Cyclometallation *via* Carbon–Fluorine Bond Activation Induced by Silver Particles

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Supporting Information Placeholder

ABSTRACT: On treatment with either freshly-prepared silver nanoparticles or silver particles mechanochemically generated by stirring silver(I) oxide in dichloromethane, the complex $[Cp*IrCl_2(\kappa C-MeNC_3H_2NCH_2C_6F_5)]$ underwent a rapid and clean cyclometallation involving carbon—fluorine bond fission to afford the product $[Cp*IrCl(\kappa C^2-MeNC_3H_2NCH_2C_6F_4)]$.

The activation of carbon–fluorine bonds by metal complexes has attracted much attention during the past two decades.[1] Breaking these strong bonds is a considerable academic challenge. Interest in C—F chemistry stems from the importance of fluorinated compounds in industry, and, in particular, their recent predominance in new pharmaceuticals.[2] The C—F bond has prime importance in the prevention of toxic responses to drug molecules. In addition, understanding the activation of cheap and readily available polyfluorinated compounds, such as perfluoroarenes,[3] could facilitate the design of improved catalytic routes to fluorinated organic compounds. One strategy to overcome the thermodynamic problem of cleaving C—F bonds is the use of intramolecular reactions. For geometric reasons these tend to be rapid, regiospecific and therefore high-yielding. A number of examples have been reported,[4] including those leading to cyclometallated products.[5] However, despite cyclometallation involving C—F bond fission being first reported over 40 years ago,[5a] it remains rare in comparison to cyclometallation involving C—H bond fission, and a working knowledge of how to manipulate fluorinated organic compounds efficiently has yet to be achieved. Here we report an unexpected cyclometallation by C—F bond fission occurring by the action of silver, either as nanoparticles or as particles generated mechanochemically from silver(I) oxide.

In an attempt to prepare $[Cp*IrCl_2(\kappa C-MeNC_3H_2NCH_2C_6F_5)]$, **1**,[6] by a one-pot synthesis, 1-pentafluorobenzyl-3-methylimidazolium bromide was stirred in the presence of an excess of silver(I) oxide in dichloromethane for 1½ h to generate the silver NHC reagent $[AgBr(\kappa C-MeNC_3H_2NCH_2C_6F_5)]$, and $[Cp*IrCl_2]_2$ was then added. Surprisingly, after stirring for a further 4 h., the cyclometallated compound, **2**, was obtained (Scheme 1) and isolated in 79% yield. The identity of **2** was confirmed by a single-crystal X-ray diffraction study (Figure 1), with which other characterizing data are entirely consistent (see "Supporting Information"). In particular, the mass spectrum displays $[M – Cl]^+$ and the ^{19}F NMR spectrum displays four resonances with equal integration at δ -114.0, -147.7, -158.4 and -165.3.
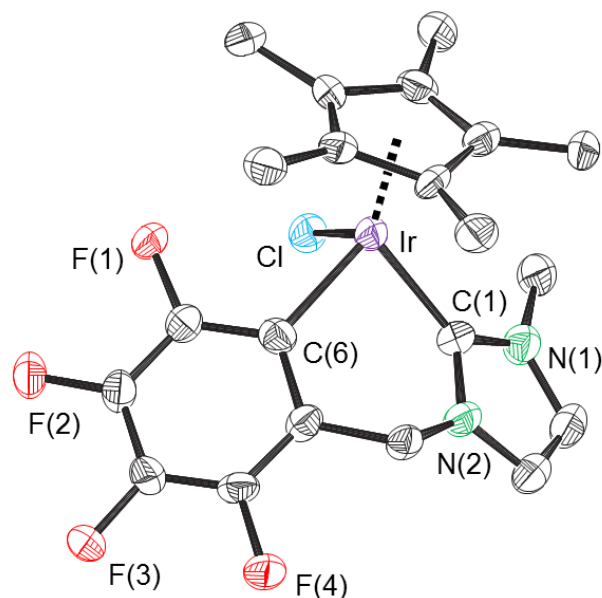

Figure 1. Molecular structure of **2**. Thermal ellipsoids represent 50% probability. Hydrogen atoms have been omitted for clarity. Selected bond distances (Å) and angles (°): Cp*—Ir 1.844(9), Ir—Cl 2.444(2), Ir—C(1) 2.015(7), Ir—C(6) 2.069(6), Cp*—Ir—Cl 124.3(2), Cp*—Ir—C(1) 127.7(3), Cp*—Ir—C(6) 128.1(3), Cl—Ir—C(1) 89.8(2), Cl—Ir—C(6) 88.2(2), C(1)—Ir—C(6) 85.7(3).

