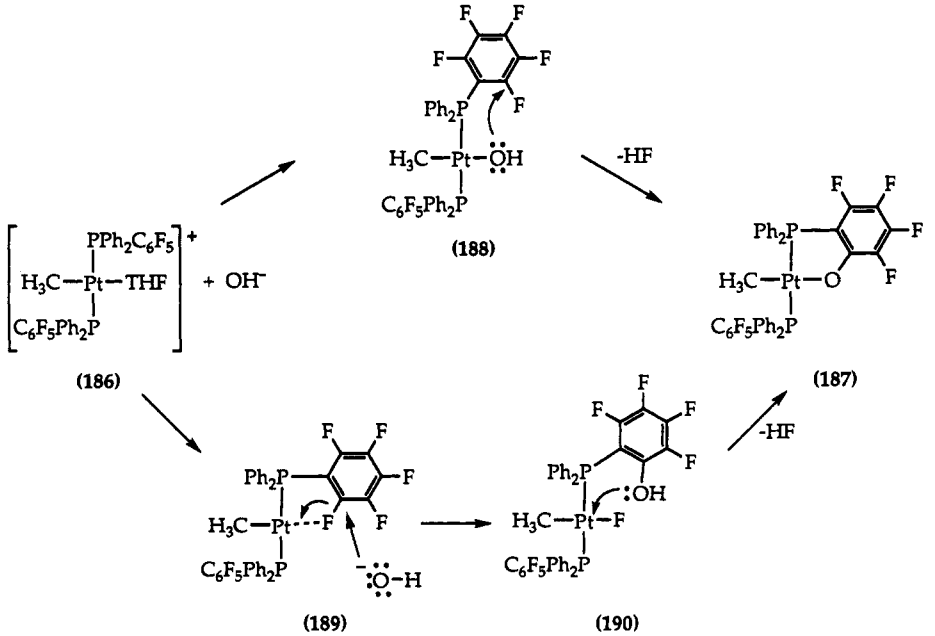
(187)

crystallography and ^1H, ^{19}F, and $^{31}P\{^1H\}$ NMR spectroscopy. The formation of the oxoplatinacycle is an unusual example of a C–F bond cleavage reaction under mild conditions. The reaction is clearly metal promoted since there is no reaction between uncoordinated $PPh_2C_6F_5$ and KOH. The product is formed by the replacement of the *ortho*-fluorine by hydroxide ion, followed by deprotonation to yield the stable five-membered ring product which resists further reaction with hydroxide ion.

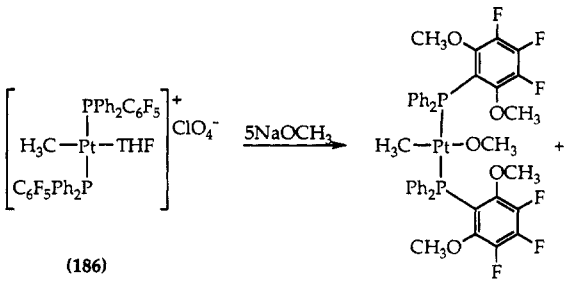
The authors have suggested two possible mechanisms for the formation of the oxaplatinacycle (Scheme 19).[272,274] Both mechanisms involve nucleophilic attack by hydroxide at the *ortho* carbon of the pentafluorophenyl ring. The first pathway involves the coordination of a hydroxy group to the platinum metal center to yield **188**, thus placing it in close proximity to the *ortho* fluorine of the coordinated phosphine, $PPh_2C_6F_5$. Subsequent intramolecular nucleophilic attack by the hydroxide lone pair at the electrophilic *ortho* carbon results in substitution to generate **187**. Similar to the nucleophilic aromatic substitution reactions involving organometallic anions,[22,150–152,154–156] formation of the platinacycle apparently deactivates the aromatic ring toward further substitution. Additionally, steric congestion upon platinacycle formation supresses reaction of the other fluorophenyl ring.[272] The second mechanism is more speculative and involves a bonding interaction between the platinum metal center and the *ortho* fluorine as in **189**. This coordination would weaken the aromatic C–F bond, making it more susceptible to nucleophilic attack by the hydroxide ion to yield **190**. Subsequent cyclization would yield **187**.

In a similar fashion, the addition of $NaOCH_3$ to *trans*-$[Pt(CH_3)(THF)(PPh_2C_6F_5)_2]ClO_4$ (**186**) results in cleavage of *ortho* C–F bonds.[272,274] However, the methoxide ion sequentially substitutes all the *ortho* fluorines in (**186**) to give *trans*-$[Pt(CH_3)(OCH_3)(PPh_2C_6F_3(OCH_3)_2\text{-}2,6)_2]$ (**191**) (eq 87). The reaction does not generate the oxoplatinacycle presumably due to the energy needed to cleave the C–O bond versus an O–H bond and the weaker coordinating properties of an ether oxygen compared to a hydroxyl oxygen. The intramolecular nature of these reactions is evidenced in that only *ortho* fluorines are substituted by methoxide.[272]

Scheme 19



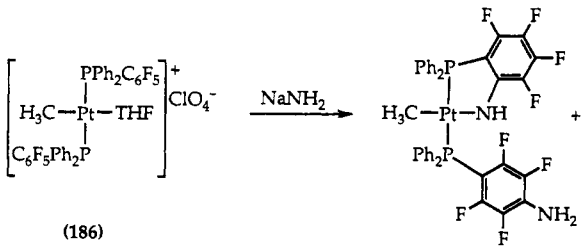
(186) (188) (187) (189) (190)



(186) (191)

$$4NaF + THF + NaClO_4 \quad (87)$$

Interestingly, both *ortho* and *para* substitution of aromatic fluorines was observed upon reaction of $NaNH_2$ with *trans*-$[Pt(CH_3)(THF)(PPh_2C_6F_5)_2]ClO_4$ (**186**) to yield the amidoplatinacycle *trans*-$[Pt(CH_3)(2\text{-}NHC_6F_4PPh_2)(PPh_2C_6F_4NH_2\text{-}4)]$ (**192**) (eq 88).[272] The

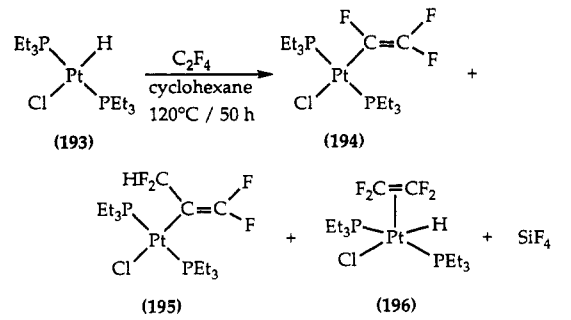


(186) (192)

$$2HF + NaClO_4 \quad (88)$$

formation of **192** demonstrates that the cyclometalation reaction is faster than the *para* substitution reaction. Deactivation of the *ortho*-substituted ring prevents the substitution of the *para* position on the same ring. Since reaction of the ligand $PPh_2C_6F_5$ and sodium amide also produces a C–F-substituted product in the *para* position, $PPh_2C_6F_4NH_2$-4, it is likely that the *para* substitution is not metal induced.[272]

Early work by Clark and Tsang[275,276] showed that the platinum(II) hydride complex *trans*-$[(Et_3P)_2PtHCl]$ (**193**) engages in C–F activation reactions with a variety of fluoroolefins in the presence of Pyrex glass. Reaction of *trans*-$[(Et_3P)_2PtHCl]$ (**193**) and tetrafluoroethylene in cyclohexane at 120 °C for 50 h afforded $[(Et_3P)_2PtCl(\eta^1\text{-}CF{=}CF_2)]$ (**194**) in 29% yield, $[(Et_3P)_2PtCl(\eta^1\text{-}C(CF_2H){=}CF_2)]$ (**195**) in 20% yield, $[(Et_3P)_2PtHCl(\eta^2\text{-}C_2F_4)]$ (**196**) in 8% yield, and SiF_4 (eq 89). The

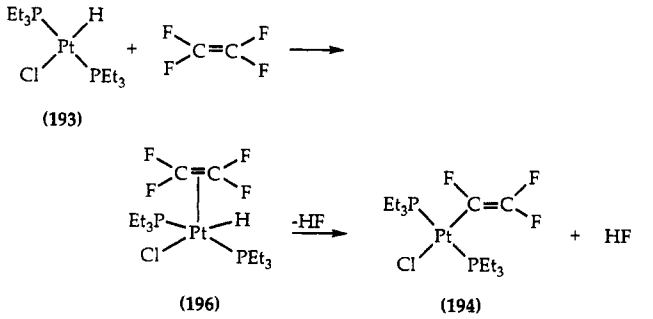


(193) (194) (195) (196)

$$+ SiF_4 \quad (89)$$

silicon tetrafluoride originates from the elimination of HF which attacks the silica in the glassware. The authors were unable to determine the origin of the platinum complex **195**. However, from low-temperature product distribution it was believed that complex **196** is an intermediate in the formation of the perfluorovinyl platinum complex **194**. Consequently, the authors postulated that initial π-coordination of tetrafluoroethylene to the platinum hydride complex **193** results in the formation of a five-coordinate species (**196**), whereby a fluorine is placed in close proximity to the metal hydride and intramolecular HF elimination would yield the observed product **194** (Scheme 20).[275,276] The

Scheme 20

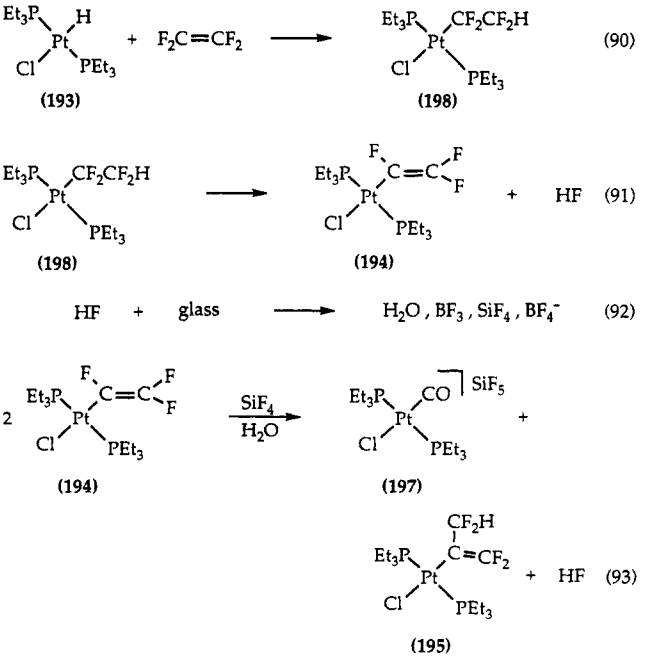


(193) (196) (194)

platinum hydride **193** was also observed to cleave a C–F bond in trifluoroethylene to form *cis* and *trans* isomers of *trans*-$[(Et_3P)_2PtCl(\eta^1\text{-}CF{=}CFH)]$ and in perfluorocyclobutene to yield $[(Et_3P)_2PtCl(\eta^1\text{-}C_4F_5)]$.[275] Both reactions are accompanied by the generation of silicon tetrafluoride.

Importantly, Clark and co-workers[277] later reported that X-ray diffraction studies revealed that the intermediate postulated to be the π-C_2F_4 complex **196** was actually the cation *trans*-$[(Et_3P)_2PtCl(CO)]SiF_5$ (**197**) which is isoelectronic with Vaska's complex, $Ir(Cl)(CO)(Ph_3)_2$. Aptly, the authors reinterpreted their previous results on the reaction of *trans*-$[(Et_3P)_2PtHCl]$ (**193**) with C_2F_4 and experimentally determined the sequence of reactions as shown in Scheme 21. Initial insertion

Scheme 21



(193) (198) (90)

(198) (194) (91)

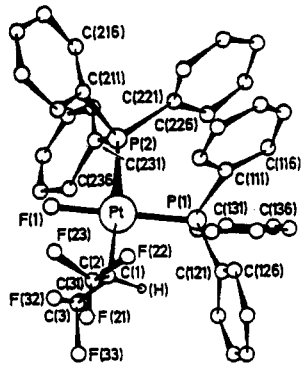
HF + glass → $H_2O, BF_3, SiF_4, BF_4^-$ (92)

(194) (197)

(195) (93)

of tetrafluoroethylene into the Pt–H bond yields the fluoroethyl complex **198** (eq 90). Elimination of HF from **198** gives the perfluorovinyl platinum complex **194** (eq 91). Finally, reaction of **194** with SiF_4 and water affords the products **195** and **197** (eq 93).[278]

Stone and co-workers[279] demonstrated that bis(trifluoromethyl)diazomethane (**199**) undergoes C–F activation upon reaction with the platinum(0) complex Pt(*trans*-stilbene)$(PPh_3)_2$ (**200**) to afford $Pt(\eta^2\text{-}C_3HF_5)(PPh_3)_2$ (**201**) in 15% yield and *trans*-$[PtF(\eta^1\text{-}CH(CF_3)_2)(PPh_3)_2]$ (**202**) in 25% yield (eq 94). The platinum complex **201** was fully characterized by NMR spectroscopic techniques, and the partially fluorinated ligand is best described as a coordinated pentafluoropropene. Interestingly, *trans*-$[PtF(\eta^1\text{-}CH(CF_3)_2)(PPh_3)_2]$ (**202**) converts to *cis*-$[PtF(\eta^1\text{-}CH(CF_3)_2)(PPh_3)_2]$ (**203**) within 5 min in refluxing benzene. The platinum fluoride complex *cis*-$[PtF(\eta^1\text{-}CH(CF_3)_2)(PPh_3)_2]$ (**203**) was confirmed by X-ray crystallographic studies (Figure 13).[280] The geometry at the platinum metal center is square planar, and a Pt–F bond distance of 2.03(1) Å and a Pt–C(1) bond distance of 2.07(2) Å were determined with a F–Pt–C(1) bond angle of 87.7(7)°.



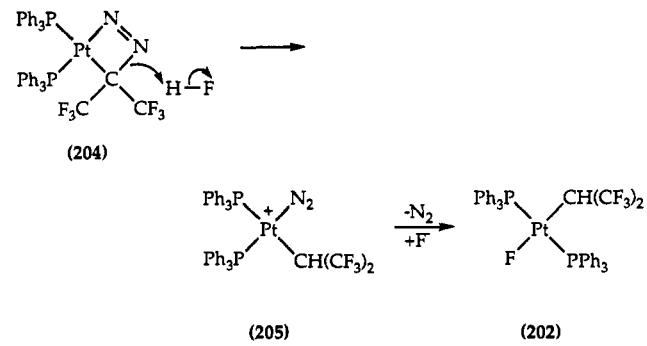
(203)

Figure 13. Reprinted with permission from ref 280. Copyright 1973 The Royal Society of Chemistry.

The authors propose that the platinum(II) fluoride complexes result from reaction of the initially formed bis(trifluoromethyl)diazomethane adduct **204** with traces of hydrogen fluoride which generates the cationic complex **205** (Scheme 22).[279] Loss of nitrogen from **205** followed by attack of fluoride affords **202**. The origin of the pentafluoropropene complex **201** was not discussed.[279]

C–F bond activation was observed by Bland and Kemmitt[281] in the reaction between the platinum complex Pt(*trans*-stilbene)$(PPh_3)_2$ (**200**) and 1,1,2-trichloro-3,3,3-trifluoropropene to produce $PtCl_2F_2(PPh_3)_2$ in 45% yield. The product was characterized by elemental analysis and infrared spectroscopy. The mechanism for this transformation is unknown.[281]

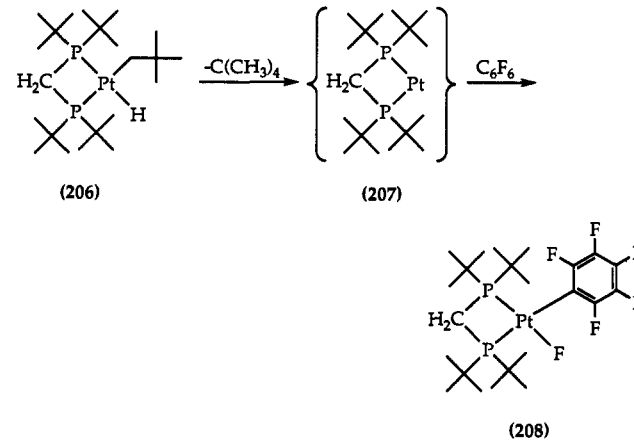
Scheme 22



(204) (205) (202)

Recently, Hofmann and Unfried[282] reported the room temperature intermolecular C–F activation of hexafluorobenzene by *cis*-hydridoneopentyl[η^2-bis(di-*tert*-butylphosphanyl)methane]platinum(II), [(dtbpm)Pt(H)$(CH_2C(CH_3)_3)$] (**206**). This platinum complex reductively eliminates neopentane, producing a very reactive 14-electron Pt(0) intermediate [(dtbpm)Pt] (**207**) which is capable of activating the C–F bonds of C_6F_6. As such, treatment of hexafluorobenzene with **206** for 1 week results in the quantitative formation of the platinum fluoride complex **208** (Scheme 23). The unique reactivity of **207** is attributed to the acute (ca. 75°) P–Pt–P bond angle which is enforced by the bridging methylene group in the ligand along with the steric bulk and strong donor ability of the dtbpm ligand.[282] The product has a *cis* arrangement of pentafluorophenyl and fluoride ligands as determined by ^1H, $^{13}C\{^1H\}$, ^{19}F, $^{31}P\{^1H\}$, and $^{195}Pt\{^1H\}$ NMR spectroscopy. The authors postulate the generation of the reactive 14-electron intermediate **207** and subsequent formation of [(dtbpm)Pt(η^2-C_6F_6)] prior to insertion into the C–F bond.[282] However, the presumed η^2-arene intermediate has not been observed. The authors could not exclude an alternative mechanism involving an initial electron transfer from **206** to C_6F_6, followed by the elimination of neopentane to generate **207**, which would insert into the C–F bond of hexafluorobenzene.[282]

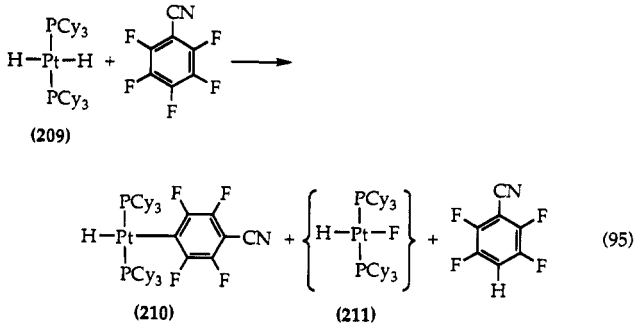
Scheme 23



(206) (207) (208)

