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Activation of C–F bonds using $Cp^*_2ZrH_2$: a diversity of mechanisms †

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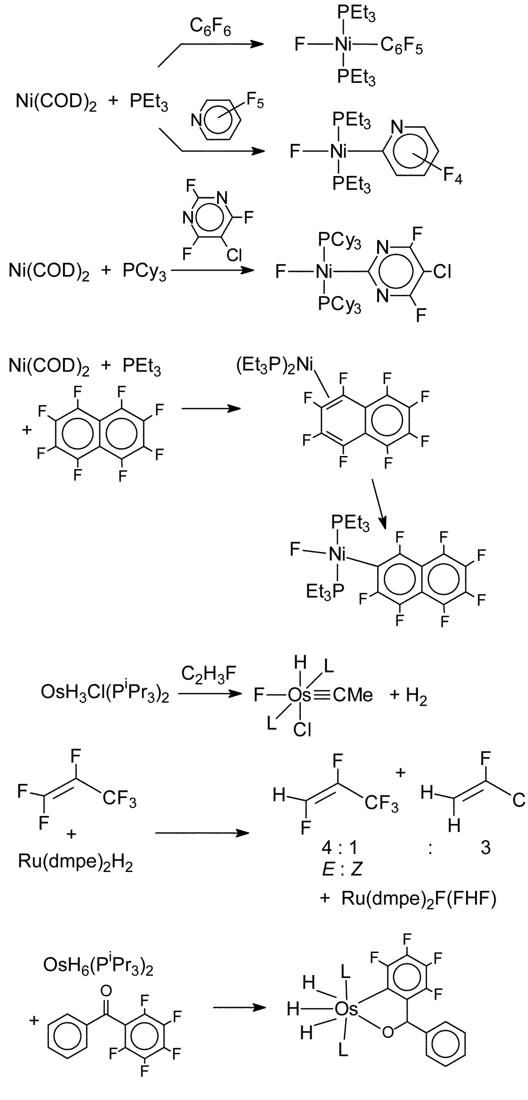
The activation of several types of carbon–fluorine bonds in alkanes, arenes and olefins, using the early transition metal complex $Cp^*_2ZrH_2$, are described. Fluoroalkanes are reduced to alkanes. Alkyl and and even aryl adducts containing β-fluorines undergo β-fluorine elimination. Evidence is presented that α-fluorine elimination is also possible, and occurs in $Cp^*_2Zr(CF_3)H$. The studies include mechanistic investigations, which show evidence for a variety of pathways depending on the specific substrate.

Introduction

Carbon–fluorine bonds are among the strongest sigma bonds known, and their inertness towards chemical reaction has made them useful in a variety of applications from frying pan coatings to artificial blood. This chemical inertness also makes the chemistry of fluorocarbons a specialized field, and new routes to transform these bonds are the subject of many investigations.[1] Transition metal complexes have been found to possess a unique ability to react with C–F bonds, although reports have focussed mainly on aromatic C–F cleavage.

Several examples of intermolecular C–F cleavage from the past three years are shown in Scheme 1. Here, the activation of the aromatic C–F bond is seen to occur with nickel,[2] osmium,[3] and ruthenium.[4] Aromatic and olefinic C–F bonds are shown to be active, although there is one report of aliphatic activation using Yb(II) complexes as reducing agents.[5]



Scheme 1 Recent carbon–fluorine bond cleavage reactions.

Earlier studies have provided many examples of polyfluoroarene reactions with a variety of metal hydrides to give reduction products. These include $Cp^*Rh(PMe_3)H_2$,[6] $Ru(dmpe)_2H_2$,[7] and, $HRh(PMe_3)_4$.[8] Oxidative addition of C–F

William D. Jones was born in Philadelphia, Pennsylvania, in 1953, and studied at Massachusetts Institute of Technology (BS, 1975). He obtained a Ph.D. degree in chemistry at California Institute of Technology (1979) with Robert G. Bergman. He moved to the University of Wisconsin as an NSF postdoctoral fellow with Chuck Casey, and in 1980 began as Assistant Professor at the University of Rochester. He was promoted to Associate Professor in 1984 and Professor in 1987, and is now the Charles F. Houghton Professor of Chemistry. Professor Jones has received several awards, including an Alfred P. Sloan Research Fellowship (1984), a Camille & Henry Dreyfus Foundation Teacher–Scholar Award (1985), a Royal Society Guest Research Fellowship (1988), a Fulbright–Hays Scholar (1988), a John Simon Guggenheim Fellow (1988), and the ACS Award in Organometallic Chemistry (2003). He also serves as Associate Editor for J. Am. Chem. Soc. *Professor Jones' research interests include organometallic research in strong C–X bond cleavage, catalysis, model studies, mechanisms, kinetics, thermodynamics, and synthetic applications.*

