

# Progress in the Synthesis of a Fluorinated Phenyl Ring System Coordinated to a Palladium (II) Metal Center

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## Abstract

The goal of this project was the synthesis of fluorinated arene ligands complexed to square planar Pd (II) metal centers to serve as precursor compounds for investigations of  $\pi$ -stacking interactions. Various fluorinated arene ligands based on diimine and diacetylpyridine backbones were synthesized and characterized. It was found that steric hindrance and electronic effects produced by the substitution pattern on the arenes influenced the synthetic yields. The fluorinated ligands were coordinated to PdCl<sub>2</sub> centers and the products were characterized. These ligand-PdCl<sub>2</sub> complexes may serve as convenient precursors to the desired dicationic bis-ligand species. However, initial attempts at preparing such compounds failed for unknown reasons.

## INTRODUCTION

The ultimate goal of this project is to observe  $\pi$ -stacking interactions between fluorinated phenyl rings bound to a metal center (Figure 1).

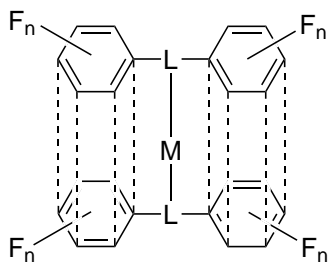


Figure 1

The preparation of tailored ligands that might give rise to both inter- and intramolecular interactions between fluorinated arenes ligated to a square planar complexes of Pd (II) is described here.

The ligands are based on a diimine or a diacetylpyridine scaffold that enforces a fixed geometry around the metal center when coordinated. Numerous examples of such ligands are known (Kliegman & Barnes, 1970; tom Dieck et al., 1981; Small & Brookhart, 1999). The ligands may be synthesized by simple condensation reactions between the alkyl and aryl constituents. However, because the ultimate purpose of this research is to study the interactions between fluorinated aryl groups, new synthetic methods for fluorinated ligands were needed. Surprisingly little information on the preparation of fluorinated diimine or diacetylpyridine ligands is available in the literature (Johansson et al., 1999). Thus, a major part of this research involves the explorato-

ry synthesis of such ligands. The ligands were complexed to metal centers by ligand substitution reactions, and attempts were made to create dicationic bis-ligand species for the  $\pi$ -interaction studies. The work to date on the synthesis of the ligands, the complexation of these ligands to useful metal starting materials, and the attempts to generate the target molecules are presented.

## RESULTS AND DISCUSSION

Suitable ligands and potential metal starting materials were required to generate the final dicationic bis-ligand Pd (II) complexes. The necessary ligands were synthesized by simple condensation reactions. Once the ligands were available, coordination to PdCl<sub>2</sub> was accomplished by ligand substitution reactions. Initial attempts to produce dicationic bis-ligand species have failed thus far.

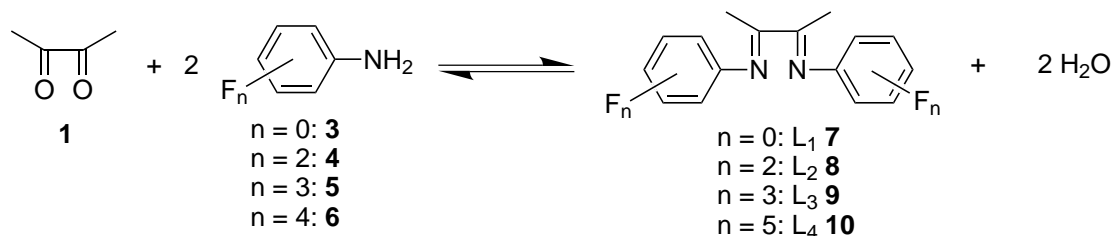
### *Synthesis of Ligands.*

Ligand synthesis involves the reaction of one equivalent of dione and two equivalents of a fluorinated aniline (or aniline in the case of L<sub>1</sub> (**7**)) in a double condensation reaction, thereby producing one equivalent of disubstituted product and two equivalents of water. The general scheme for the condensation reactions is shown in Figure 2 (next page).

