CHAPTER 5

Synthesis, Characterization and Catalytic Activity of Mononuclear Pd(II) Complex of Schiff-Base Ligand
5.1 ABSTRACT

A square planar neutral Pd (II) complex [PdLCl] of the Schiff-base ligand 2-formyl-4-methyl-6-N-ethylpiperidineiminomethylphenol (LH) has been synthesized and structurally characterized. The complex has been employed as catalyst precursor for the synthesis of ynones by coupling acyl chlorides with terminal alkynes under copper- and solvent-free conditions at room temperature.

5.2 INTRODUCTION

Ynones are compounds of substantial synthetic interest owing to their widespread occurrence among natural products and their usefulness as versatile building blocks for the synthesis of pharmaceutically significant and biologically active N-heterocyclic compounds.[1-13] Among many synthetic methods, palladium catalyzed acylation of terminal alkynes with acid chlorides has been widely used due to low catalyst loading, high yields and the versatile nature of the protocol.[14-20] However, many of the reported methods require high temperature, anhydrous solvent, inert atmosphere, and copper as co-catalyst.[14,15] The procedure typically involves the reaction of alkynyl organometallic reagents of silver,[21] copper,[22-24] sodium,[25] lithium,[26] cadmium,[27] zinc,[28] silicon,[29] or tin [30] with acid chlorides. The direct coupling of alkynyl palladium reagents with acid chlorides is an important method for the preparation of alkynyl ketones, [31-35] However, to the best of our knowledge Schiff-base complexes of palladium (II) have not yet been explored as catalyst for coupling of acyl chlorides with terminal alkynes. With the aim to explore the effectiveness of Pd(II) Schiff-base complexes as catalyst of the above mentioned reaction, we have prepared a Schiff-base complex of Pd (II) where the Schiff base is 2-formyl-4-methyl-6-N-ethylpiperidineiminomethylphenol (LH, Scheme 5.1).
The complex has been characterized by single crystal X-ray structural analysis and the well characterized complex has been exploited as catalyst in the coupling reaction of acyl chlorides with terminal alkynes to produce yrones under mild, copper- and solvent-free conditions (Scheme 5.2).

**Scheme 5.2** Syntheses of yrones by coupling of acid chloride with terminal alkynes.

### 5.3 EXPERIMENTAL SECTION

**Starting Materials**

All chemicals were obtained from commercial sources and liquid reagents were distilled before use. Solvents were dried according to standard procedure and were distilled prior to use. 4-methyl-2,6-diformylphenol was prepared on following the literature method.[36] N-(2-aminoethyl) piperidine was purchased from Alfa Aesar Chemical Company. All other chemicals were of AR grade. K₂[PdCl₄] was prepared according to literature method.[28]
Physical Measurements

Elemental analyses (carbon, hydrogen, and nitrogen) were performed using a Perkin–Elmer 240C elemental analyzer; infrared spectra were recorded on KBr disks (400–4000 cm⁻¹) with a Perkin–Elmer RXI FT-IR spectrophotometer. ¹H NMR spectra (300 MHz) and ¹³C NMR spectra (75 MHz) were recorded in the CDCl₃ solvent on a Bruker AV300 Supercon NMR spectrometer using the solvent signal as the internal standard in a 5 mm BBO probe.

Synthesis of the [PdLCl] (1) complex

A methanolic solution (5 mL) of N-(2-aminoethyl) piperidine (0.256 g, 2 mmol) was added dropwise to a heated methanolic solution (10 mL) of 2,6-diformyl-4-methyl-phenol (0.164 g, 1 mmol), and the resulting mixture was refluxed for half an hour. An aqueous solution of K₂PdCl₄ (0.164 g, 1.5 mmol) was added and the mixture was further refluxed for two hours. The resulting yellow solution was then kept in a CaCl₂ desiccator in dark. Square-shaped yellow crystals were obtained after a few days. (Yield 72%). Anal. Calcd for C₁₆H₂₁ClN₂O₂Pd; C,(46.28%); H,(5.1%); N,(6.74%); Cl,(8.54%); Found, C,(46.27%); H,(5.3%); N,(6.75%); Cl,(8.53%); I.R: ν(C=O) 1665 cm⁻¹; ν(C=N) 1630 ν(skeletal vibration) 1534 cm⁻¹; ν(H₂O) 3449 cm⁻¹. UV (DMF)/nm: 427 (ε=5560 M⁻¹    cm⁻¹).