In contrast to the *cis*-phosphine platinum system, Rüegger and associates[283] have reported that *trans*-$[PtH_2(PCy_3)_2]$ (**209**) does not react with hexafluorobenzene. However, *trans*-$[PtH_2(PCy_3)_2]$ (**209**) readily undergoes reaction with pentafluorobenzonitrile to give the platinum(II) aryl complex **210** in 32% yield, tetrafluorobenzonitrile, and the hydridofluoride *trans*-[PtH("Z")$(PCy_3)_2$] (**211**), where Z is either fluoride or

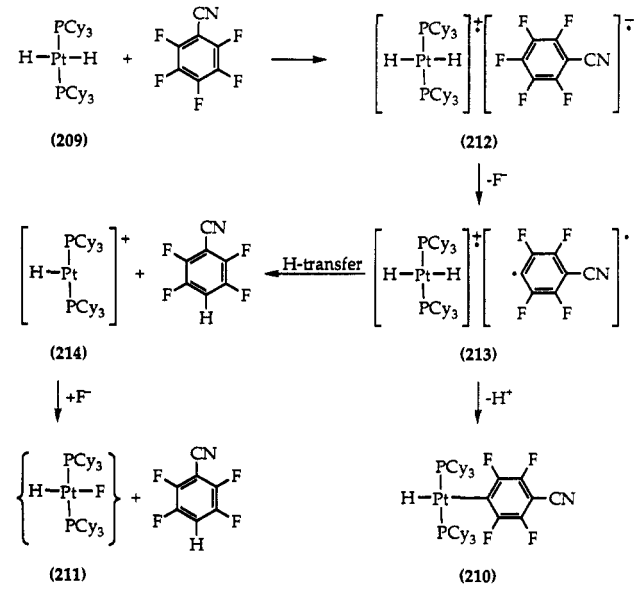
bifluoride ion, which has been detected in solution (eq 95). Importantly, the C–F activation reaction was



(209) (210) (211) (95)

equally successful when other benzonitriles, p-C_6F_4R-(CN) (R = H, CN, OCH_3), were employed; however, different substitution patterns for the platinum(II) aryl products were observed. The relative reaction rates for the nitriles paralleled their electron affinities: p-$C_6F_4(CN)_2$ > $C_6F_5(CN)$ > p-$C_6F_4H(CN)$ ≫ p-C_6F_4-$(OCH_3)(CN)$. Furthermore, ESR studies detected a radical when the reactions were performed in the presence of a spin trapping agent. Accordingly, the authors proposed an electron-transfer pathway to account for the observed C–F activation products, as illustrated in Scheme 24 for the reaction of **209** with

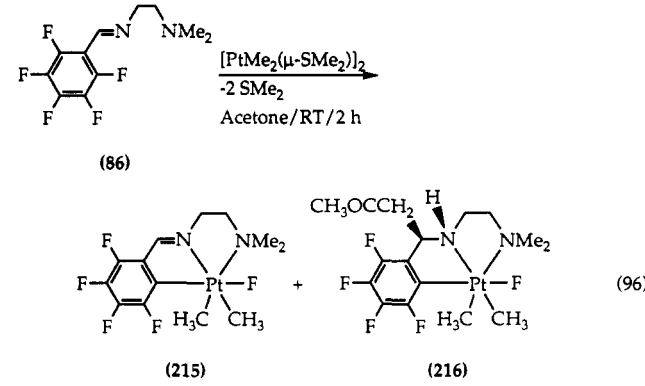
Scheme 24



(209) (212) (214) (213) (211) (210)

pentafluorobenzonitrile.[283] Initial electron-transfer from the electron-rich dihydride complex **209** to pentafluorobenzonitrile generates the π-radical complex **212**. Expulsion of fluoride from **212** would give the σ-radical complex **213** in which the unpaired electron is *para* to the nitrile. This radical can either combine with the platinum species with concomitant loss of H^+ to afford the observed platinum(II) aryl complex **210** or scavenge a hydrogen atom to give tetrafluorobenzonitrile and the cationic platinum species **214** which reacts with fluoride ion in solution to afford the hydrido fluoride complex **211**.[283] Note that this mechanism is similar to that postulated by Milstein and co-workers[257] for the addition of hexafluorobenzene to $[Ir(CH_3)(PEt_3)_3]$ (**137**) (see section VII.D).

Puddephatt and co-workers[284,285] have shown that C–F activation also occurs at a platinum(II) metal center. Reaction of the Schiff base ligand **86** with the platinum dimer $[Pt_2Me_4(\mu\text{-}SMe_2)_2]$ in acetone forms the six-coordinate platinum(IV) fluoride complexes **215** and **216** (eq 96). The reaction proceeds via a ligand



(86) (215) (216) (96)

substitution whereby the Me_2S ligands are replaced by the chelate backbone of the Schiff base ligand. The substitution product $[Pt(Me_3)_2(Me_2NCH_2$-$CH_2N{=}CHC_6F_5)]$ has been detected spectroscopically. Interestingly, the oxidative addition product **216** is formed by the addition of acetone across the imine bond in **215**. The oxidative addition product from this reaction is solvent dependent since only **215** is produced in CH_2Cl_2. The structure of **216** was determined by X-ray crystallography (Figure 14).[284,285] The six-coordinate platinum(IV) fluoride complex **216** crystallizes as a hydrogen-bonded dimer with a N(1)···F(1)–Pt bond distance of 2.805(10) Å which is appropriate for a N–H···F–Pt interaction. A Pt–C(1) bond length was determined to be 1.978(9) Å. The Pt–F bond length was found to be 2.070(5) Å with a F(1)–Pt–C(1) bond angle of 172.0(4)°. This is the longest reported Pt–F bond distance, which the authors suggest reflects the high ionic character of the bond.

C–F oxidative addition at Pt(II) can be promoted with only a single nitrogen donor atom as evidenced by the reaction of the Schiff base ligand **217** with the platinum dimer $[Pt_2Me_4(\mu\text{-}SMe_2)_2]$ in acetone for 16 h to yield the platinum(IV) fluoride complex **218** in 71% yield (eq 97).[285]

Puddephatt and co-workers postulate that the oxidative addition of C–F bonds at Pt(II) proceeds by either an electron-transfer mechanism or an S_NAr pathway. Unfortunately, attempts at kinetic studies were un-

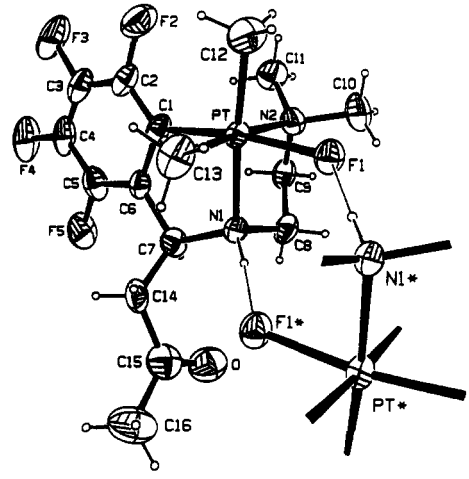
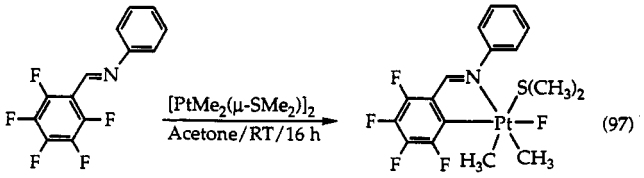


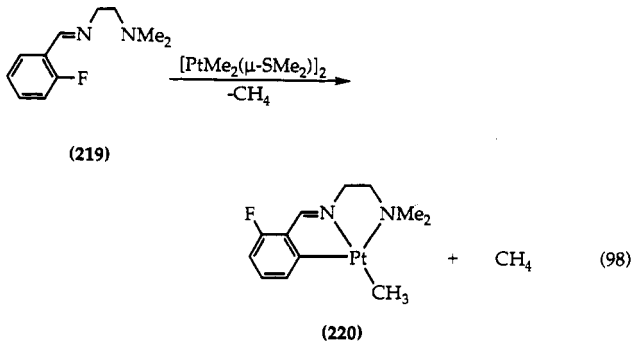
Figure 14. Reprinted with permission from ref 285. Copyright 1992 American Chemical Society.



(217) (218) (97)

successful, and so no activation parameters for these reactions are available. A concerted mechanism has been proposed for the oxidative addition of aromatic C–H, C–Cl, and C–Br bonds at Pt(II).[286]

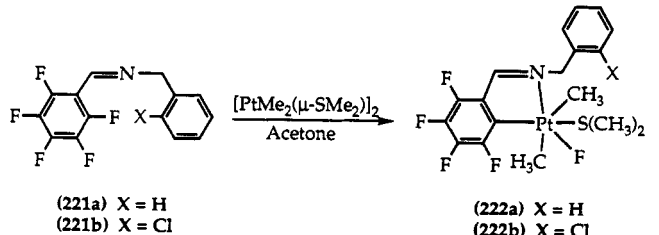
The scope of the dimethylplatinum(II) system was elucidated through a series of competition experiments. Using the bidentate ligand **219**, these researchers[285] demonstrated that C–F activation of a monofluorinated arene is more difficult than in a perfluorinated system despite the weaker C–F bond (BDE = 123 kcal/mol[37]) in the former system. Reaction of **219** with $[Pt_2Me_4(\mu\text{-}SMe_2)_2]$ affords only the *ortho*-metalated Pt(II) complex **220** by reductive elimination of methane (eq 98). *Ortho*-metalation is always observed instead of C–F



(219) (220) (98)

activation in $C_6H_nF_{5-n}$ groups.[285,287] C–F activation at Pt(II) has only been observed for pentafluorophenyl ligands and for trifluorinated aryl ligands containing two fluorine substituents in *ortho* positions.[285,287]

Additional studies with this dimethylplatinum(II) system by Crespo and associates[287,288] have shown that activation of C–F bonds takes place in the presence of weaker C–X bonds (X = H, Cl, and Br) in appropriately designed ligands. The platinum dimer $[Pt_2Me_4(\mu\text{-}SMe_2)_2]$ selectively activates a C–F bond instead of weaker C–H, C–Cl, and C–Br bonds in the monodentate ligand **221** to give the corresponding platinum(IV) fluoride complex **222** (eq 99). The ability of these



(221a) X = H
(221b) X = Cl
(221c) X = Br

(222a) X = H
(222b) X = Cl
(222c) X = Br

(99)

dimethylplatinum(II) systems to engage in C–F activation was attributed to several factors associated with ligand design. The presence of the pentafluorophenyl ligand is imperative for C–F activation. The formation of a five-membered metallacycle containing an endocyclic C=N group rather than an endocyclic C–N group has been noted for similar ligand systems.[232,237,289] The kinetics for X = H were investigated, and the following activation parameters were determined for the C–F activation process: $\Delta H^{\ddagger} = 30 \pm 4$ kJ mol^{-1} and $\Delta S^{\ddagger} = -198 \pm 14$ J K^{-1} mol^{-1}.[288] Consistent with these activation parameters, the authors propose that C–F activation proceeds by either an S_N2 mechanism or an electron-transfer pathway.

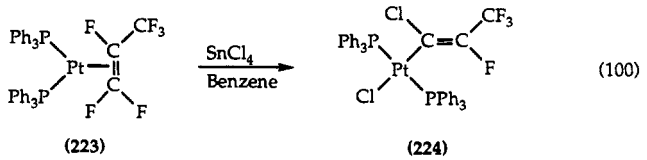
VIII. Reactions of Coordinated Ligands Involving C–F Cleavage

Despite the many diverse catalytic processes that exist, very few of these systems are well understood.[290] To promote further developments in this field a mechanistic understanding of the chemical interactions between the metal complex and the organic substrate is necessary.[291] As demonstrated in the preceding sections, several transition-metal complexes are capable of C–F oxidative addition which is one of the fundamental mechanistic steps necessary for metal-catalyzed functionalization of polyfluorinated molecules. The mild conditions of these transformations provide important implications for the development of homogeneous catalysts for fluorocarbon activation and functionalization. Unfortunately, many of these metal-promoted C–F activation reactions are recognized only because they form compounds in which a C–F bond has been ruptured, and typically a polyfluorinated ligand is coordinated to the metal center in the product. The stability of these adducts offers chemists an opportunity to study the way in which coordination modifies the reactivity of the coordinating molecules.[292] Presumably, this situation also better represents how the metal and polyfluorinated substrate interact within the coordination sphere of the metal center.[290]

Coordination of the perfluorinated moieties alters their chemical reactivity, making them susceptible to chemical attack. Consequently, there are several examples of reactions of fluorinated ligands that involve C–F cleavage. For clarity, the reactions of coordinated ligands will be organized according to ligand and type of reaction.

A. Reactions of Fluoroolefin Ligands

Several transition-metal fluoroolefin complexes have been prepared.[61,64,293–295] Upon coordination, the fluoroolefin moiety becomes rather electrophilic as evidenced by the facile addition of protic acids, such as hydrochloric acid and trifluoroacetic acid, to give fluoroethyl complexes.[296,297] In regard to this enhanced electrophilicity, coordinated fluoroolefins also tend to react readily with Lewis acids to afford vinyl complexes via fluoride abstraction. Specifically, Stone and coworkers[298] reported that reaction of the perfluoropropene platinum(0) complex **223** with stannic chloride in benzene at room temperature for 8 h gives the vinylplatinum(II) complex **224** in 63% yield (eq 100). The

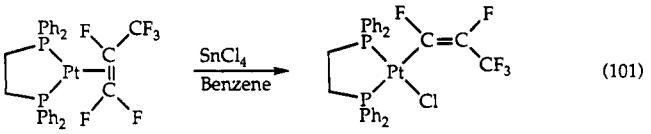


(223) (224) (100)

product platinum(II) complex **224** results from the loss

of two fluorine atoms under mild conditions, and its structure was determined by ^{19}F and ^{195}Pt NMR spectroscopy.

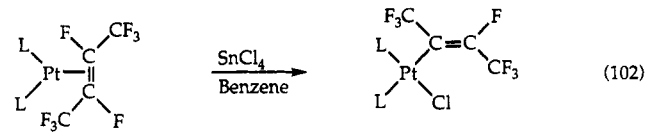
Similarly, the reaction of the perfluoropropene platinum(0) complex **225** with stannic chloride resulted in the loss of a single fluorine atom to afford the perfluoropropenyl platinum(II) complex **226** in 43% yield (eq 101). The authors note that the reaction is



(225) (226) (101)

dependent upon the nature of the ancillary ligands since displacement of the perfluoropropene by chloride was observed with PPh_2CH_3 or $AsPh_3$ as ligands.[298]

The stereospecificity of the fluoride abstraction was ascertained by reaction of perfluorobutene platinum(0) complexes **227a–c** with stannic chloride to afford the three isostructural platinum(II) complexes **228a–c**, respectively (eq 102). Again, displacement of the



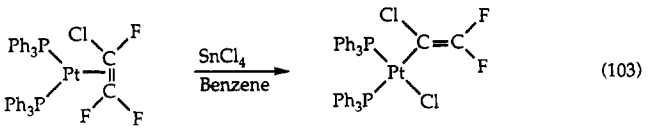
(102)

(227a) L = PPh_3
(227b) L = PPh_2CH_3
(227c) L = 1/2 Diphos

(228a) L = PPh_3
(228b) L = PPh_2CH_3
(228c) L = 1/2 Diphos

fluoroolefin by chloride was observed when the ancillary ligand was triphenylarsine.

Interestingly, treatment of the chlorotrifluoroethylene platinum(0) complex **229** with stannic chloride exclusively affords the vinylplatinum(II) complex **230** (eq 103).[298] As illustrated by the reactions of perfluoropropene complexes in Scheme 25, the authors

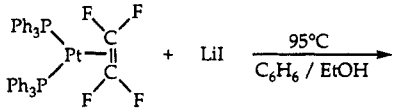


(229) (230) (103)

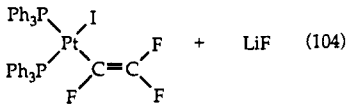
postulate a mechanism that involves the initial attack on the coordinated perfluoropropene by the Lewis acid at F_A to generate the cationic species **231**.[298] To account for the retention of configuration observed with the perfluoropropene diphos complex **225** and the perfluoro-2-butene complexes **227a–c** upon reaction with stannic chloride, the authors suggest that **231** forms an intimate ion pair which can react with chloride ion to yield the *cis*-vinyl isomer **232**. The existence of an intimate ion pair complex has been proposed to explain the retention of stereochemistry in similar "vinyl-rearrangement reactions" at iridium(I)[292] and platinum(0)[299] metal centers. An alternative and more probable mechanism involves the oxidative addition of the alkene C–Cl bond at Pt(0) followed by Lewis acid abstraction of fluoride to generate a cationic platinum carbene species which then undergoes nucleophilic attack by chloride ($SnFCl_4^-$) to afford the observed product **230**.

