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Note

Application of dimeric cyclopalladated complex of tribenzylamine as an efficient catalyst in the Heck cross-coupling reaction

Abdol R. Hajipour^{a, b, *}, Fatemeh Rafiee^a

^a Pharmaceutical Research Laboratory, Department of Chemistry, Isfahan University of Technology, Isfahan 84156, Islamic Republic of Iran ^b Department of Pharmacology, University of Wisconsin, Medical School, 1300 University Avenue, Madison, WI 53706-1532, USA

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ABSTRACT

The activity of $[Pd\{C_6H_4(CH_2N(CH_2Ph)_2)\}$ (µ-Br)]₂ complex was investigated in the Heck–Mizoroki C–C cross-coupling reaction. This complex is an active and efficient catalyst for the Heck reaction of aryl iodides, bromides and even chlorides and also arenesulfonyl chlorides. The cross-coupled products were produced in excellent yields in short reaction time using a catalytic amount of $[Pd\{C_6H_4(CH_2N(CH_2Ph)_2) (\mu-Br)]_2$ complex in NMP at 130 °C.

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1. Introduction

The formation of carbon-carbon bonds is a fundamental reaction in organic synthesis due to many vast applications in the areas of bioactive compounds, natural products and high performance materials. The Heck coupling, one of the most important palladium-catalyzed C-C bond formation reactions, is a process also described as olefin arylation. The Heck reaction has received considerable attention, primarily due to the enormous synthetic potential to generate sp²-sp² carbon-carbon bonds [1]. However, the reaction suffers from limitations that have so far precluded many industrial applications [2]. Typically, a relatively large amount of catalyst (1-5 mol%) is needed for reasonable conversions and often catalyst recycling is hampered. Various approaches towards catalyst improvement have been described [3]. Most effort was reported to be achieved with activated, electron-poor chloroarenes using highly basic, sterically hindered phosphanes [4], the use of a large excess of coordinating ligands, for example, triphenylphosphane [5] or tris(2,4-di-tert-butylphenyl)phosphate (tbp) [6], the use of heterogeneous Pd/C [7] or Pd/MgO [8], or the use of nanostructured palladium clusters [9], the use of N-heterocyclic carbenes (NHC) [10] and the use of palladacycles [11,12].

E-mail address: haji@cc.iut.ac.ir (A.R. Hajipour).

Cyclopalladated complexes are important starting materials in organometallic chemistry [13,14]. Palladacycles have been known for over 30 years [15–20] and have been acquiring great interest due to their applications in many areas, including organic synthesis [21-24], material science [25], biologically active compounds [26] and as building blocks in macromolecular chemistry [27-29]. Cyclopalladated complexes exhibit a superior catalytic efficiency in cross-coupling reactions. In particular, the phospa-palladacycles introduced by Herrmann have found application in a wide variety of palladium-catalyzed reactions [1]. Phosphine ligands, especially the electron-rich phosphines, are often toxic and sensitive to air and moisture. Bedford et al. also showed that phosphinite palladacycles exhibited better activity than structurally similar phosphite and phosphine complexes [22]. Consequently, the search for easy handling, active, thermally stable and low-cost catalysts caused the development of phosphine-free palladium catalysts such as palladium complexes bearing nitrogen-donor ligands [30]. For several years only aryl iodides and aryl bromides were employed in Heck reaction. Different efforts have been down to find better catalysts for coupling aryl chlorides as readily available and industrially important compounds by Heck reaction. The aryl chlorides react very slowly by palladium catalysts [31,32] due to the strength of the C-Cl bond which delays the oxidation addition to Pd(II) complexes [33,34]. Heck reaction of aryl chlorides with olefins was carried out by using additives containing tetraalkylammonium or tetraalkylphosphonium salts at higher temperature and

^{*} Corresponding author. Pharmaceutical Research Laboratory, Department of Chemistry, Isfahan University of Technology, Isfahan 84156, Islamic Republic of Iran. Tel.: +98 311 391 3262; fax: +98 311 391 2350.

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Scheme 1. The Heck–Mizoroki cross-coupling reaction of aryl halides with olefins by a cyclopalladated complex **A**.

high loadings of complex in long reaction times [10]. The activity with aryl chloride substrates can be greatly improved using cyclopalladated complexes as thermally stable catalyst [35–40].