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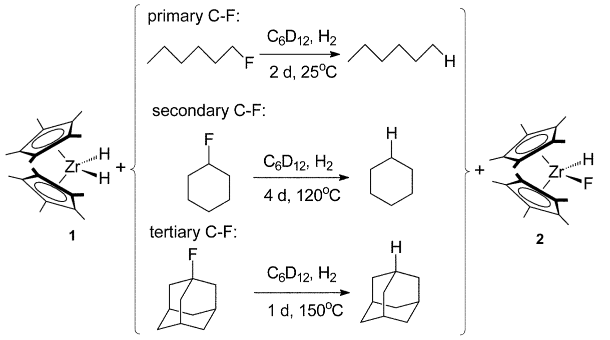
bonds to low oxidation state transition metal fragments are also known, such as with [Cp*Rh(PMe$_3$)],[9] [(Bu$^t_2$PC$_2$H$_4$PBu$^t_2$)Ni],[10] and [(PEt$_3$)$_2$Ni].[11] Examples of aliphatic C–F activation are quite rare, as exemplified by the reduction of perfluorodecalin by [CpFe(CO)$_2$]$^-$ to give metal-substituted perfluoronaphthalenes[12] and the use of Cp$_2$TiF$_2$ or Cp$_2$ZrCl$_2$/Mg or Al/HgCl$_2$ to reduce perfluorodecalin to perfluoronaphthalene.[13] Reactions of fluoroolefins with metal hydride complexes are also quite rare, with examples that include CpM(CO)$_3$H (M = Mo, W),[14] Mn(CO)$_5$H,[15] Ru(dmpe)$_2$H$_2$,[16] and HRh(PEt$_3$)$_4$.[17]

In this report, we summarize several examples of C–F cleavage found in our laboratory using the reactive early metal complex Cp*$_2$ZrH$_2$. These studies stand in contrast to much of the earlier work in the wide variety of types of C–F bonds that can be cleaved. The formation of the strong Zr–F bond provides the driving force for these reactions, and the mechanisms to achieve this thermodynamic result are varied, We also present evidence for a new cleavage pathway of α-C–F bonds.

Results and discussion

Reactions of Cp*$_2$ZrH$_2$ with fluoroalkanes

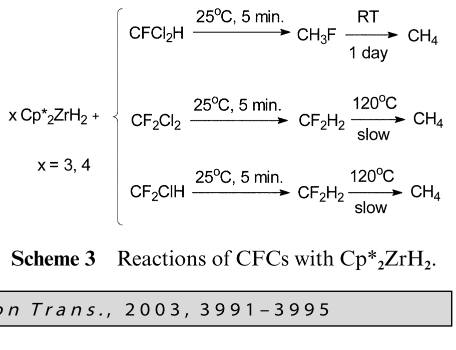
The hydrocarbon soluble dihydride Cp*$_2$ZrH$_2$ (**1**) reacts with 1-fluorohexane in cyclohexane solution over the course of several days at RT to give hexane and Cp*$_2$ZrHF (**2**). Complex **2** reacts with additional 1-fluorohexane but only slowly at elevated temperatures (120 °C). Secondary C–F bonds also react with difficulty. Fluorocyclohexane is converted to cyclohexane by **1** at 120 °C over 4 days. Under these conditions, **1** is unstable towards dihydrogen loss and dimerization, and an atmosphere of H$_2$ is employed to prevent this undesirable, but reversible, side reaction. Even tertiary C–F bonds will react, as shown by the reaction of **1** with 1-fluoroadamantane at 120 °C (25% complete in 1 week). Scheme 2 summarizes this reactivity.[18]



Scheme 2 Reactions of fluoroalkanes with Cp*$_2$ZrH$_2$.