To rationalize the formation of the chlorovinyl complex **224** from **223** the authors propose that the cationic species **231** is initially formed; however, an internal return reaction involving attack by one of the chlorine atoms at the original site of the C–F fission would afford the chlorofluoroolefin complex **233**. Subsequent fluoride abstraction (F_B) from **233** would yield the cationic intermediate **234** which would undergo a vinyl rearrangement to afford the product **235**.[298]

In related work, Kemmitt and associates[300] noted that treatment of the (tetrafluoroethylene)platinum(0) complex **236** with lithium iodide in benzene/ethanol at 95 °C affords the (perfluorovinyl)platinum(II) complex **237** in 85% yield (eq 104). Presumably, the driving



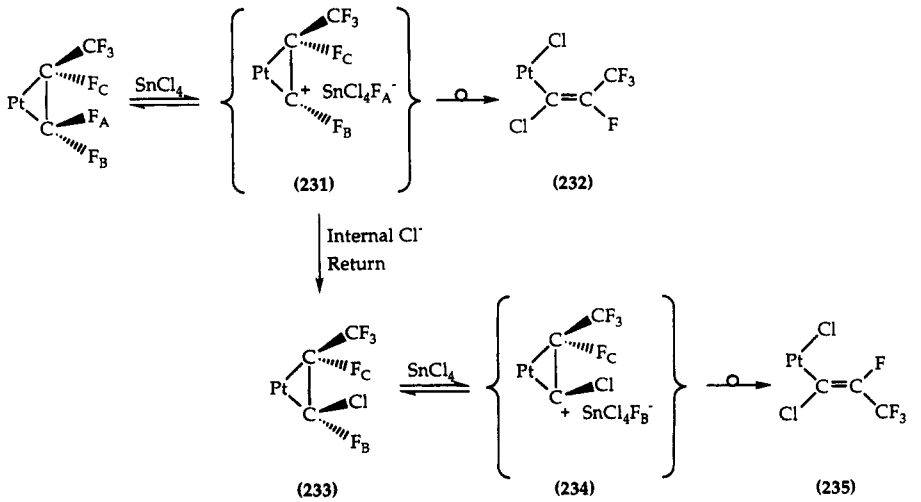
(236)



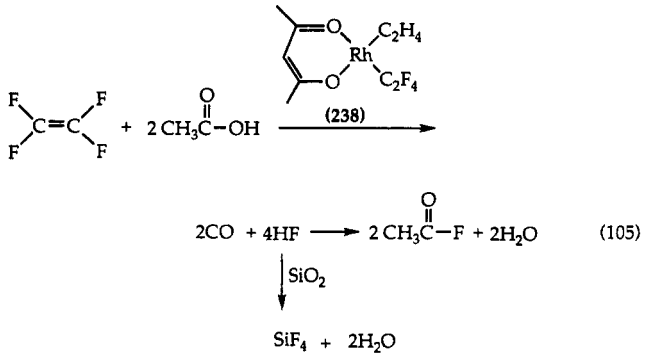
(237) (104)

force for this transformation is the high lattice energy for the formation of lithium fluoride.

Scheme 25



Parshall and Jones[62] observed that the hydrolysis of the terminal CF_2 groups of fluoroolefins is catalyzed by the complexes $Rh(acac)(CF_2{=}CF_2)(CH_2{=}CH_2)$ (**238**) and K_2PtCl_4 (**239**). In acetic acid, treatment of the complex **238** with tetrafluoroethylene affords carbon monoxide and acetyl fluoride as the fluorinated product (or SiF_4 if the reaction is done in glass) (eq 105).[301] One



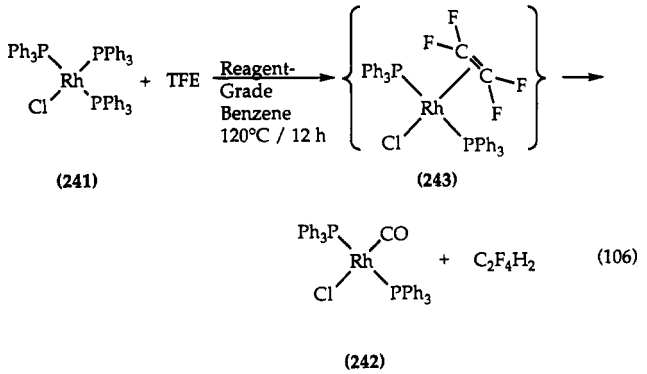
(238)

$$2CO + 4HF \longrightarrow 2\,CH_3C(=O)F + 2H_2O \qquad (105)$$

$$2CH_3C(=O)F \xrightarrow{SiO_2} SiF_4 + 2H_2O$$

mmol of the $Rh(acac)(CF_2{=}CF_2)(CH_2{=}CH_2)$ complex **238** hydrolyzes at least 30 mmol of tetrafluoroethylene.[301] The highest conversion was obtained with K_2PtCl_4 (**239**) as the catalyst pecursor which converted 60 mmol of tetrafluoroethylene to 113 mmol of carbon monoxide.[301] Presumably, the active catalysts are the monotetrafluoroethylene complexes since **239** also forms a monotetrafluoroethylene complex. No mechanistic details for this intriguing transformation were provided. Similarly, the hydrolysis of hexafluoropropylene by $Rh(acac)(CH_2{=}CH_2)_2$ (**240**) in acetic acid occurs at the terminal CF_2 group to yield 2,3,3,3-tetrafluoropropionic acid and acetyl fluoride.[301]

In related studies, Kemmitt and Nichols[302] reported that hydrolysis of tetrafluoroethylene (TFE) takes place upon reaction with Wilkinson's catalyst $[Rh(Cl)(PPh_3)_3]$ (**241**) in the presence of trace amounts of water (reagent-grade benzene) in a sealed glass tube for 12 h at 120 °C to afford CF_2HCF_2H and the carbonylrhodium complex *trans*-$Rh(Cl)(CO)(PPh_3)_2$ (**242**) in 90% yield (eq 106). The reaction was shown to involve the

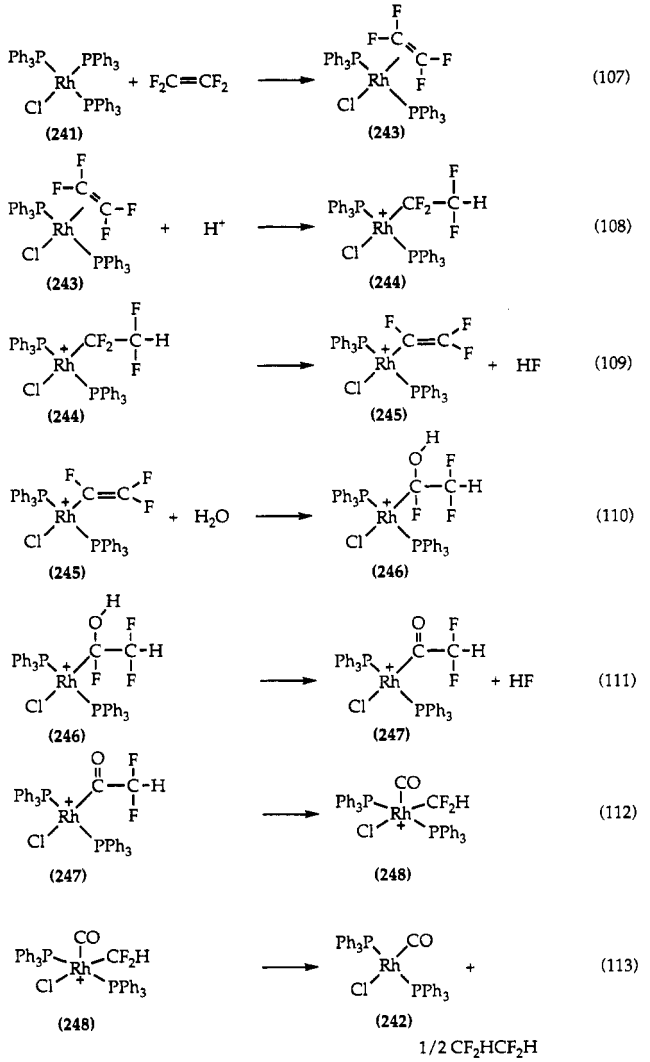


(241) (243)

(242)

intermediate formation of the corresponding olefin complex $RhCl(CF_2{=}CF_2)(PPh_3)_2$ (**243**). The gaseous product from the reaction of $RhCl(CF_2{=}CF_2)(PPh_3)_2$ (**243**) with water in a Carius tube was mainly CF_2HCF_2H; however, in a stainless steel bomb large amounts of CF_2HCF_2H and CF_2H_2 were formed. This implies that the reaction mechanism may be dependent upon the surface of the reaction vessel.

To account for the products formed in the glass tube reactions, the authors[302] suggested a series of reactions similar to those proposed by Clark and co-workers[278] (see section VII.E) for the activation of a tetrafluoroethylene C–F bond by *trans*-$[(Et_3P)_2PtHCl]$ (**193**) (eqs 107–113). Initial formation of the tetrafluoroethylene π-complex **243** is followed by the addition of water to eventually yield the α-hydroxyl complex **246** which loses a molecule of HF to afford the acyl compound **247** (eqs 107–111). This acyl complex would then undergo alkyl migration to afford the carbonyl complex **248** (eq 112). Loss of CF_2H from two molecules of **248** would yield the observed products **242** and CF_2HCF_2H (eq 113).[302] Interestingly, although treatment of $Rh(Cl)(PPh_3)_3$ (**241**) with chlorotrifluoroethylene (in a sealed Carius tube) also produced the carbonyl complex $RhCl(CO)(PPh_3)_2$ (**242**), it was noted that the chloroolefin did not afford the carbonyl complex as readily as did the fluoroolefin.



(241) (243) (107)

(243) (244) (108)

(244) (245) (109)

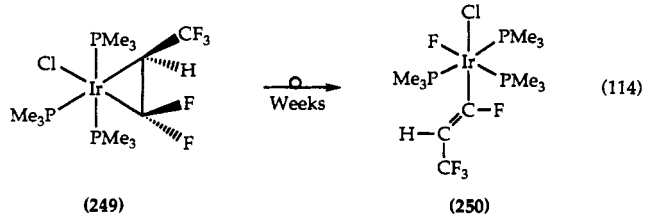
(245) (246) (110)

(246) (247) (111)

(247) (248) (112)

(248) (242) + $1/2\,CF_2HCF_2H$ (113)

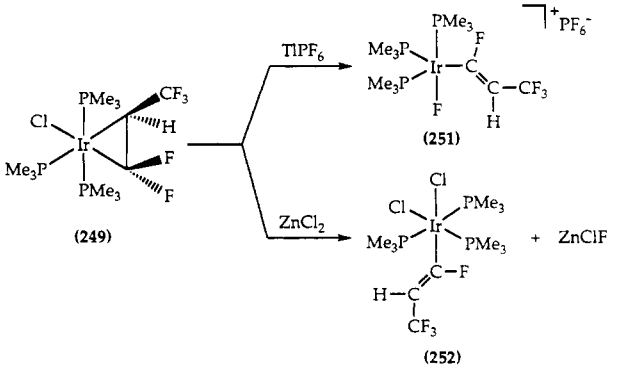
Recently, Baker[303] observed that the (fluoropropene)-iridium(I) complex **249** rearranges over a period of weeks to afford the σ-vinyliridium(III) fluoride complex **250** via vinylic C–F bond activation (eq 114). The structure



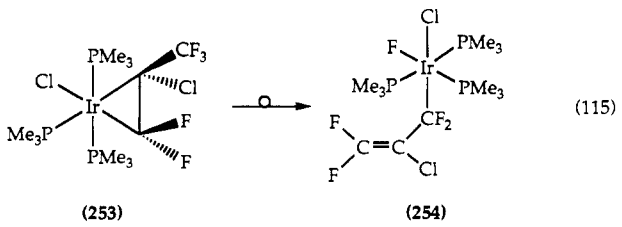
(249) (250) (114)

of the vinyliridium(III) fluoride complex **250** was determined by ^{19}F, $^{31}P\{^{19}F\}$, and $^{31}P\{^{1}H\}$ NMR spectroscopy. Baker postulates that Ir–Cl bond heterolysis initiates the rearrangement. Accordingly, treatment of **249** with 1 equiv $TlPF_6$ in tetrahydrofuran readily affords the cationic iridium(III) fluoride complex $[IrF(CF{=}CHCF_3)(PMe_3)_3]PF_6$ (**251**) in 84% yield as determined by multinuclear NMR studies (Scheme 26).[303] Chloride abstraction with $AgBPh_4$ in acetone or tetrahydrofuran also generates the cation $[IrF(CF{=}CHCF_3)(PMe_3)_3]BPh_4$ (**251**). Similarly, $ZnCl_2$ promotes vinylic C–F bond activation upon reaction with **249** to give *cis,mer*-$IrCl_2(CF{=}CHCF_3)(PMe_3)_3$ (**252**) and insoluble ZnClF (Scheme 26).

Scheme 26



A rare example of allylic C–F bond activation was observed upon rearrangement of the (fluoropropene)iridium(I) complex **253** at 25 °C to *mer*-$IrFCl(CF_2CCl{=}CF_2)(PMe_3)_3$ (**254**) (eq 115).[303] The iridium(III) fluoride product **254** was fully characterized by multinuclear NMR studies.

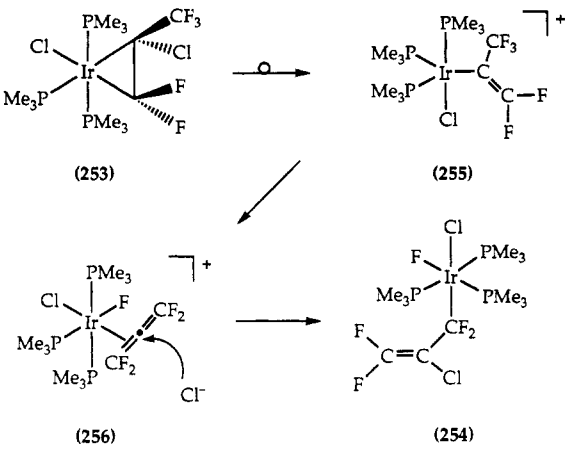


(115)

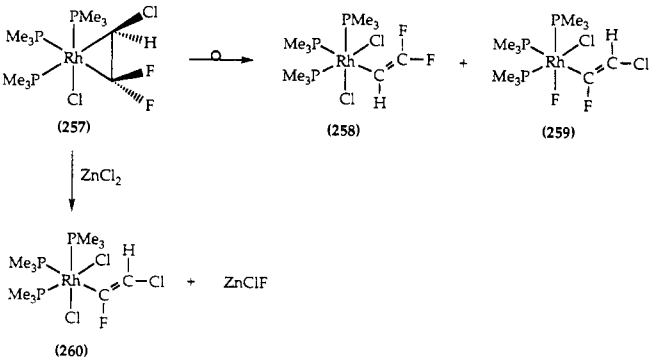
It was noted that the rate of rearrangement is dependent upon solvent polarity with acetone > tetrahydrofuran > toluene. In accord with this, Baker proposes a mechanism that involves initial Ir–Cl heterolysis followed by rearrangement to afford the cationic alkenyliridium intermediate **255** (Scheme 27).[303] This electrophilic 16-electron complex then abstracts a fluoride from the CF_3 group to generate the perfluoroallene iridium complex **256**. Subsequent attack by chloride ion at the central carbon of the coordinated allene then affords the observed product **254**.

In analogy to the above iridium systems, the fluoroolefin rhodium(I) complex **257** rearranges to a mixture of the vinylrhodium(III) complexes $RhCl_2(PMe_3)_3(CH{=}CF_2)$ (**258**) and $RhClF(PMe_3)_3(CF{=}CHCl)$ (**259**) (Scheme 28).[303] Rh–Cl bond heterolysis is also believed to initiate this rearrangement. As such, treatment of **257** with $ZnCl_2$ gives insoluble ZnClF and $RhCl_2(PMe_3)_3(CF{=}CHCl)$ (**260**) exclusively (Scheme 28). The structure of $RhCl_2(PMe_3)_3(CF{=}CHCl)$ (**260**) was confirmed by a single-crystal X-ray diffraction study.

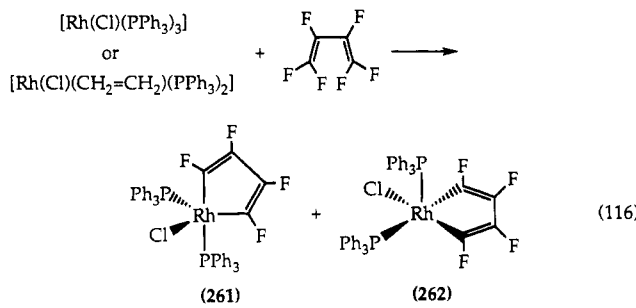
Scheme 27



Scheme 28

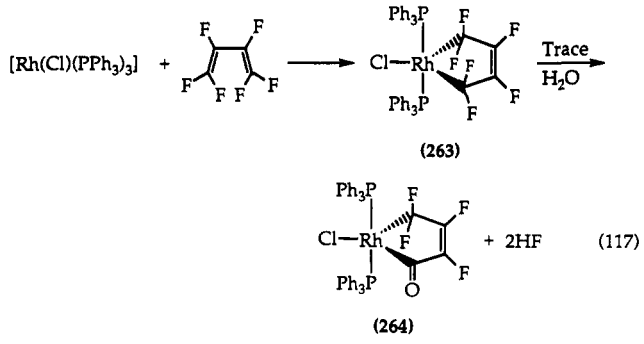


In 1968, Wilkinson and associates[304] reported that reaction of either $[RhCl(CH_2{=}CH_2)(PPh_3)_2]$ or $[Rh(Cl)(PPh_3)_3]$ with hexafluorobutadiene affords the tetrafluorometallacyclopentadiene complexes **261** and **262** via the apparent activation of two vinylic C–F bonds (eq 116). The fate of the fluorine atoms was not determined, and the structural characterization was vague and inconclusive.



