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Phosphine-free Pd–salen complexes as efficient and inexpensive catalysts for Heck and Suzuki reactions under aerobic conditions

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Abstract

Phosphine-free palladium–salen complexes, *N*,*N*′-bis(salicylidene)-ethylenediamino-palladium and *N*,*N*′-bis(salicylidene)-1,2-phenylenediamino palladium, are found to be highly active catalysts for the Heck olefination of aryl iodides and Suzuki reaction of aryl iodides and bromides giving excellent yields (70–90%) of products under aerobic conditions, in short reaction times (10–60 min).

Keywords: Heck; Suzuki; Pd–Salen; Iodobenzene; Phenylboronic acid

1. Introduction

The design of new ligands and transition metal catalysts that are effective in C–C bond forming reactions with high conversion and selectivity is an exciting and challenging area of research.[1] The palladium-catalyzed Heck and Suzuki reactions have been used extensively for the synthesis of natural products, pharmaceutical intermediates, conducting polymers, pesticides, and liquid crystals.[2–5] In homogeneous reaction medium phosphine ligands play an important role in C–C bond formation under an inert atmosphere and moisture-free conditions.[6] Since most of the phosphine ligands are air- and moisture-sensitive, P–C bond degradation sometimes occurs at elevated temperatures, which poisons the metal, leading to decomposition of the catalyst which strongly affects conversion and selectivity.[7a,b] A number of methods on the use of ligand-free palladium catalysts as well as phosphine-free ligands have been reported for the Heck and Suzuki reactions. Examples of phosphine-free ligands include the *N*-heterocyclic carbene class of compounds,[7c,d] thioureas,[7a,8] tetrazoles,[9] phenanthroline,[10] bisimidazole,[11] bispyridines,[12] amino acids,[13] and hydroxyquinolines,[14] hydrazones,[15] *N*-phenylurea,[16] and Schiff bases.[17] Herein, we report the synthesis of the symmetrical palladium(II) complexes, *N*,*N*′-bis(salicylidene)-ethylenediamino-palladium (**A**), and *N*,*N*′-bis(salicylidene)-1,2-phenylenediamino palladium (**B**) and their catalytic activity in Heck and Suzuki coupling reactions with various substrates.

The symmetrical palladium(II) complexes **A** and **B** were synthesized by the reaction of the salen ligands, *N*,*N*′-bis(salicylidene)-ethylenediamine and *N*,*N*′-bis(salicylidene)-1,2-phenylenediamine, with palladium acetate for 18–20 h at room temperature (Scheme 1), in moderate yields. The synthesis of complex **A** was previously reported by Abu-Omar and co-workers in poor yield (17–30%).[18] In our synthesis, complexes **A** and **B** were obtained as yellow and brown crystalline solids in 76% and 55% yields, respectively. The catalytic activities of complexes **A** and **B** (0.5 mol %) were studied in the Heck reaction using iodobenzene and ethyl acrylate as substrates, in the presence of triethylamine as base, at 130 °C under aerobic conditions (Scheme 2). The catalytic activity showed that complex **A** (100% in 10 min) was superior to **B** (69% in 10 min). Therefore, further reactions were optimized using complex **A**.

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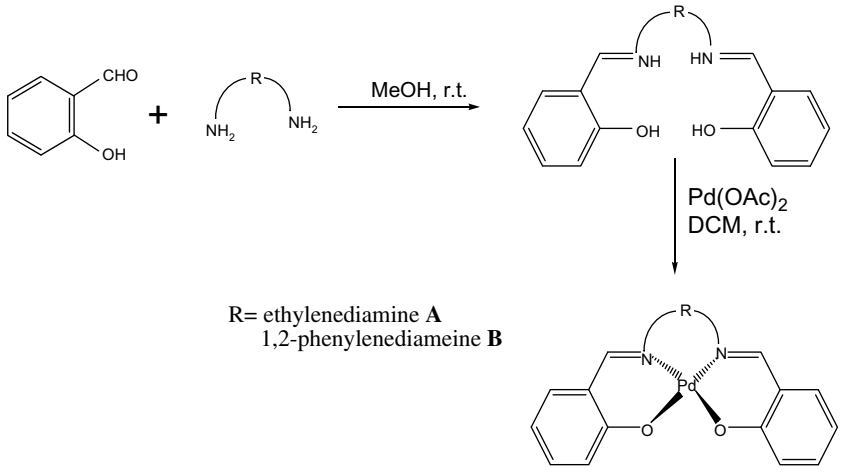
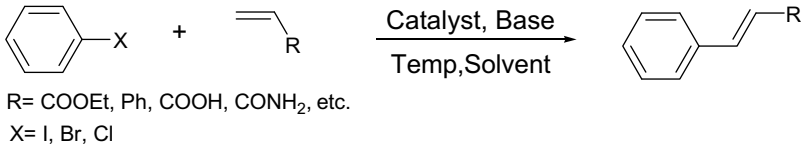


Scheme 1. General synthetic pathway for the preparation of Pd–salen complexes.



