Synthesis of palladium complexes with bis(diphenylphosphinomethyl)amino ligands: A catalyst for the Heck reaction of aryl halide with methyl acrylate

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Abstract

A series of ligands, $(Ph_2PCH_2)_2NR$ (R = $-CH_3$) (**1**), $-C(CH_3)_3$, (**2**) $-m-C_6H_4SO_3Na$ (**3**), and their Pd(II) complexes have been synthesized under nitrogen atmosphere using Schlenk method. All compounds were characterized using elemental analysis and spectroscopic techniques (AAS, NMR (^1H, ^{31}P)). Based on the analysis the complexes have been proposed as in square planar geometry. The Pd(II) complexes were applied to the Heck reaction of aryl halide (Br, Cl) with methyl acrylate. The results have exhibited that complexes $[PdCl_2((Ph_2PCH_2)_2NCH_3)]$ (**4**) and $[PdCl_2((Ph_2PCH_2)_2NC(CH_3)_3)]$ (**5**) have shown higher turnover numbers (TON) than complex $[PdCl_2(Ph_2PCH_2)_2N-m-C_6H_4SO_3Na]$ (**6**).
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Keywords: Bis(diphenylphosphinomethyl)amino; Pd complex; Heck reaction; Aryl halide

1. Introduction

Heck reactions, palladium-catalyzed cross coupling reactions, have been most powerful tools for generating a new C–C bond in organic synthesis; thus, a variety of palladium–phosphine complexes have been developed [1–3]. Aryl halides (I, Br and Cl) and activated alkenes are typical reactants for the Heck reactions. Although iodide derivatives have a high reactivity than bromide and chloride derivatives, the latter ones are preferred in synthetic routes due to their cheapness and availability [4]. Cinnamic esters as the resulting compounds of Heck reaction derived from aryl halides and alkyl acrylates have found application as UV absorbers, antioxidants in plastics, and intermediates in pharmaceuticals [5].

In recent years nitrogen containing chiral phosphines and their transition metal complexes have become increasingly important due to their improved catalytic activity [6–8]. The nature of the phosphine ligand on complexes influences on the stability of the catalysts and on the rate of catalyzed reactions [9]. Several nitrogen containing phosphine–palladium complexes have been studied in a variety of catalytic systems to reach higher yields in Heck reactions [10].

In the present paper, some bis(diphenylphosphinomethyl)amino (P–C–N) type ligands and their Pd(II) complexes have been synthesized in order to test in the Heck reactions of bromobenzene and chlorobenzene with methyl acrylate. Although *tert*-butyl substituted aminomethylphosphine used in this study was reported previously, the synthetic route was slightly different [11].

2. Results and discussion

A series of ligands, $(Ph_2PCH_2)_2NR$ (R = $-CH_3$, $-C(CH_3)_3$, $-m-C_6H_4SO_3Na$), have been by treating phosphonium salt, $([PPh_2(CH_2OH)_2]Cl)$ with appropriate primary amines according to the Mannich reaction in the presence

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of triethylamine as a base (Scheme 1). The Pd(II) complexes of the bis(diphenylphosphinomethyl)amino ligands were prepared under nitrogen atmosphere using Schlenk techniques as shown in Scheme 1.

2.1. Characterization of bis(diphenylphosphino-methyl)amino ligands and their Pd(II) complexes

Bis(diphenylphosphinomethyl)amino ligands and their Pd(II) complexes were characterized using ^{1}H NMR, ^{31}P NMR, and elemental analysis.

Assignment of ^{1}H NMR spectra of ligands and their Pd(II) complexes showed that the aromatic protons of the phenyl ring had the chemical shift value (δ) in a range of 6.9–7.52 ppm. The spectra of P–CH$_2$–N protons of ligands and their Pd(II) complexes were observed around 3.42–3.62 ppm which is in agreement with reported studies [12,13]. N–C–(CH$_3$)$_3$ proton signals of ligand **2** and complex **5** appeared in 1.21 and 1.23 ppm, respectively. Assignment of ^{1}H NMR spectra showed no remarkable differences between free ligands and their Pd(II) complexes. The P–CH$_2$–N resonance was slightly shifted to a low field compared to the free ligands, the consequence of which shows that N is not coordinated Pd. This observation is an additional evidence that the NCH$_2$ protons are situated away from the coordination sphere around the metal as reported in the literature [11–14].