(116)

Recently, Hughes and co-workers[305] carefully reexamined this intriguing transformation. These workers found that reaction of hexafluorobutadiene with $[Rh(Cl)(PPh_3)_3]$ under anhydrous conditions (with silylated glassware) affords the five-coordinate hexafluorometallacyclopentene complex **263** with loss of a PPh_3 ligand due to steric constraints. This coordinatively unsaturated 16-electron compound **263** is extremely sensitive to adventitious moisture and rapidly hydrolyzes to the tetrafluorometallacyclopentenone complex **264** (eq 117). Both complexes **263** and **264** were fully characterized by multinuclear NMR spectroscopy, and the structure of **264** was confirmed by X-ray crystallographic analysis. Interestingly, hydrolysis of only one α-CF_2 group was

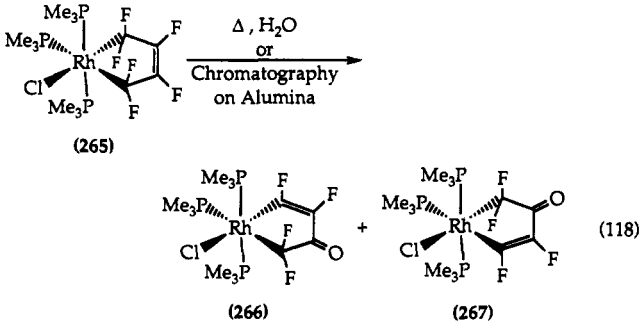


(263)

(264)

observed; subsequent hydrolysis of the second α-CF_2 group of **264** did not occur even at 60 °C.[305]

In contrast to the five-coordinate complex **263**, the six-coordinate derivative **265** is quite robust and does not react with water at room temperature. However, on heating with water or upon chromatography on alumina, compound **265** does undergo an unusual hydrolysis of a β-CF group to afford a mixture of isomers **266** and **267** (eq 118).[305] The authors offer two possible

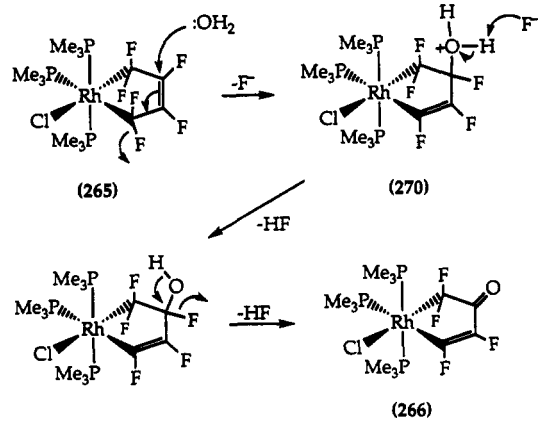


(265)

(266) (267)

mechanisms to rationalize the enhanced susceptibility of the coordinatively unsaturated rhodium(III) complex **263** toward hydrolysis (Scheme 29).[305] In the first pathway, the authors propose that the rhodium metal center acts as an internal Lewis acid in the α-elimination of fluoride to generate **268** which is then activated toward nucleophilic attack at the α-carbon by water. Subsequent elimination of HF affords the observed product **264**. Alternatively, coordination of H_2O at the rhodium would enhance the acidity of the α-carbon and promote the elimination of HF to generate **269**. Subsequent migration of OH to the α-carbon followed by loss of a second molecule of HF would also afford the observed product **264**. As a coordinatively saturated compound **265** cannot participate in the above α-hydrolysis pathways. Accordingly, the authors propose that the observed β-hydrolysis of **265** proceeds via the S_N2' mechanism illustrated in Scheme 30.[305] Attack

Scheme 30



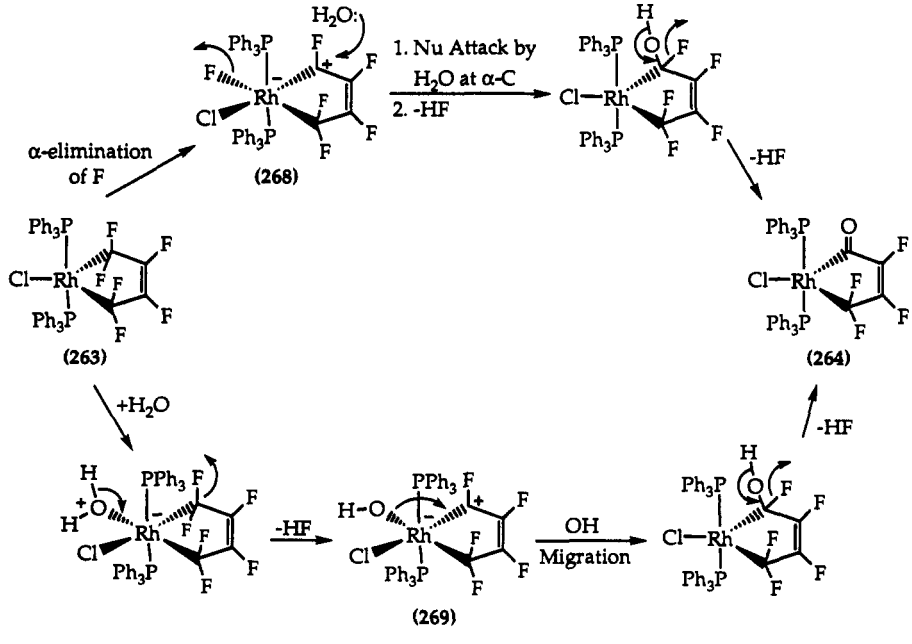
(265) (270) (266)

by water at the β-carbon results in the displacement of fluoride ion to generate **270**. Subsequent loss of two molecules of HF affords the observed major isomer **266**. In lieu of this mechanism, it is noteworthy that fluoride displacement has been observed upon reaction of perfluoropropene complexes with sodium hydroxide.[306]

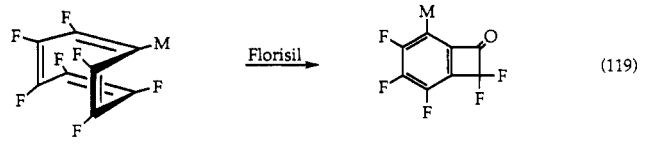
B. Reactions of the Octafluorocyclooctatetraene (OFCOT) Ligand

Several η^1-heptafluorocyclooctatraenyl iron and cobalt complexes undergo partial hydrolysis to afford the bicyclic ketone derivatives **271** upon column chromatography on Florisil (eq 119).[1,171,172] The mechanism of this transformation is unknown but clearly involves the loss of two fluorine atoms. Curiously, the ruthenium

Scheme 29



(263) (268) (264) (269)



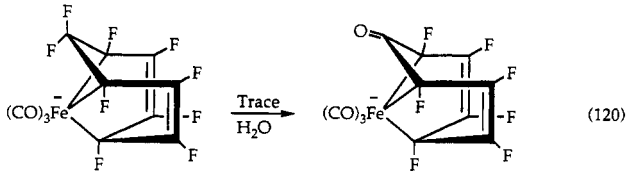
(119)

(32) M = Fe(Cp)(CO)$_2$
(34) M = Fe(Cp*)(CO)$_2$
(42a) M = Co(CO)$_3$(PPh$_3$)
(42b) M = Co(CO)$_3$(PMe$_2$Ph)
(42c) M = Co(CO)$_3$(PMe$_3$)
(42e) M = Co(CO)$_3$(PMePh$_2$)

(271a) M = Fe(Cp)(CO)$_2$
(271b) M = Fe(Cp*)(CO)$_2$
(271c) M = Co(CO)$_3$(PPh$_3$)
(271d) M = Co(CO)$_3$(PMe$_2$Ph)
(271e) M = Co(CO)$_3$(PMe$_3$)
(271f) M = Co(CO)$_3$(PMePh$_2$)

complex **36** did not form a bicyclic ketone complex upon exposure to Florisil.[172]

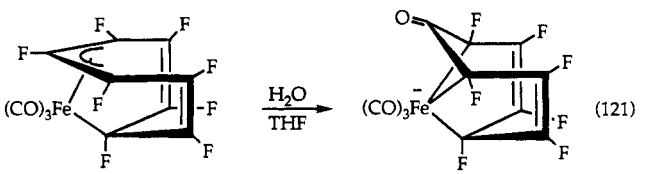
A similar conversion was observed by Hughes and co-workers[307] upon exposure of the anionic η^3-nonafluorocycloocta-2,5-diene-1,4,7-triyl complex **272** with traces of moisture to afford the $[(Me_2N)_3S]^+$ salt of the anionic 8-oxoheptafluorocycloocta-2,5-diene-1,4,7-triyl complex **273** (eq 120). Similarly, reaction of the [Fe-



(120)

(272) (273)

(1,2,3,6-η^4-C_8F_8)(CO)$_3$] complex **274** with H_2O in tetrahydrofuran gives **273** and HF (eq 121).[307] Treatment

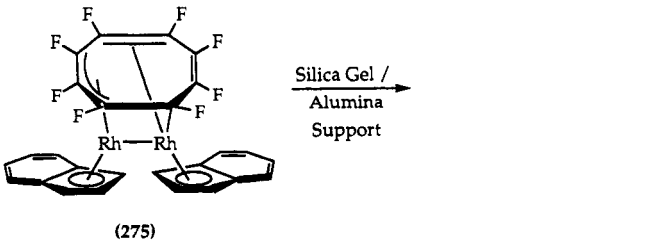


(121)

(274) (273)

of **274** with potassium hydroxide in DMSO also affords **273** as the (18-crown-6)K$^+$ salt.[307]

Remarkably, during column chromatography of the dinuclear (η^5-indenyl)rhodium complex **275**, using either a silica gel or alumina support, the complex **276** is produced in which a C–F bond has been exchanged for a much weaker C–H bond (eq 122).[308] The fate of the fluorine is unknown, as is the source of the hydrogen.



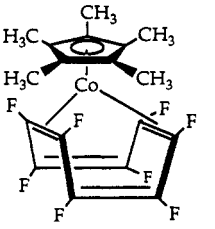
(275)

(122)

(276)

However, longer contact times on the column resulted in increased production of **276**.

Fluoride loss was observed upon electrochemical two-electron reduction of the complex [Co(η^5-C_5Me_5)-(1,2,5,6-η^4-C_8F_8)] (**277**) to afford an unidentified product with a mass spectrum peak corresponding to [Co(η^5-C_5Me_5)(C_8F_7H)]$^+$.[309] An ECE process was proposed to

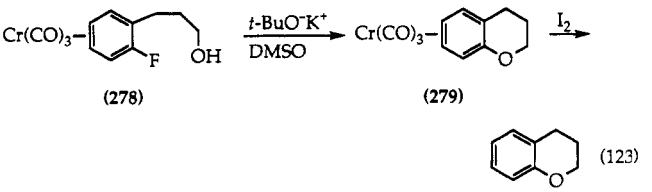


(277)

account for the loss of fluoride ion. ECE-type mechanisms have been suggested for other pertinent C–F activation processes.[310]

C. Intramolecular Nucleophilic Substitution of Coordinated Aryl Halide Ligands

Monofluoro arenes are normally inert toward nucleophilic attack as evidenced by the lack of reactivity between $[Fe(CO)_2(C_5H_5)]^-$ and fluorobenzene (see section V.A). However, π-coordination to a chromium tricarbonyl residue activates *ortho*-substituted aryl fluorides toward rapid intramolecular nucleophilic substitution accompanied by a selective cleavage of the aryl carbon–fluorine bond to afford six-membered oxygen heterocycles. Specifically, Houghton and co-workers[311,312] reported that treatment of the chromium complex **278** in dimethyl sulfoxide solution with potassium *tert*-butoxide at room temperature results in immediate cyclization to afford the chroman complex **279** in 75% yield. Subsequent oxidation by iodine in diethyl ether gives chroman in quantitative yield (eq 123). This is remarkable considering treatment of the

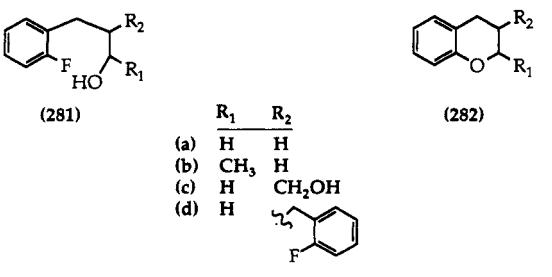


(278) (279)

(123)

parent fluoro alcohol with potassium *tert*-butoxide in dimethyl sulfoxide for 100 h at room temperature only affords a solution of the corresponding alkoxide anion.[311]

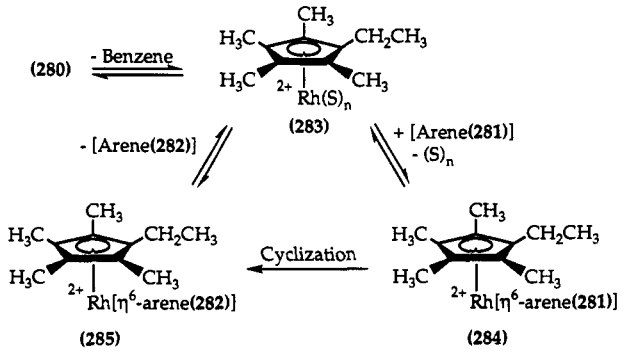
Importantly, Houghton and colleagues[311,313] further demonstrated that the rhodium(III) cation complexes $[Rh(\eta^5\text{-}C_5EtMe_4)(\eta^6\text{-}C_6H_6)][X]_2$ (X = PF_6 (**280a**); X = BF_4 (**280b**)) catalyze the cyclization of the 3-(2-fluorophenyl)propanols (**281**) in nitromethane–acetone solution at 80 °C to the corresponding chromans **282**.



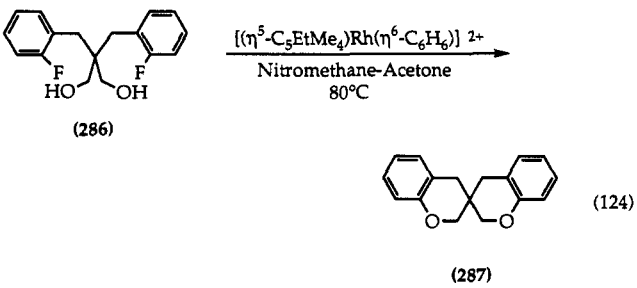
(281) (282)

	R_1	R_2
(a)	H	H
(b)	CH_3	H
(c)	H	CH_2OH
(d)	H	

Scheme 31



The authors proposed the catalytic cycle shown in Scheme 31.[311,313] The coordinated benzene in the cation **280** is reversibly displaced by solvent (either a molecule of solvent or alcohol **281** to yield the σ-solvent complex **283**. Similarly, reversible displacement of solvent affords the activated aryl fluoride complex **284** which rapidly undergoes cyclization to the chroman complex **285**. This complex would then regenerate the catalyst upon loss of the chroman product. Interestingly, under the same conditions the diol **286** afforded the spiro compound **287** in 90% yield via displacement of two fluorides (eq 124). The cyclizations proceeded at a much

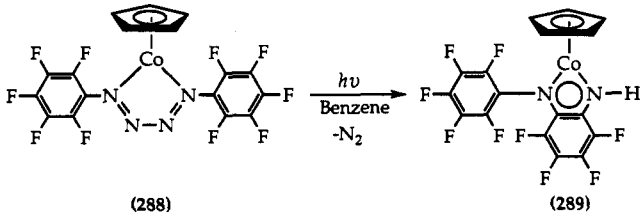


(124)

faster rate when **280a** was used as catalyst. Presumably, this is because the displacement of benzene from the cation **280** is dependent upon the counterion and occurs much more readily when the counterion is PF_6^- (**280a**) than when it is BF_4^- (**280b**).[311,313]

D. Photochemistry of the 1,4-Diaryltetraazadiene Ligand

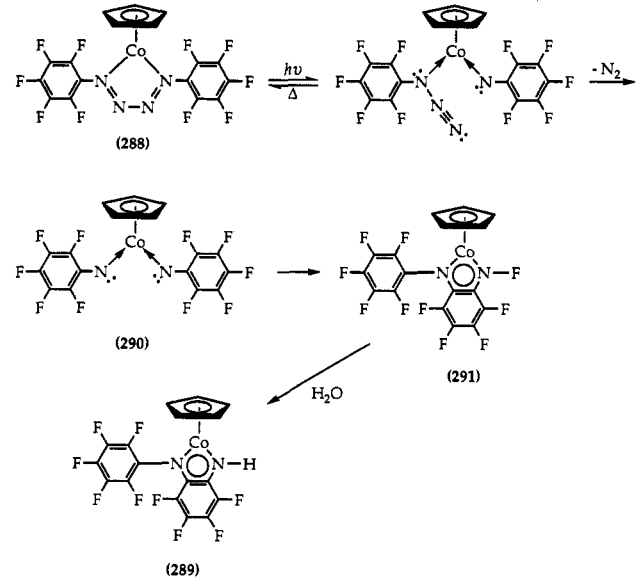
Trogler and co-workers[314–316] observed that photolysis (1200 nm > λ > 350 nm) of the cyclopentadienylcobalt 1,4-diaryltetraazadiene complex **288** in benzene affords the diimine complex **289** in which an aryl C–F bond has been cleaved (eq 125). The fate of the lost fluorine was not determined.



(125)

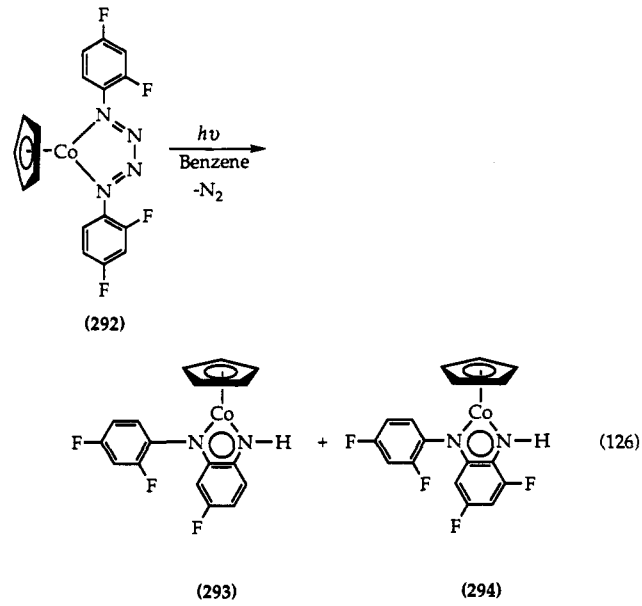
The mechanism for this intriguing rearrangement is unclear. However, an attractive pathway involves the initial formation of the bis(nitrene) intermediate **290** upon extrusion of N_2 from the starting material **288**

Scheme 32



(Scheme 32).[314,317] Abstraction of a fluorine atom in the putative bis(nitrene) intermediate would then yield the complex **291**.[315] Hydrolysis of the extremely labile N–F bond during workup would then afford the observed product **289**.[314] Alternatively, a radical mechanism has been proposed to account for this C–F cleavage reaction.[317] However, there has been no evidence (e.g., formation of HF) to support such a pathway.

In an analogous manner, irradiation of the cyclopentadienylcobalt 1,4-diaryltetraazadiene complex **292** in benzene yields a mixture of the diimine complexes **293** in 7% yield and **294** in 86% yield (eq 126).[317]



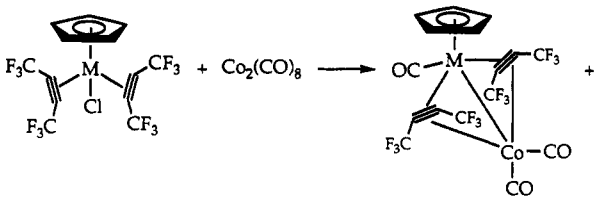
(126)

Remarkably, C–F activation is competitive with C–H bond cleavage. It is noteworthy that neither of these transformations occurs thermally.

