APPLIED ORGANOMETALLIC CHEMISTRY
Appl. Organometal. Chem. 2007; **21**: 641–644

2-Iminopyridylpalladium dichloride as highly active catalyst for the Heck reaction

Weixuan Chen, Chanjuan Xi* and Ke Yang

Key Laboratory for Bioorganic Phosphorus Chemistry and Chemical Biology (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, People's Republic of China

Received 3 February 2007; Accepted 5 February 2007

Heck reactions of bromoarenes with various olefins catalyzed by 2-iminopyridylpalladium (II) have been investigated. The scope of a coupling reaction has been tested in 1-methyl-2-pyrrolidinone at 140 °C using K_2CO_3 as base. Using 0.1% molar ratio of palladium catalysts, aryl bromides were converted into 1,2-substitutedethene products in good to high yields through coupling with both vinylarenes and alkylolefins. With butyl vinyl ether, an electron-rich olefin, however, the effective coupling reaction produced a mixture of two regio-isomers, 1,2- and 1,1-substitutedethenes. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: Heck coupling; palladium catalysts; iminopyridines; catalysis

INTRODUCTION

The Heck reaction is one of the most widely used carbon–carbon bond formation reactions catalyzed by palladium compounds in organic synthesis.[1–11] The reactions are commonly carried out in the presence of phosphine ligands, for example in the reported work by the groups of Fu,[12,13] Beller[14] and Hartwig,[15] who have made use of sterically demanded electron-rich tertiary phosphines as catalyst modifiers as well as palladacycles formed by the reaction of $Pd(OAc)_2$ and tris(*o*-tolyl)phosphine.[16–18] Palladium catalysts containing modified ligands could activate the coupling reactions with less reactive aryl bromides and aryl chlorides as well as nonactivated alkenes.[16–19] Beyond the consideration of negative environmental effect of phosphine, however, the phosphine (III) compounds are generally air-sensitive and multi-synthetic phosphine ligands add cost to the palladium catalyst. Therefore, the development of phosphine-free catalysts for Heck reaction would be important for academic and industrial applications, and some progress has appeared in the literature.[20–29] Much less attention has been paid to phosphine-free nitrogen-based palladium catalysts with bidentate *N,N*-ligands such as diimine,[30] dipyridine[31–36] and hydrazone.[37] In addition, palladium compounds ligated by iminopyridyines were proven to be efficient catalyst precursors for the ethylene oligomerization and polymerization reaction,[38,39] but limited results without detail investigation on the Heck reaction have been reported.[40,41] A series of 2-iminopyridyl palladium(II) chlorides were investigated for the Heck cross-coupling reaction and highly effective activities were observed. Herein the detail investigation and results are reported and discussed.

RESULTS AND DISCUSSION

The pyridyl-imine based palladium(II) complexes **1–7** have been prepared by the reaction of $PdCl_2(MeCN)_2$ with various pyridyl-imine ligands in dichloromethane.[40,41] The spectroscopic data and the elemental analyses are in agreement with structures depicted in Fig. 1. Complexes **1–7** have been tested as catalysts in the model reaction of bromobenzene with methyl acrylate under nitrogen atmosphere to determine the optimum reaction conditions (Table 1). In the presence of catalyst **1**, Heck cross coupling product **8** was obtained in high yield (entry 1). The effect of catalysts **1–7** in this reaction was investigated (entries 1–7). Although the catalyst **3, 6** and **7** were also effective for the Heck reaction, the use of **2** as catalyst led to a higher yield for this reaction (entry 2). In general, the difference in reactivity of these palladium complexes can be attributed to the electron-donating ability of substituent of the benzene

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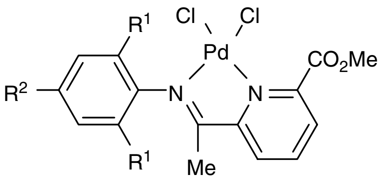
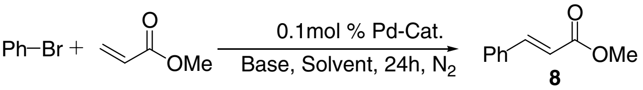
*Correspondence to: Chanjuan Xi, Department of Chemistry, Tsinghua University, Beijing 100084, People's Republic of China.
E-mail: cjxi@tsinghua.edu.cn
Contract/grant sponsor: National Natural Science Foundation of China; Contract/grant number: 20572058.