It was found that ^{31}P NMR spectra of all complexes gave more shielded signals compared with the uncoordinated aminomethyldiphosphine ligands as shown in Table 1. The results are in consistent with those of the reported studies giving coordination shifts in a range of 34.6–35.74 ppm [12,15,16]. The coordination shift values of the complexes (Δ), depending on the metal centers and the chemical structures of the ligands showed that the ligands coordinated to Pd(II) via phosphorus atoms to give chelated complexes [17]. Based on ^{31}P NMR data, Pd(II) complexes have been proposed as in square planar geometry as those of the reported studies [12,13,15]. Although nitrogen is seemed as a potential coordinating site to the metal center, many studies reported including single crystal X-ray diffraction studies clearly showed that there was no close interaction between the nitrogen atom of the amine group and the metal center [11,15,18,19].

Table 1
^{31}P NMR data for ligands and metal complexes

Compounds	δ_p (ppm)	$\Delta\delta$ (ppm)[a]
1	−27.2	–
2	−26.36	–
3	−27.53	–
4	7.4	34.6
5	8.12	34.48
6	8.21	35.74

[a] ^{31}P chemical shifts $\Delta\delta = \delta$ (complex) − δ (free ligand) [17].

Elemental analysis for C, H and N of ligands and AAS for metal contents have indicated that the metal–ligand ratio of complexes were 1:1.
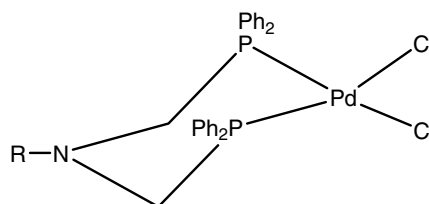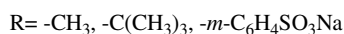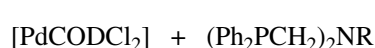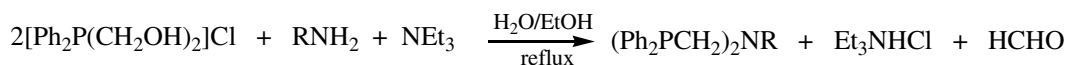
2.2. Heck reaction

Pd(II) complexes **4**, **5**, and **6** were applied to the Heck reaction of methyl acrylate with bromobenzene and chlorobenzene respectively. The reactions were carried out in the NMP solvent and using K$_3$PO$_4$ as a base at 140 °C for 14 h since these aryl halides are often unreactive towards oxidative addition under mild conditions (Scheme 2).

The percentage of conversions of the aryl halides and methyl acrylate to the methyl cinnamate was determined based on the amount of the product by GC and GC–MS. Product yields and TON's corresponding to the catalysts are presented in Table 2. The Heck reaction of bromobenzene with methyl acrylate gave better yields of the desired product than that of chlorobenzene. Additionally, the palladium complexes exhibited a better catalytic activity for the Heck reaction of bromobenzene than that of chlorobenzene with methyl acrylate in the catalytic experiments under the studied conditions. These results are in agreement with the reported studies [3,20].

It is well known that the catalytic activity depends on the type of aryl halides. While electron-withdrawing groups on the aryl ring increase the reaction rate [21], electron-donating substituent on the aryl group make the oxidative addition more difficult and, as a result, electron-poor aryl halides are often referred to as "activated", and electron-rich aryl halides as "deactivated" [20].