E. Reactions Involving F^- Migration/Abstraction

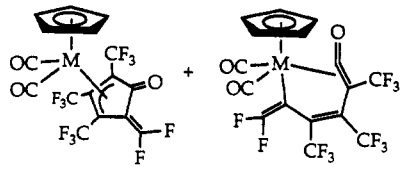
C–F bond cleavage is effected in coordinated ligands via metal-assisted fluoride abstraction or migration. For example, Davidson[318] reported that reaction of $[(\eta^5\text{-}C_5H_5)M(Cl)(CF_3C{\equiv}CCF_3)_2]$ (M = Mo (**295**); M = W

(296)) with $[Co_2(CO)_8]$ in an open system in diethyl ether affords the bis(μ-alkyne) complexes $[(\eta^5\text{-}C_5H_5)MCo(CO)_3(\mu\text{-}CF_3C{\equiv}CCF_3)_2]$ (M = Mo (**297**); M = W (**298**)) and small amounts of the complexes $[(\eta^5\text{-}C_5H_5)M(CO)_2(\eta^3\text{-}C_4(CF_3)_3CF_2CO)]$ (M = Mo (**299**), (**301**); M = W (**300**), (**302**) (eq 127). Apparently, the



(295) M = Mo
(296) M = W

(297) M = Mo
(298) M = W



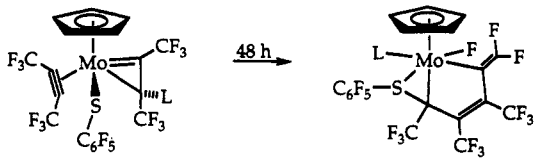
(299) M = Mo
(300) M = W

(301) M = Mo
(302) M = W

(127)

complexes **299–302** are formed as a result of fluorine abstraction from a CF_3 group by a cobalt carbonyl fragment. This is reasonable considering that hexafluoro-2-butyne readily undergoes nucleophilic attack by organometallic anions to afford metalated perfluoroallenyl complexes (see section V.A).[166]

In related studies, Davidson and co-workers[319] observed that the η^2-vinyl molybdenum complexes **303** undergo rearrangement in diethyl ether at room temperature in 48 h to afford the corresponding isomeric molybdenum fluoride complexes **304** in good yields (eq 128). Clearly, the complexes **304** follow from the



(303a) L = PEt_3
(303b) L = PMe_2Ph

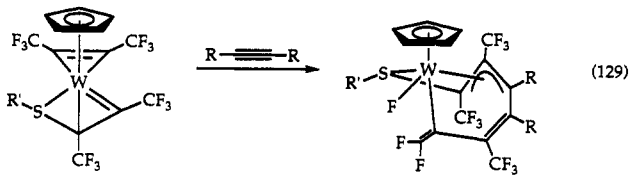
(304a) L = PEt_3
(304b) L = PMe_2Ph

(128)

transfer of fluorine from a CF_3 group to the metal. In this capacity, the molybdenum metal center appears to be acting as an internal Lewis acid. Additionally, the thiolate group has migrated onto the resulting perfluorinated ligand. Less successful fluoride migrations were noted for the tungsten analogs.[319]

Davidson, Muir, and associates[320] have also shown that the six-coordinate tungsten η^2-vinyl complexes **305** are quite susceptible to alkyne insertion into the W=C bond to predominantly afford the tungsten fluoride complexes **306** (eq 129). Upon alkyne insertion into the W=C bond migration of a fluorine atom from a CF_3 group to the tungsten metal center occurs with concomitant cleavage of a W–C(CF_3) bond. The authors claim that evidence for an agostic fluorine interaction was obtained at low temperature.[320]

Interestingly, Kiplinger et al.[76] have demonstrated that seven-coordinate tungsten fluoride η^2-vinyl complexes do not undergo further alkyne insertions. Presumably, this is a result of steric congestion at the

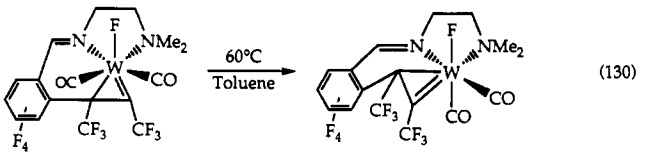


(305a) R' = Et
(305b) R' = Pr^n
(305c) R' = Pr^i
(305d) R' = Pr^i

(306a) R = CF_3, R' = Et
(306b) R = CF_3, R' = Pr^n
(306c) R = CF_3, R' = Pr^i
(306d) R = CO_2Me, R' = Pr^i

(129)

tungsten(II) metal center. However, upon heating at 60 °C an unusual η^2-vinyl isomerization is observed whereby the kinetic η^2-vinyl complex **307** converts to a thermodynamic η^2-vinyl product **308** (eq 130). The

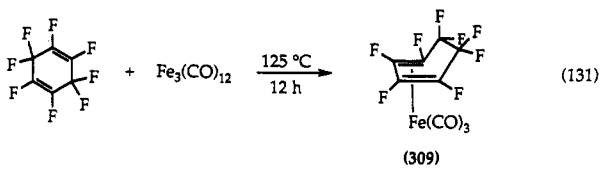


(307) (308)

(130)

driving force for the rearrangement appears to be the preference for the fluorine to be *trans* to a carbonyl ligand rather than *trans* to the inserted acetylene.[321]

Early work by Wilkinson and co-workers[322] revealed that fluoride migration occurs during the reaction of octafluorocyclohexa-1,4-diene with $Fe_3(CO)_{12}$ to afford the iron complex **309** (eq 131). The olefin was spec-

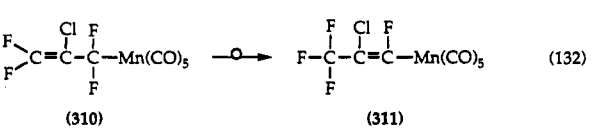


(309)

(131)

troscopically determined to be bound in a 1,3-fashion, consistent with a fluoride migration, but no mechanistic information for this transformation was provided.[322]

A rare example of intermolecular fluoride migration was reported by Goldwhite et al.[323] and is presumed to account for the thermal (≥40 °C) rearrangement of (2-chlorotetrafluoroallyl)manganese pentacarbonyl (**310**) to the propenyl isomer **311** (eq 132). Interestingly, low-



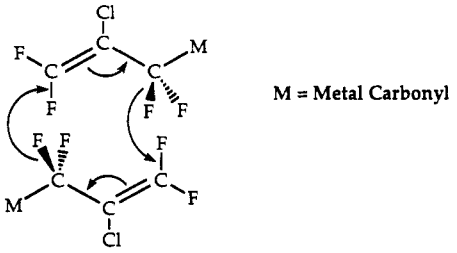
(310) (311)

(132)

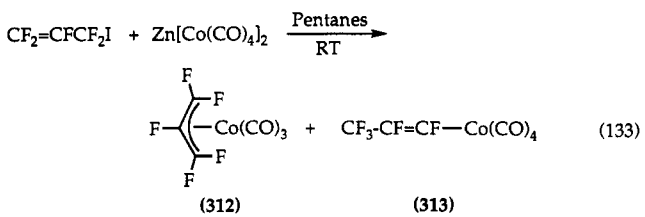
temperature treatment of 2,3-dichlorotetrafluoropropene with $[(\eta^5\text{-}C_5H_5)Fe(CO)_2]^-$ afforded only the propenyl compound $[(\eta^1\text{-}CF_3CCl{=}CF)(\eta^5\text{-}C_5H_5)Fe(CO)_2]$; it was not possible to isolate the unrearranged allyl compound from the reaction.[323,324] Presumably, the allyl complex $[(\eta^1\text{-}CF_2{=}CClCF_2)(\eta^5\text{-}C_5H_5)Fe(CO)_2]$ is formed but undergoes rearrangement under the reaction conditions.[323] Similarly, in early work by Stone and coworkers[149] and McClellan[325] it was noted that reaction between perfluoroallyl chloride and manganese pentacarbonyl anion gave exclusively the perfluoropropenyl complex $[(\eta^1\text{-}CF_3CF{=}CF)Mn(CO)_5]$. Again, the intermediacy of an allyl complex, $[(\eta^1\text{-}CF_2{=}CFCF_2)Mn(CO)_5]$, was surmised.

It is believed that the α-fluoride serves as an internal nucleophile in these compounds as a consequence of its

well-documented weakened bond strength. Although an intramolecular 1,3-fluoride shift is feasible, qualitative kinetic results suggested an intermolecular pathway via the following transition state:

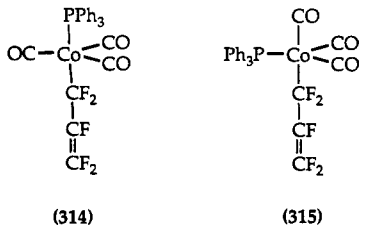


In related work, Stanley and McBride[326] noted that perfluoroallyl iodide reacts with $Zn[Co(CO)_4]_2$ to give $[(\eta^3\text{-}C_3F_5)Co(CO)_3]$ (**312**) and $[(\eta^1\text{-}CF_3CF{=}CF)Co(CO)_4]$ (**313**) (eq 133). To account for the observed



products, these authors propose the intermediacy of the allyl complex $[(\eta^1\text{-}CF_2{=}CFCF_2)Co(CO)_4]$ which undergoes an intermolecular fluoride transfer via the transition state proposed by Goldwhite et al.[323] to yield the product **313**. Alternatively, the η^1-allyl complex can lose a molecule of carbon monoxide to yield the η^3-allyl complex **312**.[326]

In support of the proposed mechanism, these authors further observed that only *trans*-$[(\eta^1\text{-}CF_2{=}CFCF_2)Co(CO)_3(PPh_3)]$ (**314**) rearranges to its corresponding propenyl complex, *trans*-$[(\eta^1\text{-}CF_3\text{-}CF{=}CF)Co(CO)_3(PPh_3)]$; *cis*-$[(\eta^1\text{-}CF_2{=}CFCF_2)Co(CO)_3(PPh_3)]$ (**315**) does not undergo rearrangement. The authors suggest

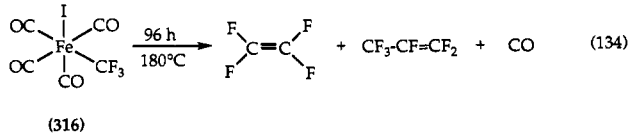


that with the bulky PPh_3 ligand in a *cis* position there are severe steric interactions in the transition state and the requisite bimolecular rearrangement cannot be attained.[326]

F. Reactions of Perfluoroalkyl Ligands

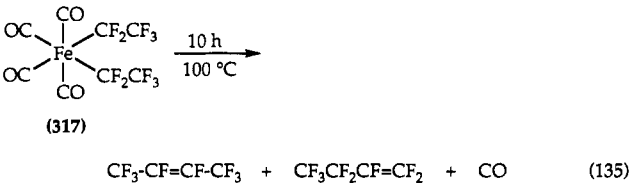
It has long been known that perfluoroalkyl transition-metal complexes possess exceptionally strong metal–carbon bonds and the carbon–fluorine bonds α to the metal center are weaker than in aliphatic compounds as evidenced by their reduced infrared stretching frequencies[68,69] and increased bond lengths.[67] As such, the carbon–fluorine bonds adjacent to the metal center in transition-metal–perfluoroalkyl complexes are susceptible to chemical attack.

(Perfluoroalkyl)transition-metal carbonyl complexes are susceptible to α-fluorine elimination decomposition pathways. Stone and co-workers[324] reported that extended pyrolysis of the (perfluoromethyl)iron tetracarbonyl iodide **316** produced tetrafluoroethylene, perfluoropropene, and carbon monoxide (eq 134). The

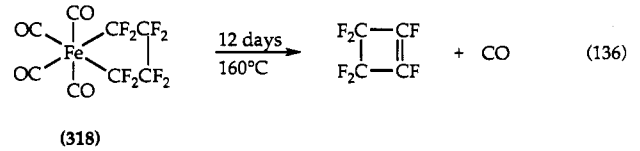


authors account for the observed products via α-fluorine elimination and the formation of the difluorocarbene intermediate, $:CF_2$. Coupling of two difluorocarbene units would give tetrafluoroethylene, and reaction of tetrafluoroethylene with $:CF_2$ would afford perfluoropropene.

Similarly, pyrolysis of $[(C_2F_5)_2Fe(CO)_4]$ (**317**) produces carbon monoxide and a mixture of the perfluorobutenes $CF_3CF{=}CFCF_3$ and $CF_3CF_2CF{=}CF_2$ (eq 135).[324]

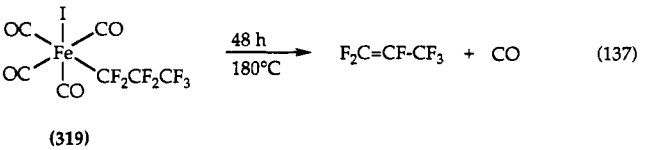


Likewise, pyrolysis of $[(CF_2)_4Fe(CO)_4]$ (**318**) quantitatively affords perfluorocyclobutene and carbon monoxide, suggesting that α-fluorine elimination is preferred to a β-fluorine elimination in the decomposition of (fluoroalkyl)iron complexes (eq 136).[327,328]



Again, the intermediacy of a difluorocarbene was invoked to account for the observed products in both systems.[324,327,328]

A rare example of β-fluorine elimination was observed by Stone and co-workers[324] upon pyrolysis of $[(C_3F_7)Fe(CO)_4(I)]$ (**319**) to give only perfluoropropene and carbon monoxide (eq 137).

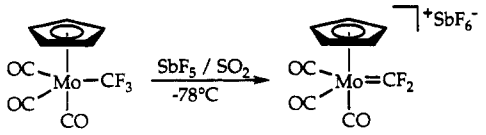


C–F cleavage was also observed by Stone and associates[329] upon vaccum pyrolysis of $[HCF_2CF_2Mn(CO)_5]$ to afford a mixture of $CF_2{=}CFH$, $CF_2{=}CH_2$, and carbon monoxide. The authors further note that sequential treatment of $[HCF_2CF_2Mn(CO)_5]$ and $[(C_3F_7)_2Fe(CO)_4]$ with 20% sodium hydroxide solution, acetic acid, and finally $CaCl_2$ affords fluoride ion as CaF_2 as the major product. Likewise, treatment of $[HCF_2CF_2Mn(CO)_5]$, $[(C_2F_5)_2Fe(CO)_4]$, and $[(C_2F_5)Mn(CO)_5]$ with hydrogen chloride gas afforded fluoride ion as SiF_4 as the major product. Apparently, the integrity of the metal–fluorocarbon bond is maintained

and only defluorination is observed since no fluorocarbons are produced from the reactions.[329]

Interestingly, the reaction chemistry of trifluoromethyl complexes remained largely unexplored until it was recognized that the weakened α carbon–fluorine bonds in these complexes rendered them susceptible to electrophilic attack. In particular, Shriver and coworkers[203-205] demonstrated that Lewis acids attack the metal-bound trifluoromethyl group to afford cationic difluorocarbene complexes which may either undergo hydrolysis to yield the corresponding cationic carbonyl complexes or undergo halide exchange upon reaction with boron trihalides to produce the corresponding trihalomethyl (X = Cl, Br, I) complexes. In related chemistry, Roper and colleagues[330] reported that treatment of transition-metal–trifluoromethyl complexes with protonic acids affords stable difluorocarbene complexes. Note that these reactions are conceptually similar to the electrophilic-assisted reactions at carbon–halogen bonds frequently observed in organic chemistry.[331] This prolific area of research has ultimately been the subject of three reviews by Roper and associates.[23,70,332] Therefore, we will only detail those difluorocarbene reactions subsequent to these reviews.

The studies by Shriver, Roper, and co-workers followed the early report by Reger and Dukes[333] concerning the generation of cationic molybdenum carbene complexes in solution (eq 138). The carbene complexes were not isolable and were monitored in solution using NMR spectroscopy.

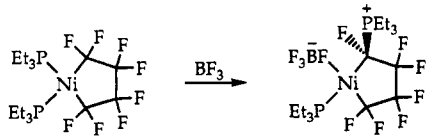


(138)

(320)

Recently, Koola and Roddick[334] reported the isolation and molecular structure of the comparable molybdenum difluorocarbene complex $[(\eta^5\text{-}C_5Me_5)Mo(CO)_3(CF_2)][OSO_2CF_3]$. This provided the first example of a structurally characterized Group 6 difluorocarbene complex. Prior attempts to isolate these complexes were typically frustrated by the undesired formation of $[(\eta^5\text{-}C_5H_5)Mo(CO)_4]^+$ as the sole decomposition product of the difluorocarbene.

