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Reagent-Dependent Formation of C−C and C−F Bonds in Pt Complexes: An Unexpected Twist in the Electrophilic Fluorination Chemistry

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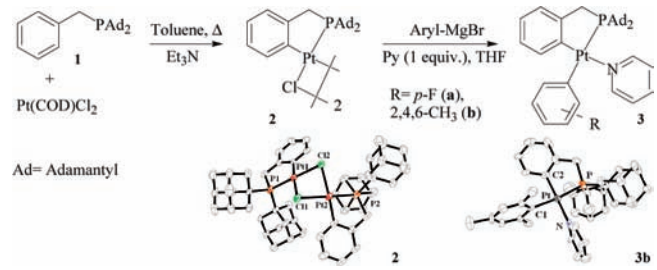
Abstract: Cyclometalated platinum(II) complexes (C−P)Pt(Aryl)py undergo oxidative addition reaction upon treatment with electrophilic fluorination reagents, XeF_2 or *N*-fluoro-2,4,6-trimethylpyridinium tetrafluoroborate, giving eventually products of C−C coupling. However, when aryl = mesityl, the two reagents give completely different products: the N−F salt still favors the C−C coupling reaction while XeF_2 gives the unprecedented benzylic fluorination of one of the *ortho*-methyl groups of the mesityl ligand.

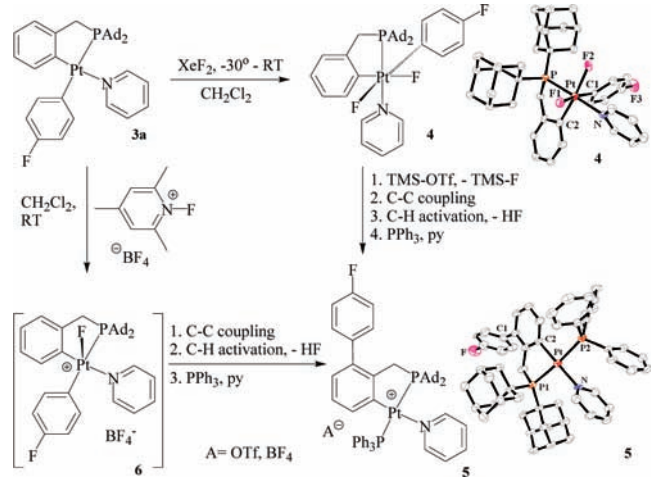
Transition-metal-mediated formation of carbon−fluorine bonds has recently become the topic of much interest[1] primarily due to the importance of the fluoroorganic compounds in the pharmaceutical and agrochemical industries. These compounds are traditionally prepared via a nucleophilic substitution reaction at an sp^2- or sp^3-hybridized carbon atom containing a halide or sulfonate leaving group.[2,3] More recently, a palladium-catalyzed ligand-assisted electrophilic fluorination emerged as a complementary technique to the nucleophilic exchange.[4] In these reactions, the C−F bond formation was proposed to take place from a Pd(IV) intermediate.[5−7] The electrophilic path offers an advantage of directly utilizing the C−H bonds in the fluorination reaction, thus reducing the number of synthetic steps and amount of waste associated with them. However, the necessity to utilize a heteroatom containing directing group (usually nitrogen) makes the palladium-assisted electrophilic fluorination relatively limited in scope. In this work, we present the first example of (1) use of Pt in making a C−F bond and (2) different reactivity patterns of different electrophilic fluorinating reagents.

A few years ago, we reported that chelating diphosphine complexes of the formula $(R_2P(CH_2)_nPR_2)Pt(Ar)_2$ (R = Alkyl, Aryl, n = 2, 3) react with XeF_2 to give products of the C−C reductive elimination: diaryl and the corresponding Pt(II) difluoride.[8] No oxidative addition Pt(IV) intermediate was observed during the reaction course. To study the reaction mechanism in more detail, we decided to slow down the C−C elimination process by making one of the aryl groups of a Pt(II) complex a part of a stable five-membered chelate. We found that reacting ligand **1**[9] with $(COD)PtCl_2$ (COD = 1,5-cyclooctadiene) gives a cyclometalated Pt(II) dimer **2**, which was fully characterized, including by X-ray analysis. Complex **2** reacted with ArMgBr giving, after the addition of pyridine, the corresponding monomeric Pt(II) diaryl precursors **3a,b** (Scheme 1). A typical $^{31}P\{^1H\}$ NMR spectrum of these complexes showed a singlet at ca. 62 ppm with a small J_{PtP} of ca. 1840 Hz, indicating the mutual trans-arrangement of the nonchelated aryl and phosphine ligands. The X-ray structure of the mesityl complex **3b** (Scheme 1) confirms the cis-positioning of the two aryl ligands, with the mesityl group being at a slightly longer distance from the Pt center than the chelated aryl group (2.057(8) Å vs 1.988(8) Å), likely due to a stronger trans-influence of the phosphine ligand compared with that of the pyridine.

