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# SYNTHESIS AND CATALYTIC ACTIVITY OF N,N'-*BIS*-(α-METHYLSALICYLIDENE)-PROPANE-1,3-DIAMINEPALLADIUM(II) AND ITS 4-METHYL DERIVATIVES IN HECK CARBON-CARBON COUPLING REACTION

## (Sintesis dan Aktiviti Pemangkinan N,N'-*Bis*-(α-Metilsalisilidina-Propan-1,3-Diamina-palladium(II) dan Terbitan 4-Metil dalam Tindak Balas Gandingan Karbon-Karbon Heck)

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**Abstract**

Carbon-carbon bond formation is an important step in organic synthesis. Palladium(II) complexes have been widely used as catalyst in the transition metal catalysed bond formation. This paper reports the synthesis, characterization and catalytic performance of two palladium(II)-Schiff base complexes obtained from the condensation of 2'-hydroxyacetophenone and its 4'-methyl derivative with 1,3-diaminopropane followed by complexation with palladium(II) acetate, $Pd(OAc)_2$. Ligands and complexes were characterized by NMR and FTIR spectroscopic methods as well as X-ray crystallographic analysis and CHN elemental analyses. The ligands acted as N,N,O,O tetradentate, coordinating to the palladium atom through both its imine nitrogens and phenolic oxygens. The efficiency of these palladium complexes were evaluated as catalysts in the Heck reaction of 4'-bromoacetophenone with methyl acrylate in the presence of sodium hydrogen carbonate as base in N,N-dimethylacetamide as solvent at reflux temperature 120 ºC. The activities of the catalysts were monitored by GC-FID. Both catalysts gave 100% conversion after 12 hours. The product of the reactions is 3-(4-Acetylphenyl)-acrylic acid methyl ester.

**Keywords**: Palladium, Schiff base, Heck reaction

**Abstrak**

Pembentukan ikatan karbon-karbon merupakan langkah penting dalam sintesis organik. Kompleks palladium(II) telah digunakan secara meluas sebagai mangkin dalam logam peralihan yang memangkinkan pembentukan ikatan. Kajian ini melaporkan hasil sintesis, pencirian dan prestasi pemangkinan bagi dua kompleks palladium(II)-bes Schiff yang telah dihasilkan daripada tindak balas kondensasi 2'-hidroksiasetofenon dan terbitan 4'-metil dengan 1,3-diaminopropan, diikuti oleh pengkompleksan dengan palladium(II) asetat, $Pd(OAc)_2$. Ligan dan kompleks ini dicirikan dengan kaedah spektroskopi RMN dan IM, diikuti oleh analisis kristalografi sinar-X dan analisis unsur CHN. Ligan ini berfungsi sebagai ligan tetradentat N,N,O,O dan terkoordinat kepada atom palladium melalui kedua-dua atom nitrogen imina dan kedua-dua atom oksigen fenolik. Kecekapan kompleks palladium ini dinilai sebagai mangkin dalam tindakbalas Heck antara 4'-bromoasetofenon dan metil akrilat dalam N,N-dimetilasetamida dengan kehadiran bes sodium hidrogen karbonat pada suhu refluks 120 ºC. Aktiviti pemangkinan ini dipantau menggunakan GC-FID. Kedua-dua mangkin ini memberikan penukaran 4-bromoasetofenon 100% selepas 12 jam tindakbalas. Hasil daripada tindak balas ini adalah 3-(4-asetilfenil)-akrilik-asid metal ester.

**Kata kunci**: Palladium, bes Schiff, tindak balas Heck

## Introduction

The Heck coupling reaction, a versatile, powerful and efficient tool for construction of new C-C bonds in organic synthesis has become one of the best methods for fine chemical production [1]. It is referred to as the palladium-catalyzed of aryl halides with alkenes derivatives. Since it was put forward mainly by Mizoroki and Heck et al. in the late 1970s, more and more chemicals especially the cinnamate derivatives and the medicine intermediates have been synthesized through this process [2,3].