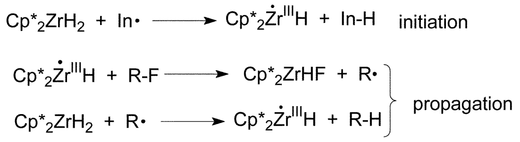
Geminal difluoroalkanes also react with **1** to give alkanes. 1,1-Difluoroethane produces ethane after 1 day at 150 °C in the presence of **1** under an atmosphere of H$_2$. 1,1,1-Trifluoropropane is vitually unreactive, giving small amounts of **2** after several weeks at 150 °C.

CFCs have proven to be reactive towards **1** to give alkanes as shown in Scheme 3. The reaction of CFCl$_2$H with an excess of **1** immediately gives CH$_3$F, which then goes on to produce methane. CF$_2$Cl$_2$ and CF$_2$ClH react immediately with **1** to give CF$_2$H$_2$, which then reacts at elevated temperatures to give methane.



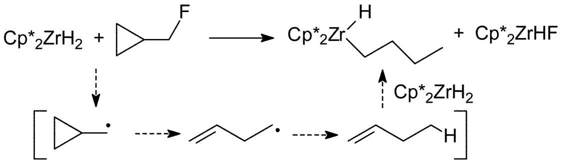
Scheme 3 Reactions of CFCs with Cp*$_2$ZrH$_2$.

Mechanistic studies were undertaken of these reactions. The mechanism proposed is a radical chain pathway, as shown in Scheme 4. While the reactivity pattern 1° > 2° > 3° argues against a radical mechanism, a number of other observations indicate that a radical chain is operative in these reductions. First, it was observed that freshly recrystallized batches of **1** react more slowly with fluoroalkanes than 'aged' batches of **1**. Second, it was found that sodium naphthalenide dramatically accelerated the reaction of **1** with 1-fluorohexane.



Scheme 4 Radical chain mechanism for fluoroalkane reduction.

Third, both radical inhibitors 9,10-dihydroanthracene and triphenylmethane showed 5–6-fold inhibition of the rate of reaction. The fourth and most definitive piece of evidence favoring a radical pathway is the reaction of **1** with cyclopropylcarbinyl fluoride. This reaction gives Cp*$_2$Zr(*n*-Bu)H plus **2** rather than methylcyclopropane. The intermediate cyclopropylcarbinyl radical ring opens to give a butenyl radical, which then produces butene that inserts into the Zr–H bond to give Cp*$_2$Zr(*n*-Bu)H (Scheme 5). The increased reactivity of primary over secondary and tertiary C–F bonds can be explained in terms of a rate determining step in which Zr^{III} abstracts a fluorine from the fluorocarbon. The steric bulk of **1** could make less-hindered substrates more reactive.[19]

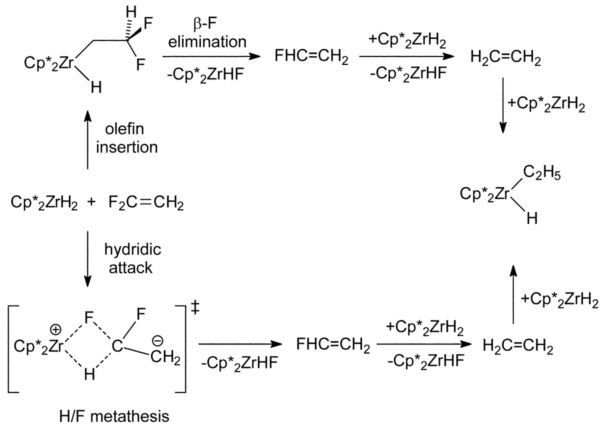


Scheme 5 Reaction of **1** with cyclopropylcarbinylfluoride.

