Insight into the Mechanism of Platinum-Catalyzed Cross-Coupling of Polyfluoroaryl Imines

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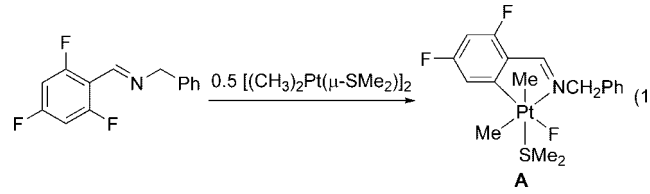
We recently reported the first examples of Pt-catalyzed methylation of polyfluorinated arenes as a means to generate partially fluorinated aromatic building blocks. The reaction is selective for cleavage of C−F bonds *ortho* to an imine substituent and allows for preferential cleavage of C−F bonds in the presence of considerably weaker bonds (e.g., C−Br). We report herein the proposed mechanism for this reaction. Initial C−F activation generates a Pt(IV)−F intermediate, which then reacts with $(CH_3)_2Zn$ via transmetalation. Subsequent reductive elimination from the Pt(IV) species generates a new sp^2-sp^3 C−C bond. In addition, we have identified a species present during the catalytic reaction and propose this to be the catalyst resting state.

Introduction

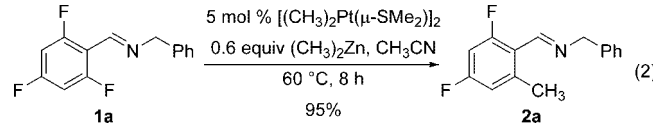
The catalytic cross-coupling of aryl fluorides has received considerably less attention than that of other aryl halides. Although several protocols have emerged,[1–3] beginning with the report from Kumada in 1973, only a few examples of these involve cross-coupling of polyfluoroarenes.[2] We recently reported the first examples of Pt-catalyzed cross-coupling of polyfluorinated aryl imines.[3] Our inspiration came from the report by Crespo and Martinez that $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$[4] effects the stoichiometric C−F activation of a number of polyfluorinated aryl imines (eq 1).[5] We sought to explore the reaction mechanism as a means to develop catalysts with broader substrate scope.

Based on detailed kinetic and mechanistic analyses, Martinez proposed the mechanism outlined in Scheme 1 for the oxidative addition of C(aryl)−X bonds (X = F, Cl, Br) to $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$.[6] Coordination of imine leads to Pt(II) intermediate **I**. Loss of SMe_2 generates Pt(II) intermediate **II**. Oxidative addition of the C−X bond leads, initially, to intermediate **III**, in which the C(aryl) and X are in a *cis* relationship. This species undergoes facile Berry pseudorotation. Consequently, upon coordination of SMe_2, the isomer with a *trans* relationship between C(aryl) and X (complex **IV**) is generated. Martinez has shown that Pt(IV) complexes of this type can undergo both dissociative[6,7] and associative[7,8] substitution reactions.



(1)

We anticipated that a Pt(IV)−F intermediate (e.g., **A** in eq 1, **III** and **IV** in Scheme 1) could undergo cross-coupling with a suitable organometallic reagent to permit formation of a new C−C bond. Consistent with this hypothesis, we found that the addition of 0.6 equiv of $(CH_3)_2Zn$ to a mixture of **1a** and 5 mol % $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$ afforded methylated product **2a** in high isolated yield (eq 2).[3] A variety of other fluoroaryl imines were successfully methylated using this protocol, including those bearing potentially reactive functional groups, such as aryl bromides and nitriles.



(2)

During the course of our investigation, we noticed considerable similarities between our catalytic results[3] and the stoichio-

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(1) (a) Kiso, Y.; Tamao, K.; Kumada, M. *J. Organomet. Chem.* **1973**, *50*, C12–C14. (b) Böhm, V. P. W.; Gstöttmayr, C. W. K.; Weskamp, T.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 3387–3389. (c) Mongin, F.; Mojovic, L.; Guillamet, B.; Trécourt, F.; Quéguiner, G. *J. Org. Chem.* **2002**, *67*, 8991–8994. (d) Terao, J.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2003**, *125*, 5646–5647. (e) Ackermann, L.; Born, R.; Spatz, J. H.; Meyer, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 7216–7219. (f) Dankwardt, J. W. *J. Organomet. Chem.* **2005**, *690*, 932–938. (g) Liu, J.; Robins, M. J. *Org. Lett.* **2005**, *7*, 1149–1151. (h) Wilhelm, R.; Widdowson, D. A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3808–3813. (i) Kim, Y. M.; Yu, S. *J. Am. Chem. Soc.* **2003**, *125*, 1696–1697. (j) Mikami, K.; Miyamoto, T.; Hatano, M. *Chem. Commun.* **2004**, 2082–2083. (k) Guo, H.; Kong, F.; Kanno, K-i.; He, J.; Nakajima, K. *Organometallics* **2006**, *25*, 2045–2048.

(2) Zr: (a) Edelbach, B. L.; Kraft, B. M.; Jones, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 10327–10331. (b) Braun, T.; Perutz, R. N.; Sladek, M. I. *Chem. Commun.* **2001**, 2254–2255. (c) Steffen, A.; Sladek, M. I.; Braun, T.; Neumann, B.; Stammler, H.-G. *Organometallics* **2005**, *24*, 4057–4064. (d) Yoshikai, N.; Mashima, H.; Nakamura, E. *J. Am. Chem. Soc.* **2005**, *127*, 17978–17979. (e) Schaub, T.; Backes, M.; Radius, U. *J. Am. Chem. Soc.* **2006**, *128*, 15964–15965. (f) Saeki, T.; Takashima, Y.; Tamao, K. *Synlett* **2005**, *11*, 1771–1774. (g) Braun, T.; Izundu, J.; Steffen, A.; Neumann, B.; Stammler, H.-G. *Dalton Trans.* **2006**, 5118–5123. (h) Korn, T. J.; Schade, M. A.; Wirth, S.; Knochel, P. *Org. Lett.* **2006**, *8*, 725–728. (i) Korn, T. J.; Schade, M. A.; Cheemala, M. N.; Wirth, S.; Guevara, S. A.; Cahiez, G.; Knochel, P. *Synthesis* **2006**, *21*, 3547–3574.

(3) Wang, T.; Alfonso, B. J.; Love, J. A. *Org. Lett.* **2007**, *9*, 5629–5631.

(4) Hill, G. S.; Irwin, M. J.; Levy, C. J.; Rendina, L. M.; Puddephatt, R. J.; Andersen, R. A.; McLean, L. *Inorg. Synth.* **1998**, *32*, 149–151.

(5) Crespo, M.; Martinez, M.; Sales, J. *Organometallics* **1993**, *12*, 4297–4304.

(6) Bernhardt, P. V.; Gallego, C.; Martinez, M. *Organometallics* **2000**, *19*, 4862–4869.