Scheme 1



Scheme 2



The reaction of **3a** with XeF_2 provided the stable oxidative addition complex **4** as the only organometallic product, which was isolated in a 92% yield after precipitation with pentane (Scheme 2). The ^{19}F NMR spectrum of **4** exhibits two multiplets due to the inequivalent fluoro ligands at −231 and −234 ppm, with an additional signal at −120 ppm due to the *para*-fluoro substituent of the nonchelated aryl ligand. The X-ray structure of **4** also shows two inequivalent fluorides, with bond distances of 2.077(3) Å and 2.167(3) Å. As the Pt−C distances for the two aryl ligands are in the same range (2.013(6) Å vs 2.041(6) Å), we can tentatively attribute the large difference in the Pt−F bond lengths to the nonlinear positioning of the axial F1 and C1 ligands (Scheme 3, C1−Pt−F1 angle of 167.77(17)°) which decreases the trans-influence of the aryl group. The significant deviation from the linearity can be the result of the steric repulsions involving the bulky adamantyl groups.

Interestingly, the removal of one of the fluoro ligands from the Pt coordination sphere by 1 equiv of trimethylsilyl triflate (TMS-OTf) resulted in instantaneous C−C reductive elimination, followed by cyclometalation at the other side of aromatic ring.[10] The consequent elimination of HF gave an unsaturated Pt(II) product, which was characterized in solution. Addition of pyridine[11] and

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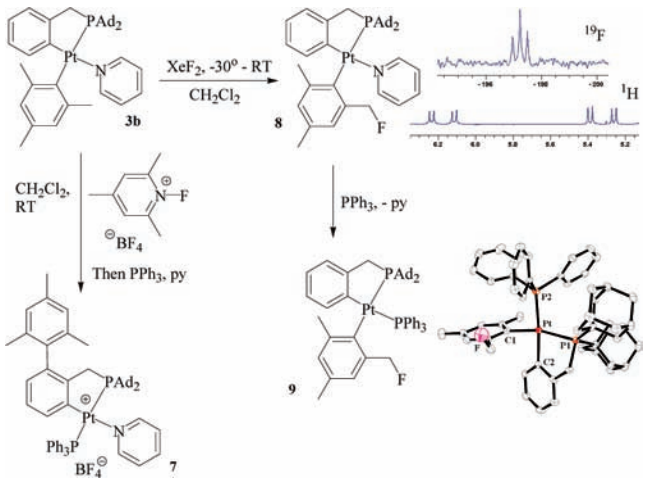
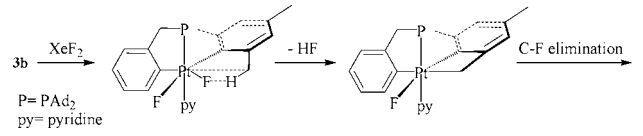
Scheme 3



PPh_3 to this species gave a 16-electron square-planar complex **5** which was isolated in a quantitative yield (Scheme 2). The ^{31}P NMR spectroscopy as well as X-ray structural analysis of **5** confirms the trans-positioning of the two phosphine ligands in solution and the solid state. As the reaction between TMS-OTf and **4** likely gives a cationic monofluoro Pt(IV) intermediate,[12] we thought that the reaction of **3a** with an electrophilic fluorinating reagent, such as *N*-fluoro-2,4,6-trimethylpyridinium tetrafluoroborate ("N−F"$^+$), would directly result in the formation of **5**, after the addition of PPh_3. Indeed, as shown in Scheme 2, complex **5** was obtained in the sequence of reactions which likely involved electrophilic fluorination, C−C reductive elimination, C−H activation, and H−F elimination; however, the reaction was not as clean as the fluoride removal from **4** with TMS-OTf giving ∼30% of unidentified byproducts. Following the reaction by ^{19}F NMR spectroscopy revealed the formation of a new Pt monofluoride complex which rapidly disappeared at RT to give the final product. This intermediate complex was assigned the structure of **6** (Scheme 2) based on the ^{31}P and ^{19}F NMR data. Subsequent addition of 1.5 equiv of $Me_4N^+F^-$ hydrate resulted in the formation of **4** as the major product. While we did not observe **6** in the reaction between **4** and TMS-OTf even at low temperatures, it is possible that the reaction proceeds via a different, more reactive Pt(IV) isomer.[13]