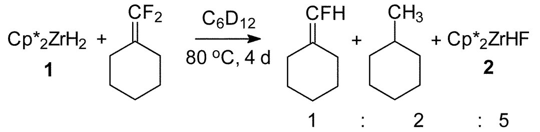
Reactions of Cp*$_2$ZrH$_2$ with fluoroolefins

Cp*$_2$ZrH$_2$ also reacts rapidly with certain fluorinated olefins. For example, **1** (3 equiv.) and 1,1-difluoroethylene react at −80 °C to give Cp*$_2$Zr(C$_2$H$_5$)H and Cp*$_2$ZrHF. No intermediates are observed, and attempts to use limiting quantities of **1** result in smaller conversions to the same products. This reaction can be explained by two reasonable mechanisms: (1) olefin insertion/β-fluoride elimination, or (2) hydride attack/fluoride metathesis as shown in Scheme 6. Olefin insertion is well known for this zirconium hydride, and regioselective insertion to attach hydride to the more electropositive carbon would give the proper isomer for β-fluoride elimination. The hydride attack mechanism would predict an unfavorable buildup of negative charge on the β-carbon during the metathesis.[20]

Examination of a different olefin helps differentiate these pathways. Reaction of **1** with 1,1-difluoromethylenecyclohexane only occurs slowly upon heating to 80 °C. One observes both the monofluoro and the difluoro reduction products, as shown in eqn. (1). This observation is inconsistent with the H/F metathesis pathway described above, which should proceed at a similar rate. An insertion/β-fluoride elimination pathway would be expected to be more difficult, since a tertiary Zr–C bond would be formed prior to β-F elimination. Tertiary alkylzirconium complexes, such as Cp$_2$Zr(CMe$_3$)Cl, have not been accessible for characterization even as intermediates.[21]



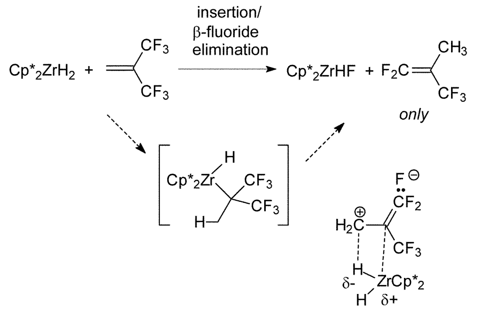
Scheme 6 Mechanisms for reduction of CH_2=CF_2 by **1**.



(1)

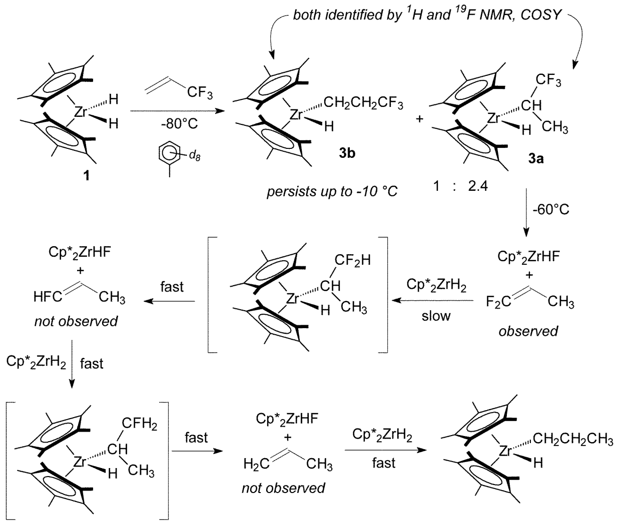
As support for the above, Caulton and co-workers showed that Cp_2ZrHCl reacts with fluoroethylene to give Cp_2ZrFCl, $Cp_2Zr(CH_2CH_3)Cl$ and Cp_2ZrF_2.[22] Again, no intermediates were observed in this reaction, but DFT calculations suggested that a metathesis mechanism was energetically disfavored over an insertion/elimination pathway. The calculations also predicted a transition state leading to the insertion product rather than an η^2-olefin complex as a stable intermediate.

Another substrate that requires insertion to give a tertiary Zr–C bond is 3,3,3-trifluoro-2-(trifluoromethyl)propene. The only products seen in this reaction are **2** and CF_2=$C(CF_3)(CH_3)$. The reaction occurs rapidly at −85 °C, and is consistent with an insertion/β-fluoride elimination. The rapidity of the reaction compared to that of 1,1-difluoromethylenecyclohexane can be associated with the presence of two electron withdrawing CF_3 groups on the carbon that attaches to zirconium. Negative hyperconjugation over two CF_3 groups could also help to account for the increase in rate (Scheme 7).[19]



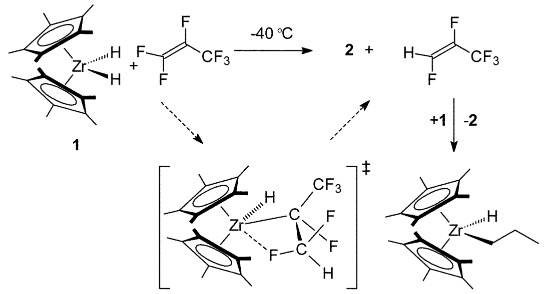
Scheme 7 Hyperconjugation effects in insertion/β-F elimination.