Scheme 2.

The effect of temperature on the activity of complex **A** was studied in the range 30 °C to 130 °C. The % conversion increased with temperature and there was no conversion observed below 80 °C. As the temperature increased from 100 to 130 °C, the conversion increased from 66% to 100% and the reaction time was also reduced considerably from 60 to 10 min with excellent selectivity for the *trans* product.

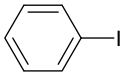
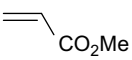
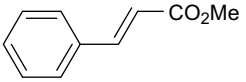
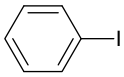
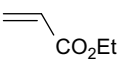
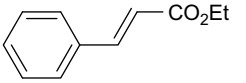
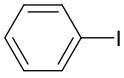
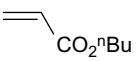
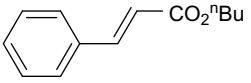
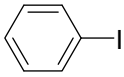
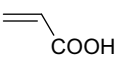
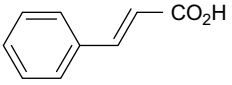
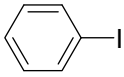
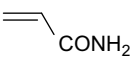
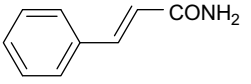
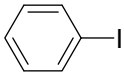
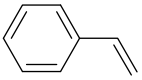
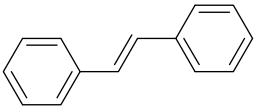
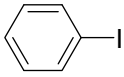
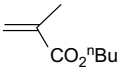
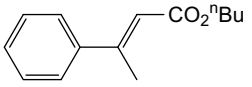
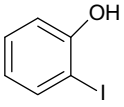
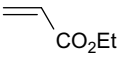
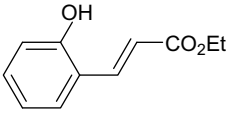
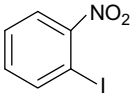
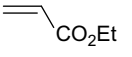
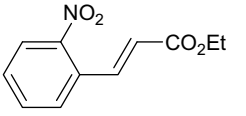
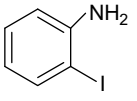
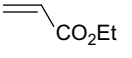
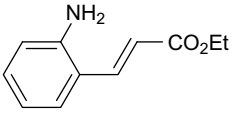
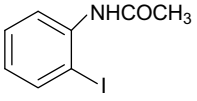
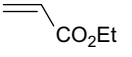
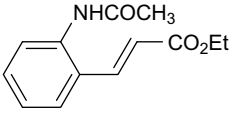
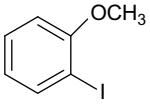
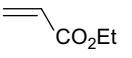
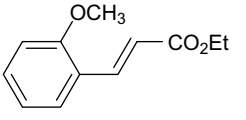
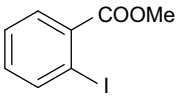
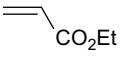
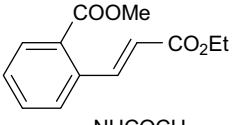
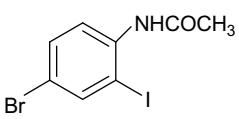
Among the various solvents studied, polar aprotic solvents DMF, NMP, DMAc, and DMSO gave excellent conversions (100%) at 130 °C in 10 min. Non-polar solvents such as xylene showed 17% conversion for the desired product even after 60 min. Water required the addition of the phase transfer catalyst tetrabutylammoniumbromide (TBAB) to deliver satisfactory conversion (59% in 60 min).

Among the various bases, triethylamine (TEA) and tributylamine (TBA) were found to be the best (100% conversion in 10 min). These organic bases were superior to inorganic bases such as K_2CO_3, Na_2CO_3, NaOAc, $NaHCO_3$, $Ca(OH)_2$, and Cs_2CO_3. This may be due to the partial inhomogeneity of inorganic bases with the organic substrate, reagent, and solvent, which lowered the conversion and increased the reaction times compared to organic bases (32–60% in 30 min). The effect of Pd concentration on the Heck reaction was studied and the results show that the reaction complete within 5 min, with excellent conversion and selectivity for the β-arylated *trans* product using 0.5 mol % Pd.