(7) Bernhardt, P. V.; Gallego, C.; Martinez, M.; Parella, T. *Inorg. Chem.* **2002**, *41*, 1747–1754.

(8) Gallego, C.; Gonzalez, G.; Martinez, M.; Merbach, A. E. *Organometallics* **2004**, *23*, 2434–2438.

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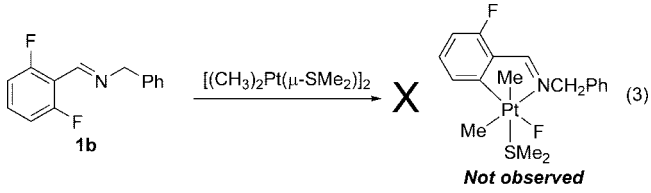
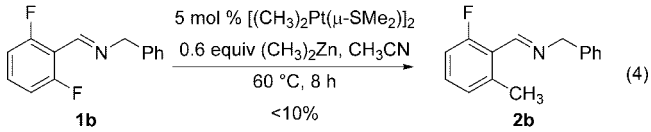
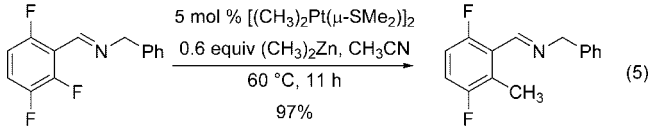
metric C−F activation results previously reported. In particular, after a detailed study, Crespo and Martinez established that at least three electron-withdrawing groups were needed in order for C−F activation to occur efficiently and that the activation barrier for C−F activation decreased as the number of fluorine substituents increased. Likewise, we found that difluoroaryl imine (**1b**), which did not undergo appreciable stoichiometric C−F activation (eq 3), also did not fare well in the catalytic reaction (eq 4). In addition, the selectivity of the cross-coupling of unsymmetrically substituted trifluoroimine **1c** is the same in both the stoichiometric and catalytic studies (eq 5). Crespo and Martinez attributed the selectivity for activation of the more hindered C−F bond to the electron-withdrawing ability of the adjacent fluorine substituent.[5]

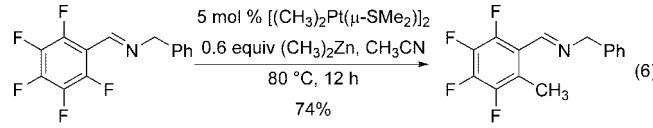


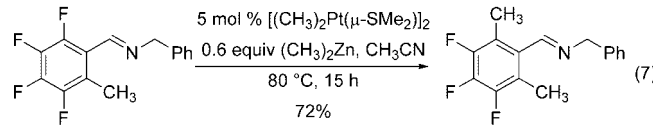




We also discovered that the reaction products could undergo a second methylation, provided that the arene ring was sufficiently electron deficient. For example, the reaction of pentafluoroimine **1d** can be selectively monomethylated in good yield; only 3% of the dimethylated product was formed (eq 6). The product of this reaction, **2d**, can subsequently be methylated with excess $(CH_3)_2Zn$ (eq 7).

These observations led us to hypothesize that the catalytic reaction does involve C−F activation (eq 1) as a catalytically relevant step. Importantly, if this hypothesis is correct, efforts to design and synthesize complexes with greater ability to promote stoichiometric C−F activation should eventually lead





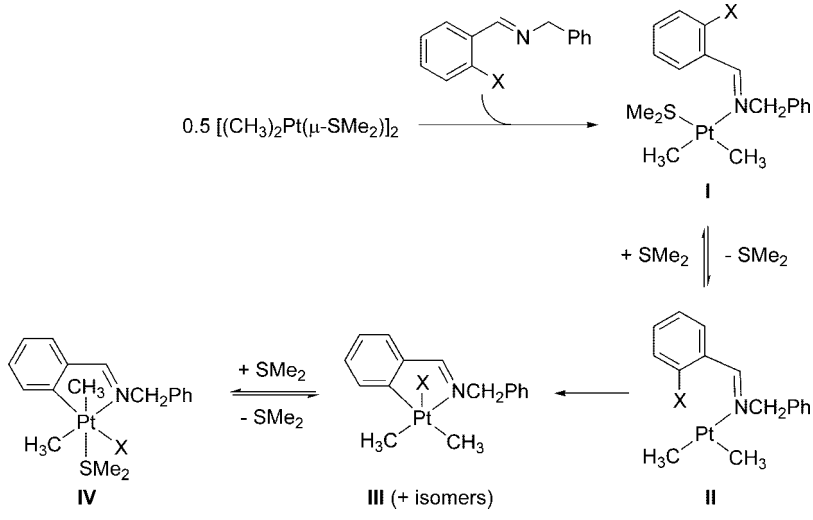
to increased substrate scope in the catalytic reaction. We report herein the results of our study.

Results and Discussion

We began by monitoring the conversion of **1a** to **2a** by ^1H and ^{19}F NMR spectroscopy. Trifluoroimine (**1a**, 8.5 mg, 0.034 mmol), $(CH_3)_2Zn$ (11.0 μL of a 2.0 M solution in toluene), and $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$ (100 μL of a 0.017 M solution in CD_3CN) were dissolved in 1.1 mL of CD_3CN in an NMR tube. The reaction was monitored over several hours at 60 °C. A plot showing the consumption of **1a** and formation of **2a** as measured by integration of the imine CH═N resonances using ^1H NMR spectroscopy (300 MHz, CD_3CN) is shown in Figure 1. During the course of the reaction, in addition to the resonances attributed to **1a** and **2a**, a number of smaller resonances were observed; importantly, **A** was not observed during the catalytic reaction.

To gain better information about these additional resonances, the reaction was repeated at higher concentration. Trifluoroimine (**1a**, 85 mg, 0.34 mmol), $(CH_3)_2Zn$ (110 μL of a 2.0 M solution in toluene), and $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$ (10 mg, 0.017 mmol) were dissolved in 1.1 mL of CD_3CN in an NMR tube. Again, in addition to **1a** and **2a**, a number of additional resonances appeared in the ^1H NMR spectrum. The chemical shifts and their relative intensities are given in Table 1. The resonance at δ 8.87 (entry 1) is attributed to the C*H*═N of a bound imine, with a Pt satellite coupling constant of 39 Hz. The multiplet at δ 4.98 is consistent with the methylene of a bound imine. The signal at δ 1.77 is assigned as coordinated SMe_2 (J_{Pt-H} = 12 Hz). The three resonances at δ 0.78, 0.41, and 0.20, which are of equivalent intensity, are attributed to Pt-CH_3 groups. The coupling constants of the signals at δ 0.78 and 0.41 (69 and 73 Hz, respectively) are consistent with methyl groups *trans* to

Scheme 1. Mechanism of C−X Activation (see refs 5 and 6)



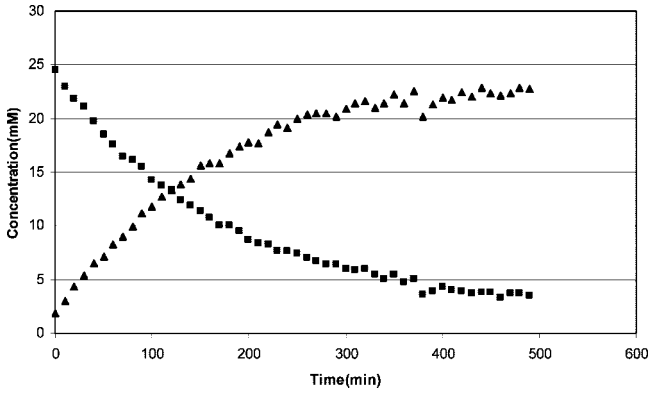


Figure 1. Plot of [**1a**] (mM) vs time (min) (■) and [**2a**] (mM) vs time (min) (▲) at 60 °C.