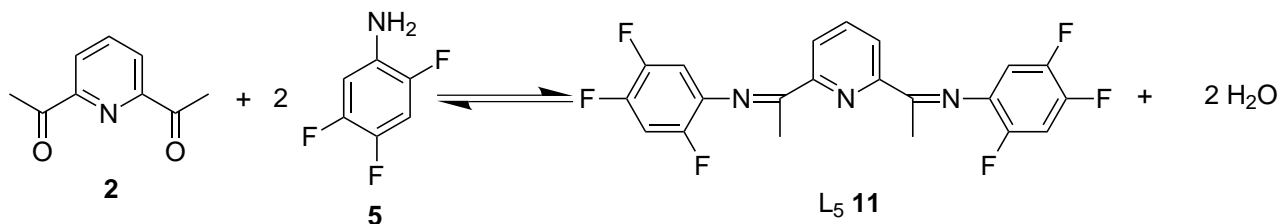
The diones used were 2,3-butanedione (**1**) and 2,6-diacetylpyridine (**2**). Four different anilines were used: aniline (**3**), 2,3-difluoroaniline (**4**), 2,4,5-trifluoroaniline (**5**) and 2,3,4,5,6-pentafluoroaniline (**6**).

To try to resolve the problem of concomitant water formation in the condensation reactions, drying agents such as molecular sieves and anhy-

### Scheme 1



### Scheme 2



**Figure 2**

drous sodium sulfate were added to the reaction mixtures. By using such materials, it was hoped that any water produced would be trapped, forcing the equilibrium towards products. An additional attempt to remove water was made using a Dean-Stark trap. However, the boiling point of the solvent azeotrope was so close to that of the 2,3-butanedione (**1**) that separation could not occur. Nevertheless, good yields of the ligands were observed, at least when minimally fluorinated anilines were used.

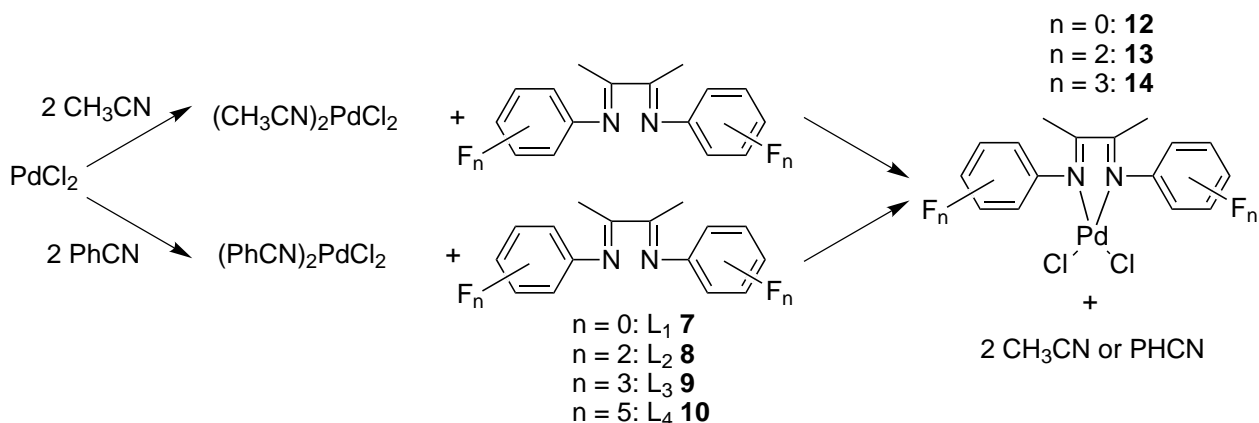
While it may be possible to conduct these reactions in air, they were best done using techniques designed to exclude oxygen and moisture. Two different sets of conditions were employed. One approach used methylene chloride under dry nitrogen as the reaction solvent and sodium sulfate as the water trap. The other procedure employed methanol under dry nitrogen and molecular sieves. In most cases both methods were used and compared for finding the optimum reaction conditions.