In a continuation of our recent investigations on the application of the palladacycle systems in Heck reactions [41–43] and cyanation reactions [44,45], we now wish to report the extension of [Pd{ $C_6H_4(CH_2N(CH_2Ph)_2)$ (µ-Br)]_2 complex, as an efficient, thermally stable and non-sensitive to air and moisture catalyst for Heck coupling reaction of various types of aryl halides under traditional heating (Scheme 1).

2. Results and discussion

Cyclopalladation of tribenzylamine proceeds in benzene at 80 °C when the amine is heated with an equimolar amount of palladium(II) acetate. Tribenzylamine did not produce isolable bis-amine complex owing to the three bulky benzyl groups on the nitrogen atom, whereas less sterically demanding amines, for example, monobenzylamine coordinated palladium much more tightly, preventing the conversion of the bis-amine adduct to the cyclopalladated complex. $[Pd\{C_6H_4(CH_2N(CH_2Ph)_2)\} (\mu-Br)]_2$ (**A**) as a palladacycle complex was prepared according to the literature [46] and its application in Heck coupling reaction was studied.

The application of palladacycle **A** as a catalyst for the Heck crosscoupling reaction was examined by optimizing both base and solvent effects. The reaction of 4-*bromoacetophenone* with methylacrylate using palladacycle **A** as the catalyst was carried out in various solvents and organic and inorganic bases under conventional heating at 130 °C, as shown in Table 1.

We found that K_2CO_3 as base and *N*-methyl-2-pyrrolidone (NMP) as solvent gave the best results (Table 1, entry 4). Various catalyst concentrations were also tested (Table 2, entry 5) and 0.1 mol% gave the best result.

These optimized reaction conditions were applied in the Heck cross-coupling reaction of different types of aryl halides with

Table 1Optimization of base and solvent under conventional heating in an oil bath.^a

Entry	Solvent	Base	Temperature (°C)	Time (min)	Conversion (%)
1	NMP	Et ₃ N	130	120	0
2	NMP	Cs ₂ CO ₃	130	120	30
3	NMP	Na_2CO_3	130	120	40
4	NMP	K ₂ CO ₃	130	40	100
5	NMP	CH₃COONa	130	40	90
6	DMF	K ₂ CO ₃	130	120	90
7	CH ₃ CN	K ₂ CO ₃	80	120	0
8	Toluene	K ₂ CO ₃	110	3	0

^a Reaction conditions: 1 mmol 4-bromoacetophenon, 2.2 mmol methylacrylate, 1.1 mmol base, 0.1 mol% palladacycle.

Гa	able 2	
D	ptimization of catalyst concentration under conventional	heating.a

Entry	Catalyst (mol%)	Time (min)	Temperature (°C)	Conversion (%)
1	None	120	130	0
2	0.01	120	130	40
3	0.03	120	130	60
4	0.05	120	130	90
5	0.1	40	130	100
6	0.2	40	130	100

 $^{\rm a}$ Reaction conditions: 1 mmol 4-bromoacetophenon, 2.2 mmol methylacrylate, 1.1 mmol $K_2 CO_3,$ 3 ml NMP and palladacycle.

different olefins under conventional heating at 130 $^\circ\text{C}$, as shown in Table 3.

The results showed that aryl halides with either electronwithdrawing or electron-donating substituents reacted with olefins rapidly and generated the coupled products with excellent yields. The coupling reactions with acrylates as the olefin were faster than styrene and methylstyrene.

The ideal substrates for coupling reactions are aryl chlorides, since they tend to be cheaper and more widely available than their bromide or iodide counterparts. Unfortunately, the high C–Cl bond strength compared with C–Br and C–I bonds disfavour oxidative addition, the first step in catalytic coupling reactions. The most reported catalyst needed to be used in high loadings, and they show little or no activity with aryl chloride substrates.

Furthermore, as shown in Table 3 (entries 13-15, 32-34) the catalytic amount of palladacyclic complex **A** can be used in the Heck coupling of even less reactive aryl chloride derivatives with olefins in good yields.

