Journal of Organometallic Chemistry 696 (2011) 795–801

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Uridate/pyridyl Pd(II) complexes: Phosphine-free high turnover catalysts for the Heck reaction of deactivated aryl bromides

Pottabathula Srinivas [a], Keesara Srinivas [a], Pravin R. Likhar [a,*], Balsubramanian Sridhar [b], Kakita Veera Mohan [c], Suresh Bhargava [d], Mannepalli Lakshmi Kantam [a,*]

[a] I & PC Division, Indian Institute of Chemical Technology, Hyderabad 500607, India
[b] X-ray Crystallography Center, Indian Institute of Chemical Technology, Hyderabad 500607, India
[c] NMR Center, Indian Institute of Chemical Technology, Hyderabad 500607, India
[d] School of Applied Sciences, RMIT University, Melbourne, Australia

ARTICLE INFO

Article history:
Received 20 July 2010
Received in revised form
29 September 2010
Accepted 30 September 2010
Available online 12 October 2010

Keywords:
Heck reaction
N-Ligand
Phosphine-free
Palladium
High turnover

ABSTRACT

The synthesis and structure of palladium(II) complexes bearing uridato/pyridyl ligands as an anionic N-donor coordination sites are reported. The complexes have been shown to be highly active catalysts for the Heck reaction of aryl bromides (TON 4.0×10^4–9.1×10^4) and moderate activity for the activation of aryl chlorides under phosphine-free conditions.

1. Introduction

The Heck reaction [1], since its popularity started to flourish in the mid 1980's, has become not only one of the most exciting organic transformations for C–C bond formation but also a benchmark to estimate the efficiency of a catalytic system [2]. This powerful reaction has received considerable attention due to its functional group tolerance and its application to a broad range of endeavors, ranging from synthetic organic chemistry to materials science [3]. Therefore, several goals have to be achieved for its industrial application, such as the use of inexpensive starting materials, achievement of high turnover numbers (TON's) with less reactive aryl bromides and aryl chlorides, and the use of stable and inexpensive ligands. In this context, the design of new ligands and their palladium complexes that can catalyze the Heck reaction of less reactive aryl bromides and aryl chlorides with both high activity and high efficiency is a current important topic of research.

As the choice of ligand plays a major role in the efficiency of the catalyst, phosphine ligands are the first choice to catalyze the Heck reaction more actively and efficiently [4]. However, they are often toxic, air-sensitive or quite expensive. Moreover, there is no need to use electron-rich phosphines to generate nucleophilic Pd(0) species for promoting the oxidative-addition step in the catalytic cycle [5]. Therefore, the development of phosphine-free Pd-catalysts has become another equally important topic of research [6].

Although palladacycles [7], *N*-heterocyclic [8] and carbocyclic [9] carbene Pd-catalysts are well performing phosphine-free catalysts, their tedious multi-step synthesis, inert atmosphere or dry conditional catalytic performance and the use of various additives, limit their use in industrial applications. In addition, alternative catalytic systems such as N-, O- and S-centered ancillary ligand complexes of Pd have appeared with moderate catalytic activity and efficiency [10]. Recently, we have shown that anionic carboxyamide is a good supporting N-donor functional group which increases the thermal stability and activity of the palladium complexes for C–C bond-formation reactions [11]. We now report the synthesis and structure of new palladium(II) complexes bearing uridato/pyridyl ligands as an anionic N-donor coordinating site, together with its performance in the Heck reaction.

* Corresponding authors. Tel.: +91 40 27193510; fax: +91 40 27160921.
E-mail addresses: plikhar@iict.res.in (P.R. Likhar), mlakshmi@iict.res.in (M.L. Kantam).

0022-328X/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2010.09.075

2. Results and discussion

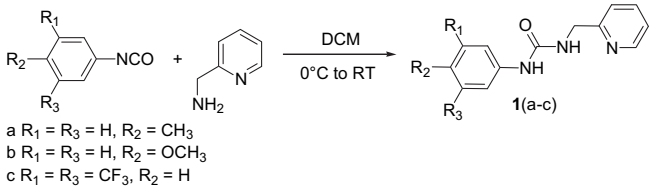
Many N-based ligands are stable and have been reported to be efficient ligands for the palladium catalyzed Heck and Suzuki reactions [10b,f,12]. Among the N-based ligands, urea derivatives are very stable and less explored ligands in C–C bond formation reactions. Recently, Liu et al. reported *N*-phenyl urea as an efficient ligand for Heck and Suzuki reactions [10d]. Since it was shown that a pyridine ring was a good neighboring group to enhance the effect of a carboxylate group in Pd catalysis [10e,11b], it was of interest to design and synthesize the ligands using urea and pyridine as pendant donor-functionalities. Thus, in a simple and high yielding reaction, uridato/pyridyl ligands were prepared by the reaction of widely available aryl isocyanates with 2-picolylamine in dichloromethane (DCM) (Scheme 1).