3,3,3-Trifluoropropene also reacts stoichiometrically with **1** to give **2**, CF_2=$CHCH_3$, $Cp^*_2Zr(n\text{-}Pr)H$, $Cp^*_2ZrF_2$ and $CF_3CH_2CH_3$ in a ratio of 23 : 12 : 4 : 2 : 1. With excess **1**, only $Cp^*_2Zr(n\text{-}Pr)H$, **2** and $Cp^*_2ZrF_2$ are seen in an 18 : 5 : 1 ratio. At room temperature, complete defluorination and formation of $Cp^*_2Zr(n\text{-}Pr)H$ is seen without any intermediate olefins being observed. At −90 °C, however, **1** and 3,3,3-trifluoropropene give a 2.4 : 1 mixture of two insertion products, **3a** and **3b**, as shown in Scheme 8. Complex **3a** Decomposes at −70 °C *via* β-fluoride elimination to give the olefin CF_2=$CHCH_3$ and **2**. Complex **3b** is more stable, however, and only decomposes at −10 °C to give $CF_3CH_2CH_3$ and unidentified Zr-containing products. While the preference for formation of the isopropyl over the *n*-propyl insertion product seems unusual in terms of steric effects, consideration of negative hyperconjugation favors hydride addition to the terminal methylene group.[18]



Scheme 8 Reaction of **1** with 3,3,3-trifluoropropene.

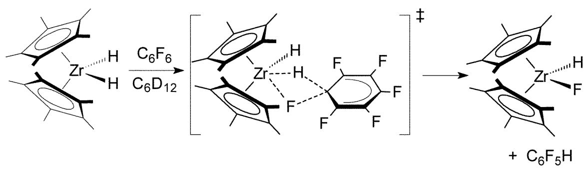
A related olefin, perfluoropropene, also reacts rapidly with **1** to give reduction products. With excess **1**, complete defluorination to give **2** and $Cp^*_2Zr(n\text{-}Pr)H$ is seen after only 15 min at room temperature. With only 1 equiv. of **1**, the olefin (*E*)-CHF=CFCF$_3$ is observed (95%) along with a trace of the *Z* isomer (~5%). Addition of more **1** results in the complete conversion to **2** and *n*-propyl hydride complex without any intermediates being observed. The formation of primarily (*E*)-CHF=CFCF$_3$ is quite unusual, as this implies that an insertion/β-fluoride elimination pathway must proceed through a specific rotamer (Scheme 9).[18] Further mechanistic studies are in progress.



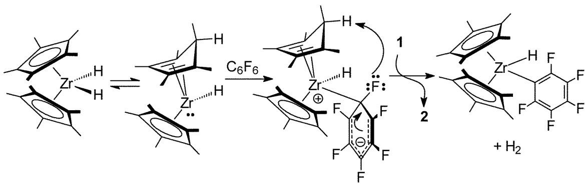
Scheme 9 Reaction of **1** with perfluoropropene.

Reactions of $Cp^*_2ZrH_2$ with fluoroarenes

$Cp^*_2ZrH_2$ reacts cleanly with an excess of hexafluorobenzene at 85 °C in cyclohexane-d_{12} to give a mixture of **2**, $Cp^*_2Zr(C_6F_5)H$ and C_6F_5H in a 2 : 1 : 1 ratio. Traces of $Cp^*_2ZrF_2$ are seen (<5%). These species are produced together as the reaction proceeds, in the same ratio. The ratio of products was unaffected whether one equivalent or neat C_6F_6 was employed. Pentafluorobenzene also reacts with **1** under similar conditions, giving **2**, $Cp^*_2Zr(C_6F_5)H$, $Cp^*_2Zr(o\text{-}C_6F_4H)H$ and $C_6F_4H_2$ (1.3 : 1; *o* : *p*) in a 3 : 2 : 1 : 1 ratio. Perfluoronaphthalene and **1** react at 85 °C to give **2**, heptafluoronaphthalene and $Cp^*_2Zr(C_{10}F_7)H$ in a 3 : 2.5 : 1 ratio. The simultaneous formation of a mixture of both metallated fluoroarenes and fluoroarene reduction products is consistent with parallel reactions leading to each type of product. The reduction pathway is consistent with bimolecular attack of hydride **1** on the fluoroarene *via* an S_NAr2 mechanism (eqn. (2)). The formation of the metallated fluoroarene could occur *via* the known initial migration of a hydride ligand to the Cp* ring, attack of the Zr^{II} on the arene ring to eliminate HF, followed by reaction of HF with **1** to produce **2** (eqn. (3)).[23]