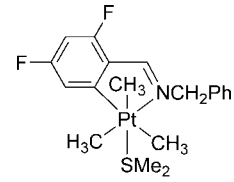
Table 1. ^{1}H NMR Spectroscopic Data for Observed Species

entry	δ	multiplicity	rel intensity
1	8.87	s (J_{PtH} = 39 Hz)	1
2	4.98	m	2
3	1.77	s (J_{PtH} = 12 Hz)	6
4	0.78	s (J_{PtH} = 69 Hz)	3
5	0.41	s (J_{PtH} = 73 Hz)	3
6	0.20	s (J_{PtH} = 46 Hz)	3

L-type ligands (presumably imine and SMe_2).[9] The coupling constant for the signal at δ 0.20 (46 Hz) is typical of a methyl group *trans* to a carbon. The six signals are present in a 1:2:6:3:3:3 ratio, which suggests that all these components are in the same species. On the basis of integration of the ^{1}H NMR spectrum, this species is present as ∼5% of the reaction mixture (i.e., ∼50% of the amount of Pt).[10] In addition, the ^{19}F NMR spectrum shows **1a** and **2a**, as well as two resonances at δ 104.1 and 111.4, which were present in considerably lower intensity than either **1a** or **2a**. On the basis of this data, we have assigned the structure as complex **D** (Figure 2). Given that this complex is observed for the duration of the reaction, this species is proposed as the resting state of the catalytic cycle.

To provide support for the C−F activation mechanism outlined in Scheme 1, we attempted the stoichiometric C−F activation of **1a** (44.0 mg, 0.177 mmol) with $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$ (50.5 mg, 0.088 mmol) in the presence of SEt_2 (15.5 mg, 0.172 mmol). Two complexes were formed in a 2.3:1 ratio; based on ^{1}H NMR spectroscopic data, we have assigned these as complex **A** (eq 1) and **A**·SEt_2, respectively. This result indicates that exchange of thioether ligands is feasible.

Our next objective was to determine whether **A** could generate **2a**. Experiments were performed in both the absence and presence of $(CH_3)_2Zn$. The reaction of 1 equiv of $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$ (9.8 mg, 0.017 mmol) with 2.0 equiv of trifluoroimine **1a** (8.5 mg, 0.034 mmol) in 1.1 mL of CD_3CN (0.016 mM in $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$) generated Pt−F complex **A** at 60 °C, as established by comparing the ^{19}F NMR spectrum to the reported data.[5,11,12] After 6 h at 60 °C, the majority of the starting material



D

Figure 2. Proposed structure of observed Pt complex.

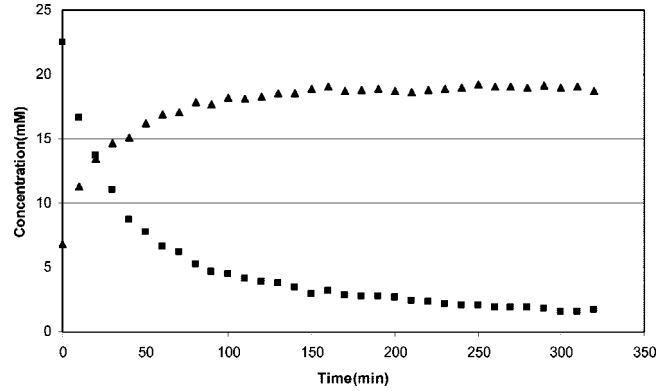


Figure 3. Plot of [**1a**] (mM) vs time (min) (■) and [**A**] (mM) vs time (min) (▲) at 60 °C.

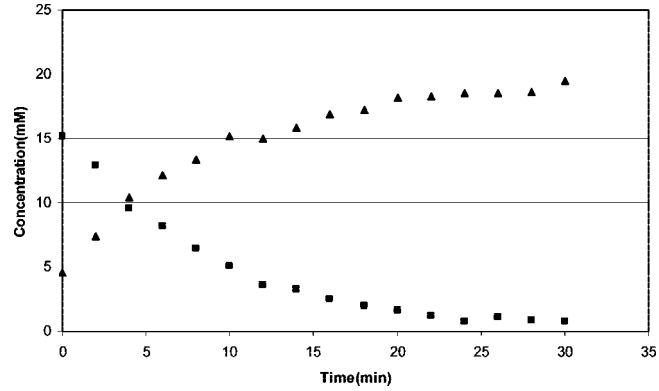


Figure 4. Plot of [**A**] (mM) vs time (min) (■) and [**2a**] (mM) vs time (min) (▲) at 60 °C.

was consumed and complex **A** was formed in 70% yield. A plot showing the consumption of **1a** and formation of **A** as measured by integration of the imine CH_2 resonances using ^{1}H NMR spectroscopy (300 MHz, CD_3CN) is shown in Figure 3. It is noteworthy that the catalytic methylation of **1a** requires 8 h at this temperature (Figure 1).

In the absence of $(CH_3)_2Zn$, **A** does not generate product **2a** (eq 8).[13] In contrast, when 1.2 equiv of $(CH_3)_2Zn$ is added to preformed **A**, the Pt−F signal of **A** in the ^{19}F NMR spectrum immediately disappears and new signals emerge in the ^{1}H NMR spectrum indicative of formation of **2a**, as well as **D**. The reaction is complete within 30 min, which is considerably faster than both the stoichiometric C−F activation and the catalytic methylation reaction (eq 9). Imine **2a** is formed in 69% overall yield from **1a** (>98% based on the amount of **A** formed from **1a**), consistent with the catalytic results (eq 2). A plot showing the consumption of **A** and formation of **2a** as measured by integration of the imine CH_2 resonances using ^{1}H NMR spectroscopy (300 MHz, CD_3CN) is shown in Figure 4. These

(9) (a) van Asselt, R.; Rjinberg, E.; Elsevier, C. J. *Organometallics* **1994**, *13*, 706–720. (b) Clegg, D. E.; Hall, J. R.; Swile, G. A. *J. Organomet. Chem.* **1972**, *38*, 403–420. (c) Ruddick, J. R.; Shaw, B. L. *J. Chem. Soc. A* **1969**, 2969–2970.

