Palladium(II) Complexes with Phosphorus−Nitrogen Mixed Donors. Efficient Catalysts for the Heck Reaction

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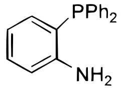
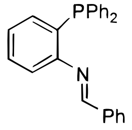
Summary: Pd(II) complexes of phosphine−nitrogen (P−N) bidentate donors act as efficient catalysts for the Heck reaction. In a typical example, reaction of phenyl iodide with methyl acrylate in N-methylpyrrolidinone (NMP) at ca. 130 °C provides the Heck product with a turnover number of up to 10^6. In addition, the coupling reaction of 4-bromoacetophenone with olefin in a quantitative yield was achieved by using the same catalyst in the presence of sodium iodide.

Introduction

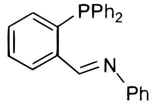
Olefination of aryl halides, known as the Heck reaction, is an important transition-metal-catalyzed reaction for organic synthesis.[1] The discovery of efficient palladium complexes for this reaction has been received much attention due to their industrial applications. It is reported that Pd(II) complexes of common P−P or N−N bidentate ligands are generally less active.[2] However, Shaw and co-workers recently demonstrated that palladium complexes of chelating diphosphines are excellent catalysts.[3] Other ligand combinations of palladium(II) providing good catalytic activity are cyclometalated phosphines[4] and imines,[5] carbene,[6] and dimethylglycine,[7] but mixed phosphorus−nitrogen donors as ligands in the Heck reaction have rarely been reported. We are currently involved in developing palladium-based catalysts with bidentate phosphine−imine (P−N) ligands, in which imine acts as a weak π-acceptor and phosphine as a good σ-donor, and demonstrated that palladium complexes with the mixed donor system $\mathbf{L_2}$ show unusual influence in stabilizing the insertion product.[8] Here we investigate the high catalytic activity of the palladium complexes associated with the ligands $\mathbf{L_1}$−$\mathbf{L_3}$ in the Heck reaction.



L_1



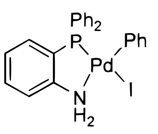
L_2



L_3

Results and Discussion

Palladium(II) Complexes. Palladium complexes [(L_n)PdPhI] (**1**, $n = 1$; **2**, $n = 2$; **3**, $n = 3$) are readily prepared by oxidative addition of phenyl iodide to a mixture of Pd(dba)$_2$ and the corresponding ligand in THF solution. All these complexes are stable in air and can be handled in the atmosphere. Formation of only one isomer, in which the phenyl ligand is cis to the phosphine donor, is evident from the appearance of a single phosphorus signal in ^{31}P NMR spectra and the crystal structures of **2** and **3**. This stereoarrangement is in general agreement with the reported [Pd(P−N)-RX] complexes.[9]



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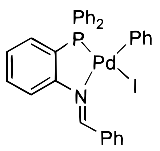

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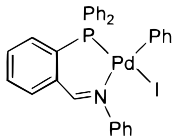

3

Heck Reaction. In a typical experiment for the reaction, aryl halides, olefins, and triethylamine in a 1:1.5:1 ratio were added to a freshly distilled *N*-methylprrolidinone (NMP) solution, followed by the addition of the catalyst. The mixture was heated in an oil bath for the specified temperature and time. After the reaction was stopped, the reaction mixture was diluted with dichloromethane and washed with 5 N HCl and water. The organic portion was separated, dried with Na$_2$SO$_4$, and concentrated. The desired product was either characterized by ^{1}H NMR spectroscopy directly or separated by column chromotography. All of the results are summarized in Table 1.

Complete conversions of phenyl iodide and methyl acrylate into methyl cinnamate were observed with catalysts **1** and **3** at various temperatures (110−130 °C),

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Table 1. Results of the Heck Reaction Catalyzed by [(P−N)PdPhI]