By varying the substitution pattern of the fluorines on the anilines, it might be expected that the reactivity of each fluoroaniline would be very different. It was observed that 2,4,5-trifluoroaniline (**5**) underwent the smoothest reaction with both diones. The products were both air- and moisture-stable. No significant decrease in the yield was observed when the reactions were performed open to the air. 2,3-difluoroaniline (**4**) proved to be more difficult to work with, potentially due to the strong dipole moment induced by the fluorines on one side of the ring. This difluoroaniline reacted with **1** to form  $\text{L}_2$  (**8**), but yielded only monosubstituted product when **2** was used as the dione starting material.

Due to the strong electronegativity of fluorine, the fluoroanilines are quite deactivated as nucleophiles. Electron density is displaced towards the outside of the ring. As such, 2,3,4,5,6-pentafluoroaniline (**6**) should be rendered quite unreactive. Even under very careful handling, only a 3 % yield of  $\text{L}_4$  (**10**) was recovered when allowed to react with **1**. Furthermore, reaction with **2** failed: only starting materials were recovered from the reaction mixture.

Another potential complication that might help to explain some of the difficulties in forming these ligands is the steric hindrance of the anilines. In these compounds, the fluorines on the phenyl rings sterically hinder the formation of the eventual C=N bond in the product. This is supported by the fact that both of the *ortho* positions of the phenyl ring in **6** are occupied by fluorines, which further decreases the reactivity of the ring. However, in both **4** and **5**, only one of the *ortho* positions is blocked by a fluorine atom, rendering the compounds less sterically hindered, and more reactive, than **6**.

All of the products were characterized by  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectroscopy and infrared spectroscopy. In each case, the NMR spectra of the ligands were compared to those of the starting materials, and significant downfield shifting was observed. Also, bands characteristic of C=N bonds were detected in the IR spectra of each ligand. Additional confirmation of the products was provided by X-ray crystallography.



**Figure 3**

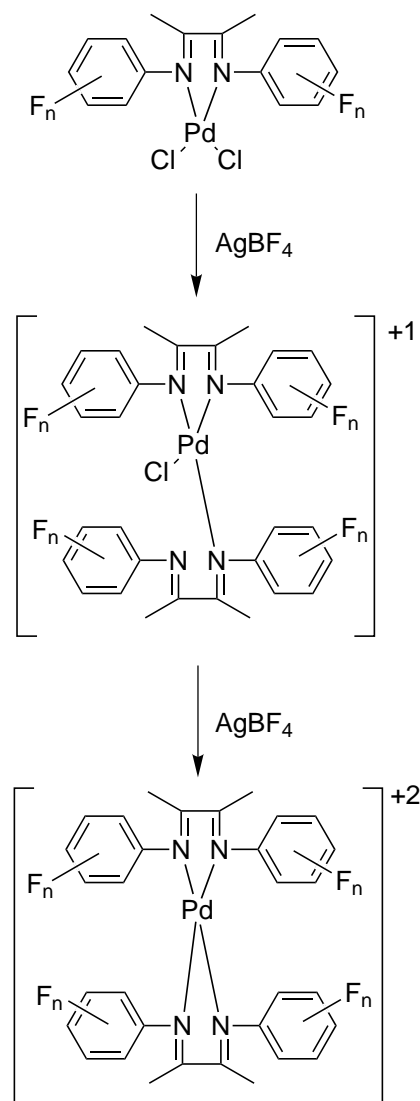
### Synthesis of Ligand-PdCl<sub>2</sub> Complexes.

The synthesis of these complexes involved ligand substitution reactions and required suitable PdCl<sub>2</sub> starting materials, obtained through two routes (see Figure 3). In the first case, (CH<sub>3</sub>CN)<sub>2</sub>PdCl<sub>2</sub> could be generated *in situ* by refluxing PdCl<sub>2</sub> in excess acetonitrile; introducing the ligand led to the precipitation of the desired compound. Similarly, (PhCN)<sub>2</sub>PdCl<sub>2</sub> could be reacted with the ligand to give the same product (Anderson & Lin, 1990).