The steric and electronic properties of these ligands can be varied by a variety of substitutions, allowing for a variety of possible coordination modes that uridato/pyridyl ligands can adopt when bonding to a metal (Fig. 1).

As depicted in Scheme 2, the new uridate/pyridyl Pd(II) complexes (**2a**–**2c**) were readily prepared, in almost quantitative yields, upon treatment of the ligands with $Pd(OAc)_2$ in the presence of $LiOH\cdot H_2O$ in MeOH at room temperature. Complexes **2a**–**2c** are insoluble in solvents such as dichloromethane, chloroform and diethyl ether, but soluble in highly polar solvents such as DMF, DMA, DMSO and methanol. The complexes have been fully characterized by NMR, MS and FT-IR techniques. The solution structure of the ligands and their complexes were studied by ^1H and ^{13}C NMR spectroscopy and showed, respectively, the presence of uridyl (RN*H*CON*H*R^1) hydrogen atoms and the presence of uridate bonding to Pd similar to amidate-Pd bonding that observed in our previous work [11]. Moreover, the molecular structure of complex **2c** was determined by X-ray diffraction analysis on a crystal obtained by slow evaporation of a methanol solution at room temperature. The molecular structure, shown in Fig. 2, and crystal data (Table 1) confirms complex **2c** is mononuclear, with distorted square planar geometry around the metal center and the uridate ligands disposed *cis* relative to each other. Bidentate N,N-coordination of the ligand to palladium atom takes place through the N-atoms of two different functionalities, namely uridate (deprotonated urea) (N2 and N5) and pyridine (N1 and N4).

In case of *N*-phenyl urea, Liu et al. [10d] proposed that *N*,*O*-coordination takes place through an anionic *O*-donor atom of deprotonated *N*-phenyl urea in the rate-determining oxidative-addition step. By analogy, the proposed intermediate in the present case may be a species containing a bidentate N,N-ligand in which the palladium atom is coordinated by anionic N-donor atom of deprotonated urea functionality and the pyridyl group.

To evaluate the usefulness of these N-donor, phosphine-free Pd (II) complexes in C–C bond forming reactions, we investigated their application to the Heck reaction of aryl bromides and chlorides. The results are tabulated in Tables 2–4. To optimize the reaction, we initially examined the reaction of 4-bromoanisole with styrene in the presence of the 'uridate' complex **2c**. A variety of reaction conditions were used in order to get a high turnover number with



Scheme 1. Synthesis of uridato/pyridyl ligands.

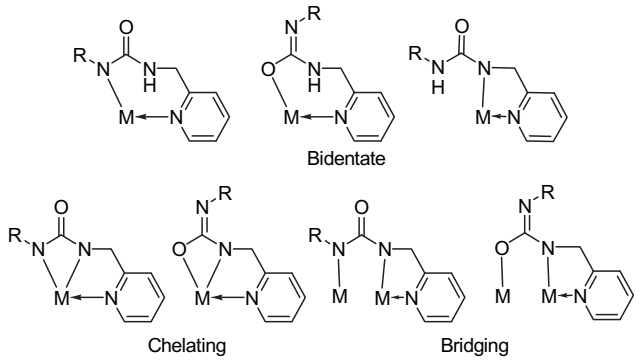
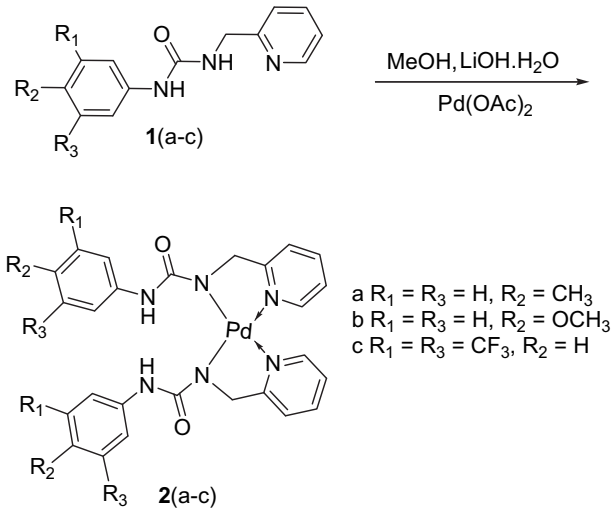


Fig. 1. Some of the possible bonding modes of uridato/pyridyl ligands.