(10) Although accurate determination of the amount is rendered difficult based on the inherent error in integration, we are able to observe the ^{13}C satellites for $PhCH_3$, indicative of a good signal-to-noise ratio.

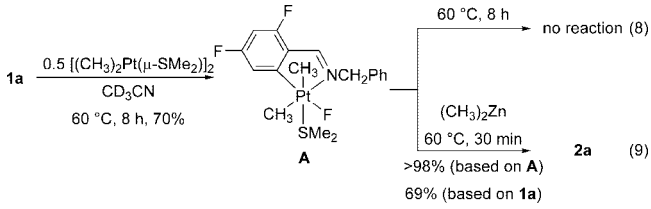
(11) Although the stoichiometric studies (ref 5) were conducted in acetone-d_6, we used CD_3CN because this is the solvent used in the catalytic study. As such, the chemical shifts in the ^{19}F NMR spectrum were slightly different than those reported in ref 5.

(12) Formation of **A** from **1a** is not quantitative; see Figure 3.

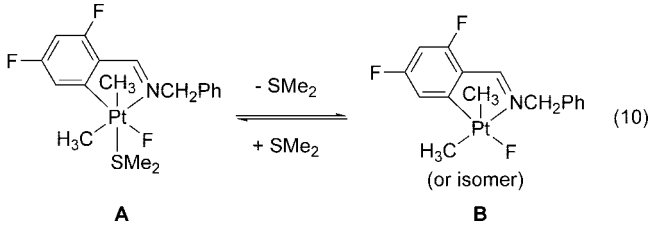
(13) Likewise, no evidence for ethane formation is observed.

results indicate that addition of $(CH_3)_2Zn$ is needed to promote formation of **2a** from **A**. During the course of the reaction of **A** with $(CH_3)_2Zn$, the ^1H NMR spectroscopic resonances for $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$, which had been depleted in the formation of **A**, re-emerge, indicating that the original Pt species can be regenerated. In addition, it is noteworthy that the conversion of **A** to **2a** is considerably faster than the conversion of **1a** to **A**.

These findings are consistent with **A** being either part of the

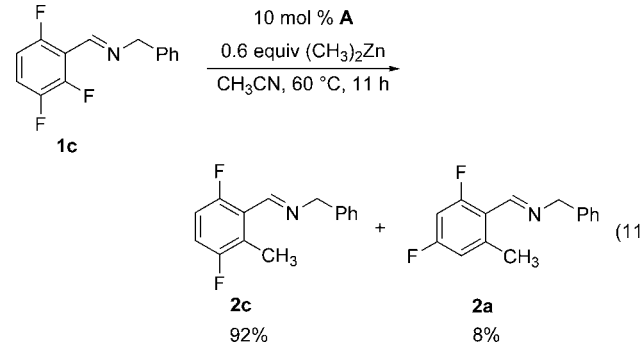


catalytic cycle or able to enter the catalytic cycle. The reaction of **A** with $(CH_3)_2Zn$ is slowed considerably by the addition of SMe_2, suggesting that conversion of **A** to **2a** involves dissociation of SMe_2. Martinez and co-workers had previously shown that the formation of complexes similar to **A** proceeds through a five-coordinate Pt(IV) complex (e.g., **III** in Scheme 1).[6] Martinez and Crespo also showed that **A** can undergo dissociative exchange of SMe_2 for PPh_3, indicating that there is an equilibrium between **A** and a five-coordinate species.[5–7] This information led us to conclude that a five-coordinate species, **B**, is part of the catalytic pathway and that **B** is in equilibrium with **A** (eq 10). This indicates that **A** should be able to enter the catalytic cycle.

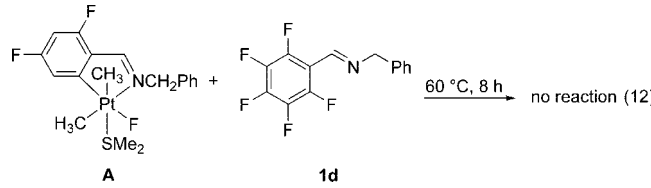


To further explore this possibility, we used **A** as a catalyst for methylation of imine **1c** (eq 11).[14] Presumably, **A** would first react with $(CH_3)_2Zn$ to generate up to 10 mol % of **2a** (equivalent to the amount of **A** added, though the formation of **A** from **1a** is not quantitative, as previously mentioned). The formation of **2a** would presumably be accompanied by the regeneration of $[(CH_3)_2Pt(SMe_2)(imine)]$, which is the species postulated to be involved in C−F activation (see Scheme 1).[5,6] This Pt(II) species could then catalyze the methylation of **1c**. Consistent with this hypothesis, we found that **A** does indeed permit the catalytic formation of **2c**, in a yield comparable to that obtained using 5 mol % $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$ (eq 5). This reaction also produces 8% of **2a**, as expected. This result is also consistent with the propensity of **A** to enter the catalytic cycle.

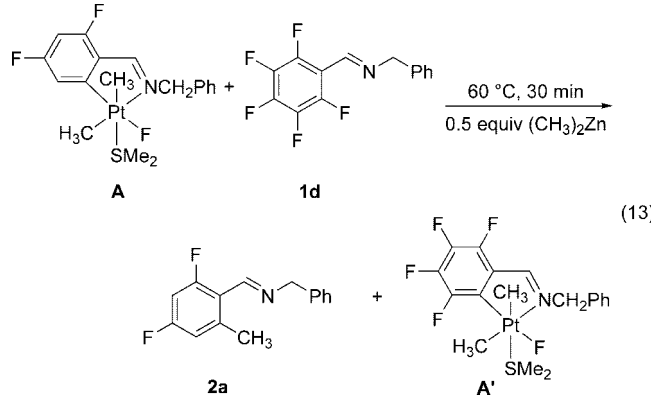
We next explored the reversibility of formation of **A**. Pentafluoroimine **1d** was selected for study, as this imine undergoes stoichiometric C−F activation at a significantly faster rate than **1a**; the experimentally determined enthalpies of activation for C−F activation of **1a** and **1d** were reported by Crespo and Martinez and are 54 ± 1 and 30 ± 4 kJ/mol, respectively.[5] Thus, if formation of **A** were reversible, we would expect to see the preferential formation of the Pt−F species



derived from **1d**. Addition of 10 equiv of **1d** to a solution of **A** in CD_3CN does not result in the formation of a new Pt−F species, based on the ^1H or ^{19}F NMR spectra, even after 8 h at 60 °C (eq 12).[15] This result indicates that formation of **A** is not reversible on the time scale of the catalytic process.