Both methods were performed without the exclusion of air or moisture and gave good to excellent yields of the products **12**, **13**, and **14**. NMR spectroscopy indicated successful complexation by changes in the chemical shifts of the coordinated ligands relative to those of the free ligands. Shifting of the C=N stretches to lower wavenumbers as compared to those of the free ligands was observed in the IR spectra. This is a typical occurrence upon coordination of free ligands to metal centers.

### Synthesis of the Dicationic Complexes.

After preparing the ligand-PdCl<sub>2</sub> complexes, an attempt to synthesize both monocationic and dicationic complexes was made. The reaction scheme for the formation of the two desired cationic molecules is shown in Figure 4. AgBF<sub>4</sub> was used to remove the chlorines in the ligand-PdCl<sub>2</sub> complex in order to open coordination sites for the eventual binding of another ligand molecule. By using a non-coordinating anion such as BF<sub>4</sub><sup>-</sup>, there should be little competition between the anion and another equivalent of ligand. Initially, the synthesis of the dicationic complex



**Figure 4**

was attempted using two equivalents of  $\text{AgBF}_4$ . Unfortunately, the solids that were formed in both reactions were not the desired products as the  $^{19}\text{F}$  NMR spectra showed only one peak corresponding to  $\text{BF}_4^-$ . In an attempt to assemble the complex in a stepwise fashion, one equivalent of  $\text{AgBF}_4$  was used to form a monocationic species, which could serve as a precursor to the desired dicationic compound. However, the same result was observed: only one peak ( $\text{BF}_4^-$ ) was seen in the  $^{19}\text{F}$  NMR spectrum. The reason for these failures is not immediately obvious, but they may involve facile decomposition of the cationic complexes.

## CONCLUSION

This project was quite successful in terms of the formation of numerous precursors for the synthesis of the cationic molecules. Given more time, optimal methods for producing the ligands, especially those of **6**, and the ligand- $\text{PdCl}_2$  complexes may be found. Hopefully, in the future, improved procedures for synthesizing the dicationic palladium complexes will be discovered so that the interactions between fluorinated arene groups will be able to be observed directly in the systems.

## EXPERIMENTAL

**General Methods.** Unless otherwise noted, all reactions were performed under dry nitrogen using either Schlenk or dry box technique.  $^1\text{H}$  or  $^{19}\text{F}$  NMR spectroscopy was conducted on a Varian XL-300 spectrometer using  $\text{C}_6\text{D}_6$ , acetone- $d_6$  or acetonitrile- $d_3$ . Infrared data were obtained on a Perkin-Elmer 1600 series FTIR instrument using either  $\text{CH}_2\text{Cl}_2$  solution or KBr pellets. X-ray crystallography was conducted at the University of Delaware.

**Synthesis of 2,3-N,N'-diphenylbisiminobutane, **L**<sub>1</sub> (**7**):** 2,3-Butanedione (**1**) (10 g, 0.12 mol) was added to a Schlenk flask (150 mL) and dissolved in methanol (15 mL). The solution was cooled to 0 °C with an ice bath for 10 minutes with stirring. Aniline (**3**) (22 g, 0.24 mol) was added to the solution dropwise and the reaction was allowed to stir for 2 h. The ice bath was removed and molecular sieves were added. This mixture was then allowed to stir for 24 h. The molecular sieves were filtered off, and the solvent was evaporated. Hexanes (15 mL) were added, and the resulting layers were separated. The brown bottom layer was extracted again with hexanes (10 mL) and the combined hexanes solution was dried over  $\text{Na}_2\text{SO}_4$ . The  $\text{Na}_2\text{SO}_4$  was removed by filtration and the filtrate was evaporated to dryness to give a yellow solid. This material was recrystallized using chilled methanol. The shiny yellow solid (4.6 g, 0.02 mol) was isolated in 17 % yield and was identified by comparison of its spectroscopic data previously recorded (tom Dieck & Renk, 1971).