In particular, palladium complexes associated with phosphine ligands which stabilize palladium species serve as highly active systems for carbon-carbon bonds formation [4]. However, these ligands are undesirable in industry due to the toxicity, high price and water and air sensitivity [5]

To date, many efforts have been made to search for more phosphine-free ligands for Heck catalytic reaction [6]. In this present work, the Schiff base ligands have been chosen for this purpose. The palladium(II)-Schiff base complexes have been widely studied due to the versatility of their steric and electronic properties, which can be fine-tuned by choosing the amine precursors and ring substituents [7]. N,O-bidentate and $N_2O_2$-tetradentate ligands possess many advantages such as facile approach, readily adjusted ancillary ligands, and tunable steric and electronic coordination environments on the metal centre [8] Due to these properties, the $N_2O_2$-tetradentate ligands and their transition metal complexes often act as catalysts.

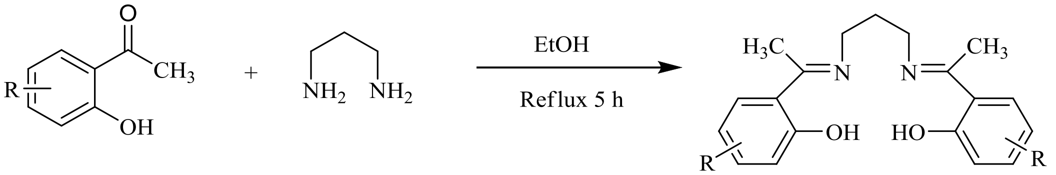
In our attempt to evaluate a phosphine free conditions of Heck coupling reaction, the Schiff bases derived from the condensation between 1,3-diaminopropane with 2'-hydroxyacetophenone and its 4'-methyl derivative have been chosen. In this present work, the performance of the corresponding palladium(II) complexes as catalysts have been evaluated in the Heck reactions of 4'-bromoacetophenone and methyl acrylate. The reactions were carried out in N,N-dimethylacetamide as a solvent in the presence of sodium hydrogen carbonate as base at 120 °C.

## Materials and Methods

All glasswares were dried overnight in an oven. Commercial grade solvents were distilled according to normal procedures and dried over molecular sieves (Å) before used. All reagents were purchased either from Aldrich, Merck or Fluka and were used without further purification. All reactions were carried out in an inert atmosphere of dry nitrogen.

The melting point of the solid products was determined using an Electrothermal Digital Melting Point Apparatus and were uncorrected. Infrared spectra were recorded as KBr pellets on a Perkin Elmer Spectrum One FTIR spectrometer in the range of 4000-400 $cm^{-1}$. NMR spectra were recorded in $CDCl_3$ on a Bruker Avance 400MHz spectrometer. The chemical shifts are reporetd in ppm using tetramethylsilane (TMS) as internal standard. Elemental analysis was performed on a Thermo Finnigan CE 125 CHN analyzer. The single crystal X-ray crystallographic measurements were performed on a Bruker AXS Ltd, Siemens SMART APEX 4K CCD model using graphite-monochromated Mo-Kα radiation ($\lambda = 0.71073$ Å). The structures were solved by direct methods and all calculations were carried out with the aid of the SHEXTL software package [9]. Gas Chromatography (GC) analyses were carried out on a Hewlett-Packard 6890H gas chromatograph equipped with a 30 m x 250 µm x 0.25 µm nominal capillary column (UTRA-1.0.05, 100% dimethylpolysiloxane) and Flame Ionization Detector (FID). The microliter samples were injected at 50 ºC. The temperature increment was at 15 ºC per minute and the final temperature was 300 ºC.