To test whether the conversion of **A** to **2a** is accompanied by the regeneration of a species capable of subsequent C−F activation, we examined the reaction of **A**[16] with $(CH_3)_2Zn$ (8.5 μL of a 2.0 M solution in toluene, 0.5 equiv relative to **1a**) in the presence of **1d** (19.4 mg, 0.068 mmol, 2.0 equiv relative to **1a**). Within 30 min at 60 °C, **A** was completely consumed. Product **2a** was formed in 79% yield, along with a 75% yield of complex **A′** (eq 13).[17] This result is consistent with initial reaction of **A** with $(CH_3)_2Zn$ to generate **2a**, similar to that outlined in eqs 9 and 11. The resultant Pt(II) species then reacts with **1d** (which is more reactive toward C−F activation than **2a**) to generate **A′** upon coordination of SMe_2.



Based on these observations, a plausible mechanism is outlined in Scheme 2. The platinum dimer $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$ reacts with imine **1a** to generate $[(CH_3)_2Pt(SMe_2)(imine)]$.[5–7] After dissociation of SMe_2, $[(CH_3)_2Pt(imine)]$ undergoes rate-limiting C−F activation of **1a** to produce **B** (or an isomer).[18] This species is in equilibrium with **A**, consistent with the results

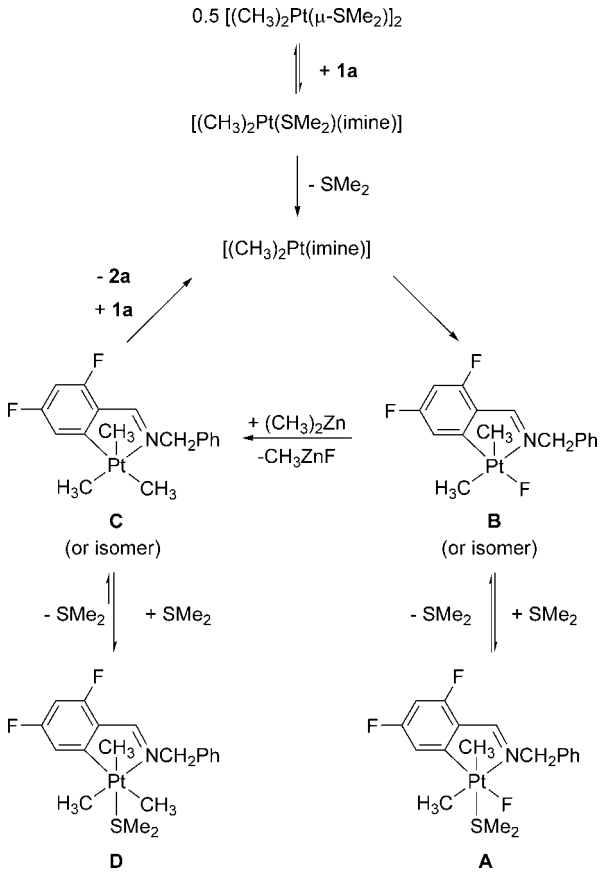
(14) The use of metal fluorides to catalyze cross-coupling of aryl fluorides has been previously reported. See refs 2b,c,g.

(15) The Pt−F signal of **A** diminishes over time, presumably due to decomposition.

(16) Complex **A** was formed from the stoichiometric reaction of **1a** and $[(CH_3)_2Pt(\mu\text{-}SMe_2)]_2$, as in eqs 8 and 9.

(17) Yields for formation of **2a** and **A′** are based on the percent yield of **A** formed from the stoichiometric reaction of **1a** with $(CH_3)_2Zn$.

Scheme 2. Proposed Mechanism of Cross-Coupling



of Crespo and Martinez.[5] Complex **B** then undergoes transmetalation with $(CH_3)_2Zn$ to provide **C** (or an isomer).[18,19] Intermediate **C** can react in two ways: (1) coordination of SMe_2 to generate **D**, the species observed during the catalytic reaction, or (2) reductive elimination to provide **2a** and, after association of another equivalent of imine **1a**, $[(CH_3)_2Pt(imine)]$.

Reductive elimination of both sp^3-sp^3 C−C bonds[20] and sp^2-sp^2 C−C bonds[21] from five-coordinate Pt(IV) species is well-documented. Alternatively, reductive elimination could occur directly from **D**; sp^2-sp^2 C−C bond formation from six-coordinate Pt(IV)[22,23] has been observed. Given that **D** builds up and accounts for approximately half of the Pt in the reaction (vide infra), as well as the observation that excess SMe_2 slows the conversion of **A** to **2a**, we propose that complex **D** is not part of the catalytic cycle.[24] As such, reductive elimination would occur from the five-coordinate species, **C**. We are currently attempting to isolate complex **D** to verify its structure, as well as its ability to undergo reductive elimination. In addition, a detailed kinetic investigation of the transmetalation and reductive elimination steps is underway.

Conclusions

In conclusion, we have established the general mechanism for the Pt-catalyzed methylation of polyfluorinated aryl imines and that the process does involve C−F activation as a fundamental step. Given that C−F activation is substantially slower than the subsequent transmetalation and reductive elimination steps and that aryl fluorides that cannot undergo stoichiometric C−F activation also do not undergo catalytic cross-coupling, we are currently developing new Pt(II) complexes capable of C−F activation with an expanded substrate scope.

Experimental Section

General Procedures. Manipulation of organometallic compounds was performed using standard Schlenk techniques under an atmosphere of dry nitrogen or in a nitrogen-filled Vacuum Atmospheres drybox (O_2 < 2 ppm). NMR spectra were recorded on Bruker Avance 300 or Bruker Avance 400 spectrometers. ^1H and ^{13}C chemical shifts are reported in parts per million and referenced to residual solvent. ^{19}F NMR spectra are reported in parts per million and referenced to C_6F_6 in acetone−d_6 (−162.9 ppm). Coupling constant values were extracted assuming first-order coupling. The multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m = multiplet. All spectra were obtained at 25 °C. Mass spectra were recorded on a Kratos MS-50 mass spectrometer.

Materials and Methods. Acetonitrile was dried by heating to reflux over calcium hydride. Acetonitrile-d_3 and all organic reagents were obtained from commercial sources and used as received. K_2PtCl_4 was purchased from Strem Chemicals and was used without further purification. $PtCl_2(SMe_2)_2$ was prepared by a previously reported procedure.[4] $Pt_2Me_4(SMe_2)_2$ was prepared by a previously reported procedure.[3,4] All imines were prepared by previously reported procedures.[3,5] Dimethyl zinc (2.0 M solution in toluene) was purchased from Aldrich.

Preparation of N-(4,6-Difluoro-2-methylbenzylidene)benzylamine (2a). In a 20 mL vial, *N*-(2,4,6-trifluorobenzylidene)benzylamine (**1a**) (0.4 mmol, 100.0 mg) and $Pt_2Me_4(SMe_2)_2$ (0.02 mmol, 11.5 mg) were dissolved in CH_3CN (3 mL). The resulting solution was transferred into a test tube fitted with a screw cap containing a septum. Me_2Zn (0.240 mmol, 120 μL of a 2.0 M solution in toluene) was then added by syringe. The resulting solution was heated at 60 °C for 8 h. The solution was then cooled to room temperature, and the solvent was removed by rotary evaporation. *n*-Pentane (3 × 20 mL) was then added, and the resulting mixture was shaken. The *n*-pentane solution was collected and filtered through Celite. The filtrate was concentrated by rotary

(18) Berry pseudorotation in five-coordinate Pt(IV) species is assumed to be fast, on the basis of precedent from Martinez and others.