Burch and colleagues[335] reported that treatment of the perfluorometallacyclopentane complex $Ni(PEt_3)_2(CF_2)_4$ (**321**) with 1 equiv of BF_3 affords the phosphonium ylide $[Ni(PEt_3)(BF_4^-)(CF)(PEt_3^+)(CF_2)_3]$ (**322**) (eq 139). The structure of the unusual product **322** was

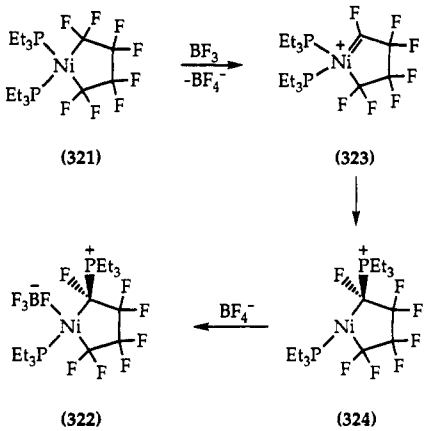


(139)

(321) (322)

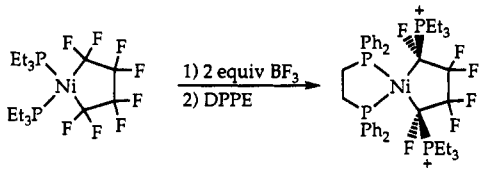
determined by a single-crystal X-ray diffraction study. The reaction is believed to proceed via fluoride abstraction from the α carbon by BF_3 to generate the fluorocarbene **323** which undergoes phosphine migration to afford the ylide-like structure **324** (Scheme 33).[335] Subsequent coordination of BF_4^- gives the observed product **322**. Presumably, reaction of the complex Ni-

Scheme 33



(321) (323) (322) (324)

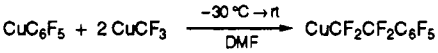
$(PEt_3)_2(CF_2)_4$ (**321**) with 2 equiv of BF_3 results in two fluoride abstractions followed by phosphine migrations. The solid obtained readily reacts with bis(diphenylphosphino)ethane (DPPE) to yield the crystallographically determined bis(ylide) dicationic compound **325** (eq 140).[335]



(140)

(321) (325)

An intriguing example of C–F cleavage involving (trifluoromethyl)copper as a CF_2 transfer reagent has been noted by Burton and co-workers.[336] Reaction of (pentafluorophenyl)copper with 2 equiv of $CuCF_3$ in dimethylformamide afforded $CuCF_2CF_2C_6F_5$ (**326**) in 70–80% yield (eq 141). It is believed that the $CuCF_3$



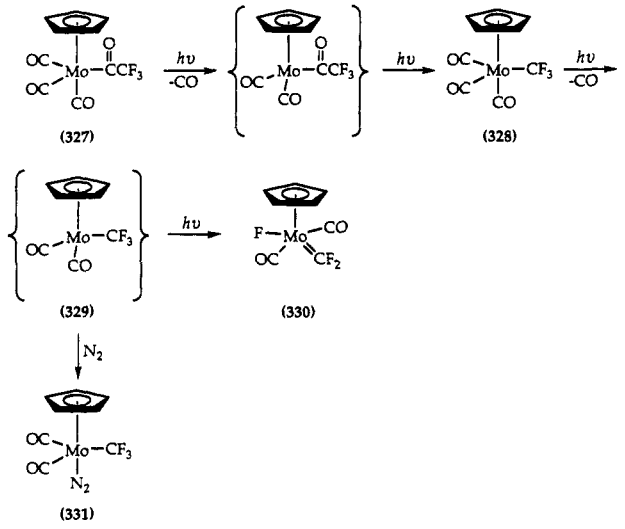
(141)

(326)

is in equilibrium with the copper difluorocarbene complex, (F)Cu=CF_2, which inserts into the carbon–copper bond of CuC_6F_5 to form $CuCF_2C_6F_5$ which then reacts with another (F)Cu=CF_2 to yield the product **326**. The authors note that only the double insertion product is observed since $CuCF_2C_6F_5$ is more reactive toward insertion than CuC_6F_5.[336]

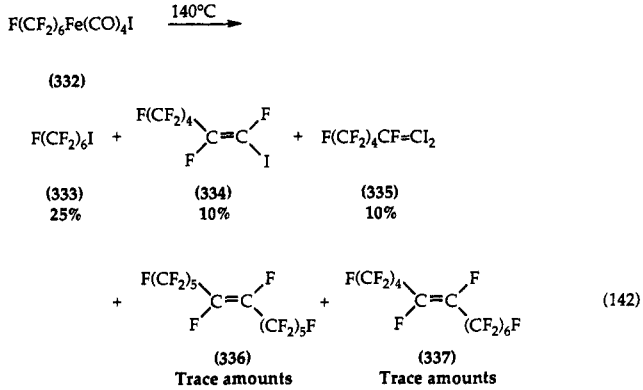
A rare example of intramolecular α-fluorine abstraction to generate a difluorocarbene complex was spectroscopically demonstrated by Rest and co-workers[337] upon photolysis of $[(\eta^5\text{-}C_5H_5)Mo(CO)_3(COCF_3)]$ (**327**) in frozen gas matrices at 12 K (Scheme 34). Photolysis of the fluoroacetyl complex $[(\eta^5\text{-}C_5H_5)Mo(CO)_3(COCF_3)]$ (**327**) effects CO loss and CF_3 migration to yield the 18-electron species $[(\eta^5\text{-}C_5H_5)Mo(CO)_3(CF_3)]$ (**328**). Continued photolysis results in further CO loss to generate the coordinatively unsaturated 16-electron complex $[(\eta^5\text{-}C_5H_5)Mo(CO)_2(CF_3)]$ (**329**) which rapidly undergoes α-fluorine elimination to afford the observed difluorocarbene product *trans*-$[(\eta^5\text{-}C_5H_5)Mo(CO)_2(CF_2)F]$ (**330**). In this context, the electron-deficient metal could be viewed as an internal Lewis acid abstracting the α-fluorine to give the difluorocarbene complex, not unlike the intermolecular fluorine abstraction reactions mentioned earlier. Interestingly,

Scheme 34



in nitrogen matrices the photolysis produces the dinitrogen complex *cis*-[(η^5-C_5H_5)Mo(CO)$_2$(CF_3)N_2] (**331**).[337]

Krespan[338] has reported a synthesis of fluorinated vinyl iodides that involves intermolecular α-fluorine abstraction by an iron metal center. Pyrolysis of the perfluoroalkyliron tetracarbonyl iodide [$F(CF_2)_6$Fe(CO)$_4$I] (**332**) at 140 °C gave the products detailed in eq 142. Note that this system decomposes quite dif-



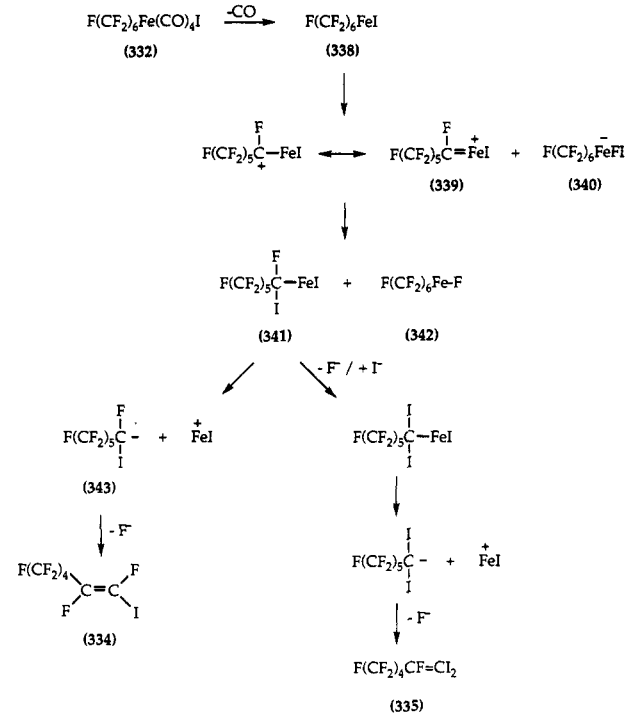
(142)

ferently than those reported by Stone and co-workers[324] for perfluoroalkyliron tetracarbonyl iodide complexes. In fact, virtually no perfluoro-1-hexene, arising from β-fluorine elimination, was observed from the pyrolysis of **332**.[338]

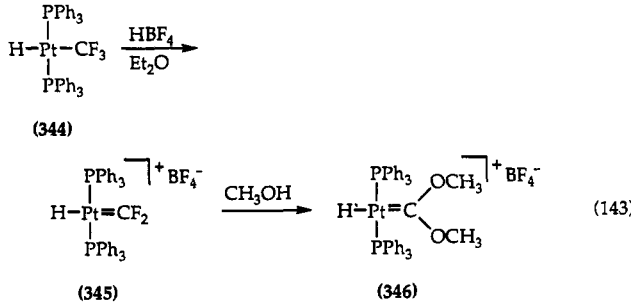
To account for the observed products Krespan proposed a mechanism that involves initial loss of CO to generate the iron iodide species **338** (Scheme 35).[338] The electron-deficient iron center in **338** could then serve as a Lewis acid and abstract the α-fluorine from another molecule to afford a mixture of the fluorocarbene cation (**339**) and the iron fluoride anion (**340**) complexes which would easily undergo halide exchange to afford the neutral iron complexes **341** and **342**. Heterolysis of **341** would form the carbanion **343** which would undergo β-fluorine elimination to generate the observed monoiodide **334**. Alternatively, complex **341** could generate another iron carbenoid and undergo a second halide exchange to eventually afford the diiodide **335**.

Michelin and associates[339,340] observed that the C–F bond in *trans*-[PtH(CF_3)(PPh_3)$_2$] (**344**) undergoes electrophilic cleavage by HBF_4 to afford the platinum

Scheme 35



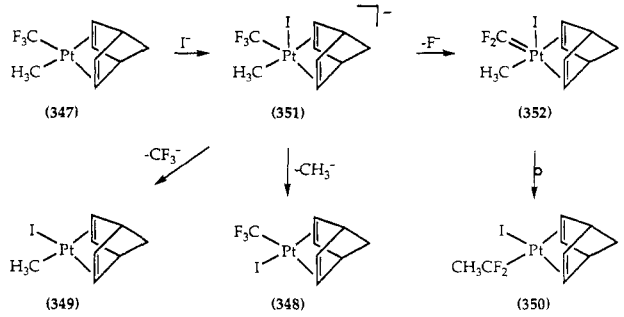
difluorocarbene complex **345** which in the presence of an alcohol, such as methanol, affords the corresponding hydrido carbene complex *trans*-[PtH(=C(OCH_3)$_2$)(PPh_3)$_2$][BF_4] (**346**) (eq 143). The intermediate difluorocarbene complex **345** was fully characterized using low-temperature multinuclear NMR spectroscopic techniques. Analogous reactions were observed using *trans*-[PtCl(CF_3)(PMe_2Ph)$_2$].[339,340]



(143)

In contrast, Appleton and associates[341] recently reported that reaction of the mixed alkyl compound Pt(CH_3)(CF_3)(norbornadiene) (**347**) with iodide affords a mixture of Pt(CF_3)(I)(norbornadiene) (**348**), Pt(CH_3)(I)(norbornadiene) (**349**), and Pt(CF_2CH_3)(I)(norbornadiene) (**350**), the product of a formal insertion of difluorocarbene into a Pt–CH_3 bond. The authors proposed the initial formation of the five-coordinate anionic complex **351** (Scheme 36).[341] Apparently, the negative charge on this complex promotes the loss of fluoride ion from the trifluoromethyl group to yield the neutral difluorocarbene complex **352**. Methyl migration to the difluorocarbene group would then yield the product **350**. Analogous reactions involving hydride migration to a difluorocarbene group have been observed in rhodium[342] and iridium systems[343] by Roper and co-workers. Alternatively, the common intermediate **351** could lose either CH_3^- or CF_3^- to give the products **348** and **349**, respectively. It is interesting to note that treatment of *cis*-[Pt(CF_3)$_2$(norbornadiene)]

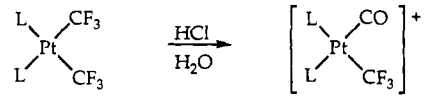
Scheme 36



(347) (351) (352) (349) (348) (350)

with iodide results in initial displacement of the norbornadiene moiety to give $[\{Pt(CF_3)_2(\mu\text{-}I)\}_2]^{2-}$ which readily loses fluoride ion to generate a difluorocarbene complex which forms *cis*-$[Pt(CF_3)(CO)I_2]^-$ in the presence of adventitious moisture.[341]

Interestingly, Hall and co-workers[344] observed that with the related bis(trifluoromethyl)platinum complexes *cis*-$[Pt(CF_3)_2L_2]$ (L_2 = bipyridine (bipy) (**353**), *N,N,N',N'*-tetramethylethylenediamine (tmen) (**354**); L = pyridine (**355**)) only one CF_3 group undergoes reaction with aqueous hydrochloric acid to afford the corresponding monocarbonyl complexes *cis*-$[Pt(CO)(CF_3)L_2]^+$ **356–358** (eq 144). Even with $HClO_4$ the



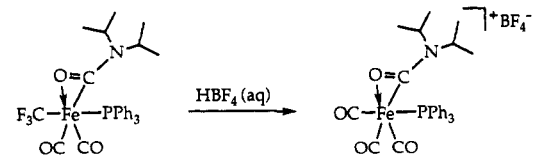
(144)

(353) L = bipy
(354) L = tmen
(355) L = pyridine

(356) L = bipy
(357) L = tmen
(358) L = pyridine

remaining trifluoromethyl group does not undergo electrophilic attack. The authors postulate that this is a consequence of decreasing the electron density on the platinum center upon conversion of one CF_3 group to a CO group leaving the remaining CF_3 group immune to further chemical attack.[344]

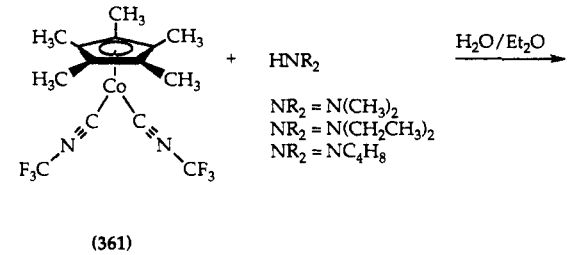
Recently, Anderson, Hill, and Clark[345] provided an example of difluorocarbene formation at an iron metal center by reaction of the (trifluoromethyl)carbamoyliron complex $[Fe(CF_3)\{\eta^2\text{-}CON^iPr_2\}(CO)_2(PPh_3)]$ (**359**) with aqueous HBF_4 to afford $[Fe\{\eta^2\text{-}CON^iPr_2\}(CO)_3(PPh_3)][BF_4]$ (**360**) (eq 145).



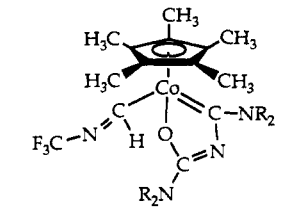
(145)

(359) (360)

In the course of their work on fluoroisocyanides, Lentz and Marschall[346] reported that the complex $[(\eta^5\text{-}C_5Me_5)Co(CNCF_3)_2]$ (**361**) reacts with amines in wet diethyl ether to afford the cobalt(III) heterocycles **362–364** (eq 146). These products all contain an *N*-(trifluoromethyl)formimidoyl moiety, and the structure of **362** was confirmed by X-ray crystallography. Three C–F bonds are cleaved with fluoride removed as HF. Using the reaction between **361** and dimethylamine as an example, the authors postulated a mechanism that involves initial attack by the amine at an isocyanide



(361)

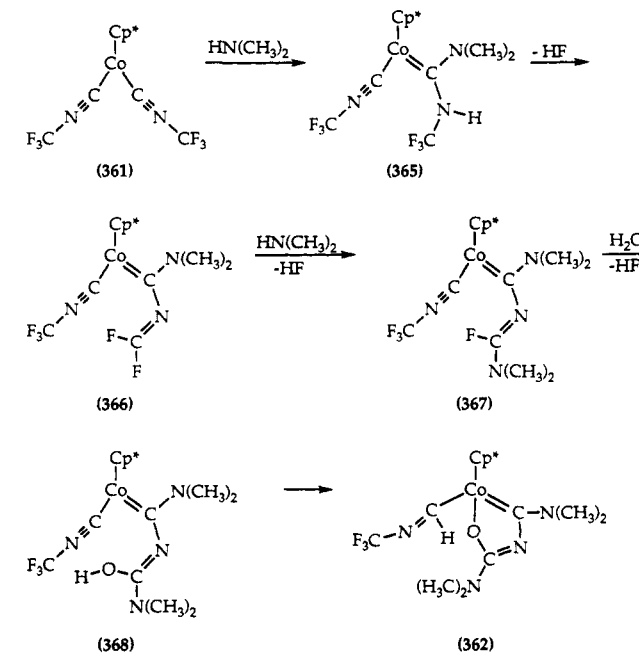


(146)

(362) $NR_2 = N(CH_3)_2$
(363) $NR_2 = N(CH_2CH_3)_2$
(364) $NR_2 = NC_4H_8$

carbon in **361** to form the cobalt carbene species **365** which loses HF to afford the difluorocarbene complex **366** (Scheme 37). This difluorocarbene ligand then

Scheme 37



undergoes nucleophilic attack by another amine to give the imine complex **367**. Subsequent hydrolysis followed by proton transfer would afford the observed product **362**.[346]

IX. Activation of C–F Bonds in Biological Systems

In recent years, there has been a substantial amount of research and development concerning the microbial degradation of halogenated organic compounds.[347] Several microbial strains have demonstrated the ability to successfully break down even recalcitrant chlorinated[348–350] and in rare instances fluorinated[351] compounds.[352,353] This subject has been extensively reviewed.[353–356] Five major pathways for enzymatic degradation of halogenated compounds have been discovered: reductive dehalogenation, dehydrohalo-

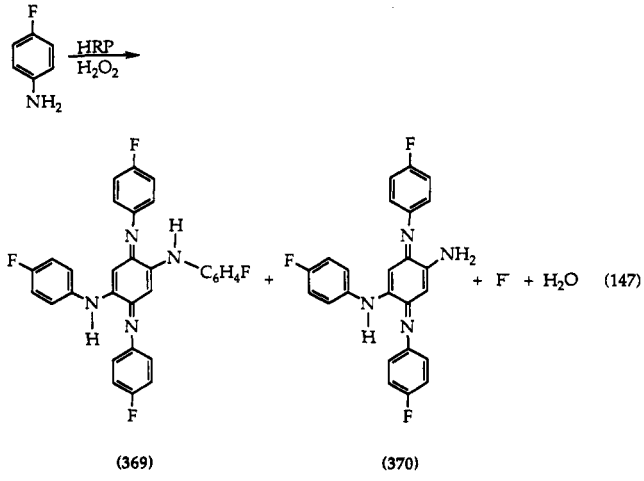
genation, hydrolytic dehalogenation, epoxidation, and oxidative displacement.[355–357]

The activation of C–F bonds in biological systems has been an area of considerable interest. Of particular relevance are the often lethal effects imparted by the substitution of fluorine for hydrogen in a substrate of an enzyme.[17] Often the fluorinated analog acts as an irreversible inhibitor of the enzyme through the formation of covalent bonds and/or loss of fluoride. This toxicity is evident by the lethal *in vivo* synthesis of fluorocitrate from fluoroacetate.[18] Fluorocitrate inhibits the enzyme aconitase and results in the accumulation of citric acid which leads to cell death. Interestingly, difluoroacetate and trifluoroacetate are nontoxic for steric reasons, and these molecules can no longer mimic acetic acid like fluoroacetate.[18]

With the evolution of bioinorganic chemistry, researchers have explored the fundamentals of these microbally induced metabolic reactions in biological systems that contain a transition metal such as coenzymes, hematin, and porphyrin-based proteins. In fact, several metal-containing coenzymes have been shown to catalyze the reductive dehalogenation of halogenated alkanes, chloroethylenes, and chlorinated aromatic compounds.[358–361] Remarkably, C–F bond activation has been shown to occur in metal-containing biological systems dating as far back as 1954, although mechanistic study in this area is still in its infancy. As we shall see for these biological systems, the C–F bond activation occurs at the metal center, and radical mechanisms are typically invoked to account for observed products.