**Synthesis of 2,3-N,N'-bis(2,3-difluorophenyl)bisiminobutane, **L**<sub>2</sub> (**8**):** *Method A.* 2,3-Difluoroaniline (**4**) (1.0 g, 7.75 mmol) and 2,3-butanedione (**1**) (0.33 g, 3.83 mmol) were dissolved in  $\text{CH}_2\text{Cl}_2$  (10 mL) in a round-bottom flask (250 mL) containing a magnetic stirring bar. Ten drops of 97 % formic acid were added to the mixture along with an excess amount of  $\text{Na}_2\text{SO}_4$ . The reaction mixture was allowed to stir for 48 h. The solvent was removed by vacuum evaporation and the resultant solid was redissolved in  $\text{CH}_2\text{Cl}_2$  (15 mL). After filtration to remove the  $\text{Na}_2\text{SO}_4$ , the solvent was removed by rotary evaporation. The product was rinsed twice with hexanes (15 mL) and dried under vacuum to give a brownish white powder (0.49 g, 1.59 mmol) in 41 % yield.  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ ): 6.50 (apparent t, 4H,  $\text{C}_6\text{H}_3\text{F}_2$ ); 6.24 (m, 2H,  $\text{C}_6\text{H}_3\text{F}_2$ ); 1.97 (s, 6H,  $\text{CH}_3$ ).  $^{19}\text{F}$  NMR: -137.7 (d,  $^3J_{\text{FF}} = 24.3$  Hz, 2F, *o*- $\text{C}_6\text{H}_3\text{F}_2$ ); -151.5 (d,  $^3J_{\text{FF}} = 24.3$  Hz, 2F, *m*- $\text{C}_6\text{H}_3\text{F}_2$ ). IR ( $\text{CH}_2\text{Cl}_2$  solution,  $\text{cm}^{-1}$ ):  $\nu_{\text{C}=\text{N}} = 1628$ . *Method B.* Using a procedure similar to Method A, 2,3-difluoroaniline (**4**) (1.0 g, 7.75 mmol) and 2,3-butanedione (**1**) (0.33 g, 3.83 mmol) were dissolved in methanol (10 mL) in a round-bottom flask (250 mL). Molecular sieves were added and the mixture was allowed to stir for 48 h. Following the procedure described above, the desired compound (0.02g, 0.65 mmol) could be isolated in 2 % yield.

**Synthesis of 2,3-N,N'-bis(2,4,5-trifluorophenyl)bisiminobutane, **L**<sub>3</sub> (**9**):** The procedures described above for **L**<sub>2</sub> (**8**) were used with the following amounts of materials in the synthesis of **L**<sub>3</sub>. *Method A and B:* 2,4,5-trifluoroaniline (**5**) (1.0 g, 6.80 mmol), 2,3-butanedione (**1**) (0.29 g, 3.37 mmol). Method A gave golden yellow **L**<sub>3</sub> (**9**) (0.50 g, 1.45 mmol) in 43 % yield.  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ ): 6.38 (m, 2H,  $\text{C}_6\text{H}_2\text{F}_3$ ); 6.17 (m, 2H,  $\text{C}_6\text{H}_2\text{F}_3$ ); 1.88 (s, 6H,  $\text{CH}_3$ ).  $^{19}\text{F}$  NMR: -128.0 (m, 2F, *o*- $\text{C}_6\text{H}_2\text{F}_3$ ); -139.8 (m, 2F, *p*- $\text{C}_6\text{H}_2\text{F}_3$ ); -142.1 (m, 2F, *m*- $\text{C}_6\text{H}_2\text{F}_3$ ). IR ( $\text{CH}_2\text{Cl}_2$  solution,  $\text{cm}^{-1}$ ):  $\nu_{\text{C}=\text{N}} = 1649$ . Method B produced shiny yellow **L**<sub>3</sub> (0.60 g, 1.74 mmol) in 51 % overall yield.