Using the optimized reaction conditions, we explored the general applicability of Pd–salen complex **A** with different olefins and aryl halides containing electron withdrawing or donating substituents, and the results are shown in Table 1. Iodobenzene reacts with various olefins such as acrylates, acrylic acid, acryl amide, and styrene, delivering the corresponding products in good to excellent yields (entries 1–7). Ethyl acrylate was found to be the most reactive amongst the olefins studied (entry 2). As expected, the most electron rich olefin, acryl amide reacted more slowly than the other acrylates, whereas methyl butyl acrylate reacted very sluggishly under these reaction conditions which may be due to steric hindrance (entry 7). Styrene was less reactive than the acrylates. Among the various substituted aryl iodides, both deactivated (electron rich) and activated (electron poor) examples were converted efficiently to the desired products in good to excellent yields within 10–60 min (entries 8–16). In general, the *ortho*-substituted aryl iodides required longer reaction times than *para*-substituted aryl iodides. The biscoupled product was obtained exclusively when 1,3-diiodobenzene was used (entry 19). The comparatively less reactive bromobenzene did not undergo any conversion even after 12 h, whereas activated 4-bromoacetophenone gave only 20% conversion (entry 22).

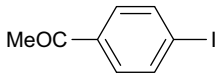
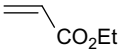
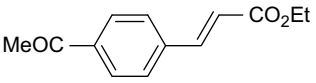
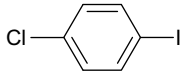
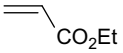
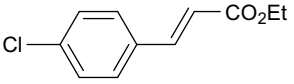
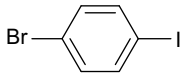
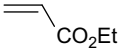
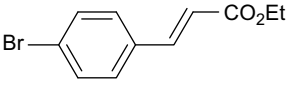
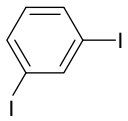
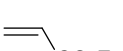
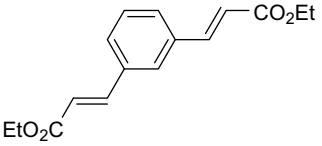
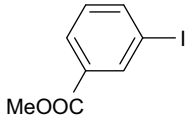
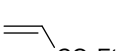
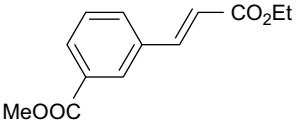
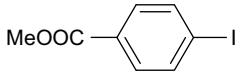
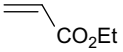
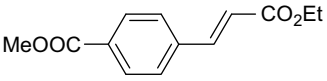
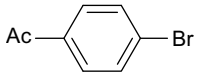
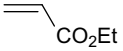
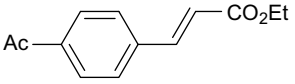
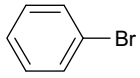
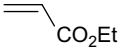
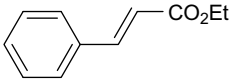
Further, under these optimized conditions we investigated the usefulness of Pd–salen complex **A** in the Suzuki reaction involving cross-coupling of an aryl halide with phenyl boronic acid (Scheme 3). Table 2 illustrates that the reaction was effective in the presence of a wide variety of functional groups on the aryl iodides, bromides, and chlorides, giving good to excellent conversions to the corresponding products, within 15–180 min. Earlier, Phan and co-workers reported on a polymer-supported salen type

Table 1
Heck reactions of aryl halides with olefins using Pd–salen complex **A**[a]

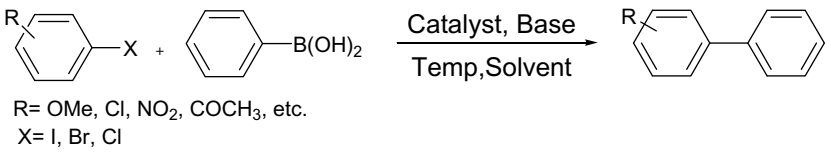
Entry	Aryl halide	Olefin	Product	Time (min)	Conversion[b] (%)
1				15	95
2				10	96
3				12	91
4				10	93
5				30	74
6				60	79
7				60	12
8				10	93
9				60	92
10				15	88
11				10	97
12				30	81
13				15	84
14[c]				30	89[d]
15				10	85