0.001 mol% **2c**, and the progress of the reaction was monitored by gas chromatography (see Table 2). We were pleased to find that the olefination of less reactive 4-bromoanisole proceeded smoothly in *N*,*N*-dimethylformamide when $LiOH\cdot H_2O$ was used as the base. Thus, we obtained the product 4-methoxy-*trans*-stilbene in 76% yield by carrying out the reaction at 145 °C for 10h, with a turnover number of 10^5 (entry 8). This is of particular interest to industry as catalyst with TON's of 10^5 or higher minimizes industrial problems such as the high cost of the metal catalyst and contamination of the product by metal-leaching [13].

The activity of the catalysts **2a** and **2b** were also tested in the Heck reaction, and the cross coupled product was obtained in good yields (Table 2, entries 12 and 13). Thus, the electronic properties of the phenyl ring of the uridato/pyridyl ligands do not appear to have a significant effect on the reactivity of their palladium complexes. As it is always advisable to compare the activity of new complexes with ligandless Pd-catalysts [13,14], the Heck coupling reaction using $Pd(OAc)_2$ and our optimized reaction condition was undertaken. In this case, the 4-methoxy-stilbene product was only obtained in a yield of 8%, considerably less than the 76% using **2c** as catalyst (Table 2, entries 14 and 8).

Having optimized the reaction conditions (0.001 mol% **2c**, 1.2 equiv $LiOH\cdot H_2O$, DMF, 145 °C), we next examined the coupling of less reactive aryl bromides on a 30 mmol scale and the results are listed in Table 3. Reactions involving deactivated aryl bromides bearing a methyl or methoxy group with either styrene or 4-methyl



Scheme 2. Synthesis of uridato/pyridyl-based palladium(II) complexes.

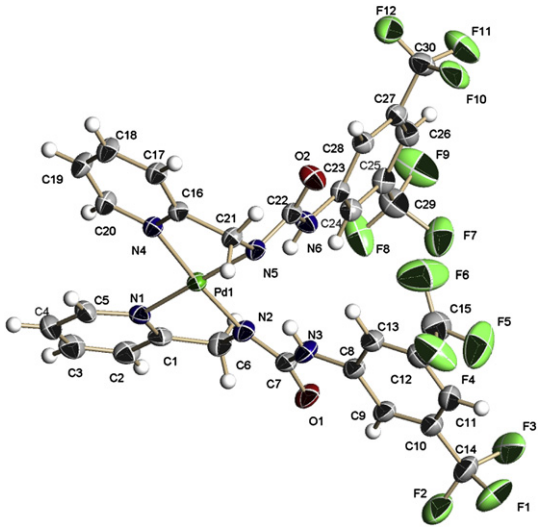


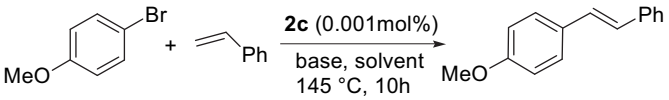
Fig. 2. X-ray structure of Pd(II) complex **2c** (hydrogen atoms are included to highlight uridate anion bonding to palladium atom). Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius. Selected bond lengths [Å] and bond angles [°]: Pd1–N2 = 2.006(2); Pd1–N5 = 2.009 (2); Pd1–N1 = 2.040(2); Pd1–N4 = 2.060(2); ∠N2–C7–N3 = 114.2(3); ∠N5–C22–N6 = 113.0(2).

styrene (entries 5–11) gave high yields of the coupled product. Sterically hindered 2-bromoanisole could also be coupled in moderate yields using as low as 0.001 mol% catalyst loading (entries 9 and 10). We also applied these optimized reaction conditions to coupling of deactivated aryl bromides and *n*-butyl acrylate. However, the best results could be obtained with increasing the catalyst concentration by 0.01 mol% in presence of Li_2CO_3 as a base (entries 12–14). Although the above optimized reaction conditions were ineffective for the Heck reaction of aryl chlorides (Table 4, entry 1), moderate yields of the coupled products could be obtained by increasing the catalyst loading to 1 mol% and using *N*,*N*-dimethylacetamide (DMA) as solvent at 160 °C (Table 4).