Figure 5.1 FTIR spectrum of [Pd(II)LCl] complex
Synthesis of 1-(4-methoxyphenyl)-3-p-tolylpropynone

A mixture of 4-methoxyphenyl acyl chloride (341 mg, 2 mmol), 4-ethynyl toluene (253 μL, 232 mg, 2 mmol), and Et₃N (278 μL, 202 mg, 2 mmol) was taken in a round-bottom flask under anhydrous condition in presence of the Pd-Schiff-base catalyst (16 mg, 2 mol%) and the mixture was stirred at room temperature for 20 minutes. After completion of the reaction (confirmed by TLC analysis) the mixture was diluted with water (10 ml) and extracted with ethyl acetate (20 mL). The organic phase was dried over Na₂SO₄. The crude product obtained on evaporation of solvent was subjected to column chromatography to get the analytically pure compound (400 mg, 80%). I.R: ν(C=O) 1593 cm⁻¹; ν(C≡C) 2188 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 8.16 (d, J = 7.8Hz, 2H), 7.50 (d, J = 7.8Hz, 2H), 7.15 (d, J = 7.5Hz, 2H), 6.95 (d, J = 7.8Hz, 2H), 2.32 (s, 3H), 3.83 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 176.4, 164.2, 141.0, 132.7 (2C), 131.6 (2C), 130.0, 129.2 (2C), 116.9, 113.6 (2C), 92.7, 86.5, 55.2, 21.4; Anal.Calcd. for C₁₇H₁₄O₂: C, 81.58; H, 5.64; Found: C, 81.46; H, 5.52.

X-ray Data Collection and Structural Description

Diffraction data for compound 1 was collected at room temperature on a Nonius DIP-1030H system equipped with Mo-Kα radiation (λ = 0.71073 Å). Cell refinement, indexing and scaling of the data set were carried out using Denzo [38] and Scalepack.[38] The structure was solved by direct methods and subsequent Fourier analyses [39] and refined by the full-matrix least-squares method based on F² with all observed reflections. All the calculations were performed using the WinGX System, Ver 1.80.05.[40] Crystallographic data and details of refinements are as follows. 

Crystal data: C₁₆H₂₀ClN₂O₂Pd, M = 414.19, orthorhombic, space group Pbca, a = 16.935(3), b = 9.627(2), c = 20.667(4) Å, V = 3369.4(11) Å³, Z = 8, Dc = 1.637 g/cm³, μ( Mo-Kα) = 1.268 mm⁻¹, F(000) = 1680, θ max = 27.10°. Final R1 = 0.0367, wR2 = 0.0904, S = 0.872 for 200 parameters and 48500 collected reflections, 3560 unique [R(int) = 0.0792], of which 1912 with I > 2σ(I), max positive and negative peaks in ΔF map 0.423, -0.463 e. Å⁻³.

[a] R1 = Σ ||Fo|| - |Fc| / Σ |Fo|, wR2 = [Σw (Fo² - Fc²)² / Σw (Fo²)²]½.
5.4 RESULT AND DISCUSSION

Synthesis procedure and characterization

The Schiff-base complex of Pd(II) was prepared by adopting template synthesis technique by treating the water solution of K$_2$PdCl$_2$ with the tridentate Schiff-base ligand formed \textit{in situ} between 2,6-diformyl-4-methylphenol and 2-aminoethylpiperidine. Infrared spectrum of the complex shows bands at 1630 cm$^{-1}$ due to C=N stretching, skeletal vibration at 1534 cm$^{-1}$ and C=O stretching at 1665 cm$^{-1}$.

Description of Crystal Structure

The X-ray structure determination of the complex reveals that the neutral mononuclear complex displays slightly distorted square planar arrangement around the Pd center. An ORTEP view of the complex is depicted in Figure 5.2 and selected bond distances and angles are presented in Table 5.1.

![ORTEP view](https://example.com/figure52.png)

**Figure 5.2** ORTEP view (30% thermal ellipsoids probability) of the complex with atom labeling scheme.
Table 5.1 Selected bond lengths (Å) and angles (°).