(*continued on next page*)

Table 1 (*continued*)

Entry	Aryl halide	Olefin	Product	Time (min)	Conversion[b] (%)
16				15	91
17				10	94
18				15	91
19				10	86
20				10	97
21				15	94
22				6 h	20
23				12 h	NR

[a] Conditions: aryl halide (1 mmol), olefin (3 mmol), triethylamine (3 mmol), DMF (4.0 mL), 0.5 mol % Pd catalyst **A**, 130 °C.
[b] Conversions were determined by GC ($\Delta_{rel} = \pm 5\%$).
[c] Reaction was monitored by TLC.
[d] Isolated yield after silica gel column chromatography (9:1 hexane/ethyl acetate).

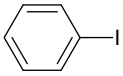
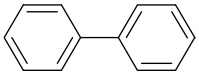
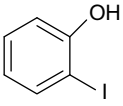
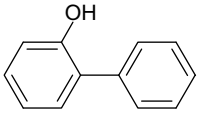
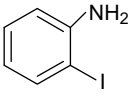
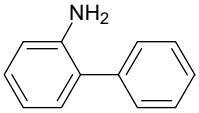
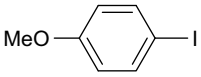
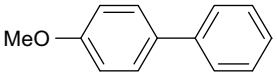
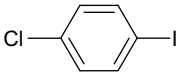
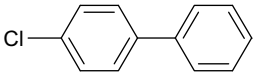
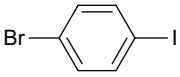
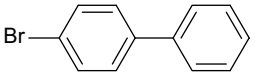
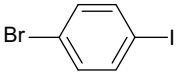
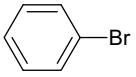
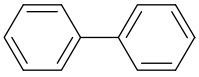
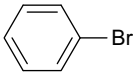
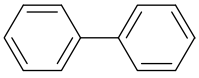
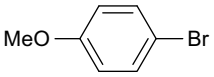
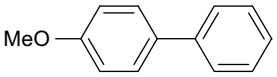
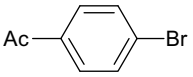
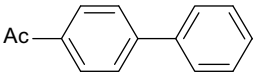
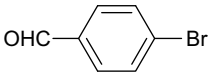
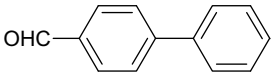
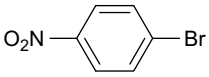
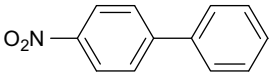
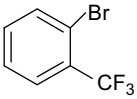
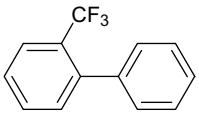


Scheme 3.

complex for the Suzuki reaction in 24 h at 90 °C under a nitrogen atmosphere.[17c] In our studies, the *ortho*-substituted aryl iodides required longer reaction times to give satisfactory conversions which might be due to steric hindrance. Complete regioselectivity was observed for 4-bromo and 4-chloroiodobenzene on reaction with 1.0 equivalent of phenyl boronic acid (entries 5 and 6). 4-Bromoiodobenzene gave the diarylated product on reaction with 2.2 equiv of phenyl boronic acid (entry 7). The less reactive chlorobenzene showed low conversion. However, the activated aryl chloride, 4-nitrochlorobenzene gave the corresponding product in moderate yield, using 1.0 mol % of palladium. The reaction of 2-bromopyridine with phenyl boronic acid resulted in a low yield of the product, which may be due to the coordination of the pyridine nitrogen with palladium metal (entry 17).

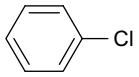
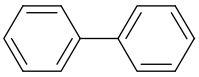
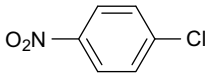
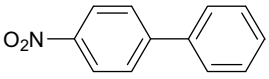
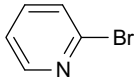
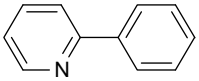
In summary, we have shown that the palladium–salen complex **A** efficiently catalyzes the Heck olefination of aryl

Table 2
Suzuki reaction of aryl halides with phenyl boronic acid using Pd–salen complex **A**[a]

Entry	Aryl halide	Product	Temp (°C)	Time (min)	Conversion[b]
1			100	15	100
2			100	60	72
3			100	60	47
4			100	60	84
5			100	60	96
6[c]			100	15	78
7[d]			100	120	83
8			100	120	87
9			110	90	88
10			110	90	94
11			110	30	100
12			110	30	100
13			110	60	81
14			110	90	51