## Synthesis of N,N,O,O Ligands



**1a** R = H
**1b** R = 4-$CH_3$

Figure 1. Synthesis of N,N,O,O–tetradentate ligands

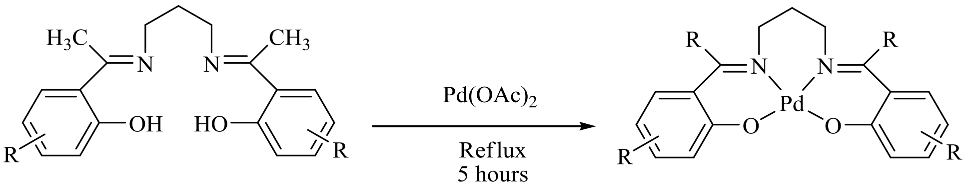
***N,N'-bis(α-methylsalicylidene)-propane-1,3-diamine*** **(1a)**

Stoichiometric amount of 1,3-diaminopropane (5.0mmol) with two equivalents of 2-hydroxyacetophenone are mixed together in 10 mL anhydrous ethanol (Figure 1). The resulting mixture was refluxed under $N_2$ atmosphere for 5 h after which a yellow solid had precipitated out. This was separated by vacuum filtration, washed with cold ethanol and dried in vacuum. Yield 80%. m.p. = 95-96°C. Calc. for $C_{19}H_{22}N_2O_2$: C, 73.52; H, 7.14; N, 9.03%. Found: C, 75.31; H, 7.28; N, 9.55%. IR (KBr) $\nu_{max}$ $cm^{-1}$: 3445 (OH), 1614 (C=N), 1161 (C-O). $^1$H-NMR ($CDCl_3$), $\delta_H$: 12.28 (s, 2H, OH), 7.54-7.52 (dd, 2H, J=8.2 Hz Ar-H), 7.32-7.28 (t, 2H, J=8.0 Hz, Ar-H), 6.95-6.92 (dd, 2H, J=8.2 Hz, Ar-H), 6.81-6.77 (t. 2H, J=8.0 Hz, Ar-H), 3.78-3.74 (t, 4H, N-$CH_2$), 2.37 (s, 6H, $CH_3$) and 2.29-2.20 (m, 2H, $CH_2$). $^{13}$C-NMR ($CDCl_3$), $\delta_C$: 172.36 (CC=N), 164.09 (C-OH), 132.59, 128.02, 119.17, 118.76, 117.05 (arom. C), 46.46 (N-$CH_2$), 30.82 (C$CH_2$) and 14.53 (C$CH_3$).

***N,N'-bis(4-methyl-α-methylsalicylidene)-propane-1,3-diamine*** **(1b)**

The 4-methyl analogue was prepared in 85% yield in a similar manner to the method described for **1a**. Suitable crystal for **1b** was obtained by slow evaporation of acetone solvent. m.p. = 111-112°C. Calc. for $C_{21}H_{26}N_2O_2$: C, 74.52; H, 7.74; N, 8.28 %. Found: C, 73.81; H, 7.37; N, 8.31%. IR (KBr) $\nu_{max}$ $cm^{-1}$: 3436 (OH), 1611 (C=N), 1154 (C-O). $^1$H-NMR ($CDCl_3$), $\delta_H$: 12.30 (s, 2H, OH), 7.40-7.38 (d, 2H, J=8.0 Hz, Ar-H), 6.74 (s, 2H, Ar-H), 6.60-6.58 (d, 2H, J=8.0 Hz, Ar-H), 3.74-3.71 (t, 4H, N-$CH_2$), 2.33-2.31 (d, 6H, $CH_3$), 2.26-2.20 (m, 2H, $CH_2$) and 1.82 (s, 6H, $CH_3$). $^{13}$C-NMR ($CDCl_3$), $\delta_C$: 172.06 (CC=N), 164.63 (C-OH), 143.50, 127.88, 119.11, 118.17, 116.67 (arom. C), 46.11 (N$CH_2$), 30.80 (C$CH_2$), 21.57 (N=C$CH_3$) and 14.38 (C$CH_3$).