<table>
<thead>
<tr>
<th>Bond</th>
<th>Distance (Å)</th>
<th>Bond</th>
<th>Distance (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd-N(1)</td>
<td>1.956(3)</td>
<td>N(1)-C(8)</td>
<td>1.288(5)</td>
</tr>
<tr>
<td>Pd-N(2)</td>
<td>2.081(3)</td>
<td>N(1)-C(9)</td>
<td>1.467(6)</td>
</tr>
<tr>
<td>Pd-O(1)</td>
<td>1.990(3)</td>
<td>O(1)-C(1)</td>
<td>1.306(5)</td>
</tr>
<tr>
<td>Pd-C(l1)</td>
<td>2.3315(12)</td>
<td>O(2)-C(7)</td>
<td>1.204(5)</td>
</tr>
<tr>
<td>N(1)-Pd-N(2)</td>
<td>84.57(15)</td>
<td>O(1)-Pd-N(2)</td>
<td>176.66(13)</td>
</tr>
<tr>
<td>N(1)-Pd-O(1)</td>
<td>92.37(14)</td>
<td>N(2)-Pd-Cl(1)</td>
<td>95.67(10)</td>
</tr>
<tr>
<td>N(1)-Pd-Cl(1)</td>
<td>174.53(10)</td>
<td>O(1)-Pd-Cl(1)</td>
<td>87.51(9)</td>
</tr>
</tbody>
</table>

The tridentate chelating ligand is clearly coordinated to Pd ion through two nitrogen, a phenolate oxygen, and a chloride ion, forming a five- and a six-membered ring. The Pd-N(1) bond distance, of 1.956(3) Å, is slightly shorter than the Pd-N(2), 2.081(3) Å, for the different nature of the involved donors (imino vs amine N). The Pd-O and Pd-Cl bond lengths are of 1.990(3) and 2.331(12) Å, respectively, which are in agreement with typical values for Pd(II) complexes comprising of similar ligands. In particular the present geometry is close to that found in a neutral [PdL’Cl] complex, where L’= tridentate ligand having a dimethylamine nitrogen, a tertiary amine nitrogen, and a phenolate oxygen as donor atoms,[41] with the following values Pd-N(1) = 2.059(2), Pd-N(2) = 2.042(2), Pd-O1 = 2.013(2), and Pd-Cl(1) = 2.2996(6) Å.

It is worth to note that among the coordination angles the larger value of N(2)-Pd-Cl(1) compared to the O(1)-Pd-Cl(1), (95.67(10) vs. 87.51(9)°) likely dictated by steric reasons. The phenolato mean plane forms a dihedral angle 15.7(1)° with the N₂OCl coordination plane, likely accomplished for packing requirements. No classical H bonds are present in crystal packing, but C-H…O (2.737(6), 3.163(6) Å) and C-H…Cl (3.784(5), 3.451(5) Å) contacts are noticed. Figure 5.3 presents the crystal packing viewed down axis a which looks the wave like arrangement.
Optimization study