(*continued on next page*)

Table 2 (*continued*)

Entry	Aryl halide	Product	Temp (°C)	Time (min)	Conversion[b]
15[e]			110	120	22
16[e]			110	180	48
17			110	90	28

[a] Conditions: substrate (1.0 mmol), phenyl boronic acid (1.25 mmol), base (2.0 mmol), DMF + H_2O (1:1), Pd (0.5 mol %).
[b] Conversions were determined by GC ($\Delta_{rel} = \pm 5\%$).
[c] 1.0 equiv of phenyl boronic acid were used.
[d] 2.2 equiv of phenyl boronic acid were used.
[e] 1.0 mol % of Pd was used.

iodides with various alkenes and the Suzuki cross coupling of aryl iodides, bromides, and activated chlorides with phenyl boronic acid under aerobic conditions.

2. Experimental

2.1. General procedure for the synthesis of Pd–salen complexes *A* and *B*

To a stirred solution of 2-hydroxybenzaldehyde (1 mmol) in 5 mL of methanol, 1,2-diamine (0.5 mmol ethylenediamine for complex **A** and phenylenediamine for complex **B**) was added dropwise and the reaction stirred for 20 min at room temperature. To the above solution, dichloromethane (DCM) (5 mL) was added to dissolve the formed precipitate. To this solution $Pd(OAc)_2$ (0.5 mmol) in DCM (5 mL) was added dropwise. The resulting reaction mixture was stirred for 18 to 20 h at room temperature and then allowed to cool to 0 °C. The product was filtered and washed with DCM and methanol to remove the unreacted ligand.

2.1.1. Complex *A*

(*N*,*N*′-Bis(salicylidene)-ethylenediamino-palladium), yield 76%, yellow solid, ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.19 (s, 2H), 7.36 (d, *J* 7.7 Hz, 2H), 7.28 (t, 2H), 6.81 (d, *J* 8.5 Hz, 2H), 6.54 (t, 2H), 3.82 (s, 4H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 59.5, 114.2, 120.2, 120.7, 134.3, 134.5, 160.2, 168.4. FTIR (cm^{-1}): 1629, 1600, 1446, 1192, 1136, 742. Mass: *m*/*z* 372, 325, 238, 132, 91, 77, 51. Anal. Calcd for $C_{16}H_{14}N_2O_2Pd$: C, 51.56; H, 3.79; N, 7.52. Found: C, 51.76; H, 3.75; N, 7.50.

2.1.2. Complex *B*

(*N*,*N*′-Bis(salicylidene)-1,2-phenylenediaminopalladium), yield 57%, brown solid, ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.18 (s, 2H), 8.31–6.70 (m, 12H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 115.1, 117.0, 120.5, 120.7, 128.0, 136.0, 136.1, 142.9, 154.7, 165.8. FTIR (cm^{-1}): 1626, 1444, 1319, 1197, 1145, 746. Mass: *m*/*z* 420, 313, 257, 210, 167, 106, 91, 77, 65, 44. Anal. Calcd for $C_{20}H_{14}N_2O_2Pd$: C, 57.09; H, 3.35; N, 6.66. Found: C, 57.34; H, 3.42; N, 6.58.

2.2. Typical experimental procedure for the Heck reaction

To a 20 mL two neck round-bottom flask were added aryl halide (1 mmol), olefin (3 mmol), triethylamine (3 mmol), and Pd–salen complex (0.5 mol %) and 4.0 mL of DMF. The reaction mixtures were heated at 130 °C for the appropriate time.

2.3. Typical experimental procedure for the Suzuki reaction

To a 20 mL two neck round-bottom flask were added aryl halide (1 mmol), phenyl boronic acid (1.25 mmol), Na_2CO_3 (2 mmol), and Pd–salen complex **A** (0.5 mol %) in DMF−H_2O (1:1), and the reaction mixtures were heated at the appropriate temperatures and durations.

Both reactions were monitored by gas chromatography. After the completion of the reaction, the mixture was extracted with ethyl acetate three times. The combined organic extracts were dried over anhydrous sodium sulfate solvent evaporated on reduced pressure. The crude products were purified by column chromatography [hexane or hexane/ethyl acetate (9:1)]. The products were analyzed by GC, GCMS, FTIR, and NMR.

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