**Synthesis of 2,3-N,N'-bis(2,3,4,5,6-pentafluorophenyl)bisiminobutane, **L**<sub>4</sub> (**10**):** 2,3-butanedione (**1**) (0.38 g, 4.41 mmol) was dissolved in methanol (1 mL) in a Schlenk flask (125 mL), containing a magnetic stirring bar. 2,3,4,5,6-pentafluoroaniline (**6**) (2.0 g, 0.01 mol) was then added to the solution along with 5 drops of 97 % formic acid. The reaction mixture was allowed to stir for 5 days. The solvent in the cloudy solution was evaporated and additional methanol (15 mL) was added. The solution was filtered leaving a yellow **L**<sub>4</sub> (0.07g, 0.17 mmol) in a 3% yield.  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ ): 1.84 (s, 6H,  $\text{CH}_3$ ).  $^{19}\text{F}$  NMR: -152.0 (d,  $^3J_{\text{FF}} = 24.3$  Hz, 2F, *o*- $\text{C}_6\text{F}_5$ ); -161.2 (t,  $^3J_{\text{FF}} = 24.3$  Hz, 2F, *p*- $\text{C}_6\text{F}_5$ ); -163.1 (d,  $^3J_{\text{FF}} = 24.3$  Hz, 2F, *m*- $\text{C}_6\text{F}_5$ ). IR ( $\text{CH}_2\text{Cl}_2$  solution,  $\text{cm}^{-1}$ ):  $\nu_{\text{C}=\text{N}} = 1604$ .

**Synthesis of 2,6-bis[1-(2,4,5-trifluorophenylimino)ethyl]pyridine, **L**<sub>5</sub> (**11**):** 2,6-diacetylpyridine (**2**) (0.50 g, 3.06 mmol) and 2,4,5-trifluoroaniline (**4**) (0.90 g, 6.12 mmol) were dissolved in methanol (20 mL) in a round bottom flask (250 mL).  $\text{Na}_2\text{SO}_4$  was added to the solution along with ten drops of 97 % formic acid. The solution was allowed to stir for 2 days. The solvent in the milky white solution was removed by vacuum, and  $\text{CH}_2\text{Cl}_2$  was added. The material was rinsed with a hexane/toluene (25:1) solution and was thoroughly dried under vacuum to give **L**<sub>5</sub> (0.20 g, 0.47 mmol) in 16 % overall yield.  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ ): 8.27 (d,  $^3J_{\text{HH}} = 7.8$  Hz, 2H,  $\text{C}_6\text{H}_2\text{F}_3$ ); 7.13 (d,  $^3J_{\text{HH}} = 8.1$  Hz, 2H,  $\text{C}_6\text{H}_2\text{F}_3$ ); 6.43 (m, 4H,  $\text{C}_6\text{H}_2\text{F}_3$ ); 2.17 (s, 6H,  $\text{CH}_3$ ).  $^{19}\text{F}$  NMR: -128.2 (br. s, 2F, *o*- $\text{C}_6\text{H}_2\text{F}_3$ ); -140.6 (m, 2F, *p*- $\text{C}_6\text{H}_2\text{F}_3$ ); -142.2 (m, 2F, *m*- $\text{C}_6\text{H}_2\text{F}_3$ ). IR ( $\text{CH}_2\text{Cl}_2$  solution,  $\text{cm}^{-1}$ ):  $\nu_{\text{C}=\text{N}} = 1644$ .

**Synthesis of L<sub>1</sub>-PdCl<sub>2</sub> (12):** Excess acetonitrile (150 mL) and PdCl<sub>2</sub> (0.25 g, 1.41 mmol) were added to a round-bottom flask (250 mL) and were heated to reflux until complete dissolution of the starting material occurred. The heat was removed, and the mixture was allowed to cool. To this was added L<sub>1</sub> (7) (0.33 g, 1.40 mmol) and the reaction mixture was allowed to stir for 24 h. During this time, an orange solid precipitated. Hexanes (15 mL) were added, and the mixture was filtered. The collected solid was washed with hexanes (15 mL) and dried under vacuum to give bright yellow-orange L<sub>1</sub>-PdCl<sub>2</sub> (12) (0.40 g, 0.97 mmol) in 69 % overall yield. <sup>1</sup>H NMR (acetonitrile-d<sub>3</sub>, δ): 7.46 (m, 2H, C<sub>6</sub>H<sub>5</sub>); 7.38 (m, 2H, C<sub>6</sub>H<sub>5</sub>); 7.10 (m, 2H, C<sub>6</sub>H<sub>5</sub>); 2.07 (s, 6H, CH<sub>3</sub>). IR (KBr, cm<sup>-1</sup>): ν<sub>C=N</sub> = 1586.

