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Group IV Metallocene-Mediated Synthesis of Fluoroaromatics via Selective Defluorination of Saturated Perfluorocarbons

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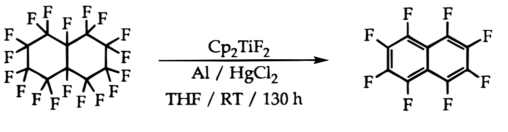
Fluorocarbons are noted for their chemical inertness, which is a manifestation of the great strength of the C−F bond and the weak nature of metal fluorocarbon interactions. These same thermodynamic and kinetic considerations which tend to disfavor C−F activation have also been exploited in useful technological and medical applications of fluorocarbons.[1] A recent example is the development of the "fluorous biphase system" by Horváth and Rábai at Exxon[2] in which the low hydrocarbon solubility of catalysts decorated with perfluoroalkyl chains allows for facile separation of products from catalysts under homogeneous conditions.

Activation and functionalization of C−F bonds provides a chemical challenge akin to that of C-H activation in analogous hydrocarbon compounds. Although it is well known that strong reducing agents such as sodium in liquid ammonia can completely destroy fluorocarbons to afford carbon and fluoride ions,[3] the crucial problem is one of *selective* activation of C−F bonds rather than complete defluorination. In the past decade, numerous examples of C−F bond activation using organometallic complexes have been reported,[4] but only recently has homogeneous catalytic hydrogenation of a C−F bond been noted.[5] Like nearly all examples of C−F activation, this latter work utilizes hexafluorobenzene as a substrate. Homogeneous reaction chemistry of saturated perfluorocarbons is limited to complete defluorination using aryl thiolates,[6] substoichiometric reactions with $[CpFe(CO)_2]^-$,[7] Cp_2Co,[8] or alkali metal organic radical anions,[9] and radical-based hydrogen for fluorine exchange using Cp_3UCMe_3.[10] Most recently, Crabtree and coworkers[11] have combined NH_3 with Hg photosensitization to reduce and functionalize saturated perfluorocarbons. We report here the first examples of transition metal-catalyzed synthesis of perfluoroaromatic compounds by room temperature reductive defluorination of saturated perfluorocarbons. In addition, a mild hydrogenation of aromatic carbon−fluorine bonds is reported. The key feature of this work is the use of early transition metallocenes to mediate electron transfer from readily available terminal reductants such as magnesium and aluminum metals.

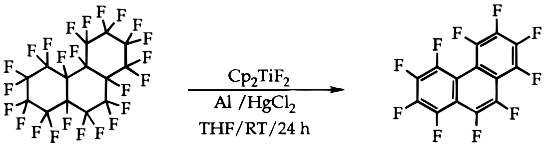
Zirconocene complexes have become firmly entrenched in the application of organometallic reagents in organic synthesis;[12] however, examples of their chemistry with fluorocarbons are rare.[4] This can be attributed to the great strength of the early transition metal−fluoride bond which is thought to preclude catalytic chemistry. Thus, the key challenge in early transition metal organometallic fluorocarbon chemistry is not merely breaking a C−F bond but developing a system in which catalytic turnover is possible.[13]

As depicted in eq 1, reaction of 6.2 mmol of perfluorodecalin **(1)** with 0.026 mmol of Cp_2TiF_2 in the presence of excess Al (87 mmol)/$HgCl_2$ (0.19 mmol) as the terminal reductant in THF solution at room temperature results in *catalytic* production of octafluoronaphthalene **(2)** (3.2 mmol, 12 turnovers).[14] Over 120 fluorides are removed per titanium metal center, and Cp_2TiF_2 can be recovered from the reaction mixture. It is important to note that initial activation of the fluorocarbon appears to be the slow step in this reaction because unreacted starting material can be recovered with subsequent defluorination and formation of the aromatic products as rapid events. Control experiments demonstrate that the metallocene fragment is necessary for the observed chemistry since the activated aluminum does not exhibit any reactivity with perfluorodecalin or perfluoronaphthalene at room temperature. The Cp_2TiF_2-mediated chemistry can be extended to other ring systems such as perfluoro(tetradecahydrophenanthrene) (**3**) to afford decafluorophenanthrene (**4**) (eq 2). Our studies also show that Cp_2ZrCl_2 and Cp_2ZrF_2 (in the presence of Mg/$HgCl_2$) are equally effective in mediating the tranformation depicted in eq 1.[15] However, these reactions tend to be rather exothermic, and so great care should be exercised when the chemistry is performed on large scales. The important observation that Cp_2TiF_2 and Cp_2ZrF_2 can mediate these transformations provides evidence that early transition metal fluoride complexes do *not* preclude catalytic chemistry.



1 **2**

(1)



3 **4**

(2)

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(13) Due to the oxophilicity of titanium, cleavage of the Ti−O bond in titanium oxametallacycles to regenerate the titanium catalyst also presents a notable challenge. For recent examples of catalytic reductive cyclization of enones using $Cp_2Ti(PMe_3)_2$, see: (a) Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1995**, *117*, 6785−6786. (b) Crowe, W. E.; Rachita, M. J. *J. Am. Chem. Soc.* **1995**, *117*, 6787−6788.

(14) Integration of the crude reaction mixture was performed using fluorobenzene as an internal standard. The perfluoronaphthalene was isolated following chromatography on silica with pentane. The fraction was collected, and rotatory evaporation yielded 0.665 g (2.44 mmol, 40%) of white crystalline perfluoronaphthalene.