Although this procedure could active CeCl, however in the compounds containing both Br and Cl substituent, by using a stoichiometric amount of olefins only the Br was substituted, which may be due to the higher activity of Br compared with Cl.

Arenesulfonyl chlorides could be used as electrophilic partners under desulfinylation conditions in place of aryl halides (Table 3, entries 16, 35, 36 and 40). Arenesulfonyl chlorides are inexpensive and readily available compounds and more reactive than corresponding bromides and chlorides. The reactive Pd^0 catalyst undergoes oxidative addition of the SO₂–Cl bond to give first a chloro palladium^{II} sulfinate (Ar–SO₂–Pd^{II}–Cl). Desulfinylation occurs rapidly at high temperature (130 °C) and R–Pd–Cl complex forms, which is followed by the reversible coordination of the olefin to it. The Pd^0 formed in the main catalytic cycle, after β -hydride and reductive elimination steps [47].

Production of exclusively the trans isomers and complete conversions by this method are great advantages of the presented catalyst.

3. Experimental

3.1. General

¹H NMR spectra were recorded at 500 and 400 MHz in CDCl₃ solutions at room temperature on a Bruker, Avance 500 instrument (Rheinstetten, Germany) and Varian 400 NMR (TMS was used as an internal standard). The FT-IR spectra were recorded on a spectro-photometer (Jasco-680, Japan). Furthermore, we used GC (BEIFIN 3420 Gas Chromatograph equipped a Varian CP SIL 5CB column – 30 m, 0.32 mm, 0.25 μ m) for examination of reaction completion and yields. All chemical materials were purchased from Merck and Aldrich and were used as received.

Table 3 Heck reacti	ion of arvl ha	lides under conventional heating conditions in an oil bath.
	A	
EIIIIV	AľX	K'CH=CH ₂

Entry	ArX	R'CH=CH2	Product	Time (min)	Yield (%)
1	$X = I, Br, Cl, SO_2Cl$ (Respectively)	OMe	O OMe O U	20 35 110 50	96 94 80 93
2		OMe	H O	60	90
3	OMe	OMe	MeO OMe	25	96
4	Cl	OMe	CI OMe	35	95
5	Cl	OMe	OMe	40	90
6	Br	OMe	OMe	100	87
7	NC	OMe	O OMe NC	35	95
8	$H_{3}C$ X = Br, Cl (Respectively)	OMe	H ₃ C O O	40 80	93 85
9	H ₃ C Br	OMe	H ₃ C OMe	70 (continued o	87 on next page)

Table 3 (continued)



Table 3 (continued)

Entry	ArX	R'CH=CH ₂	Product	Time (min)	Yield (%)
19	Cl		CI	45	92
20	CI Br		CI	60	90
21	$H_{3}C$ $X = Br, Cl$ (Respectively)		H ₃ C	65 110	91 83
22	H ₃ C Br		H ₃ C	120	80
23	CH ₃		CH ₃	200	67
24	NC		NC	70	92
25	Br			140	85
26	Br			200	87
27	H ₃ C SO ₂ Cl		H ₃ C	110 (continued o	90 on next page)

Table 3 (continued)



3.2. General procedure for Heck cross-coupling reaction

In a round-bottom flask equipped with a magnetic stirring bar to a mixture of K_2CO_3 (1.1 mmol), olefin (2.2 mmol) and aryl halide (1 mmol) in NMP (3 ml) were added 0.1 mol% of palladacycle complex (**A**) and equipped with a condenser for refluxing. The above mixture was heated at 130 °C in an oil bath. The reaction's progress was monitored by TLC (hexane/EtOAc, 80:20) and gas chromatography (GC). After completion of the reaction the mixture was diluted with n-hexane and water. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by recrystallization from ethanol and water. The products were characterized by comparing their m.p., IR, ¹H, ¹³C NMR spectra with those found in the literature [41–43].

4. Conclusion

Using dimeric orthopalladate complex [Pd $\{C_6H_4(CH_2N(CH_2Ph)_2)\}$ (µ-Br)]₂ as an efficient catalyst for Heck reaction of aryl bromides, aryl iodides, aryl chlorides and arene-sulfonyl chlorides was reported. The catalytic amount of palladium complex in NMP at 130 °C led to C–C bond formation and corresponding products were produced in good yields.

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