From the obtained results it can be concluded that the presence of Pd(II) complexes of bis bis(diphenylphosphi-

$$2[Ph_2P(CH_2OH)_2]Cl + RNH_2 + NEt_3 \xrightarrow[reflux]{H_2O/EtOH} (Ph_2PCH_2)_2NR + Et_3NHCl + HCHO$$

$$[PdCODCl_2] + (Ph_2PCH_2)_2NR \xrightarrow{CH_2Cl_2}$$

R= -CH$_3$, -C(CH$_3$)$_3$, -m-C$_6$H$_4$SO$_3$Na

Scheme 1. Synthesis of bis(diphenylphosphinomethyl)amino ligands and their Pd(II) complexes.
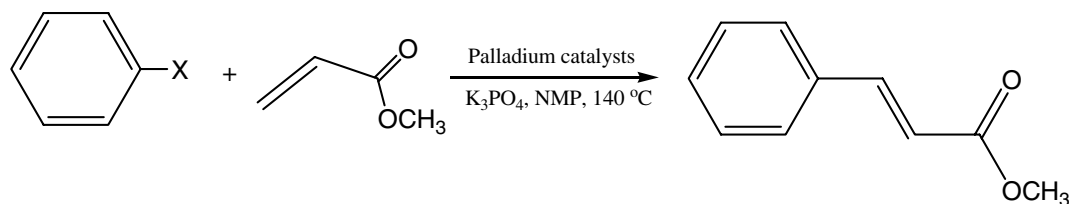
Scheme 2. Heck reaction of aryl halide with methyl acrylate.

Table 2
Heck reaction[a] of aryl halide with methyl acrylate catalysed by palladium complex

Entry	X	Catalysts	Conversion (%)[b,c]	TON
1	Br	[PdCl$_2$((Ph$_2$PCH$_2$)$_2$NCH$_3$)]	94	5220
2	Cl	[PdCl$_2$((Ph$_2$PCH$_2$)$_2$NCH$_3$)]	65	3600
3	Br	[PdCl$_2$(Ph$_2$PCH$_2$)$_2$NC(CH$_3$)$_3$]	96	5330
4	Cl	[PdCl$_2$(Ph$_2$PCH$_2$)$_2$NC(CH$_3$)$_3$]	68	3780
5	Br	[PdCl$_2$(Ph$_2$PCH$_2$)$_2$N-m-C$_6$H$_4$SO$_3$Na]	87	5560
6	Cl	[PdCl$_2$(Ph$_2$PCH$_2$)$_2$N-m-C$_6$H$_4$SO$_3$Na]	53	4000

[a] Reaction conditions: aryl halide (0.56 mmol), methyl acrylate (0.67 mmol) potassium phosphate (0.67 mmol) (0.018 mmol) catalyst in 1 mL NMP, 140 °C, 14 h.
[b] GC yields are based on the amount of aryl halide and methyl cinnamate.
[c] Determined by GC and GC–MS.

nomethyl)amino ligands were found to be catalysis Heck reaction with bromobenzene and chlorobenzene. The results are consistent with the literature [10].

In addition, the electron-withdrawing ability of the P–C–N linkage increases the π-acidity character of the phosphine ligands. Thus, it can be assumed that the pre-activation of the metal, Pd(II) to the active Pd(0) species is a low energy process since the low oxidation state of the metal [22].

The catalytic activity of the Pd(II) complexes depending on the nature of the nitrogen substituent, and increasing in order to: tert-butyl (5) > methyl (4) > m-C$_6$H$_4$-SO$_3$Na (6). The trend seems to fit the electronic nature of the substituents, while the most electron-donating group (tert-butyl) compared to the most electron-withdrawing group (-phenyl) [8]. The sulfonated derivative of the phosphine ligand and its metal complex were prepared to find out catalytic activity for further study on some reactions in the polar solvent system.

3. Conclusion

The complexes of Pd(II) with bidentate tertiary bis(diphenylphosphinomethyl)amino ligands have been synthesized and characterized by using spectroscopic techniques. ^{31}P NMR spectra of the complexes have indicated that coordination of aminomethyldiphosphine ligand to metal center gives deshielded chemical shift value compared with free ligand.

Catalytic activities of Pd(II) complexes have been tested for the Heck reaction. The results show that, these complexes catalyze the reaction of methyl acrylate with bromobenzene and with chlorobenzene to give methyl cinnamate in good yields. The Heck reaction of bromobenzene with methyl acrylate is better catalyzed than chlorobenzene. Complexes 4 and 5 were found to be better catalysts than complex 6 which contained the deactivated group of –SO$_3$.