1. R^1 = Me, R^2 = H
2. R^1 = Me, R^2 = Me
3. R^1 = *i*-Pr, R^2 = H
4. R^1 = F, R^2 = H
5. R^1 = Cl, R^2 = H
6. R^1 = Br, R^2 = H
7. R^1 = Br, R^2 = Me

Figure 1. 2-Iminopyridylpalladium (II) complexes.

Table 1. Optimization of reaction conditions on Heck reaction of bromobenzene with methyl acrylate[a]



Entry	Catalyst	Base	Solvent	Temperature (°C)	Yield (%)
1	1	K_2CO_3	NMP	140	81
2	2	K_2CO_3	NMP	140	97
3	3	K_2CO_3	NMP	140	91
4	4	K_2CO_3	NMP	140	11
5	5	K_2CO_3	NMP	140	23
6	6	K_2CO_3	NMP	140	70
7	7	K_2CO_3	NMP	140	82
8	2	K_3PO_4	NMP	140	42
9	2	Pip	NMP	140	Trace
10	2	CsF	NMP	140	50
11	2	K_2CO_3	DMF	130	33
12	2	K_2CO_3	Toluene	110	NR
13	2	K_2CO_3	CH_3CN	80	NR

[a] Reaction conditions: bromobenzene (1 mmol), methyl acrylate (2.5 mmol) base (1.1 mmol), solvent (3 ml), catalyst (0.001). [b] NMR yields.

ring. Using K_2CO_3 as a base, the reaction gave a high yield of the desired product (entry 2 vs entries 8–10). When K_3PO_4 and CsF were used as base instead of K_2CO_3, the desired product was obtained in moderate yield (entries 8 and 10). When an organic base such as Pip (piperidine) was used as base, trace amount of product was obtained (entry 9). In this condition, several commonly used solvents were tested (entries 11–13). Solvents such as toluene and CH_3CN were not effective (entries 12 and 13) for this reaction. DMF was also not effective (entry 11). We found the following optimized conditions: using the catalyst **2**, the reaction proceeded with 97% in 1-methyl-2-pyrrolidinone (NMP) with K_2CO_3 at 140 °C for 24 h under nitrogen atmosphere (entry 2). In addition, these complexes were not sensitive to oxygen or moisture; no change in their reaction efficiencies was observed even if the Heck reactions were carried out under aerobic conditions.

The results of the catalytic Heck reaction of aryl bromides and olefins using pyridyl-imine based catalyst **2** are summarized in Table 2.

First, we investigated the effect of varying the olefins in the Heck reaction using 1-bromobenzene as substrate under the optimized reaction conditions (entries 1–10). Styrene or *para*-substituted styrene led to excellent yields of the desired products (entries 1 and 2). 4-Vinylpyridine also gave a high yield of the Heck reaction product (entry 3). Using acrylate led to excellent yields of the desired product (entries 4 and 5). The above-mentioned reactions proved highly regioselective (>99 : 1 *E* selectivity). It is noteworthy that this catalytic system was also active for simple linear alkenes such as oct-1-ene, which led to 1-aryl substituted alkenes as major products in good to high yields (entries 6–9). We also tried the coupling reaction using electron-rich olefins such as 1-(vinyloxy)butane. Although the reaction proceeded smoothly, the desired internal olefin was obtained along with terminal olefin in 1 : 1 ratio, according to ^1H NMR analysis (entry 10). We next investigated the effect of neutral and activated aryl bromides in the Heck reaction using styrene as substrate (entries 1 and 11–13). The use of 4-substituted aryl bromides also led to excellent yields of the Heck reaction products (entries 11 and 12). Using 1-bromonaphthalene resulted in good yield of the desired product (entry 13).