Previous studies[6] and subsequent syntheses of **1**, indicated that the C—F bond activation does not occur with the imidazolium salt or the silver NHC compound. Consequently the reaction occurs only when the NHC is coordinated to iridium. Heating a solution of **1** in chloroform at 70⁰C for 10 h. induced no reaction and so a spontaneous reaction can be discounted. Neither did reaction occur on treatment of **1** with [AgBr(κC-MeNC$_3$H$_2$NCH$_2$C$_6$F$_5$)]. However, **2** was afforded when **1** was added to a suspension of silver(I) oxide in dichloromethane that had previously been stirred for 2 h. Base-induced cyclometallation in complexes of non-fluorinated benzyl-substituted ligands has been reported previously.[7] Indeed cyclometallation induced by silver(I) oxide has recently been reported for a series of piano stool ruthenium NHC complexes.[8] However, an *in situ* NMR study indicated that there is no reaction on treatment of **1** with triethylamine. Since the latter reagent would generate hydroxide ions under the hydrous conditions of the experiment, their involvement, either as base or reducing agent,[9] can be ruled out. Devising a mechanism for the reaction to occur between **1** and silver(I) oxide is problematic: a carbon atom undergoes a formal reduction from +1 to -1 on C—F bond fission and Ir—C bond formation, but there is no corresponding oxidation. Silver(I) oxide has been found to react with a related rhodium NHC complex, but the reaction involves intramolecular nucleophilic attack by an oxide or a related species, and the oxygen atom is retained in the product.[10] Clearly this pathway is not applicable to the reaction between **1** and silver(I) oxide.

**Scheme 1. Reaction between Complex 1 and Silver Particles**
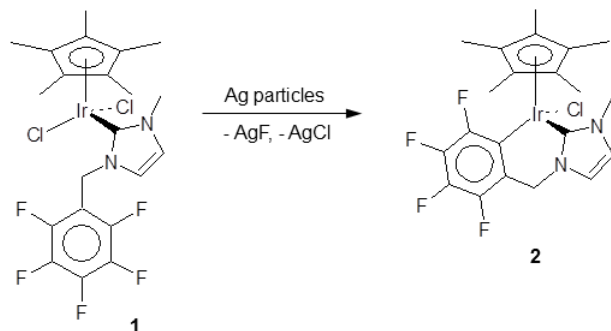
Since silver(I) oxide is unlikely to be directly responsible for cyclometallation, the possible involvement of elemental silver was considered. In this case the reduction of the carbon atom would be matched by oxidation of two silver atoms to afford silver(I) chloride and fluoride. The hypothesis was supported by the identification of both these by-products in the residue (see "Supporting Information"). Furthermore, an *in situ* NMR study found that when **1** was treated with silver nanoparticles, prepared from silver nitrate and triethylamine,[11] **2** was formed rapidly and cleanly. The generation of silver nanoparticles when an excess of silver(I) oxide was used to prepare silver NHC compounds has been noted as an interesting observation,[12] but no explanation was suggested, and no subsequent investigation was undertaken.