Table 1
Crystallographic data for **2c**.

Empirical formula	$C_{30}H_{20}F_{12}N_6O_2Pd$	
Formula weight	830.92	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	$P\bar{1}$	
Unit cell dimensions	a = 9.3740(4) Å	α = 90.723(1)°.
	b = 12.1320(5) Å	β = 100.252(1)°.
	c = 15.2710(6) Å	γ = 108.489(1)°.
Volume	1616.32(12) Å^3	
Z	2	
Density (calculated)	1.707 Mg/m^3	
Absorption coefficient	0.683 mm^{-1}	
F(000)	824	
Crystal size	0.17 × 0.11 × 0.08 mm^3	
θ range for data collection	1.36–25.00°.	
Index ranges	−11<=h<=11, −14 <=k<=14, −18<=l<=18	
Reflections collected	15559	
Independent reflections	5669 [R(int) = 0.0183]	
Completeness to θ = 25.00°	99.7%	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	5669/218/532	
Goodness-of-fit on F^2	1.047	
Final R indices [$I > 2\sigma(I)$]	$R1$ = 0.0332, wR2 = 0.0891	
R indices (all data)	$R1$ = 0.0359, $wR2$ = 0.0912	
Largest diff. peak and hole	0.573 and −0.407 e Å^{-3}	

Table 2
Heck reaction between 4-bromoanisole and styrene.[a]



Entry	Base	Solvent	Yield (%)[b]	TON	TOF[c]
1	Na_2CO_3	DMF	59	59000	5900
2	Li_2CO_3	DMF	42	42000	4200
3	K_2CO_3	DMF	28	28000	2800
4	NaOAc	DMF	37	37000	3700
5	K_3PO_4	DMF	24	24000	2400
6	DIPEA	DMF	10	10000	1000
7	MDCHA	DMF	0	–	–
8	LiOH·H_2O	DMF	76	76000	7600
9	LiOH·H_2O	DMSO	9	9000	900
10	LiOH·H_2O	DMA	74	74000	7400
11	LiOH·H_2O	NMP	46	46000	4600
12	LiOH·H_2O	DMF	73[d]	73000	7300
13	LiOH·H_2O	DMF	74[e]	74000	7400
14	LiOH·H_2O	DMF	8[f]	8000	800

[a] Reaction conditions: 4-bromoanisole (1 mmol), styrene (2 mmol), catalyst (0.001 mol%), base (1.2 mmol), solvent (2 mL).
[b] Isolated yields.
[c] TOF-turnover frequency (mol product per mol catalyst h^{-1}).
[d] Complex **2a** was used.
[e] Complex **2b** was used.
[f] $Pd(OAc)_2$ used as catalyst. DIPEA = *N*,*N*-diisopropylethylamine, MDCHA = *N*-Methyl-dicyclohexylamine.

The uridate/pyridyl Pd(II) complexes find their superiority over most of the phosphine-free catalysts with at least one of the following advantages: facile synthesis, thermal stability and structural versatility, easy handling, catalytic performance in air without any additives [9a,15], achievement of high TON's and TOF's with deactivated aryl bromides and with hindered aryl bromides [9b,12c,16], and activation of less reactive aryl chlorides [5a,17].

3. Conclusion

New palladium(II) complexes containing uridato/pyridyl ligands have been prepared and their ability to catalyze the Heck reaction under phosphine-free reaction conditions has been studied. High turnover numbers can be achieved in the coupling of aryl bromides and olefins, including sterically hindered deactivated 2-bromoanisole. The complexes also show moderate catalytic activity for the coupling of aryl chlorides. The concept of anionic urea as an ancillary ligand with a number of possible modes of coordination opens a new opportunity for the development of phoshpine-free metal catalysts.