CONCLUSIONS

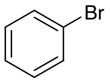
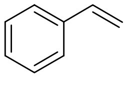
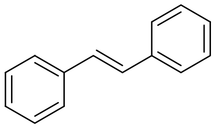
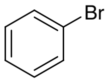
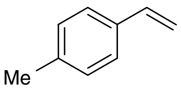
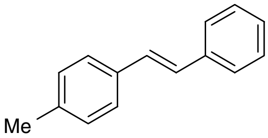
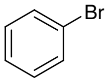
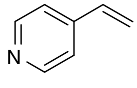
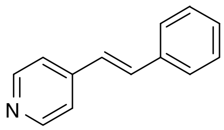
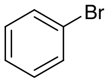
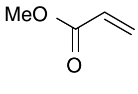
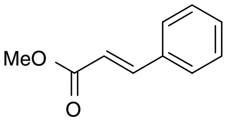
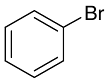
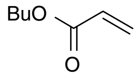
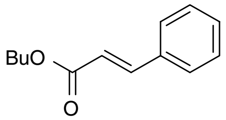
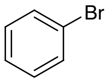
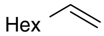
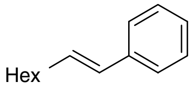
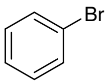
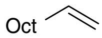
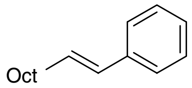
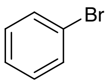
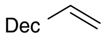
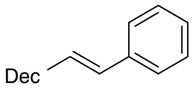
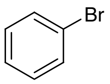
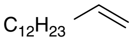
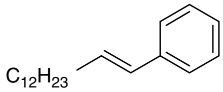
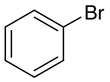
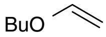
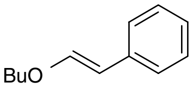
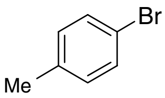
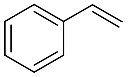
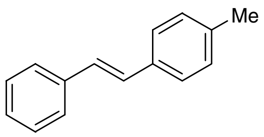
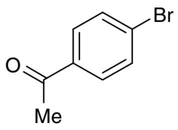
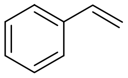
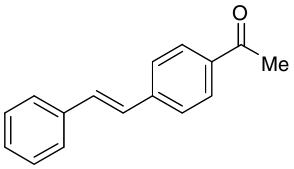
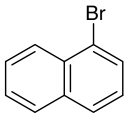
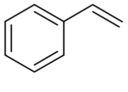
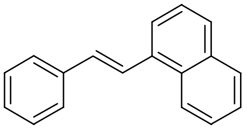
It can be concluded that the Heck reaction of aryl bromides and olefins can be performed under phosphine-free conditions based on Pd(II) catalyst with pyridyl-imine ligand. This catalyst system is air-, water- and heat-stable. With electron-rich olefin, mixtures of two isomers (1,2- and 1,1-substitutedethene) are obtained. With the other olefins, the major isomer is 1,2-substitutedethene.

EXPERIMENTAL

General

All manipulations were conducted in a Schlenk tube and under nitrogen with a slightly positive pressure. GC analyses were preformed on a gas chromatograph equipped with a flame ionization detector using a capillary column (CBP1-M25-025). The GC yields were determined using suitable hydrocarbons as internal standards. Unless otherwise noted, all starting materials were commercially available and were used without further purification. ^1H NMR and ^{13}C NMR spectra were recorded on Jeol 300 NMR spectrometer with TMS as internal standard. Elemental analyses were performed on a Flash EA 1112 instrument. Melting points were determined with a digital electrothermal apparatus without calibration. The IR spectra were obtained on a Perkin–Elmer FT-IR 2000 spectrophotometer using the KBr disc in the range 4000–400 cm^{-1}.

Table 2. Heck reaction of aryl bromide with olefin using pyridyl-imime based catalyst **2a**[a]

Entry	Aryl bromide	Olefin	Time (h)	Product	Yield (%)[b]	TON[c]
1			12		99 (98)	990
2			12		99 (81)	990
3			12		94 (75)	940
4			24		97(85)	970
5			24		97(82)	970
6			24		94 (86)	940
7			24		78(50)	780
8			24		81(59)	810
9			24		83 (65)	830
10			12		99 (60)[d]	990
11			12		99	990
12			12		99 (80)	990
13			12		85 (60)	850

[a] Reaction conditions: aryl bromide (1 mmol), olefin (2.5 mmol), K_2CO_3 (1.1 mmol), NMP (5 ml), catalyst **2** (0.001 mmol). [b] NMR yields, isolated yields were given in parentheses. [c] TON = mol of product/mol of the catalyst. [d] Regioselectivity as determined by ^{1}H NMR spectroscopic analysis, 1 : 1 ratio of internal : terminal alkene products.