A. Horseradish Peroxidase

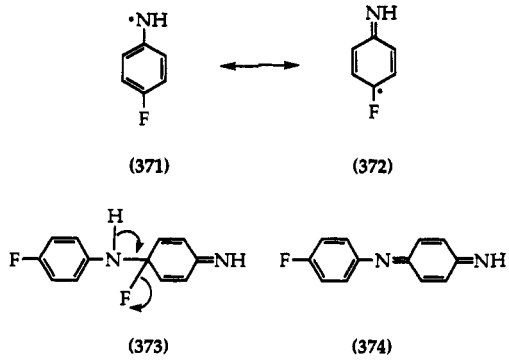
In 1954, Hughes and Saunders[362,363] provided the first reports of a metal-containing enzyme, horseradish peroxidase (HRP), that engages in C–F activation.[364] HRP is an iron-containing protein.[364] Treatment of *p*-fluoroaniline with HRP, at ambient temperature and pH 4.5, results in the immediate formation of compounds **369** and **370** in a cummulative 30% yield (eq 147). The reaction involves the catalytic rupture of a



(369) (370) (147)

covalent C–F bond with elimination of fluorine as F^-. The formation of **369** and **370** requires that one fluorine atom should be eliminated between five and four molecules of *p*-fluoroaniline, respectively. Unfortunately, the process is self-poisoning since the enzyme reaction is retarded by F^-.[362,363]

Although the authors do not offer a detailed mechanism, they do propose the initial generation of the radicals **371** and **372**[365] resulting from either direct loss of a hydrogen atom or by electron-removal followed by loss of a proton via action of the HRP. The unsymmetrical pairing of radical **372** yields **373**, which upon loss of HF gives the imine **374**. It is not certain as to whether the loss of HF involves a one-step or a two-step process. However, this sequence, which is reminiscent of a nucleophilic aromatic substitution, accounts for both the observed fall in pH and the production of F^-. The authors subsequently allude to a "series of



(371) (372) (373) (374)

established addition and oxidation reactions"[363] that could occur with **374** to afford the observed products.

In view of the availability of the fluoride selective electrode since 1966, it is surprising that this intriguing observation was not pursued further until 1978 by MacDonald and Kelly[366] who realized the bioanalytical importance of this reaction. Using a fluoride ion-selective electrode, the liberated F^- may be used as a marker for the quantification of HRP or its substrates.[366,367] Siddiqi and associates[368,369] have since demonstrated that several other organofluorine compounds are similarly susceptible to C–F bond rupture and are attractive for use as indicator reactions for the enzyme immunoassay technique ELISA (enzyme linked immino-sorbant assay).

B. Cytochrome P-450

Another iron-containing protein that has been recognized for its ability to catalytically cleave C–F bonds is liver microsomal cytochrome P-450. Cytochrome P-450 is able to reductively dehalogenate halothane (2-bromo-2-chloro-1,1,1-trifluoroethane). Interestingly, halothane was originally designed as the prototype of stable halogenated anesthetics.[370,371] However, biodegradation of halothane in humans was later established.[372,373]

Early studies using ^{14}C-labeled halothane demonstrated that a reductive pathway accounted for the halothane decomposition with covalent binding of ^{14}C-metabolites to lipids from ^{14}C-halothane. In fact, under anaerobic conditions the production of fluoride was observed through *in vitro*[374] and *in vivo*[375] experiments. The anaerobic metabolites of halothane were determined to be 2-chloro-1,1,1-trifluoroethane (CTE) and 2-chloro-1,1-difluoroethylene (CDE), the latter clearly a result of a reductive defluorination process.[376] Unfortunately, these early reports offered only vague and inconclusive mechanisms concerning the direct interaction, if any, of the metal center with halothane.

In 1974, there was a report by Ullrich and associates[377] on the mechanism of halothane reductive dehalogenation by microsomal cytochrome P-450 which was essentially qualitative in nature and based on comparisons of UV–vis difference spectra. Since the difference spectrum obtained with halothane and reduced liver microsomal cytochrome P-450 (λ_{max} = 470 nm) was nearly identical to the difference spectrum obtained by the addition of trifluorodiazoethane to dithionite reduced microsomal cytochrome P-450 (λ_{max} = 468 nm), the authors concluded that a trifluoromethyl ferrous carbene complex **375** was formed between the reduced cytochrome P-450 and halothane. Specifically, upon forming an enzyme–substrate complex with halothane, cytochrome P-450 could form the ferrous carbene complex via a two-electron reduction of the halothane (eq 148).[377]

$$(\text{P-450})\text{Fe}^{\text{II}} + \text{CF}_3\text{-CHClBr} \xrightarrow[-\text{Cl}^-,\,-\text{Br}^-]{+2e^-} (\text{P-450})\text{Fe}^{\text{II}}{=}\text{C}(\text{H})\text{-CF}_3 \quad (148)$$

(375)

Doubt was later cast on this assignment when a study[378] of the products of reductive halothane metabolism revealed that the intermediate complex with the Soret band at 470 nm decomposes spontaneously to the olefin CF_2=CHCl, which is best explained as the product of a β-fluoride elimination from the ferric carbanion complex **376**. This is consistent with related

$$(\text{P-450})\text{Fe}^{\text{III}}\cdots{}^-\text{CHClCF}_3$$

(376)

work in which it was observed that tetrachloroethylene was produced in 99.5% yield upon the reductive dehalogenation of hexachloroethane by reduced cytochrome P-450 under anaerobic conditions (eq 149).[379]

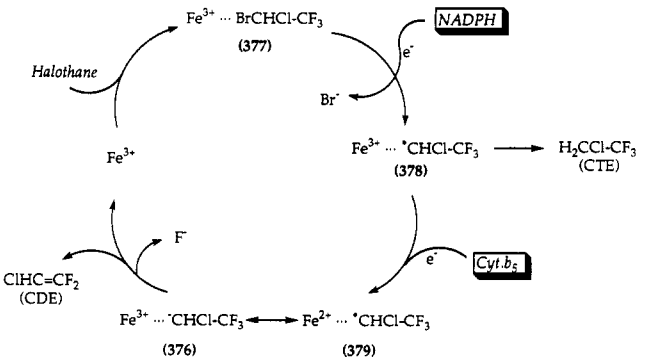
$$\text{Cl}_3\text{CCCl}_3 + (\text{P-450})\text{Fe}^{\text{III}} \xrightarrow[-2\text{Cl}^-]{\text{NADPH (+2e}^-)} \text{Cl}_2\text{C}{=}\text{CCl}_2 \quad (149)$$

To account for the alkene product the researchers suggested that the reduction proceeds by two subsequent one-electron reductions forming first a radical and then a carbanion. This carbanion can then form an alkene through β-elimination of chloride.[379]

The anaerobic oxidation of NADPH by microsomes (liver cytochrome P-450) in the presence of halothane afforded both 2-chloro-1,1,1-trifluoroethane and 2-chloro-1,1-difluoroethylene (major product). The *in vitro* study was treated as an appropriate measure of the reductive metabolism of halothane. To ensure that both metabolites, CDE and CTE, were indeed formed reductively by cytochrome P-450 it was shown that carbon monoxide inhibited the production of CDE by 98% and CTE by 94%.[378]

The authors proposed that cytochrome P-450 binds to halothane to form an enzyme–substrate complex (**377**) which undergoes a one-electron reduction by NADPH in the absence of dioxygen (Scheme 38).[380] The reduced ferrous cytochrome then donates its electron to the substrate and forms a radical (**378**) after releasing a bromide anion. The free radical $[CF_3CHCl]^\bullet$ from **378** is then able to pick up a hydrogen from

Scheme 38

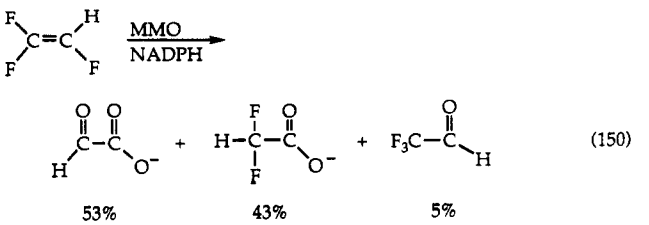


available microsomal proteins and unsaturated lipids to afford CTE. This would account for the early observations of halothane metabolites covalently bound to lipids.[374,375] In the presence of NADPH, the radical complex can alternatively accept a second electron to form the cytochrome P-450 anion complex **376**. The anion complex with a σ-bond could then release fluoride via β-elimination to form CDE.[378] Interestingly, the mechanism proposed closely resembles the mechanism of oxygen activation by cytochrome P-450.[381,382]

The carbanion complex of halothane and cytochrome P-450 was determined to be a low-spin ferric complex via electron-spin resonance studies (g = 2.71, 2.27, and 1.80).[383] In addition, Ruf and co-workers[383] demonstrated that iron(III) porphyrin model complexes, $[Fe(TPP)(CF_3CHCl)(RS)]^-$, having both the carbanion CF_3CHCl^- and thiolate RS^- as axial ligands, showed hyperporphyrin spectra, ESR signals, and ligand field parameters similar to those for **376**.

C. Methane Monooxygenase

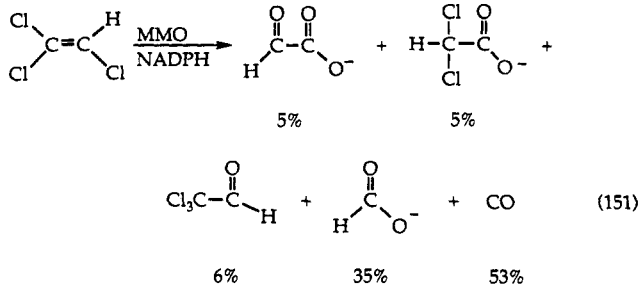
Lipscomb and colleagues[384] demonstrated that methane monooxygenase (MMO) is capable of catalytically oxidizing a variety of halogenated alkenes including trichloroethylene (TCE), chlorotrifluoroethylene, and trifluoroethylene. Methane monooxygenase is a nonheme iron oxygenase enzyme containing an oxo-bridged binuclear iron cluster. Treatment of trifluoroethylene with methane monooxygenase (isolated from *Methylosinus trichosporium* OB3b and contains 40-kDa NADH oxidoreductase + 16-kDa protein termed component B + 245-kDa hydroxylase) for 30 min in 3-(*N*-morpholino)propanesulfonic acid (pH = 7.5) and in the presence of NADH at 23 °C affords a mixture with glyoxylate in 53%, difluoroacetate in 43%, and fluoral in 5% yield as determined by normalization to trifluoroethylene (eq 150).[384] Presumably, the fluoral arises



(150)

from an intramolecular fluoride migration that occurs during the enzymatic oxidation reaction. Clearly, the formation of all three products involves the activation of a C–F bond. Under identical reaction conditions, the oxidation of chlorotrifluoroethylene by methane monooxygenase produces only oxalate in 15% yield.[384]

The oxidation of trichloroethylene by methane monooxygenase affords glyoxylate, dichloroacetate, chloral, formate, and CO (eq 151). For all of these halogenated

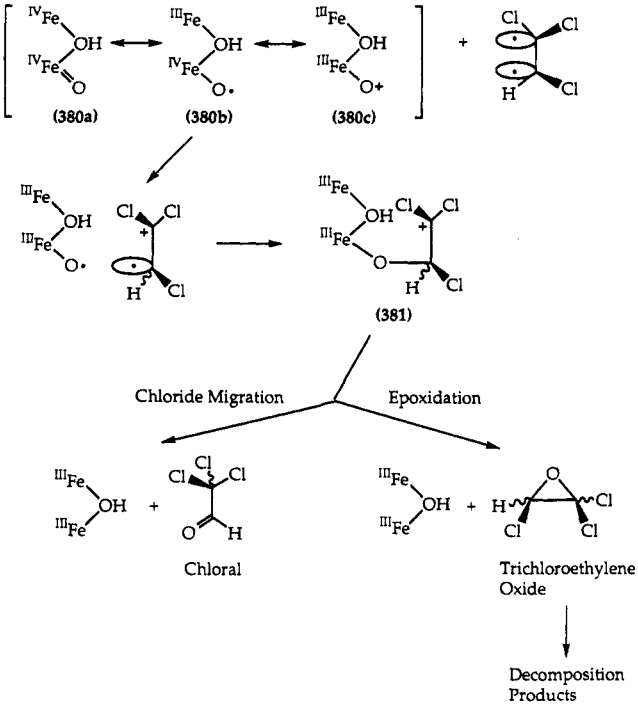


(151)

alkenes, the oxidation products formed are indicative of the transient existence of product epoxides. However, only stable epoxides were detected for trichloroethylene.

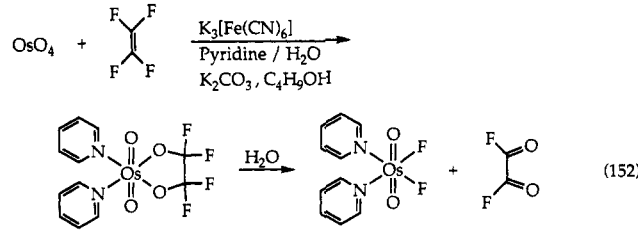
As a representative mechanism that accounts for the observed products, the authors proposed that the oxidation for trichloroethylene by methane monooxygenase involves the cleavage of the O–O bond resulting in the initial formation of a powerful oxene electrophile species **380** (Scheme 39).[384] It was suggested that the

Scheme 39



hydrolase component of methane monooxygenase, which contains only μ-oxo-bridged binuclear iron clusters, provides the two electrons needed to stabilize the electrophilic oxene. The oxene species then initiates oxidation by direct attack on the π-bond of the haloalkene to afford a carbocationic intermediate **381**.[385] This cationic species can either (1) undergo chloride migration to yield chloral or (2) undergo epoxidation and ultimately afford the observed epoxide decomposition products.[384]

An abiotic chemical system undergoes similar transformations. Herrmann and co-workers[386] have reported the isolation of oxalyl fluoride from the catalytic oxidation of fluorinated olefins, such as tetrafluoroethylene, by osmium tetraoxide with $K_3[Fe(CN)_6]$ as cooxidant (eq 152). The products were afforded upon



(152)

hydrolysis of their fully characterized osmate esters. Importantly, ketones, or 1,2-diketones, were produced upon sponaneous elimination of HF from their corresponding α-fluoro alcohols.[386]

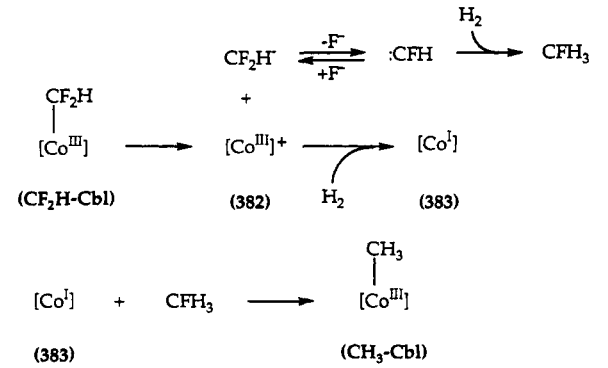
D. Vitamin B_{12} and Analogues

Vitamin B_{12}, or cyanocobalamin, is considered as the first known example of a naturally occurring organometallic complex, since it contains a covalent cobalt–carbon bond.[387] The chemistry and biochemistry of the organometallic derivatives of vitamin B_{12}, or organocorrinoids, in the context of C–F activation is the focus of intensive research.

In 1970, Wood and associates[388] noted unexpected C–F bond activation in a study of fluoroalkylcobalamins and their effectiveness as competitive inhibitors for methylcobalamin in enzymatic methane formation by cell extracts of the methanogenic bacterium strain MOH. Cobalamin analogs containing $CFCl_2$, CF_2Cl, and CF_3 in place of CH_3 were shown to be competitive inhibitors for methylcobalamin. However, (difluoromethyl)cobalamin ($CHCF_2$-Cbl) replaces methylcobalamin (CH_3-Cbl) as a substrate in the methane system, and in the presence of ATP and hydrogen as a source of electrons, this analog yields methane as the major product upon incubation for 45 min at 45 °C.[388] The formation of methane undoubtedly involves the activation of two C–F bonds in $CHCF_2$-Cbl.

The authors suggested that the methane is derived from the carbon atom bound to the cobalt and proposed a mechanism that involves a heterolytic cleavage of the Co-CF_2H bond leaving CF_2H^- and a Co^{III} species (**382**) (Scheme 40).[388] This carbanion could then decompose

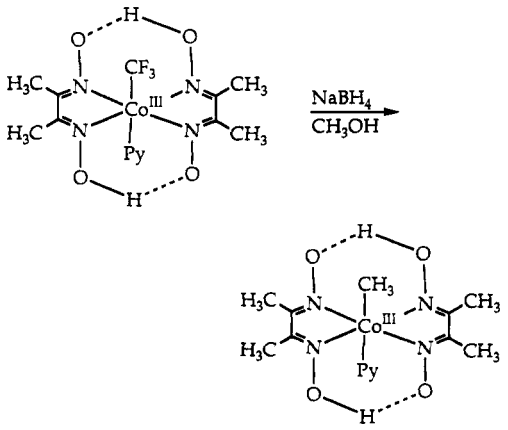
Scheme 40



to :CFH. The authors further propose that this fluorocarbene reacts with H_2 to form CFH_3; however, more recent gas-phase studies show that this reaction seems unlikely.[389] With H_2 present as a source of electrons, **382** could undergo a two-electron reduction to form a Co^I species (**383**) which could be realkylated by CFH_3 to give methylcobalamin, which in turn could

act as a substrate to evolve methane. The reaction between the carbene and H_2 is postulated to proceed simultaneously with the alkylation step. This mechanism was supported by the detection of CH_3F and not CF_2H_2 in the mass spectrum of the atmosphere over the reaction mixture.[388]

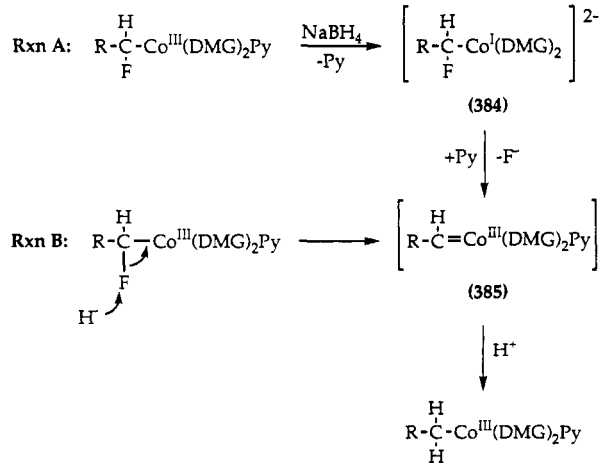
Reductive dehalogenation of α-(haloalkyl)cobalt complexes was first reported by Gaudemer and co-workers[390] for α-(haloalkyl)cobaloximes and (trifluoromethyl)-cobaloximes. In particular, treatment of (trifluoromethyl)Co^{III}(dimethylglyoxime)$_2$(pyridine), [CF_3Co^{III}-(DMG)$_2$(Py)], with $NaBH_4$ in methanol afforded [CH_3-Co^{III}(DMG)$_2$(Py)] in 50–70% yield (eq 153). Presum-



(153)

ably, the reduction occurs via (difluoromethyl)- and (fluoromethyl)cobaloxime intermediates. In contrast to Wood and associates,[388] these workers showed that carbon–cobalt bond cleavage did not occur during these conversions and that reduction of trifluorocobaloxime with $NaBH_4$ in CH_3OD led to the formation of (trideuteriomethyl)cobaloxime.[390] They proposed a mechanism in which trifluorocobaloxime undergoes a two-electron reduction to afford a Co^I complex (**384**) (Scheme 41, reaction A). Loss of α-fluoride from **384**

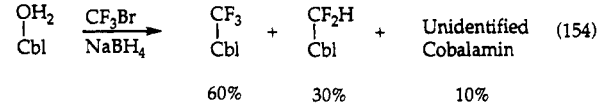
Scheme 41



leads to the formation of a carbene-like cobalt(III) complex **385** which then protonates to give methylcobaloxime as the observed product.[390] The authors note that the formation of the carbene-like cobalt(III) complex **385** by direct attack of H^- on the fluorine cannot be excluded (Scheme 41, reaction B).