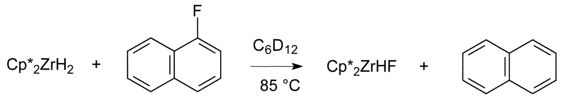


(2)



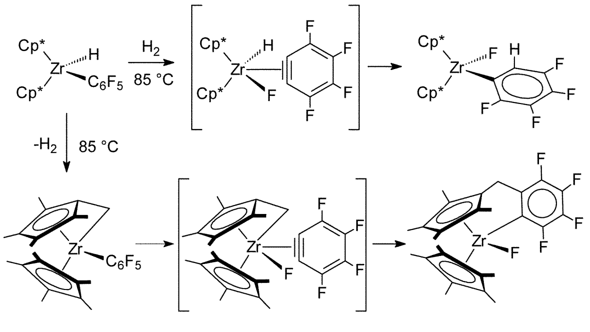
(3)

The simple monofluoroarene fluorobenzene reacts with **1** at 85 °C over a month to give a 1 : 1 : 0.75 mixture of **2**, benzene and $Cp^*_2Zr(C_6H_5)F$. 1-Fluoronaphthalene reacts under the same conditions over 4 days to give only naphthalene and **2** (eqn. (4)).



(4)

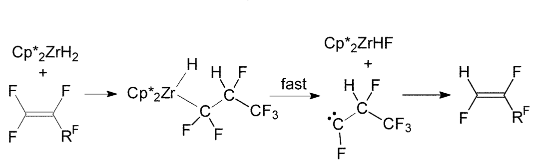
One of the more novel reactions observed with fluoroaryl ligands is that of $Cp^*_2Zr(C_6F_5)H$, prepared from **1** and $Hg(C_6F_5)_2$. Heating to 100 °C under an atmosphere of hydrogen leads to the rearrangement to the isomeric $Cp^*_2Zr(o\text{-}C_6F_4H)F$. Heating in the absence of hydrogen, however, leads to hydrogen loss and formation of a tetramethylfulvene complex, which then rearranges *via* β-fluoride elimination to give a tetrafluorobenzyne intermediate that goes on to form an insertion product (Scheme 10).[24] This mechanism appears to be general, in that in the reaction of **1** with C_6H_5F also appears to generate $Cp^*_2Zr(o\text{-}C_6H_4F)H$ as an intermediate, which then rearranges (*via* a benzyne complex) to give the observed product, $Cp^*_2Zr(C_6H_5)F$.



Scheme 10 Rearrangement of fluoroaryl complex.

Olefin insertion/α-fluoride elimination

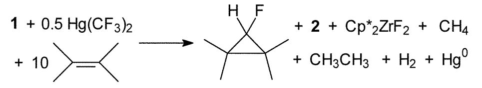
One possible mechanism to explain vinylic C–F activation products that has not been considered is olefin insertion into the Zr–H bond followed by α-fluoride elimination to give **2** and a fluorocarbene (eqn. (5)). The fluorocarbene could then quickly insert into the adjacent C–H bond to give the observed H/F substitution at the vinylic carbon.