Although no difference between a fresh sample of commercial silver(I) oxide (Sigma Aldrich) and a sample that had been stirred in dichloromethane for 2 h. was discernible visibly or by SEM (Figure 2), EDS and qualitative analytical tests[13] revealed that the former was silver(I) oxide, whereas

the latter was predominantly elemental silver (see "Supporting Information"). Silver(I) oxide is known to undergo autocatalytic thermal decomposition to silver and oxygen,[14] but this decomposition route is not consistent with the reaction conditions. Whilst most silver salts are well known to be photosensitive, to our knowledge there are no reports of light causing the decomposition of silver(I) oxide, although in the presence of aqueous hydroxide, in which silver hydroxide is formed, slow, light-induced deposition of elemental silver has been reported.[15] Decomposition by ball-milling has been reported recently,[16] although the decomposition, monitored by powder X-ray diffraction, was slow, taking more than 90 h. to reach completion. Furthermore, the heat generated by the technique may have contributed to the decomposition. It is improbable that a reaction of silver(I) oxide with dichloromethane yields silver and not also silver chloride, which would have been detected in the sample. Consequently silver(I) oxide decomposition by the mechanical action of stirring was considered. The standard Gibbs free energy, $\Delta G_f^{\ominus}$, for silver(I) oxide is only -2.7 kcal mol^{-1},[17] and it is plausible that the collision of stirred particles imparts sufficient energy. The facile nature of the decomposition was confirmed by grinding *ca.* 0.2 g of silver oxide manually for 15 mins., which afforded a *ca.* 1:1 mixture of silver and silver(I) oxide, and by stirring *ca.* 0.2 g of silver oxide, in the absence of solvent, for 2 h., which produced *ca.* 90% of elemental silver. Further evidence for this reaction is provided by the common appearance of silver on the thread of bottles of silver(I) oxide, which is formed by the mechanical action of screwing and unscrewing the top. It is hard to reconcile the facile decomposition on stirring with the slow decomposition observed on ball-milling,[16] but the different nature of the silver(I) oxide particles and the quantities used (*ca.* 0.2 g *cf.* 9.75 g) may account for the observations.

Figure 2. SEM images of a commercial (Sigma Aldrich) sample of silver(I) oxide as purchased ((a) and (c)) and after stirring in dichloromethane for 2 h. ((b) and (d)).
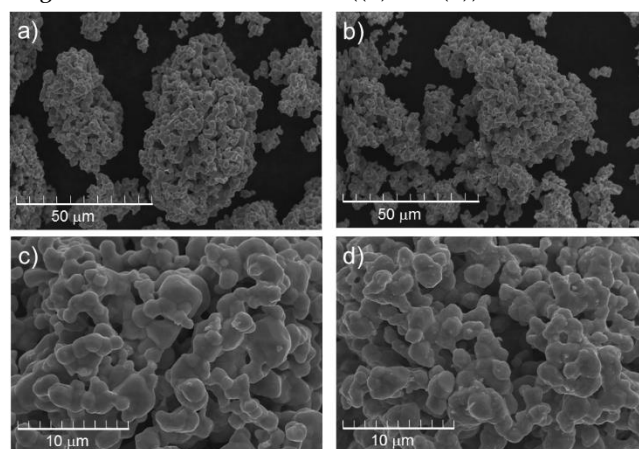
The regiospecificity of the reaction between **1** and silver particles suggests that C—F bond fission is not the initial step, because the *para* position is typically the most activated position in pentafluorophenyl compounds. A possible mechanism involves reduction of iridium and abstraction of chloride giving an anionic iridium(I) center, which performs nucleophilic attack on an *ortho* carbon atom of the phenyl ring. Although it is unlikely that bulk silver metal is capable of reducing **1**, silver nanoparticles are known to display a size-dependent reduction potential that is lower than that of the

bulk metal.[18] In support of this mechanism the reaction between **1** and zinc powder in the presence of aqueous hydrochloric acid produced **2**, although significantly less cleanly than observed with silver particles.

In summary, silver particles, generated by simply stirring silver(I) oxide in dichloromethane, induce a rapid and clean cyclometallation reaction in [Cp*IrCl$_2$(κC-MeNC$_3$H$_2$NCH$_2$C$_6$F$_5$)], which occurs *via* regiospecific carbon—fluorine bond activation.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, characterizing data, spectra and associated figures
Crystallographic data for **2**

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Author Contributions

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Notes
The authors declare no competing financial interests.

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