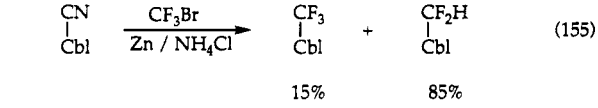
In related work, Brown et al.[391] reported that reductive alkylation of aquocobalamin or cyanocobalamin with CF_3Br produces mixtures of (trifluoromethyl)cobalamin (CF_3-Cbl) and (difluoromethyl)cobalamin (CF_2H-Cbl) because the former is reductively converted to the latter by reducing agents commonly employed for reduction of cobalt(III) cobalamins to cob(I)alamin. Confirmation of the identity of these two organocobalamins was acquired through ^{19}F NMR studies and by observation of the gaseous products formed upon anaerobic pyrolysis. CF_3-Cbl gave CF_3H as the only detectable gaseous organic product, whereas CF_2H-Cbl gave only CF_2H_2; both of the fluorocarbon products were positively identified by mass spectrometry.

Using $NaBH_4$ as the reducing agent, treatment of aquocobalamin with CF_3Br afforded CF_3-Cbl in 60% yield, CF_2H-Cbl in 30% yield, and an unidentified cobalamin in 10% yield (eq 154).[391] Interestingly, with



(154)

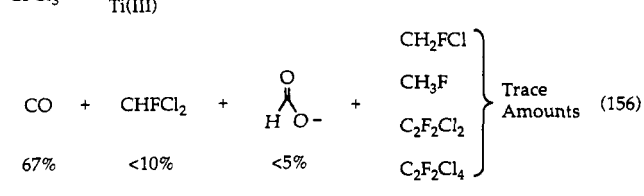
zinc and ammonium chloride as the reducing agent,[392] treatment of cyanocobalamin with CF_3Br produced CF_3-Cbl in 15% yield and CF_2H-Cbl in 85% yield, thus demonstrating that a hydride reducing agent is not required for the conversion (eq 155).[391] Surprisingly,



(155)

these workers suggested a mechanism identical to that proposed by Gaudemer and co-workers[390] but with CF_2H-Cbl being stable to further reduction (see Scheme 41). It is interesting to note that these authors did not consider the possibility of Lewis acid-assisted hydrolysis.

Hogenkamp and colleagues[358,393] reported the corronoid-catalyzed reductive dehalogenation of CCl_4, $CFCl_3$, CF_2Cl_2, and CF_3Cl to CO (and in the case of $CFCl_3$, also to formate) with titanium(III) citrate as the electron donor. CF_4 was not reduced and the rate of CO and formate formation paralleled that of fluoride release. Both rates decreased in the series $CFCl_3$ > CF_2Cl_2 > CCl_4 > CF_3Cl. Specifically, treatment of Freon-11 with titanium(III) citrate in the presence of aquocobalamin afforded CO (67%), $CHFCl_2$ (<10%), formate (<5%), and lesser amounts of CH_2FCl, CH_3F, $C_2F_2Cl_2$, and $C_2F_2Cl_4$ (eq 156).[393] The recovery of

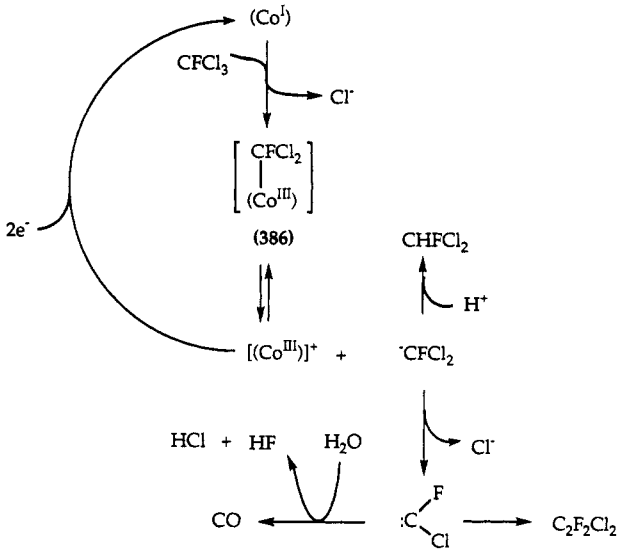


(156)

identified products was 90%. The aquocobalamin-catalyzed reductive dehalogenations of Freon-12 and Freon-13 to CO were found to occur but at much lower rates than the rate of Freon-11.

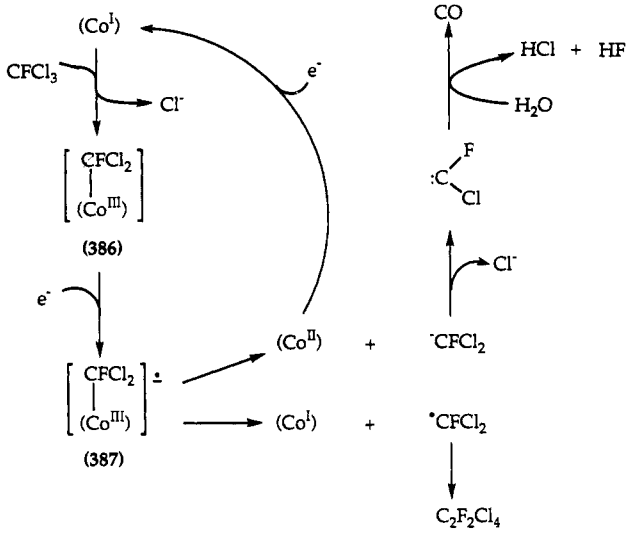
In accordance with the product pattern for the reductive dehalogenation of $CFCl_3$, the authors postulated a mechanism involving the nucleophilic attack of a Co^I cobalamin on $CFCl_3$ to yield a dichlorofluoromethyl cobalamin (**386**) that reversibly yields a

Scheme 42



dichlorofluoro carbanion and a Co^{III} corrinoid species (Scheme 42). This dichlorofluoro carbanion is either protonated to afford $CHFCl_2$ or eliminates chloride ion to give chlorofluorocarbene.[394] The :CClF can either hydrolyze to CO, HF, and HCl or dimerize to dichlorodifluoroethylene.[393] The presence of 1,1,2,2-tetrachloro-1,2-difluoroethane as a product from the reductive dehalogenation of $CFCl_3$ necessarily results from the coupling of dichlorofluoromethyl radicals. To account for the generation of radical intermediates, the authors alternatively suggested a mechanism that invokes a one-electron reduction of (dichlorofluoromethyl)cobalamin (**386**) to generate the radical anion **387** (Scheme 43). This radical anion **387** could undergo

Scheme 43



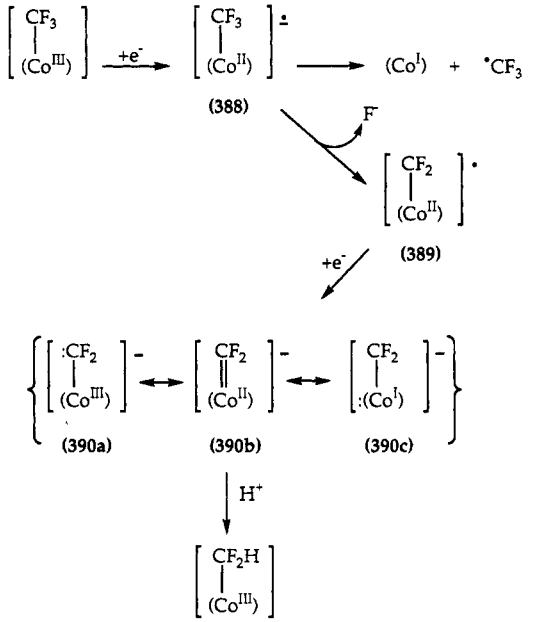
either homolytic cleavage of the carbon–cobalt(III) bond to yield a dichlorofluoromethyl radical and a Co^{I} corrinoid or heterolytic cleavage of the carbon–cobalt(III) bond to generate a dichlorofluoromethyl anion and a Co^{II} corrinoid species.[393] Hogenkamp and co-workers believe that the cobalt–carbon bond was not cleaved in these transformations since the catalytic efficiency of the alkylcobalamins increased in the series CH_3-Cbl < CFH_2-Cbl < CF_2H-Cbl < CF_3-Cbl. If the Co–C bond had been cleaved, then these cobalamins would have behaved identically to aquocobalamin after one turnover.[393]

In 1991, Brown et al.[395,396] reexamined the alkylation of α-(alkyl)cobalt complexes and found that when (trifluoromethyl)cobamide was treated with zinc reductants in a variety of media (20% H_3PO_4, 10% CH_3CO_2H, and 10% NH_4Cl) or subjected to controlled-potential reduction in buffered aqueous media at potentials between −1.0 and −1.2 V, the (trifluoromethyl)cobamide (CF_3-Cba) disappears with the simultaneous appearance of (difluoromethyl)cobamide (CF_2H-Cba) and (after aerobic sampling) the dealkylated cobamide as aquocobalamin (H_2O-Cbl) or diaquocobinamide ($(H_2O)_2$-Cbi). For the zinc reductants, the yields of CF_2H-Cba's were ~30%, while the controlled potential gave defluorination in 47% yield and dealkylation in 53% yield.[396]

The authors noted that under all of these conditions the rates of disappearance of the CF_3-Cba and the rates of appearance of the defluorinated and dealkylated products were identical. Furthermore, the dealkylation was shown to result exclusively from CF_3-Cba because CF_2H-Cba was indefinitely stable to reductive alkylation by any of the employed reducing agents.[396] Using controlled-potential coulometry, it was shown that the net defluorination of β-CF_3-Cbl results in a consumption of two electrons.

Consequently, the authors suggested a mechanism in which a one-electron reduction of CF_3-Cba leads to the radical anion **388** which can either undergo carbon–cobalt bond cleavage to afford a Co^{I} corrinoid species and a trifluoromethyl radical or undergo elimination of fluorine to form the radical Co^{II} species **389** (Scheme 44). Complex **389** then undergoes an additional one-

Scheme 44



electron reduction to form the difluorocarbene–Co^{II} species **390a–c** which is protonated to afford the product CF_2H-Cba.[396] Interestingly, CF_3-Cbl treated with zinc in 10% acetic acid-*d* affords CF_2D-Cbl. The deuterium in the difluoromethyl ligand is nonexchangeable as determined by ^1H, ^{19}F, and ^2H NMR spectroscopy. However, reduction of CF_3-Cbl with $NaBH_4$ in D_2O yields nondeuterated derivatives, while reduction with $NaBD_4$ in H_2O affords deuterated derivatives. Thus, Brown et al.[396] concluded that defluorination of CF_3-Cba by borohydride must occur by the mechanism

initially proposed by Gaudemer and co-workers[390] involving the direct attack of H^- on the fluoride as illustrated in Scheme 41, reaction B.

E. Hematin

Lovley and Woodward[397] recently reported that hematin, an iron porphyrin coenzyme, activates C–F bonds under anaerobic conditions. The study focused on the consumption of Freon-11 and Freon-12 by hematin under anaerobic conditions. When Freon-11 was incubated for 24 h in the presence of hematin as well as cysteine, the reductant used to maintain the iron in a reduced state, 35.2% of the $CFCl_3$ was consumed. Hematin in the absence of a reducing agent did not consume Freon-11, nor did the cysteine alone. There was no loss of Freon-12 in the presence of reduced or oxidized hematin, although CF_2Cl_2 was readily consumed via microbial degradation in the presence of the anaerobic microorganism *Clostridium pasteurianum*. These results provide a model for the nonenzymatic uptake of Freon-11 in the heat-killed sediments.

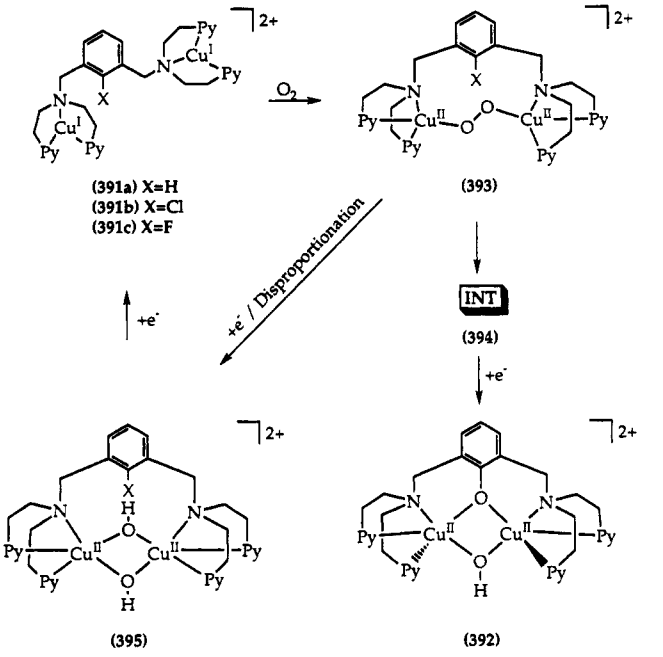
No intermediates in the Freon-11 degradation were observed during the sediment incubations. The authors suggested a mechanism for the reductive dehalogenation of Freon-11 identical to that reported by Hogenkamp and co-workers[393] for the corrinoid-catalyzed reductive dehalogenation of $CFCl_3$ and CF_2Cl_2 in the presence of titanium(III) citrate as reductant (see section IX.D). Hogenkamp and co-workers observed reductive dehalogenation in the presence of large CFC concentrations with CO as the major end product.[393] Unfortunately, due to the steady-state pool sizes of CO present in the anaerobic sediments, Lovley and Woodward noted that any CO produced from the low concentrations of $CFCl_3$ or CF_2Cl_2 was not detectable.[397]

F. Copper Model Systems

Since unequivocal structure determination is difficult to obtain for large metal-containing proteins, smaller model systems are designed to mimic the functions of the larger biological systems. In doing so, considerable advances have been made in the understanding of how the heme centers in proteins, such as hemoglobin, bind to dioxygen and how the heme center in cytochrome P-450 binds to and activates O_2.[398] Similarly, Karlin and associates[398–400] have focused their efforts on the design of model compounds for the analysis of O_2-binding and O_2-activating copper proteins. Specifically, Karlin's copper complexes serve as model systems for hemocyanins, which bind and transport O_2 in the hemolymph of mollusks and arthropods.[398]

Karlin and co-workers[400] reported that their copper monooxygenase model system, a three-coordinate dinuclear Cu(I) complex (**391a**), reacts with dioxygen resulting in the oxygenation of the ligand and formation of the phenoxo- and hydroxo-bridged dinuclear Cu(II) complex (**392**) (Scheme 45). Oxidative dehalogenation was achieved through efficacious ligand design. The first example of copper-mediated oxidative dechlorination was achieved with X = Cl.[399] Treatment of **391b** with O_2 and Zn dust (as reductant) in CH_2Cl_2 afforded the oxidatively dechlorinated product **392** in 75% overall yield. Interestingly, when X = F only a trace of the oxidatively dehalogenated products **392** was observed.[399] Treatment of **391c** with O_2, even in the presence of extra reductant, resulted in the exclusive formation of the peroxo Cu(II) complex **393**.[399,400] In terms of a mechanism for oxidative dechlorination, the authors postulated that **391b**, in the presence of a reductant and O_2, initially forms the peroxo Cu(II) complex as has been established when X = F. Subsequent attack upon the arene substrate **393** occurs to give an intermediate **INT** (**394**) which can undergo hydroxylation to afford product **392**. Alternatively, **393** can undergo disproportionation or reduction to give complex **395**. The hydroxylation of **393** is inefficient when X = Cl unless zinc is present as a reductant. In the presence of Zn, the intermediate **394** can be reduced to **392** and **395** can be reduced to **391b** so the cycle can be repeated until either the chlorinated ligand or zinc are depleted.[399] The substrate reactivity follows in the series C–F ≪ C–Cl < C–H.

Scheme 45



X. Conclusions and Future Prospects

A wide variety of metals are capable of activating the carbon–fluorine bond under the appropriate conditions. The fluoride affinity of the highly electrophilic early transition metals tends to preclude their use in catalysis. Similarly, the alkali and alkaline earth metals are not suitable as C–F activation catalysts due to their propensity to form ionic salts with fluoride. Thus, further developments should be sought employing low-valent electron-rich transition metals. Several ligand-based systems show promise and should be further exploited as model compounds for systematic studies directed toward catalytic C–F bond activation processes. Unfortunately, biological systems are not as well-developed as their wholly chemical counterparts and require more investigation to be synthetically applicable. Undoubtedly, the next challenge appears to be the activation of saturated perfluorocarbons. From this work it is evident that significant progress has been made in the area of metal-assisted C–F bond activation. Early efforts typically employed forcing conditions and obtained low yields. C–F activation can now be accomplished under extremely mild conditions using a suitable transition-metal complex. Future efforts ought

to utilize these mild C–F bond cleavage processes directed toward the ultimate functionalization of the C–F bond.

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XII. References and Notes

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