4. Experimental

4.1. General

All reactions were carried out under nitrogen atmosphere using conventional Schlenk glassware. All solvents and 1-methyl-2-pyrrolidone (NMP) were dried using established procedures and then immediately distilled under nitrogen atmosphere prior to use. The phosphonium salt ([PPh$_2$(CH$_2$OH)$_2$]Cl) and [PdCl$_2$(COD)] were prepared described in the literatures [23,24].

The metal contents of the complexes were determined using a Hitachi 180–80 Polarized Zeiman atomic absorption spectrometer. Elemental analysis was performed on a LECO CHNS 932. ^{1}H NMR and ^{31}P NMR spectra were recorded at 25 °C in DMSO-d^6 and CDCl$_3$ on a Varian Mercury 200 MHz NMR spectrometer. ^{31}P NMR spectra were recorded with complete proton decoupling and reported in ppm using 85% H$_3$PO$_4$ as an external standard. The catalyst products were analyzed on Shimadzu GC 14 A with a 30 m × 0.25 mm ZB-5 column and Thermo Finnigan GC–MS Electron impact (70 eV) with a 60 m × 0.25 mm × 0.25 μm ZB-5 column.

4.2. Synthesis of bis(diphenylphosphinomethyl)amino ligands and their Pd(II) complexes

4.2.1. [(Ph$_2$PCH$_2$)$_2$NCH$_3$] (1)

Bis(diphenylphosphinomethyl)aminomethane ([(Ph$_2$P-CH$_2$)$_2$NCH$_3$]) were prepared according to the literature methods [16].

4.2.2. [(Ph$_2$PCH$_2$)$_2$NC(CH$_3$)$_3$] (2)

Phosphonium salt (0.260 g, 0.92 mmol) was dissolved in 2:1 H$_2$O:EtOH (15 mL) solvent system. NEt$_3$ (0.5 mL, 3.65 mmol) was added to a stirred solution of [Ph$_2$P-(CH$_2$OH)$_2$]Cl, followed by the addition of tert-butylamine (46 μL, 0.46 mmol). The mixture was refluxed for 1 h and

then the formed product was extracted with CH_2CI_2 and dried over Na_2SO_4. The solvent was removed under vacuum. Yield: 0.173 g (80%). Elemental analysis calculation for $[(Ph_2PCH_2)_2NC(CH_3)_3]$: C, 76.75; H, 7.04; N, 2.98%. Found: C, 77.14; H, 7.15; N, 3.07. ^1H NMR (CDCI$_3$, 25 °C): δ 7.34–7.18 [m, 20H, 4Ph], 3.42 [d-br, 4H, 2 (P–CH_2–N)], 1.21 [s, 9H, 2 (N–C–(CH_3)$_3$)] ppm ^{31}P NMR (CDCI$_3$, 25 °C): δ −27.2 [s, PPh$_2$–CH$_2$] ppm.

4.2.3. [(Ph₂PCH₂)₂N-m-C₆H₄SO₃Na] (3)

NEt$_3$ (0.8 mL, 5.84 mmol) was added to a stirred solution of $[Ph_2P(CH_2OH)_2]Cl$ (0.5 g, 1.77 mmol) in 2:1 H_2O:MeOH (15 mL) solvent system followed by the addition of sodium 3-aminobenzenesulfonate (0.175 g, 0.9 mmol) dissolved in CH_2Cl_2. The mixture was refluxed for 2 h and then allowed to cool to room temperature. The formed product was extracted with CH_2Cl_2 and dried over Na_2SO_4. The solvent was removed under vacuum. Yield: 0.346 g (66%). Elemental analysis calculation for $[(Ph_2PCH_2)_2N-m-C_6H_4SO_3Na]$: C, 64.97; H, 4.74; N, 2..37%. Found: C, 65.40; H, 4.57; N, 2.53%. ^1H NMR (CDCI$_3$, 25 °C): δ 7.52–7.32 [m, 20H, 4P–Ph], δ 6.90 [m, 4H, N–Ph], 3.50 [m, 4H, P–CH_2–N] ppm. ^{31}P NMR (CDCI$_3$, 25 °C): δ −26.36 [s, PPh$_2$–CH$_2$] ppm.