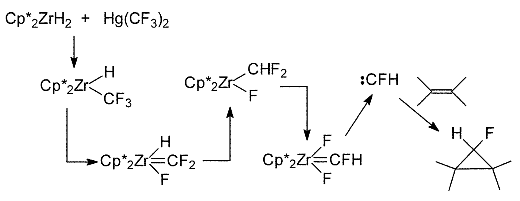
(5)

As a precedent for α-elimination, $CpMo(CO)_3(COCF_3)$ was shown to decompose photochemically to form the difluorocarbene complex, $CpMo(CO)_2(=CF_2)F$, through a pathway involving initial dissociation of CO, trifluoromethyl group migration, another CO dissociation, and finally α-fluoride elimination.[25] The α-F elimination process occurred very rapidly and could only be observed using frozen matrix isolation techniques. There is some precedence that α-F elimination processes by zirconocene complexes are also quite facile. Morrison has shown that $Cp^*_2ZrCl_2$ reacts with $Cd(CF_3)_2\cdot DME$ at −25 °C to give $Cp^*_2ZrF_2$ in 91% isolated yield. An intermediate $Cp^*_2Zr(CF_3)_2$ species was proposed, but was evidenced only by a small transient peak in the ^{19}F NMR spectrum.[26]

In further pursuit of the possibility of an α-fluoride elimination process and fluorocarbene formation, **1** was reacted with $Hg(CF_3)_2$.[27] Elemental mercury was observed, and H_2, Cp^*_2ZrHF, $Cp^*_2ZrF_2$ and trace amounts of CH_3F, CH_4 and CH_3CH_3 were detected by ^1H and ^{19}F NMR spectroscopy. A few transient resonances were observed in the ^{19}F NMR spectrum at −70 °C, but could not be assigned to a $Cp^*_2Zr(CF_3)H$ species. The reaction was repeated in the presence of excess tetramethylethylene, a carbene trap.[28] The same products along with 1-fluoro-2,2,3,3-tetramethylcyclopropane were observed (eqn. (6)).[29] The difluorocarbene adduct, 1,1-difluoro-2,2,3,3-tetramethylcyclopropane, was not observed.



(6)



Scheme 11 Carbene mechanism for C–F activation

One possible explanation is indicated in Scheme 11. Once the CF_3 group is transferred by $Hg(CF_3)_2$, an α-F elimination would generate a carbene species, $Cp^*_2ZrHF(=CF_2)$, which could then insert into the Zr–H bond to give $Cp^*_2Zr(CF_2H)F$. A subsequent α-F elimination would lead to a carbene complex, $Cp^*_2ZrF_2(=CFH)$, or $Cp^*_2ZrF_2$ and free :CFH, which could then be trapped to form the observed monofluorinated cyclopropane product.

Although not well established, an α-F elimination to generate fluorocarbenes may be possible, and might account for the hydrodefluorinated olefins observed. Multiple α-C–F eliminations would be favored by maximizing the number of Zr–F bonds formed. However, in an attempt to trap a fluorocarbene in the reactions of **1** with perfluoropropene in tetramethylethylene solvent, no carbene–tetramethylethylene adduct was observed, so the possibility of this pathway remains open to debate. Theory is currently being used to attempt to sort out different reaction pathways.

Conclusions and outlook

At least three different mechanisms have been identified for carbon–fluorine bond activation by $Cp^*_2ZrH_2$. Aliphatic fluorocarbons undergo a radical chain reaction *via* Zr^{III} to give alkane products. Fluorinated aromatics are susceptible to S_NAr2 attack to give either reduced fluoroaromatics or new zirconium–aryl products. Olefins undergo insertion followed by β-fluoride elimination to give new reduced olefins. Evidence is provided that fluoroalkyl groups on zirconium containing α-fluorines can undergo α-fluoride elimination to generate a free carbene. In all cases, formation of a strong zirconium–fluoride bond provides the driving force for the reaction.

Future developments in this chemistry are likely to arise from extension to other types of fluorocarbon substrates. Perfluoroolefins and cyclic olefins are currently under investigation. While the strong Zr–F bond is favorable for enhanced reactivity, it also presents a barrier to the development of catalytic processes. One challenge that remains is to find a sink for the fluoride other than zirconium, so that the system can be recycled in a catalytic fashion.

Acknowledgements

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References

1 J. Burdeniuc, B. Jedlicka and R. H. Crabtree, *Chem. Ber./Recueil.*, 1997, **130**, 145.

2 T. Braun and R. N. Perutz, *Chem. Commun.*, 2002, 2749; M. I. Sladek, T. Braun, B. Neumann and H.-G. Stammler, *J. Chem. Soc., Dalton Trans.*, 2002, 297; T. Braun, L. Cronin, C. L. Higgitt, J. E. McGrady, R. N. Perutz and M. Reinhold, *New J. Chem.*, 2001, **25**, 19.