## Synthesis of Palladium(II)-Schiff base Complexes



2a R = H
2b R = 4-$CH_3$

Figure 2. Synthesis of palladium(II)-Schiff base complexes

***N,N'-bis(α-methylsalicylidene)-propane-1,3-diaminepalladium(II)*** **(2a)**

The ligand **1a** (0.5 mmol) dissolved in 10 mL acetonitrile was added to a solution of palladium(II) acetate (0.5 mmol) in 10 mL acetonitrile in a three necked round bottom flask (Figure 2). The mixture was refluxed under $N_2$ atmosphere for 5 hours after which it was filtered and evaporated to low volume. The required palladium complex **2a** was obtained as brown needles. This was filtered off and dried in vacuum. Yield 77.44%. m.p. = 335-336°C.

Calc. for $C_{19}H_{20}N_2O_2Pd$: C, 55.02; H, 4.86; N, 6.75%. Found: C, 54.76; H, 4.77; N, 6.79%. IR (KBr) $\nu_{max}$ $cm^{-1}$: 1597 (C=N), 1141 (C-O). $^1H$-NMR ($CDCl_3$), $\delta_H$: 7.31-7.28 (dd, 2H, J=8.0 Hz, Ar-H), 7.18-7.14 (t, 2H, J=8.0 Hz, Ar-H), 7.07-7.06 (d, 2H, J=8.0 Hz, Ar-H), 6.56-6.52 (t, 2H, J=8.0 Hz, Ar-H), 3.35-3.33 (t, 4H, N-$CH_2$), 2.78-2.76 (m, 2H, $CH_2$), 2.35 (s. 6H, $CH_3$). $^{13}C$-NMR ($CDCl_3$), $\delta_C$: 169.18 (CC=N), 166.50 (C-OH), 133.44, 129.94, 127.02, 121.84, 114.83 (arom. C), 53.43 ($NCH_2$), 32.14 ($CCH_2$), 19.83 ($CCH_3$).

***N.N'-bis(4-methoxysalicylidene)-2,2-dimethylpropane-1,3-diaminepalladium(II)*** (**2b**)

The corresponding palladium complex **2b** was prepared and isolated as green solid in 75.25% yield after treating palladium(II) acetate with one mole equivalent of ligand **1b** in a similar manner to the method described for **2a**. m.p. = 341-343°C. Calc. for $C_{21}H_{24}N_2O_2Pd$: C, 56.96; H, 5.46; N, 6.33%. Found: C, 56.64; H, 5.42; N, 6.61%. IR (KBr) $\nu_{max}$ $cm^{-1}$: 1607 (C=N), 1165 (C-O). $^1H$-NMR ($CDCl_3$), $\delta_H$: 7.20-7.18 (d, 2H, J=8.0 Hz, Ar-H), 6.90 (s, 2H, Ar-H), 6.37-6.35 (d, 2H, J=8.0 Hz, Ar-H), 3.34-3.32 (t, 4H, N-$CH_2$), 2.76-2.74 (m, 2H, $CH_2$), 2.33 (s, 6H, $CH_3$) and 2.22 (s, 6H, $CH_3$). $^{13}C$-NMR ($CDCl_3$), $\delta_C$: 168.76 (CC=N), 166.48 (C-OH), 144.25, 129.73, 124.48, 121.80, 116.47 (arom. C), 53.28 ($NCH_2$), 32.18 ($CCH_2$), 21.39 ($N{=}CCH_3$) and 19.62 ($CCH_3$).

**Catalytic Study**

4-bromoacetophenone (1 mmol; 0.20 g), methyl acrylate (3 mmol; 0.3 mL), sodium hydrogen carbonate (2.4 molar equiv.), palladium complex **2a** (1 mol %; 0.01 mmol) and N,N-dimethylacetamide solvent (2.5 mL) were mixed together in a Radley's 12-placed reaction carousel whilst purging with nitrogen (Figure 3). The reaction carousel was then heated to 120 °C with the temperature carefully controlled by a contact thermometer (± 1 °C) for 3, 6 and 12 h. The conversion of reaction was monitored by GC-FID. The Heck reaction was repeated by using complex **2b** as catalyst.