(19) We do not observe buildup of CH_3ZnF during the catalytic reaction. Presumably, the CH_3ZnF generated upon transmetalation reacts with another equivalent of **B**, as only 0.6 equiv of $(CH_3)_2Zn$ was used in the catalytic reaction. Consistent with this hypothesis, we have found that CH_3ZnCl reacts rapidly with **B**. In contrast, in the stoichiometric reaction of **A** with $(CH_3)_2Zn$, a new species with a ^1H NMR chemical shift of −0.86 ppm in CD_3CN is observed, which is presumably CH_3ZnF. For comparison, $(CH_3)_2Zn$ has a ^1H NMR chemical shift of −0.76 ppm in CD_3CN.

(20) (a) Brown, M. P.; Puddephatt, R. J.; Upton, C. E. E. *J. Chem. Soc., Dalton Trans.* **1974**, 2457–2465. (b) Roy, S.; Puddephatt, R. J.; Scott, J. D. *J. Chem. Soc., Dalton Trans.* **1989**, 2121–2125. (c) Goldberg, K. I.; Yan, J.; Winter, E. L. *J. Am. Chem. Soc.* **1994**, *116*, 1573–1574. (d) Goldberg, K. I.; Yan, J. Y.; Breitung, E. M. *J. Am. Chem. Soc.* **1995**, *117*, 6889–6896. (e) Hill, G. S.; Puddephatt, R. J. *Organometallics* **1997**, *16*, 4522–4524. (f) Williams, B. S.; Holland, A. W.; Goldberg, K. I. *J. Am. Chem. Soc.* **1999**, *121*, 252–253. (g) Hill, G. S.; Yap, G. P. A.; Puddephatt, R. J. *Organometallics* **1999**, *18*, 1408–1418. (h) Crumpton, D. M.; Goldberg, K. I. *J. Am. Chem. Soc.* **2000**, *122*, 962–963. (i) Williams, B. S.; Goldberg, K. I. *J. Am. Chem. Soc.* **2001**, *123*, 2576–2587. (j) Crumpton-Bregel, D. M.; Goldberg, K. I. *J. Am. Chem. Soc.* **2003**, *125*, 9442–9456. (k) Procelewska, J.; Zahl, A.; Liehr, G.; van Eldik, R.; Smythe, N. A.; Williams, B. S.; Goldberg, K. I. *Inorg. Chem.* **2005**, *44*, 7732–7742. (l) Luedtke, A. T.; Goldberg, K. I. *Inorg. Chem.* **2007**, *46*, 8496–8498.

(21) Yahav-Levi, A.; Goldberg, I.; Vigalok, A.; Vedernikov, A. N. *J. Am. Chem. Soc.* **2008**, *130*, 721–731.

(22) Edelbach, B. L.; Lachiotte, R. J.; Jones, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 2843–2853.

(23) Gallego, C.; Martinez, M.; Safont, V. S. *Organometallics* **2007**, *26*, 527–537.

(24) Excess SMe_2 could slow transmetalation, reductive elimination, or both. Excess SMe_2 is also known to slow stoichiometric C−F activation (see ref 5).

evaporation to provide the crude imine product. Column chromatography (SiO_2, 70-230 mesh, *n*-pentane−Et_3N = 100:6 as eluant) provided imine product **2a** as a yellow oil in 95% yield. NMR spectroscopic data of **2a** correspond with those previously reported.[3]

Preparation of *N*-(6-Fluoro-2-methylbenzylidene)benzylamine (2b). In a 20 mL vial, *N*-(2,6-difluorobenzylidene)benzylamine (**1b**) (0.034 mmol, 8.5 mg) was dissolved in CD_3CN (1.1 mL). $Pt_2Me_4(SMe_2)_2$ (0.0017 mmol, 100 μL of a 0.017 M solution in CD_3CN) and 1,3,5-trimethoxybenzene (0.034 mmol, 100 μL of a 0.34 M solution in CD_3CN) were then added by syringe. The resulting solution was transferred into an NMR tube, which was then fitted with a screw cap containing a septum. Me_2Zn (0.022 mmol, 11 μL of a 2.0 M solution in toluene) was then added by syringe. The resulting solution was heated at 60 °C for 8 h. The reaction progress was monitored by ^1H NMR and ^{19}F NMR spectroscopy. The yield of **2b** was <10%, based on ^1H NMR spectroscopy by comparison of the methyl resonance of **2b** with the aryl resonances of the internal standard 1,3,5-trimethoxybenzene.

Preparation of *N*-(3,6-Difluoro-2-methylbenzylidene)benzylamine (2c). In a 20 mL vial, *N*-(2,3,6-trifluorobenzylidene)benzylamine (**1c**) (0.034 mmol, 8.5 mg) was dissolved in CD_3CN (1.1 mL). $Pt_2Me_4(SMe_2)_2$ (0.0017 mmol, 100 μL of a 0.017 M solution in CD_3CN) and 1,3,5-trimethoxybenzene (0.034 mmol, 100 μL of a 0.34 M solution in CD_3CN) were then added by syringe. The resulting solution was transferred into an NMR tube fitted with a screw cap containing a septum. Me_2Zn (0.022 mmol, 11 μL of a 2.0 M solution in toluene) was then added by syringe. The resulting solution was heated at 60 °C for 11 h. The sample was monitored by ^1H NMR and ^{19}F NMR spectroscopy. The yield of **2c** was 97%, based on ^1H NMR spectroscopy by comparison of the methyl resonance of **2c** with the aryl resonance of the internal standard 1,3,5-trimethoxybenzene. NMR data of **2c** correspond with those previously reported.[3]

Preparation of *N*-(3,4,5,6-Tetrafluoro-2-methylbenzylidene)benzylamine (2d). In a 20 mL vial, *N*-(2,3,4,5,6-pentafluorobenzylidene)benzylamine (**1d**) (0.034 mmol, 9.7 mg) was dissolved in CD_3CN (1.1 mL). $Pt_2Me_4(SMe_2)_2$ (0.0017 mmol, 100 μL of a 0.017 M solution in CD_3CN) and 1,3,5-trimethoxybenzene (0.034 mmol, 100 μL of a 0.34 M solution in CD_3CN) were added by syringe. The resulting solution was transferred into an NMR tube fitted with a screw cap containing a septum. Me_2Zn (0.022 mmol, 11 μL of a 2.0 M solution in toluene) was then added by syringe. The resulting solution was heated at 80 °C for 12 h. The sample was monitored by ^1H NMR and ^{19}F NMR spectroscopy. The yield of **2d** was 74%, based on ^1H NMR spectroscopy by comparison of the methyl resonance of **2d** with the aryl resonance of the internal standard 1,3,5-trimethoxybenzene. NMR data correspond with those previously reported.[3]