4. Experimental section

4.1. Typical procedure for the preparation of ligands (*1a*–*1c*)

To an RB-flask containing 2-(aminomethyl)pyridine (1g, 9.24 mmol) in 20 mL dichloromethane (DCM) was added drop wise to a solution of aryl isocyanate (1.5 equiv) in DCM (10 mL) at 0 °C and the resulting mixture was allowed to stir at room temperature for 10 h. The solvent was removed under reduced pressure and the residue was purified by repeated crystallization from ethyl acetate to give the desired product in 80–90% yield.

4.1.1. 1-(Pyridin-2-ylmethyl)-3-p-tolylurea (*1a*)

^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6, TMS) δ 2.24 (s, 3H), 4.43 (d, J = 5.2 Hz, 2H), 6.59 (t, J = 5.2 Hz, 1H), 6.96 (d, J = 7.8 Hz, 2H), 7.17

Table 3
Heck reaction of aryl bromides and olefins.[a]

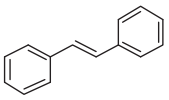
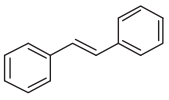
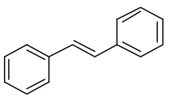
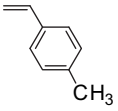
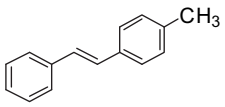
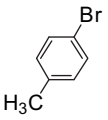
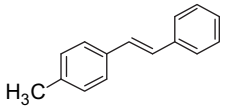
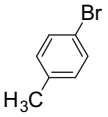
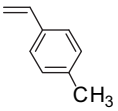
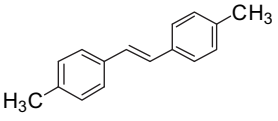
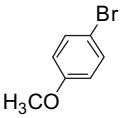
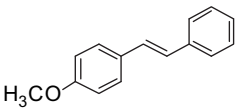
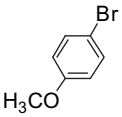
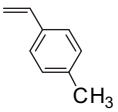
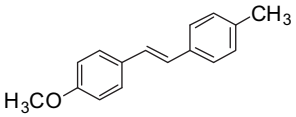
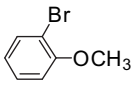
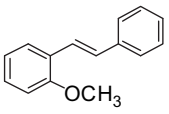
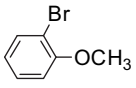
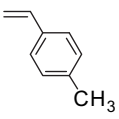
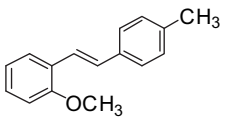
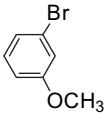
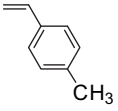
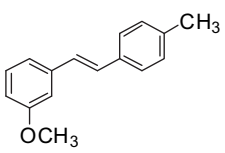
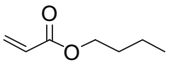
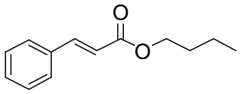
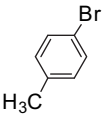
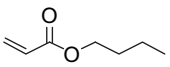
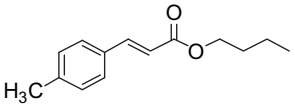
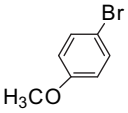
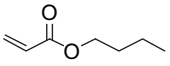
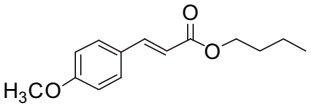
Entry	Arylh alide	Olefin	Product	Yield (%)[b]	Time (h)	TON	TOF
1				91	10	91000	9100
2				82[c]	10	82000	8200
3				83[d]	10	83000	8300
4				90	10	90000	9000
5				82	10	82000	8200
6				83	10	83000	8300
7				76	10	76000	7600
8				80	10	80000	8000
9				40	10	40000	4000
10				52	10	52000	5200
11				73	10	73000	7300

Table 3 (*continued*)

Entry	Arylh alide	Olefin	Product	Yield (%)[b]	Time (h)	TON	TOF
12				92[e]	12	9200	766
13				86[e]	12	8600	716
14				63[e]	12	6300	525

[a] Reaction conditions: aryl bromide (30 mmol), olefin (60 mmol), **2c** (0.001 mol%), $LiOH\cdot H_2O$ (36 mmol), DMF (50 mL) at 145 °C.
[b] Isolated yields.
[c] Complex **2a** was used.
[d] Complex **2b** was used.
[e] With **2c** (0.01 mol%), Li_2CO_3 (2 eq).