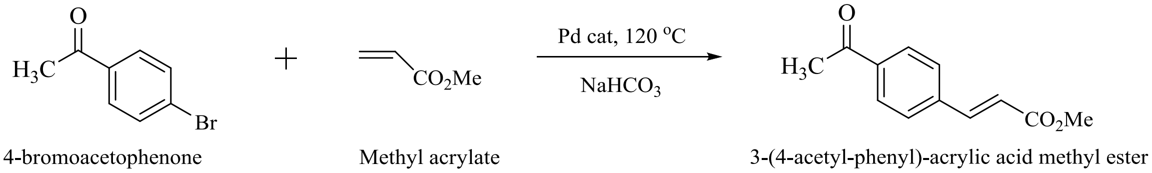


Figure 3. Heck reaction catalyzed by Pd(II) catalysts

## Results and Discussion

The Schiff base ligands, N,N'-bis(α-methylsalicylidene)-propane-1,3-diamine (**1a**) and N,N'-bis(4-methyl-α-methylsalicylidene)-propane-1,3-diamine (**1b**) were obtained as a yellow solid in high yield through condensation reaction between 1,3-diaminopropane with 2-hydroxyacetophenone and the 4-methyl derivative respectively. These Schiff bases were fully characterised. Elemental analytical, IR, $^1H$ and $^{13}C$ NMR data are in the Experimental section. The synthesis of the palladium(II) complexes are outlined as in Figure 2. Microanalytical data for the ligands and the palladium complexes are consistent with the calculated empirical formula values.

The IR spectrum of the Schiff bases **1a** and **1b** showed the appearance of a very strong azomethine ν(C=N) stretching bands at 1615 and 1611 $cm^{-1}$ respectively. These values are consistent with other similar imine compounds [10]. Besides that, the absorption bands for ν (-$NH_2$) stretching mode from 1,3-diaminopropane and ν (C=O) stretching mode from 2-hydroxyacetophenone and its 4-methyl derivative have totally disappeared, demonstrating that ligands **1a** and **1b** have been successfully synthesized.

Meanwhile, the IR spectrum of the palladium(II) complexes **2a** and **2b** exhibit the strong and sharp ν(C=N) stretching band at 1597 and 1607 $cm^{-1}$ respectively. The slight displacement of the ν (C=N) from 1615 and 1611 $cm^{-1}$ in the free ligands to 1597 and 1607 $cm^{-1}$ in the complexes respectively suggested the coordination of the azomethine nitrogen atom to the palladium metal. This results show that the contribution of C=N stretching have been reduced as the nitrogen atoms are involved in bond formation with the metal ion. Besides, the broad O-H bands at 3245 and 3421 cm$^{-1}$ in the ligands **1a** and **1b** respectively are absent in the IR spectrum of the complexes, suggesting the coordination of phenolic oxygen atom to the metal centre.

In the $^{1}$H NMR spectrum, the signal of the acidic OH proton for **1a** and **1b** appeared as single resonance at low field at δ12.28 ppm and δ 12.30 ppm respectively. These signals have totally disappeared in the $^{1}$H spectra for the complexes, further indicating the coordination of oxygen atoms to the palladium metal due to the participation of OH group in chelating to metal ion through proton displacement [11]. Meanwhile, the $^{13}$C NMR spectral data showed the displacement to low field of the imine carbon (C=N) resonance from δ172.36 ppm for **1a** and δ172.03 ppm for **1b** in the free ligand to the δ169.18 ppm and δ168.76 ppm respectively in the complexes due to the coordination of azomethine nitrogen atom to the palladium metal.