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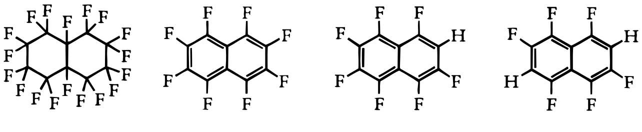
Several additional experiments support the notion that a nascent low-valent metallocene species is mediating the observed reductive defluorination chemistry. Treatment of **1** with "Cp_2Zr" (generated from 1 equiv of Cp_2ZrCl_2 and 2 equiv of *n*-BuLi) affords **2**.[16] Independent generation of "Cp_2Zr" and "Cp_2Ti" (photochemically via reductive elimination of biphenyl from Cp_2ZrPh_2 and Cp_2TiPh_2, respectively[17]) in the presence of **1** similarly affords **2**, thus confirming that the low-valent zirconocene and titanocene reagents are stoichiometrically competent to carry out intermolecular C−F bond activation of the saturated perfluorocarbon.

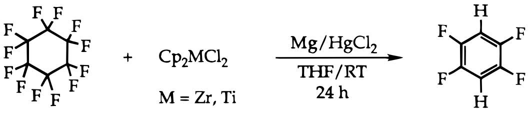
Interestingly, the zirconocene system (Cp_2ZrCl_2 + $Mg/HgCl_2$) is also active for the stepwise hydrogenation of aromatic C−F bonds at room temperature. For instance, a THF solution of 2.9 mmol of perfluorodecalin and 3.5 mmol of Cp_2ZrCl_2 with 12 mmol of magnesium turnings (3.8 mmol of $HgCl_2$) was prepared at room temperature, and a ^{19}F NMR spectrum recorded after 2 h showed that all of the perfluorodecalin (**1**) had reacted and that octafluoronaphthalene (**2**) and 1,3,4,5,6,7,8-heptafluoronaphthalene (**5**, identified and quantified by ^{19}F NMR spectroscopy[18] and GC/MS) were the principal organic products in 55% and 35% yields, respectively. After the solution was mixed for 14 h at room temperature, the dominant organic product was 1,3,4,5,7,8-hexafluoronaphthalene (**6**) (Chart 1). Deuterium incorporation in **5** and **6** from THF-d_8 demonstrates that the solvent is the proton source. In contrast to the high temperatures and pressures typically required for C−F hydrogenation reactions, it is remarkable that these selective hydrogenations can be performed under such mild conditions.[19]

Chart 1



1 2 5 6

This chemistry is not limited to substrates with tertiary C−F centers. Stirring Cp_2ZrCl_2 (or Cp_2TiCl_2) with 5 equiv of perfluorocyclohexane (**7**) in the presence of activated magnesium in THF solution for 24 h affords unreacted perfluorocyclohexane and 1,2,4,5-tetrafluorobenzene (**8**) in ~35% yield based upon zirconium as determined using ^{19}F NMR spectroscopy[20] and confirmed by comparison with commercial samples (eq 3).



(3)

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Under identical reaction conditions, hexafluorobenzene also affords 1,2,4,5-tetrafluorobenzene. The quantitative generation of pentafluorobenzene is observed prior to the formation of 1,2,4,5-tetrafluorobenzene.[21] As above, deuterium incorporation was observed in THF-d_8. Unlike the more reactive substrates that contain tertiary C−F bonds, perfluorocyclohexane and hexafluorobenzene do not exhibit any reactivity with activated magnesium in the absence of metallocene.

The above results suggest that an electron-transfer mechanism is operative whereby the metallocene fragment serves as an "electron shuttle" in transferring electrons from the terminal reductant to organic fluorinated substrates. Burk and co-workers proposed an electron-transfer mechanism for fluoride abstraction from tetrakis(trifluoromethyl)cyclopentadienone by a bis(cyclopentadienyl)titanacyclobutane complex.[22] It is unclear whether M^{II} or M^{III} (M = Ti, Zr) species are involved in this chemistry; however, reversible III/IV couples are well known for titanocene and zirconocene complexes.[12a] Mechanistic studies on these intriguing transformations are currently in progress.

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Supporting Information Available: Complete experimental procedures and spectroscopic data for known organic products (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any currrent masthead page for ordering information and Internet access instructions.

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(15) A 100 mL Schlenk flask was charged with 0.147 g of Cp_2ZrCl_2 (0.502 mmol), 1.50 g of $HgCl_2$ (5.52 mmol), 1.38 g of magnesium turnings (56.9 mmol), and 25 mL of freshly distilled THF. The resulting slurry was degassed, and 1.50 mL of perfluorodecalin (6.19 mmol) was added by syringe. The reaction mixture was stirred at room temperature for 3 h. The reaction affords 1.50 mmol of octafluoronaphthalene (30 fluorides removed per zirconium metal center or three turnovers based on Cp_2ZrCl_2) as determined by ^{19}F NMR spectroscopy using added fluorobenzene as an internal standard.

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(20) A 100 mL Schlenk flask was charged with 0.0795 g of Cp_2ZrCl_2 (0.272 mmol), 0.0887 g of $HgCl_2$ (0.327 mmol), 1.35 g of magnesium turnings (55.6 mmol), and 10 mL of freshly distilled THF. Perfluorocyclohexane (0.475 g, 1.58 mmol) was added, and the resulting mixture was degassed and allowed to stir at room temperature. After 24 h, the resulting yellow solution consists of primarily tetrafluorobenzene and unreacted perfluorocyclohexane. The reaction affords 0.0962 mmol of tetrafluorobenzene (35.4% based on Cp_2ZrCl_2) as determined by ^{19}F NMR spectroscopy using added fluorobenzene as an internal standard.

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