entry	ArX (amt, mmol)	alkene (amt, mmol)	catalyst (amt, mmol)	*t* (h)	temp, °C	yield (%) (TON)
1	PhI (10)	MA (15)	**1** (3.5×10^{-5})	21	120	100 (285 700)[a]
2	PhI (50)	MA (75)	**1** (3.5×10^{-5})	137	120	55 (785 700)[a]
3	PhI (10)	styrene (15)	**1** (3.5×10^{-5})	22	120	36 (102 800)[b]
4	PhI (10)	MA (15)	**2** (3.5×10^{-5})	22	120	53 (151 400)[a]
5	PhI (50)	styrene (75)	**2** (3.5×10^{-4})	48	130	80 (114 800)[b]
6	PhI (10)	MA (15)	**3** (3.5×10^{-5})	22	130	100 (285 700)[a]
7	PhI (10)	MA (15)	**3** (3.5×10^{-5})	22	110	100 (285 700)[a]
8	PhI (50)	MA (75)	**3** (3.5×10^{-5})	168	130	80 (1 142 800)[a]
9	bap (10)	MA (15)	**2** (3.5×10^{-4})	94	140	43 (12 285)[a]
10[g]	bap (10)	MA (15)	**2** (3.5×10^{-4})	94	140	100 (28 570)[a,c]
11[g]	bap (10)	styrene (15)	**2** (3.5×10^{-4})	97	140	100 (28 570)[a]
12[g]	bap (10)	MA (15)	**1** (3.5×10^{-4})	70	130	100 (28 570)[a,c]
13[g]	bap (10)	styrene (15)	**1** (3.5×10^{-4})	95	130	40 (11 428)[a]
14[g]	bap (10)	MA (15)	**3** (3.5×10^{-4})	70	120	50 (14 285)[a,d]
15[g]	bap (10)	MA (15)	**2** (3.5×10^{-5})	70	140	35 (100 000)[a,e]
16[g]	bnb (10)	styrene (15)	**2** ($3.5 \times 10^{-.3}$)	60	130	26 (744)[b]
17[g]	PhBr(10)	MA(15)	**2** (1.75×10^{-3})	72	140	10 (571)[b,f]
18	PhI (50)	MA (75)	$Pd(dba)_2 + \mathbf{L_2}$ (3.5×10^{-2})	21	130	57 (814)[b]
19	PhI (10)	styrene (15)	$Pd(dba)_2 + \mathbf{L_2}$ (3.5×10^{-2})	91	130	65 (185)[b]
20	bab (10)	styrene (15)	$Pd(dba)_2 + \mathbf{L_1}$ (1.0×10^{-1})	147	130	43 (43)[b]

[a] NMR yield. [b] Isolated yield. [c] A mixture of methyl 3-(4-acetylphenyl)acrylate and sodium 3-(4-acetylphenyl)acrylate (25:75). [d] Only methyl 3-(4-acetylphenyl)acrylate. [e] A mixture of methyl 3-(4-acetylphenyl)acrylate and sodium 3-(4-acetylphenyl)acrylate (20:80). [f] Pure sodium 3-(4-acetylphenyl)acrylate. [g] NaI promotor added.

respectively (entries 1, 6, and 7). On the other hand, compound **2** shows a lower conversion with respect to **1** and **3** (compare entry 4 with entries 1 and 7). The lower activity of **2** is thought to be due to its steric arrangement, determined by crystal structure analysis (crystallography). Catalysts **1** and **3** appear to be active even for a longer period of time at high temperature (entries 2 and 8). No deposition of palladium black during these reactions was observed, indicating the stability of these complexes. In fact, the catalyst remains active upon the addition of more substrates when the reaction is complete. High yields and high turnover number (TON up to 10^6, entry 8) shows the efficiency of these catalysts, which is comparable with the most active catalysts reported so far.[3−7]

As for the aryl bromide, a lower conversion rate was observed for the reaction of 4-bromoacetophenone (bap) with methyl acrylate. For example, a reaction carried out at 140 °C for 94 h only provides 43% of the Heck product (entry 9). However, the addition of sodium iodide to the reaction mixture readily improves the yield and a complete conversion was obtained (entry 10). However, under such reaction conditions, the hydrolysis product sodium 3-(4-acetylphenyl)acrylate becomes the major product. Addition of NaI is also effective in the coupling of 4-bromoacetophenone with styrene to yield 4-acetylstilbene (entry 13). A maximum TON of 10^5 was achieved with bap and methyl acrylate at lower concentrations of catalyst (entry 15). With regard to the higher conversions in the presence of added NaI salt, it is already known that addition of salts such as alkali-metal halides, Bu_4NX (X = Cl, Br), facilitates the Heck reaction by promoting the oxidative addition step.[10,11] However, such a promoter was not necessary for aryl iodides, which undergo a faster oxidative addition with Pd(0) species. Simple bromobenzene is also found to undergo a coupling reaction with methyl acrylate, but at a very slow conversion rate (entry 17). When the study is extended further, reaction of *p*-bromonitrobenzene (bnb) with styrene gave *p*-nitrostilbene in 26% yield (Eentry 16). However, no coupling product was observed with *p*-bromoanisole or 2-chloropyridine and methyl acrylate.