Unexpectedly, while the reaction of **3b** with the "N−F"$^+$ salt proceeded similarly to the reaction of **3a**, giving the product of the C−C coupling and consequent cyclometalation **7** as the major species, treating **3b** with XeF_2 did not give the analogous to **4** difluoro Pt(IV) product. Instead, quantitative fluorination of one of the *ortho*-benzylic positions of the mesityl ligand was obtained in this case giving complex **8** (Scheme 3). To the best of our knowledge, this is the first fluorination of a C−H bond assisted by a platinum complex[14] and first fluorination at the ortho-position not requiring a heteroatom directing group.[15] While the $^{31}P\{^1H\}$ NMR spectrum of **8** shows a signal very similar to that of **3b**, the triplet at 197.2 ppm (J_{HF} = 50 Hz) in the ^{19}F NMR spectrum unambiguously confirms the fluorination in the benzylic position. The CH_2F group gives rise to two low-field doublets of doublets in the ^1H NMR spectrum due to the inequivalent hydrogen atoms (Scheme 3, insert). Unlike **3b**, complex **8** shows considerable solubility in nonpolar solvents, such as pentane, and proved extremely difficult to crystallize. Fortunately, the replacement of pyridine in **8** with PPh_3 gave complex **9**, which was crystallized[16] from CH_2Cl_2−MeOH. The X-ray structure of **9** (Scheme 4) confirms the selective fluorination of one of the *ortho*-methyl groups of the mesityl ligand, with the overall geometry of the complex being very similar

Scheme 4



to that of **3b** (taking into account a different auxiliary ligand). For example, the Pt−mesityl distance of 2.057(6) Å remained virtually unchanged when compared with that in **3b**. The long 4.028 Å distance between the benzylic fluorine atom and platinum center suggests that there is no interaction between the two atoms in the solid state.

While the mechanistic studies of the new fluorination reaction are still underway, we believe that the formation of a transient Pt(IV) difluoro species (similar to **4**) takes place followed by the fluoride-assisted metalation of one of the methyl groups of the mesityl ligand.[17] The reaction is probably facilitated by high steric congestion around the metal center. The benzylic C−F reductive elimination from a Pt(IV) complex furnishes the final product (Scheme 4).

In summary, we demonstrated that Pt complexes can be used in the electrophilic fluorination of a benzylic C−H bond. In addition, using different electrophilic fluorinating reagents can lead to different reaction outcomes, which can be important in the design of new fluorination methods. Further studies on the reactivity of Pt complexes in fluorination reactions are ongoing in our laboratory.

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Supporting Information Available: Synthesis and characterization of complexes **2**−**9** (PDF). X-ray data for complexes **2**, **3b**, **4**, **5**, and **9** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) The pyridine ligand was sometimes lost with the eliminated HF. To maintain the 16e configuration it was necessary to add more pyridine along with PPh_3.
(12) Such cationic intermediates have been shown to be highly reactive in the C−C reductive elimination from Pt(IV) complexes; for example, see: Procelewska, J.; Zahl, A.; Liehr, G.; van Eldik, R.; Smythe, N. A.; Williams, B. S.; Goldberg, K. I. *Inorg. Chem.* **2005**, *44*, 7732.
(13) A nearly identical to **6** intermediate complex was also observed, along the way to **5**, when *N*-fluoro-2,4,6-trimethylpyridinium *triflate* was used, suggesting that the anion has little role in the overall transformation.
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(15) Under the same conditions, no benzylic fluorination of mesitylene with XeF_2 takes place in the absence of platinum.
(16) The complex cocrystallized with an additional PPh_3 molecule, which was omitted from Scheme 3 for clarity.
(17) A Pt(IV)−Cl interaction with the ligand CH_3 group *without* cyclometallation was recently reported: Mamtora, J.; Crosby, S. H.; Newman, C. P.; Clarkson, G. J.; Rourke, J. P. *Organometallics* **2008**, *27*, 5559.

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