**Synthesis of L<sub>2</sub>-PdCl<sub>2</sub> (13):** *Method A:* (PhCN)<sub>2</sub>PdCl<sub>2</sub> (0.25 g, 0.65 mmol) (Anderson & Lin, 1990) was added to a Schlenk flask (25 mL), containing a magnetic stirring bar, along with CH<sub>2</sub>Cl<sub>2</sub> (40 mL). In a separate flask, L<sub>2</sub> (8) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and was added dropwise to the flask. The reaction mixture was allowed to stir for 24 h. The solvent was evaporated under vacuum, and the resulting solid was washed with hexanes (15 mL). After drying under vacuum, orange-brown L<sub>2</sub>-PdCl<sub>2</sub> (13) (0.24 g, 0.49 mmol) was recovered in 75 % yield. <sup>1</sup>H NMR (acetone-d<sub>6</sub>, δ): 7.30 (m, 4H, C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>); 6.97 (m, 2H, C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>); 2.21 (s, 6H, CH<sub>3</sub>). <sup>19</sup>F NMR: -139.7 (m, 2F, *o*-C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>); -145.5 (m, 2F, *m*-C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>). IR (KBr, cm<sup>-1</sup>): ν<sub>C=N</sub> = 1620. *Method B:* Following the procedures described for L<sub>1</sub>-PdCl<sub>2</sub> (12) the following amounts were used: PdCl<sub>2</sub> (0.14 g, 0.79 mmol), L<sub>2</sub> (8) (0.25 g, 0.81 mmol). Orange L<sub>2</sub>-PdCl<sub>2</sub> (13) (0.38 g, 0.78 mmol) was recovered in 97 % overall yield.

**Synthesis of L<sub>3</sub>-PdCl<sub>2</sub> (14):** Preps above for L<sub>2</sub>-PdCl<sub>2</sub> (13) were used in this synthesis. *Method A:* L<sub>3</sub> (9) (0.22 g, 0.64 mmol) and (PhCN)<sub>2</sub>PdCl<sub>2</sub> (0.25 g, 0.65 mmol) (Anderson & Lin, 1990). Orange-brown L<sub>3</sub>-PdCl<sub>2</sub> (14) was obtained in 71 % overall yield. <sup>1</sup>H NMR (acetonitrile-d<sub>3</sub>, δ): 7.34 (m, 2H, C<sub>6</sub>H<sub>2</sub>F<sub>3</sub>); 7.21 (m, 2H, C<sub>6</sub>H<sub>2</sub>F<sub>3</sub>); 2.21 (s, 6H, CH<sub>3</sub>). <sup>19</sup>F NMR: -122.7 (br. s, 1F, *o*-C<sub>6</sub>H<sub>2</sub>F<sub>3</sub>); -122.2 (br. s, 1F, *o*-C<sub>6</sub>H<sub>2</sub>F<sub>3</sub>); -135.2 (m, 2F, *p*-C<sub>6</sub>H<sub>2</sub>F<sub>3</sub>); -143.2 (m, 2F, *m*-C<sub>6</sub>H<sub>2</sub>F<sub>3</sub>). IR (KBr, cm<sup>-1</sup>): ν<sub>C=N</sub> = 1628. *Method B:* PdCl<sub>2</sub> (0.13 g, 0.73 mmol) and L<sub>3</sub> (9) (0.25 g, 0.73 mmol) were used and orange L<sub>3</sub>-PdCl<sub>2</sub> (14) was given in an 82 % overall yield.

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Ivana Chow '00 is a Chemistry major and an Economics minor. She is currently applying to jobs that are related to the dental field and plans to attend dental school in 2001.