General procedure for the synthesis of palladium complexes 1–7

All the 2-ethoxycarbonyl-6-iminopyridines and their palladium complexes were prepared according to the literature method.[41–43] Herein only the synthesis of palladium complex **2** is described in detail as an example.

To ligand **L2** (0.296 g, 1 mmol) and $PdCl_2(CH_3CN)_2$ (0.259 g, 1.0 mmol) was added 10 mL freshly distilled dichloromethane at room temperature. The reaction mixture was stirred for 24 h, and 10 mL diethyl ether was added to precipitate the complex. The desired complex, ethyl 6-[1-(mesitylimino)ethyl]picolinate palladium dichloride **2** (0.384 g, 0.81 mmol) was obtained in 81% yield. IR (Nujol, cm^{-1}): 1741 ($COOCH_3$); 1586, 1612 (C=N). ^1H NMR (d6-DMSO) δ 8.23 (d, 1H, Py-H), 8.13 (m, 2H, Py-H), 6.91 (s, 2H, Ar-H), δ 3.90 (s, 3H, OCH_3), 2.19 (s, 6H, *o*–Ar–CH_3), 2.13 (s, 3H, *p*-Ar-CH_3), 1.87 (s, 3H, N=C–CH_3); ^{13}C NMR (d6-DMSO): δ 167.2, 165.4, 156.3, 153.4, 147.5, 146.2, 139.3, 138.5, 32.1, 130.1, 128.9, 126.8, 124.9, 53.4, 21.1, 18.9, 18.6, 18.0. Anal. calcd for $C_{19}H_{22}Cl_2N_2O_2Pd \cdot CH_2Cl_2$: C, 40.85; H, 3.97; N, 5.01. Found: C, 40.69; H, 3.95; N, 5.05. NMR data for complexes **1** and **3–7** were in accordance with literature values.[41]

Heck reaction

General procedure

Under nitrogen atmosphere, K_2CO_3 (1.1 mmol), olefin (2.5 mmol), aryl bromide (1 mmol) and NMP (5 ml) were added in turn to a Schlenk tube equipped with a magnetic stirring bar. A 20 µl NMP solution containing 0.002 mmol of complex (about 1.1 mg) was added to the Schlenk tube. The mixture was stirred at 140 °C and monitored by GC. After 12–24 h, the mixture was quenched by 1N HCl and extracted by ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using petroleum ether or mixture of petroleum ether and ethyl acetate.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (20572058). We thank Mr Peng Hao for his kind discussions.