For comparison, the catalytic system generated by the conventional manner was studied (entries 18−20). A mixture of $Pd(dba)_2$ and ligand acting as the catalyst in the reaction provides the low conversion of phenyl iodide into *trans*-cinnamate and *trans*-stilbene. In fact, a small amount of palladium black precipitated during the reaction. This outcome clearly suggests that the catalytic behavior of complexes **1**−**3** is different from that of the in situ generated species.

Crystallography. Single crystals suitable for X-ray analysis of complexes **2** and **3** are obtained by slow evaporation of dichloromethane/hexane solutions. The crystal data are given in Table 2. ORTEP drawings of these complexes are depicted in Figures 1 and 2, respectively, and selected bond distances and bond angles are summarized in Table 3.

Both palladium(II) complexes are square planar. Phenyl and phosphine ligands are *cis* to each other in both **2** and **3**. Pd−C distances are in the range 2.008−2.03 Å and are typical palladium−aryl carbon lengths.[12] All other bond distances and bond angles lie within the normal range, except the larger deviation of P−Pd−I (166.56 (7)°) for **2**. This angular deviation is attributed to the steric effect of the phenyl group of the imine moiety, which lies perpendicular to the plane. Such steric hindrance might also be responsible for the lower reactivity of the palladium complex **2** on the oxidative addition of aryl halides. At the same time, from entries 1 and 6 (Table 1), it is clear that the ring size of the complexes does not have an influence on the efficiency of the catalysts.

In conclusion, the [Pd(P−N)PhI] complexes reported here show a very high activity for aryl iodides and activated bromides for the Heck reaction. Further investigation in understanding the scope of these ligand systems for commercially cheaper aryl chlorides is presently underway.

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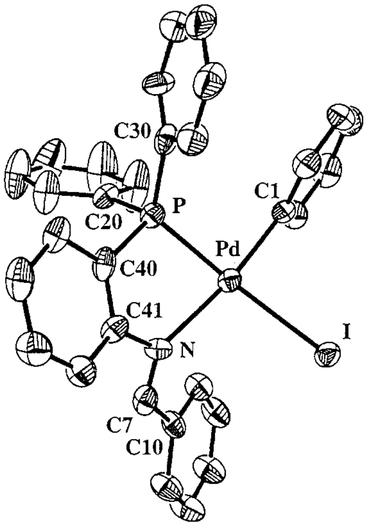

Figure 1. ORTEP plot of **2**.

Table 2. Crystal Data of 2 and 3

	2	**3**
formula	$C_{31}H_{25}INPPd$	$C_{31}H_{25}INPPd$
fw	675.79	675.49
cryst syst	monoclinic	triclinic
space group	$P2_1/c$	$P\bar{1}$
a, Å	12.9791(2)	9.339(2)
b, Å	10.4526(2)	11.044(2)
c, Å	23.8338(5)	13.179(3)
α, deg	90	87.49(3)
β, deg	100.256(1)	85.50(3)
γ, deg	90	82.98(3)
Z	4	2
V, Å^3	3181.8(1)	1344.1(5)
D_{calcd}, g cm^{-3}	1.411	1.670
μ, mm^{-1}	1.621	1.670
radiation	Mo Kα (0.7107 Å)	Mo Kα (0.7107 Å)
temp, K	295(2)	293(2)
F(000)	1328	664
cryst size, mm	0.56 × 0.10 × 0.02	0.25 × 0.30 × 0.35
θ range, deg	1.59−26.39	1.55−24.97
index limits	$-15 \le h \le 16$ $-13 \le k \le 13$ $-29 \le l \le 26$	$-10 \le h \le 11$ $0 \le k \le 13$ $-15 \le l \le 15$
no. of rflns collected	14 881	4710
no. of indep rflns	6423 ($R_{int} = 0.0810$)	4710 ($R_{int} = 0.00$)
abs cor	empirical, SADABS	semiempirical from ψ scan
max, min transmissn	0.8015, 0.4840	0.656, 0.497
refinement method	full-matrix least-squares on F^2	
goodness of fit on F^2	1.049	1.068
final R ($I > 2\sigma(I)$)	R1 = 0.0700, wR2 = 0.1687	R1 = 0.0336, wR2 = 0.0900
largest diff peak and hole, e Å^{-3}	1.461, 0.744	1.369, −0.925

Experimental Section

General Information. All reactions, manipulations, and purifications steps were performed under a dry nitrogen atmosphere. Tetrahydrofuran was distilled under nitrogen from sodium benzophenone ketyl. Dichloromethane and acetonitrile were dried with CaH_2 and distilled under nitrogen. Other chemicals and solvents were of analytical grade and were used as received unless otherwise stated.