3 G. Ferrando-Miguel, H. Gerard, O. Eisenstein and K. G. Caulton, *Inorg. Chem.*, 2002, **41**, 6440; P. Barrio, R. Castarlenas, M. A. Esteruelas, A. Lledos, F. Maseras, E. Onate and J. Tomas, *Organometallics*, 2001, **20**, 442.

4 M. S. Kirkham, M. F. Mahon and M. K. Whittlesey, *Chem. Commun.*, 2001, 813.

5 G. B. Deacon, G. Meyer and D. Stellfeldt, *Eur. J. Inorg. Chem.*, 2000, 1061.

6 B. L. Edelbach and W. D. Jones, *J. Am. Chem. Soc.*, 1997, **119**, 7734.

7 M. K. Whittlesey, R. N. Perutz and M. H. Moore, *Chem. Commun.*, 1996, 787.

8 M. Aizenberg and D. Milstein, *J. Am. Chem. Soc.*, 1995, **117**, 8674.

9 W. D. Jones, M. G. Partridge and R. N. Perutz, *J. Chem. Soc., Chem. Commun.*, 1991, 264.

10 I. Bach, K.-R. Pörschke, R. Goddard, C. Kopiske, C. Krüger, A. Rufinska and K. Seevogel, *Organometallics*, 1996, **15**, 4959.

11 L. Cronin, C. L. Higgitt, R. Karch and R. N. Perutz, *Organometallics*, 1997, **16**, 4920.

12 R. G. Harrison and T. G. Richmond, *J. Am. Chem. Soc.*, 1993, **115**, 5303.

13 J. L. Kiplinger and T. G. Richmond, *Chem. Commun.*, 1996, 1115.

14 P. M. Treichel, J. Morris and F. G. A. Stone, *J. Chem. Soc.*, 1963, 720.

15 P. M. Treichel, E. Pitcher and F. G. A. Stone, *Inorg. Chem.*, 1962, **1**, 511.

16 M. S. Kirkham, M. F. Mahon and M. K. Whittlesey, *Chem. Commun.*, 2001, 813.

17 T. Braun, D. Noveski, B. Neumann and J.-G. Stammler, *Angew. Chem., Int. Ed.*, 2002, **41**, 2745.

18 B. M. Kraft, R. J. Lachicotte and W. D. Jones, *J. Am. Chem. Soc.*, 2000, **122**, 8559.

19 B. M. Kraft, R. J. Lachicotte and W. D. Jones, *J. Am. Chem. Soc.*, 2001, **123**, 10973.

20 B. M. Kraft and W. D. Jones, *J. Am. Chem. Soc.*, 200, **124**, 8681.

21 P. J. Chirik, M. W. Day, J. A. Labinger and J. E. Bercaw, *J. Am. Chem. Soc.*, 1999, **121**, 10308.

22 L. A. Watson, D. V. Yandulov and K. G. Caulton, *J. Am. Chem. Soc.*, 2001, **123**, 603.

23 B. M. Kraft and W. D. Jones, *J. Organomet. Chem.*, 2002, **658**, 132.

24 B. M. Kraft, R. J. Lachicotte and W. D. Jones, *Organometallics*, 2002, **21**, 727.

25 A. K. Campen, K. A. Mahmoud, A. J. Rest and P. A. Willis, *J. Chem. Soc., Dalton Trans.*, 1990, 2817.

26 J. A. Morrison, *Adv. Organomet. Chem.*, 1993, **35**, 211.

27 Mercury reagents have been effective for the stoichiometric synthesis of fluoroaryl hydride derivatives of $Cp^*_2ZrH_2$. See ref. 19.

28 M. Kamel, W. Kimpenhaus and J. Buddrus, *Chem. Ber.*, 1976, **109**, 2351; $Cp^*_2ZrH_2$ is unreactive with tetramethylethylene even with heating at 85 °C.

29 The adduct, 1-fluoro-2,2,3,3-tetramethylcyclopropane, was observed in 54% yield based on ^1H NMR integration. No CH_3F was observed when the reaction was performed in the presence of the carbene trap.