REFERENCES

1. Negishi E. *Handbook of Organopalladium Chemistry for Organic Synthesis*, Vol. 1. Wiley-Interscience: New York, 2002; 1133.
2. Whitcombe NJ, Hii KK, Gibson SE. *Tetrahedron* 2001; **57**: 7449.
3. Beletskaya IP, Cheprakov AV. *Chem. Rev.* 2000; **100**: 3009.
4. Hegedus LS. *Transition Metals in the Synthesis of Complex Organic Molecules*, 2nd edn. University Science Books: Sausalito, CA, 1999; Chapter 4.6.
5. Brase S, de Meijere A. *Metal-catalyzed Cross-coupling Reactions*, Diederich F, Stang PJ (eds). Wiley-VCH: Weinheim, 1998; Chapter 3.
6. Link JT, Overman LE. *Metal-catalyzed Cross-coupling Reactions*, Diederich F, Stang PJ (eds). Wiley-VCH: Weinheim, 1998; Chapter 6.
7. Crisp GT. *Chem. Soc. Rev.* 1998; **27**: 427.
8. Cabri W, Candiani I. *Acc. Chem. Res.* 1995; **28**: 2.
9. Mizoroki T, Mori K, Ozaki A. *Bull. Chem. Soc., Jpn* 1971; **44**: 581.
10. Dieck HA, Heck RF. *J. Am. Chem. Soc.* 1974; **96**: 1133.
11. Dieck HA, Heck RF. *J. Org. Chem.* 1975; **40**: 1083.
12. Littke AF, Fu GC. *J. Org. Chem.* 1999; **64**: 10.
13. Littke AF, Fu GC. *J. Am. Chem. Soc.* 2001; **123**: 6989.
14. Ehrentraut A, Zapf A, Beller M. *Synlett* 2000; 1589.
15. Shaughnessy KH, Kim P, Hartwig JF. *J. Am. Chem. Soc.* 2001; **123**: 2123.
16. Spencer A. *J. Organomet. Chem.* 1983; **258**: 101.
17. Herrmann WA, Brossmer C, Öfele K, Reisinger CT, Priermeier T, Beller M, Fischer H. *Angew. Chem., Int. Edn Engl.* 1995; **34**: 1844.
18. Zapf A, Beller M. *Chem. Eur. J.* 2001; **13**: 2908.
19. Berthiol F, Doucet H, Santelli M. *Tetrahedron Lett.* 2003; **44**: 1221.
20. Herrmann WA, Elison M, Fischer J, Köcher C, Artus GRJ. *Angew. Chem., Int. Edn Engl.* 1995; **34**: 2371.
21. Ohff M, Ohff A, Milstein D. *Chem. Commun.* 1999; 357.
22. Tulloch AAD, Danopoulos AA, Tooze RP, Cafferkey SM, Kleinhenz S, Hursthouse MB. *Chem. Commun.* 2000; 1247.
23. Gruber AS, Zim D, Ebeling G, Monteiro AL, Dupont J. *Org. Lett.* 2000; **2**: 1287.
24. Peris E, Loch JA, Mata J, Crabtree RH. *Chem. Commun.* 2001; 201.
25. Bergbreiter DE, Osburn PL, Liu Y-S. *J. Am. Chem. Soc.* 1999; **121**: 9531.
26. Reetz MT, Westermann E. *Angew. Chem., Int. Edn* 2000; **39**: 165.
27. Reetz MT, Westermann E, Lohmer R, Lohmer G. *Tetrahedron Lett.* 1998; **39**: 8449.
28. Vries AHM, Mulders JMCA, Mommers JHM, Henderickx HJW, Vries JG. *Org. Lett.* 2003; **5**: 3285.
29. Widegren JA, Finke RG. *J. Mol. Chem. A: Chem.* 2003; **198**: 317.
30. Grasa GA, Singh R, Stevens ED, Nolan SP. *J. Organomet. Chem.* 2003; **687**: 269.
31. Cabri W, Candiani I, Bedeschi A, Santi R. *J. Org. Chem.* 1993; **58**: 7421.
32. Buchmeiser MR, Wurst K. *J. Am. Chem. Soc.* 1999; **121**: 11101.
33. Silberg J, Schareina T, Kempe R, Wurst K, Buchmeiser MR. *J. Organomet. Chem.* 2001; **622**: 6.
34. Buchmeiser MR, Schareina T, Kempe R, Wurst K. *J. Organomet. Chem.* 2001; **634**: 39.
35. Kawano T, Shinomaru T, Ueda I. *Org. Lett.* 2002; **4**: 2545.
36. Nájera C, Gil-Moltó J, Karlström S, Falvello LR. *Org. Lett.* 2003; **5**: 1451.
37. Mino T, Shirae Y, Sasai Y, Sakamoto M, Fujita T. *J. Org. Chem.* 2006; **71**: 6834.
38. Chen R, Mapolie SF. *J. Mol. Catal. A: Chem.* 2003; **193**: 33.
39. Zhang W, Sun W-H, Wu B, Zhang S, Ma H, Li Y, Chen J, Hao P. *J. Organomet. Chem.* 2006; **691**: 4759.
40. Pelagatti P, Carcelli M, Costa M, Lanelli S, Pelizzi C, Rogolino D. *J. Mol. Chem. A: Chem.* 2005; **226**: 107.
41. Clark JH, Macquarrie DJ, Mubofu EB. *Green Chem.* 2000; **2**: 53.
42. Tang X, Sun W-H, Gao T, Hou J, Chen J, Chen W. *J. Organomet. Chem.* 2005; **690**: 570.
43. Sun W-H, Tang X, Gao T, Wu B, Zhang W, Ma H. *Organometallics* 2004; **23**: 5037.

DOI: 10.1002/aoc