4.2.4. [PdCl₂((Ph₂PCH₂)₂NCH₃)] (4)

Ligand **1** (0.28 g, 0.655 mmol) was added to a stirred solution of $[PdCl_2(COD)]$ (0.185 g, 0.21 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for a further 1 h at room temperature. The addition of diethylether gave the pale yellow solid which was then filtered and dried. Yield: 0.353 g (88%). Elemental analysis calculation for $[PdCl_2((Ph_2PCH_2)_2NCH_3)]$: C, 53.6; H, 4.21; N, 2.03%. Found: C, 52.6; H, 4.58; N, 2.36%. ^1H NMR (CDCI$_3$, 25 °C): δ 7.37–7.87 [m, 20H, 4Ph], 3.24 [d, 4H, P–CH_2–N], 2.52 [s, 3H, N–Me] ppm. ^{31}P NMR (CDCI$_3$, 25 °C): δ 8.21 [Pd–PPh$_2$] ppm.

4.2.5. [PdCl₂((Ph₂PCH₂)₂NC(CH₃)₃)] (5)

Ligand **2** (0.10 g, 0.213 mmol) was added to a stirred solution of $[PdCl_2(COD)]$ (0.08 g, 0.21 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for a further 2 h at room temperature. The addition of diethylether gave the yellow solid which was then filtered and dried. Yield: 0.12 g (88%). Elemental analysis calculation for $[PdCl_2((Ph_2PCH_2)_2NC(CH_3)_3)]$: C, 55.69; H, 5.10; N, 2.17%. Found: C, 55.89; H, 5.40; N, 2.31%. ^1H NMR (CDCI$_3$, 25 °C): δ 7.77–7.46 [m, 20H, 4Ph], 3.62 [d, 4H, P–CH_2–N], 1.23 [s, 9H, N–C–(CH_3)$_3$] ppm. ^{31}P NMR (CDCI$_3$, 25 °C): δ 7.4 [br, Pd–PPh$_2$] ppm.

4.2.6. [PdCl₂(Ph₂PCH₂)₂N-m-C₆H₄SO₃Na] (6)

Ligand **3** (0.176 mmol) was added to a stirred solution of $[PdCl_2(COD)]$ (0.06 g, 0.16 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for a further 2 h at room temperature. The addition of diethylether gave the yellow solid which was then filtered and dried. Yield: 0.10 g (81%).

Elemental analysis calculation for $[Pd(Ph_2PCH_2)_2N-m-C_6H_4SO_3Na]Cl_2$: C, 49.97; H, 3.64; N, 1.82%. Found: C, 50.6; H, 3.85; N, 2.02%. ^1H NMR (CDCI$_3$, 25 °C): δ 7.83–7.42 [m, 20H, 4Ph], 6.87 [m, 4H, N–Ph] 3.62 [d, 4H, P–CH_2–N], ppm. ^{31}P NMR (CDCI$_3$, 25 °C): δ 8.12 [br, Pd–PPh$_2$] ppm.

4.3. Heck reactions

An oven-dried Schlenk flask was charged with potassium phosphate (K_3PO_4) (0.67 mmol) and NMP (1 mL) under N_2 atmosphere. Bromobenzene (0.56 mmol), methylacrylate (0.67 mmol) and complex **4** (0.018 mmol) were added into the flask. The flask was then sealed under N_2 atmosphere and placed in an oil bath preheated to 140 °C. The reaction mixture was stirred for 14 h and then allowed to cool to room temperature. The reaction mixture was poured into water (20 mL) and extracted with ethyl acetate (3×20 mL). The extracts were washed with brine, and dried over $MgSO_4$. Similar procedures were used for complexes **5**, **6** and for chlorobenzene with each complexes.

Acknowledgments

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