Initially we have carried out the coupling reaction between phenylacetylene with benzoyl chloride in neat conditions using 1 mol% of Pd-catalyst in presence of triethyl amine (1 equiv) at room temperature. The reaction proceeds rapidly and almost completed within 20 minutes. The desired coupling product was isolated with 75% yield. Encouraged by this result, we have optimized the reaction conditions varying the amount of catalyst, base, and solvent (Table 5.2). High yield (85%) is obtained using 2 mol% of the catalyst under solvent-free condition. However, no significant enhancement in yield is noticed on using higher amount (5 mol%) of the catalyst. Interestingly, when the reaction was carried out by changing the reaction condition such as, with increasing the polarity of the organic solvents (THF, CH$_3$CN and DMF) and using the bulky base (di isopropyl ethylamine, DIPEA), low conversions are observed. The yield of the coupling product decreases (55%) dramatically. Finally we have achieved the optimized state by using 2 mol% of Pd catalyst, 1 equivalent of Et$_3$N, room temperature and the absence of any solvent. With these optimized conditions, we optimized the reaction time in comparison to the Karami’s study.[42] We also obtained better yield.
### Table 5.2 Optimization of the reaction conditions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pd-catalyst (mol%)</th>
<th>Base (1 equiv)</th>
<th>Solvent</th>
<th>Yield b (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(1 mol%)</td>
<td>___</td>
<td>___</td>
<td>&lt;10</td>
</tr>
<tr>
<td>2</td>
<td>(1 mol%)</td>
<td>Et₃N</td>
<td>___</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>(2 mol%)</td>
<td>Et₃N</td>
<td>___</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>(3 mol%)</td>
<td>Et₃N</td>
<td>___</td>
<td>86</td>
</tr>
<tr>
<td>5</td>
<td>(4 mol%)</td>
<td>Et₃N</td>
<td>___</td>
<td>86</td>
</tr>
<tr>
<td>6</td>
<td>(2 mol%)</td>
<td>DIPEA</td>
<td>___</td>
<td>78</td>
</tr>
<tr>
<td>7</td>
<td>PdCl₂-catalyst (5 mol%)</td>
<td>Et₃N</td>
<td>___</td>
<td>55</td>
</tr>
<tr>
<td>8</td>
<td>(2 mol%)</td>
<td>Et₃N</td>
<td>THF</td>
<td>42</td>
</tr>
<tr>
<td>9</td>
<td>(2 mol%)</td>
<td>Et₃N</td>
<td>DMF</td>
<td>45</td>
</tr>
<tr>
<td>10</td>
<td>(2 mol%)</td>
<td>Et₃N</td>
<td>CH₃CN</td>
<td>47</td>
</tr>
</tbody>
</table>

All the reactions were carried out for 20 min. bIsolated yield.

### Substrate scope and results

To expand the general applicability of this coupling reaction, we have briefly investigated the substrate-scope and the results are shown in Table 5.3. A variety of aroyl chlorides having both
activating and deactivating groups such as Me, OMe, Cl, and NO₂ undergo coupling smoothly with aromatic terminal alkynes within very short times. Heteroaryl acyl chloride such as 2-furoyl chloride also reacts efficiently with phenylacetylene without accompanying of self-condensation or ring cleave. Cinnamoyl chloride produces the coupling product in high yield under the present reaction conditions without concomitant double-bond isomerization. Other aryl terminal alkyne such as 4-ethynyl toluene efficiently couples with acyl chlorides under the same reaction conditions as well. In general the reactions are clean, very fast, and the desired products are obtained in high yields. Regarding the mechanistic path of the present reactions in the absence of copper as cocatalyst we assume that it follows a similar route as that proposed by Najera.\[33\] Accordingly, the possible mechanism will be the initial formation of acyl palladium intermediate coupled with an incipient acetylide followed by reductive elimination to afford the ynone as originally described by Cassar \[43\] and Heck.\[44\]
Table 5.3 Synthesis of ynones.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R1</th>
<th>R2</th>
<th>Time (min)</th>
<th>Yield $^a$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Ph</td>
<td>Ph</td>
<td>20</td>
<td>79-87</td>
</tr>
<tr>
<td>2.</td>
<td>4-MeC₆H₄</td>
<td>Ph</td>
<td>20</td>
<td>76-82</td>
</tr>
<tr>
<td>3.</td>
<td>4-OMeC₆H₄</td>
<td>Ph</td>
<td>25</td>
<td>78-89</td>
</tr>
<tr>
<td>4.</td>
<td>4-ClC₆H₄</td>
<td>Ph</td>
<td>20</td>
<td>80-87</td>
</tr>
<tr>
<td>5.</td>
<td>4-NO₂C₆H₄</td>
<td>Ph</td>
<td>15</td>
<td>78-90</td>
</tr>
<tr>
<td>6.</td>
<td>Ph-C=C</td>
<td>Ph</td>
<td>30</td>
<td>56-65</td>
</tr>
<tr>
<td>7.</td>
<td><img src="image" alt="Furan" /></td>
<td>Ph</td>
<td>20</td>
<td>61-70</td>
</tr>
<tr>
<td>8.</td>
<td><img src="image" alt="Benzene" /></td>
<td>Ph</td>
<td>20</td>
<td>77-87 $^b$</td>
</tr>
<tr>
<td>9.</td>
<td>Ph</td>
<td>4-MeC₆H₄</td>
<td>20</td>
<td>82-86</td>
</tr>
<tr>
<td>10.</td>
<td>4-OMeC₆H₄</td>
<td>4-MeC₆H₄</td>
<td>20</td>
<td>69-80</td>
</tr>
</tbody>
</table>