NMR spectra were recorded on Bruker AC-E 200 or AM-300 spectrometers. Elemental analyses were determined with a Perkin-Elmer 240C instrument.

General Procedure for Preparation of 1−3. To a mixture of $Pd(dba)_2$ (575 mg, 1 mmol) and the corresponding ligand (1 mmol) in 15 mL of THF was added 0.5 mL (4 mmol) of phenyl iodide, and the mixture was stirred at room temperature for 1 h. The resulting precipitate was filtered, washed with a small amount of ether, and dried under vacuum.

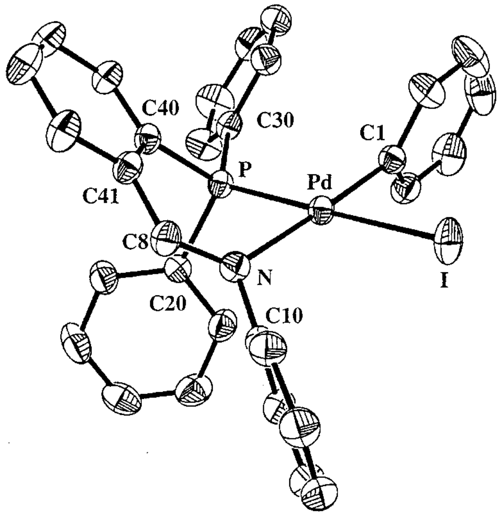

Figure 2. Molecular structure of **3** (thermal ellipsoids drawn at the 30% probability level).

Table 3. Selected Bond Distances (Å) and Bond Angles (deg)

	2	**3**
Pd−C1	2.03(1)	2.008(4)
Pd−P	2.235(3)	2.236(1)
Pd−N	2.188(8)	2.182(3)
Pd−I	2.6697(9)	2.6374(9)
C7−N	1.25(1)	
N−C8		1.277(5)
P−Pd−N	80.3(2)	84.47(9)
P−Pd−C1	92.7(3)	93.6(1)
P−Pd−I	166.56(7)	177.39(3)
C7−N−Pd	132.3(7)	
C7−N−C41	114.3(8)	
N−C8−C41		127.0(4)
C8−N−Pd		126.6(3)

Complex **1**: yield 460 mg (70%); ^{1}H NMR δ (CD_2Cl_2) 4.76 (s, 2H, NH_2), 6.72−7.53 (m, 19H, aromatic); ^{31}P NMR δ 34.3. Anal. Calcd for $C_{24}H_{21}NPIPd{\cdot}THF$: C, 51.28; H, 3.84; N, 2.13. Found: C, 50.96; H, 3.57; N, 1.98.

Complex **2**: yield 525 mg (78%); ^{1}H NMR δ ($CDCl_3$) 6.52−7.58 (m, 22H, aromatic), 8.64 (m, 3H, imine proton + two aromatic protons); ^{31}P NMR δ 22.83. Anal. Calcd for $C_{31}H_{25}NPIPd$: Calcd: C, 55.10; H, 3.72; N, 2.10. Found: C, 54.74; H, 3.52, N, 2.12.

Complex **3**: yield 545 mg (80%); ^{1}H NMR δ ($CDCl_3$) 6.44−7.65 (m, 24H, aromatic), 8.14 (s, 1H, imine); ^{31}P NMR δ 23.15. Anal. Calcd for $C_{31}H_{25}NPIPd$: C, 55.10; H, 3.72; N, 2.10. Found: C, 54.62; H, 3.76; N, 1.87.

Crystallography. Crystals of **2** and **3** were obtained by recrystallization from slow evaporization of a solution in dichloromethane/hexane. Cell parameters of **2** and **3** were determined on a Siemens SMART CCD instrument and refined by full-matrix least squares on F^2. The crystal data are listed in Table 2, and selected bond distances and bond angles are collected in Table 3. Other crystallographic data are supplied as Supporting Information.

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Supporting Information Available: Complete description of the X-ray crystallographic structure determination of **2** and **3**, including tables of atomic coordinates, isotropic and anisotropic thermal parameters, and bond distances and angles. This material is available free of charge via the Internet at http://pubs.acs.org.

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