Preparation of *N*-(3,4,5-Trifluoro-2,6-dimethylbenzylidene)benzylamine (3d). *N*-(3,4,5,6-Tetrafluoro-2-methylbenzylidene)benzylamine (**2d**) was prepared as above. Additional Me_2Zn (0.022 mmol, 11 μL of a 2.0 M solution in toluene) was then added by syringe into the NMR tube containing **2d**. The resulting solution was heated at 80 °C for an additional 15 h. The yield of **3d** was 72%, based on ^1H NMR spectroscopy by comparison of the methyl resonance of **3d** with the aryl resonance of the internal standard 1,3,5-trimethoxybenzene. ^1H NMR (acetonitrile-d_3, 300 MHz): δ 8.65 (s, 1H), 4.84 (s, 2H), 2.29 (t, J = 2.0 Hz, 6H). (Resonances of aryl protons overlapped with aryl resonances for toluene). ^{19}F NMR (acetonitrile-d_3, 282 MHz): δ −141.2 (d, J = 19.8 Hz, 2F), −160.3 (t, J = 19.8 Hz, 1F). HRMS (EI) *m/z* calcd for $C_{16}H_{14}F_3N$: 277.1078; found: 277.1080.

Formation of 2a monitored by ^1H NMR spectroscopy (Figure 1). In a 20 mL vial, *N*-(2,4,6-trifluorobenzylidene)benzylamine (**1a**) (0.034 mmol, 8.5 mg) was dissolved in CD_3CN (1.1 mL). $Pt_2Me_4(SMe_2)_2$ (0.0017 mmol, 100 μL of a 0.017 M solution in CD_3CN) and 1,3,5-trimethoxybenzene (0.034 mmol, 100 μL of a 0.34 M solution in CD_3CN) were then added by syringe. The resulting solution was transferred into an NMR tube fitted with a screw cap containing a septum. Me_2Zn (0.022 mmol, 11 μL of a 2.0 M solution in toluene) was then added by syringe. The resulting solution was heated in the NMR machine at 60 °C. The reaction was monitored by ^1H NMR spectroscopy every 10 min for 9 h. The concentration of **2a** did not change after 8 h. During the course of the reaction, in addition to the resonances attributed to **1a** and **2a**, a number of smaller resonances were observed, which are attributed to complex **D**.

Formation of Complex D (Figure 2). In a 20 mL vial, *N*-(2,4,6-trifluorobenzylidene)benzylamine (**1a**) (0.34 mmol, 85 mg) and $Pt_2Me_4(SMe_2)_2$ (10.0 mg, 0.017 mmol) were dissolved in 1.1 mL of CD_3CN. The resulting solution was transferred into an NMR tube, which was then fitted with a screw cap containing a septum. Me_2Zn (0.22 mmol, 110 μL of a 2.0 M solution in toluene) was subsequently added by syringe. The resulting solution in a NMR tube was heated at 60 °C and monitored by ^1H NMR and ^{19}F NMR spectroscopy. ^1H NMR (acetonitrile-d_3, 300 MHz): δ 8.87 (s, J_{Pt-H} = 39.0 Hz, 1H), 4.98 (m, 2H), 1.77 (s, J_{Pt-H} = 12.0 Hz, 6H), 0.78 (s, J_{Pt-H} = 69.2 Hz, 3H), 0.41 (s, J_{Pt-H} = 72.6 Hz, 3H), 0.20 (s, J_{Pt-H} = 45.9 Hz, 3H). (Resonances of aryl protons overlapped with aryl resonances for **1a** and toluene). ^{19}F NMR (acetonitrile-d_3, 282 MHz): δ −104.1 (m, this resonance overlapped with resonance for **1a**), −111.4 (m).

Preparation of Pt−F Complex A (Figure 3). In a 20 mL vial, *N*-(2,4,6-trifluorobenzylidene)benzylamine (**1a**) (0.034 mmol, 8.5 mg) and $Pt_2Me_4(SMe_2)_2$ (0.017 mmol, 9.8 mg) were dissolved in CD_3CN (1.1 mL). 1,3,5-Trimethoxybenzene (0.034 mmol, 100 μL of a 0.34 M solution in CD_3CN) was then added by syringe. The resulting solution was transferred into an NMR tube, which was then fitted with a screw cap containing a septum. The NMR tube was placed in the NMR machine at 60 °C. The reaction was monitored by ^1H NMR spectroscopy every 10 min for 8 h. No evidence of formation of **2a** was observed (eq 8). ^1H NMR (acetonitrile-d_3, 400 MHz): δ 8.78 (s, J_{Pt-H} = 47.5 Hz, 1H), 5.05 (m, 2H), 1.90 (s, J_{Pt-H} = 12.1 Hz, 6H), 1.11 (d, J_{Pt-H} = 65.6 Hz, J_{F-H} = 7.1 Hz, 3H), 0.72 (d, J_{Pt-H} = 68.3 Hz, J_{F-H} = 7.1 Hz, 3H). (Resonances of aryl protons overlapped with aryl resonances for **1a**). ^{19}F NMR (acetonitrile-d_3, 282 MHz): δ −103.2 (m, 1F), −111.9 (m, 1F), −262.3 (br s, 1F).

Preparation of 2a by the reaction between Pt−F complex A and Me_2Zn (eq 9, Figure 4). *Step 1: Preparation of Pt−F Complex* **A***:* In a 20 mL vial, *N*-(2,4,6-trifluorobenzylidene)benzylamine (**1a**) (0.034 mmol, 8.5 mg) and $Pt_2Me_4(SMe_2)_2$ (0.017 mmol, 9.8 mg) were dissolved in CD_3CN (1.1 mL). 1,3,5-Trimethoxybenzene (0.034 mmol, 100 μL of a 0.34 M solution in CD_3CN) was subsequently added by syringe. The resulting solution was transferred into an NMR tube, which was then fitted with a screw cap containing a septum. The NMR tube was heated at 60 °C for 8 h to obtain Pt−F complex **A** in situ, as evidenced by ^1H and ^{19}F NMR spectroscopy. *Step 2: Reaction between Pt−F Complex* **A** *and Me_2Zn:* Me_2Zn (0.044 mmol, 22.0 μL of a 2.0 M solution in toluene) was added by syringe to the NMR tube containing **A** in CD_3CN. The reaction was heated at 60 °C in the NMR machine, and the reaction was monitored by ^1H NMR spectroscopy every 2 min for 1 h. The formation of **2a** was completed in 30 min. The yield of **2a** was 69%, based on ^1H NMR spectroscopy by comparison of the methyl resonance of **2a** with the aryl resonance of the internal standard 1,3,5-trimethoxybenzene.