$^a$Isolated Yields, $^b$phenyl acetylene (2 equiv), Pd cat (4 mol%), Et₃N (1 equiv) were used.
\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 8.14(d, J=8.1Hz,2H), 7.70(d, J=8.1Hz,2H), 7.41-7.53(m,3H), 7.34(d, J=7.8Hz,2H), 2.45(s,3H).

**Figure 5.4** \(^1\)H-NMR spectra of 3-Phenyl-1-p-tolyl-propynone (entry 2, Table 5.3).
\[13\text{C NMR (75 MHz, CDCl}_3\]): \delta 177.7, 145.2, 134.6, 132.9, 130.6, 130.1, 129.6, 129.5(2C), 129.3, 129.1, 128.6, 118.1, 92.5, 86.9, 21.8.\]

**Figure 5.5** \(13\text{C-NMR spectra of 3-Phenyl-1-p-tolyl-propynone (entry 2, Table 5.3).}\)
$^1$H NMR (300 MHz, CDCl$_3$): δ 8.19 (d, $J = 7.2$ Hz, 2H), 7.65 (d, $J = 6.6$ Hz, 2H), 7.39-7.49 (m, 3H), 6.98 (d, $J = 7.2$ Hz, 2H), 3.87 (s, 3H).

**Figure 5.6** $^1$H-NMR spectra of 1-(4-Methoxy-phenyl)-3-phenyl-propynone (entry 3, Table 5.3).
$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 176.5, 164.4, 132.8(2C), 131.9(2C), 130.5, 130.2(2C), 128.6, 120.2, 113.8(2C), 92.2, 86.8, 55.5.

**Figure 5.7** $^{13}$C-NMR spectra of 1-(4-Methoxy-phenyl)-3-phenyl-propynone(entry 3, Table 5.3).
$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.92(d,J=16.2Hz,1H), 7.54-7.83(m,4H), 7.26-7.50(m,6H), 6.87(d,J=16.2Hz,1H).

**Figure 5.8** $^1$H-NMR spectra of 1,5-Diphenyl-pent-1-en-4-yn-3-one (entry 6, **Table 5.3**).
\[ ^{13}\text{C} \text{NMR (75 MHz, CDCl}_3\text{): } \delta 178.1, 148.5, 148.2, 133.9, 133.6, 132.6, 131.0, 130.5, 129.0, 128.6, 128.4(2C), 127.1, 120.1, 116.6, 91.4, 86.5. \]

**Figure 5.9** \[^{13}\text{C}-\text{NMR spectra of 1,5-Diphenyl-pent-1-en-4-yn-3-one (entry 6, Table 5.3).}**
$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.61-7.68(m,3H), 7.36-7.49(m,4H), 6.58-6.60(m,1H).

Figure 5.10 $^1$H-NMR spectra of 1-Furan-2-yl-3-phenyl-propynone (entry 7, Table 5.3).
13C NMR (75 MHz, CDCl3): δ 164.5, 153.0, 147.9, 132.87, 130.7, 128.5, 120.8, 119.6, 112.5, 91.7, 86.0.

Figure 5.11 13C-NMR spectra of 1-Furan-2-yl-3-phenyl-propynone (entry 7, Table 5.3).

Table 5.4 represents synthesis of yrones reported by several groups using variety of reaction conditions. In most cases the synthesis involves the use of CuI₂ and most of the reactions are performed in some organic solvents. In our case, we perform the synthesis without using any copper salt co-catalyst or any solvent. Again, as per as reaction time is concerned our method needs very minimum time for completion and the method used by Cox et al. and Bakherad et al. are only comparable with us in this regard.
4.5 CONCLUSION

In summary, we have demonstrated for the first time a Pd(II)-Schiff-base complex catalyzed synthesis of ynone. The simple procedure, mild conditions, short reaction time, and good yields are the notable advantages of our method.
4.6 REFERENCES