### Single X-ray Crystallography

Suitable crystals of ligand **1b** for X-ray diffraction analysis were successfully grown by slow evaporation from a solution of acetone at room temperature. The structure is shown in Figure 4. The selected bond lengths and angles are listed in Table 1.

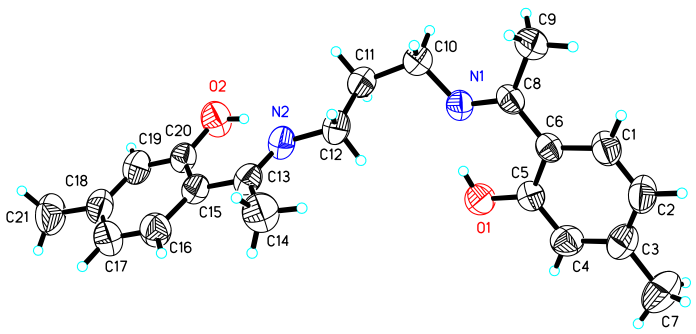


Figure 4. The ORTEP drawing of ligand **1b**

Table 1. Selected bond length (Å) and bond angles (°) for ligand **1b**

| Bond | Dist. |
|---|---|
| N(1)-C(8) | 1.286(3) |
| N(2)-C(13) | 1.284(3) |
| O(1)-C(5) | 1.339(3) |
| O(2)-C(20) | 1.343(3) |
| **Angle** | **(°)** |
| C(5)-O(1)-H(1B) | 105(3) |
| C(20)-O(2)-H(2B) | 107(2) |
| N(1)-C(8)-C(6) | 117.6(2) |
| N(2)-C(13)-C(15) | 117.3(2) |

The bond lengths and angles of the compound is in agreement with the analogues of N,N’-*bis*-(5-methyl-methylsalicylidene)-2,2-dimethylpropane-1,3-diamine [12]. From analysis showed that bond lengths of azomethine C8=N1, 1.286(3) Å and C13=N2, 1.284(3) Å in the molecule are in normal range and consistent with other similar imine compounds [13].

## Catalytic Studies

The palladium complexes **2a** and **2b** were applied to the Heck reaction (Figure 3) of methyl acrylate with 4-bromoacetophenone in N,N-dimethylacetamide at 120°C for 12h, using sodium hydrogen carbonate as base. Catalytic reactions were performed under an atmosphere of nitrogen. Catalytic loading was kept to 1.0 mol%, so as to give an expected turnover number of 100 if 100% conversion was achieved. The reaction was monitored by % conversion of the starting material, 4-bromoacetophenone, using GC-FID. A control experiment was also performed for comparison. The results are summarized in Table 2. The catalytic data obtained indicate that these palladium(II) complexes efficiently catalyse the Heck reaction of 4-bromoacetophenone with methyl acrylate, giving more than 90% conversion after 6h. The effect of temperature, solvent, base and amount of catalyst on the catalytic properties of the palladium(II) complexes is currently in progress.

Table 2. Heck reaction of 4-bromoacetophenone with methyl acrylate catalysed by palladium complexes **2a** and **2b**

| **Catalyst** | **% Conversion** | | |
|---|---|---|---|
| | *AFTER 3H* | **After 6h** | **After 12h** |
| Complex **2a** | 59.65 | 97.07 | 100 |
| Complex **2b** | 64.90 | 97.76 | 100 |
| Without catalyst | 3.89 | 7.09 | 13.7 |

## Conclusion

In summary, we have synthesised and characterised two chelated palladium(II) complexes with Schiff bases obtained from the condensation reaction between 1,3-Diaminopropane and 2-hydroxyacetophenone or 2-hydroxy-4-methoxyacetophenone. These complexes efficiently catalyse the Heck reaction of 4'-Bromo- acetophenone with methyl acrylate. The influence of temperature, solvent, bases and catalyst loading on the catalytic performance on the Heck or other palladium catalysed carbon-carbon coupling reactions is currently been investigated.

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