Cross-Coupling Reaction between 1c and Me_2Zn Catalyzed by Pt−F Complex A (eq 11). *Step 1: Preparation of Pt−F Complex* **A***:* In a 20 mL vial, *N*-(2,4,6-trifluorobenzylidene)benzylamine (**1a**) (0.0034 mmol, 100 μL of a 0.034 M solution in CD_3CN) and $Pt_2Me_4(SMe_2)_2$ (0.0017 mmol, 100 μL of a 0.017 M solution in CD_3CN) were dissolved in CD_3CN (1.1 mL). The resulting solution was transferred into an NMR tube, which was

then fitted with a screw cap containing a septum. The NMR tube was heated at 60 °C for 8 h to obtain Pt−F complex **A** in situ, as evidenced by ^{1}H and ^{19}F NMR spectroscopy. *Step 2: Cross-coupling of* **1c** *and Me_2Zn Catalyzed by Pt−F Complex* **A***: N*-(2,3,6-Trifluorobenzylidene)benzylamine (**1c**) (0.034 mmol, 8.5 mg) was weighed into a 20 mL vial. The solution of Pt−F complex **A** prepared above was transferred into the vial from the NMR tube. 1,3,5-Trimethoxybenzene (0.034 mmol, 100 μL of a 0.34 M solution in CD_3CN) was then added by syringe. The resulting solution was transferred back into the NMR tube, which was then fitted with a screw cap containing a septum. Me_2Zn (0.022 mmol, 11.0 μL of a 2.0 M solution in toluene) was subsequently added by syringe. The resulting solution was heated at 60 °C, and the reaction was monitored by ^{1}H NMR and ^{19}F NMR spectroscopy over 11 h. The yield of **2c** was 92%, based on ^{1}H NMR spectroscopy integration of methyl resonance of **2c**, compared to integration of the aryl resonance of the internal standard 1,3,5-trimethoxybenzene. The yield of **2a** was 8%, based on ^{1}H NMR spectroscopy by comparison of the methyl resonance of **2a** with the internal standard 1,3,5-trimethoxybenzene.

Reaction between Pt−F Complex A and 1d (eq 12). *Step 1: Preparation of Pt−F Complex A:* In a 20 mL vial, *N*-(2,4,6-trifluorobenzylidene)benzylamine (**1a**) (0.034 mmol, 8.5 mg) and $Pt_2Me_4(SMe_2)_2$ (0.017 mmol, 9.8 mg) were dissolved in CD_3CN (1.1 mL). 1,3,5-Trimethoxybenzene (0.034 mmol, 100 μL of a 0.34 M solution in CD_3CN) was subsequently added by syringe. The resulting solution was transferred into an NMR tube, which was then fitted with a screw cap containing a septum. The tube was heated at 60 °C for 8 h to obtain Pt−F complex **A** in situ, as evidenced by ^{1}H and ^{19}F NMR spectroscopy. *Step 2: Reaction between Pt−F Complex* **A** *and 1d: N*-(2,3,4,5,6-Pentafluorobenzylidene)benzylamine (**1d**) (0.34 mmol, 97.3 mg) was weighed into a 20 mL vial. The solution of Pt−F complex **A** prepared above was transferred into the vial from the NMR tube. The resulting solution was transferred back into the NMR tube fitted with a screw cap containing a septum. The tube was heated in oil bath at 60 °C for 8 h. Reactions were monitored by ^{1}H NMR and ^{19}F NMR spectroscopy. No evidence was observed for complex **A′**, and the resonance of Pt−F of complex **A** decreased with time.

Reaction between Pt−F Complex A, Me_2Zn, and 1d (eq 13). *Step 1: Preparation of Pt−F Complex* **A***:* In a 20 mL vial, *N*-(2,4,6-trifluorobenzylidene)benzylamine (**1a**) (0.034 mmol, 8.5 mg) and $Pt_2Me_4(SMe_2)_2$ (0.017 mmol, 9.8 mg) were dissolved in CD_3CN (1.1 mL). 1,3,5-Trimethoxybenzene (0.034 mmol, 100 μL of a 0.34 M solution in CD_3CN) was subsequently added by syringe. The resulting solution was transferred into an NMR tube, which was then fitted with a screw cap containing a septum. The NMR tube was heated at 60 °C for 8 h to obtain Pt−F complex **A** in situ, as evidenced by ^{1}H and ^{19}F NMR spectroscopy. *Step 2: Reaction between Pt−F Complex* **A***, Me_2Zn, and* **1d***: N*-(2,3,4,5,6-Pentafluorobenzylidene)benzylamine (**1d**) (0.068 mmol, 19.4 mg) was weighed into a 20 mL vial. The solution of Pt−F complex **A** prepared above was transferred into the vial from the NMR tube. The resulting solution was transferred back into the NMR tube, which was then fitted with a screw cap containing a septum. Me_2Zn (0.017 mmol, 8.5 μL of a 2 M solution in toluene) was subsequently added by syringe. The tube was heated at 60 °C for 30 min. The reaction was monitored by ^{1}H NMR and ^{19}F NMR spectroscopy. Complex **A′** was evidenced by ^{1}H NMR and ^{19}F NMR spectroscopic data, with a yield of 75%, and the yield of **2a** was 79%.

Reaction between 1a, $Pt_2Me_4(SMe_2)_2$, and SEt_2. In a 20 mL vial, *N*-(2,4,6-trifluorobenzylidene)benzylamine (**1a**) (0.18 mmol, 44 mg) and $Pt_2Me_4(SMe_2)_2$ (0.088 mmol, 50 mg) were dissolved in CD_3CN (1.1 mL). The resulting solution was transferred into an NMR tube, which was then fitted with a screw cap containing a septum. Diethyl sulfide (18.5 μL, 0.172 mmol) was subsequently added by syringe. The NMR tube was heated at 60 °C for 9 h and then cooled to room temperature. The complex **A**·SEt_2 was as observed in the ^{1}H and ^{19}F NMR spectra. ^{1}H NMR (acetonitrile-d_3, 400 MHz): δ 8.76 (s, J_{Pt-H} = 46.9 Hz, overlapped with CH═N for complex **A**), 5.05 (m, overlapped with CH_2Ph for complex **A**), 2.44 (m, overlapped with CH_2 for free SEt_2), 1.15 (d, J_{Pt-H} = 66.0 Hz, J_{F-H} = 7.0 Hz, 3H), 0.98 (t, J_{H-H} = 7.4 Hz, 3H), 0.72 (d, J_{Pt-H} = 68.3 Hz, J_{F-H} = 7.1 Hz, 3H). (Resonances of aryl protons overlapped with aryl resonances for **1a** and **A**.) ^{19}F NMR (acetonitrile-d_3, 282 MHz): δ −103.3 (m, overlapped with resonances for complex **A**), −112.0 (m, overlapped with resonances for complex **A**), −262.0 (br s).

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Supporting Information Available: Complete experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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