(t, J = 6.0 Hz, 1H), 7.24 (d, J = 8.6 Hz, 2H), 7.31 (d, J = 7.8 Hz, 1H), 7.66 (t, J = 7.8 Hz, 1H), 8.38 (s, 1H), 8.49 (d, J = 4.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 19.5, 44.0, 117.2, 120.3, 120.9, 128.0, 129.5, 135.5, 136.5, 147.7, 154.9, 157.6; IR (KBr, cm^{-1}): 3340, 3301 (CONH), 1633 (C=O); ESI-MS (m/z): $(M + H)^+$ = 242, $(M + Na)^+$ = 264; HRMS (m/z): calcd for $C_{14}H_{15}N_3ONa$ $(M + Na)^+$ = 264.1112, found: 264.1122.

*4.1.2. 1-(4-Methoxyphenyl)-3-(pyridin-2-ylmethyl)urea (**1b**)*

^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6, TMS) δ 3.73 (s, 3H), 4.51 (d, J = 5.1 Hz, 2H), 6.56 (t, J = 5.1 Hz, 1H), 6.76 (d, J = 8.8 Hz, 2H), 7.14–7.17 (m, 1H), 7.28–7.31 (m, 3H), 7.63 (t, J = 6.6 Hz, 1H), 8.23 (s, 1H), 8.49 (d, J = 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 44.5, 54.6, 113.2, 119.7, 120.7, 121.3, 132.4, 135.9, 148.0, 154.0, 155.6, 158.0; IR (KBr, cm^{-1}): 3329, 3286 (CONH), 1630 (C=O); ESI-MS (m/z): $(M + H)^+$ = 258; HRMS (m/z): calcd for $C_{14}H_{15}N_3O_2Na$ $(M + Na)^+$ = 280.1061, found: 280.1071.

*4.1.3. 1-(3,5-Bis(trifluoromethyl)phenyl)-3-(pyridin-2-ylmethyl) urea (**1c**)*

^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6, TMS) δ 4.49 (d, J = 4.4 Hz, 2H), 6.66 (t, J = 4.4 Hz, 1H), 7.14 (t, J = 5.9 Hz, 1H), 7.26–7.34 (m, 2H), 7.61 (t, J = 7.3 Hz, 1H), 7.89 (s, 2H), 8.46 (d, J = 5.1 Hz, 1H), 9.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 44.6, 113.9, 117.2, 121.4, 121.9, 124.4, 130.8, 131.1, 131.4, 131.8, 136.5, 141.5, 148.4, 155.1, 157.4; IR (KBr, cm^{-1}): 3364, 3279 (CONH), 1685 (C=O); ESI-MS (m/z): $(M + H)^+$ = 364; HRMS (m/z): calcd for $C_{15}H_{12}F_6N_3O$ $(M + H)^+$ = 364.0884, found: 364.0888.

*4.2. Typical procedure for the preparation of palladium complexes (**2a**–**2c**)*

A single-necked 25 mL RB-flask was charged with the ligand (**1a**–**1c**) (2.2 mmol), $LiOH\cdot H_2O$ (3 equiv) and MeOH (10 mL). To this stirred solution, $Pd(OAc)_2$ (1 mmol) was added in one portion at room temperature. After stirring the solution for 24 h at room temperature, a yellow colored precipitate was obtained. The solvent was removed under reduced pressure and the resulting solid was washed with water to remove excess base (note: complex is insoluble in water). The solid was then washed with ethyl acetate to remove water and excess ligand. The resulting solid was dried under high vacuum to obtain the pure complexes (**2a**–**2c**) in 94–96% yield.

*4.2.1. Complex **2a***

Mp: decomposed to black metal at 202 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + CD_3OD, TMS) δ 2.22 (s, 6H), 4.67 (d, J = 16.8 Hz, 2H), 5.45 (d, J = 16.8 Hz, 2H), 6.98 (d, J = 8.1 Hz, 4H), 7.20 (d, J = 8.1 Hz, 4H), 7.30–7.40 (m, 2H), 7.66 (d, J = 7.3, Hz, 2H), 7.93 (t, J = 7.3 Hz, 2H), 8.16 (d, J = 4.4 Hz, 2H), 8.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ 20.4, 56.3, 118.3, 118.4, 121.6, 123.5, 129.0, 130.6, 137.7, 137.8, 139.3, 147.9, 163.2, 166.8; IR (KBr, cm^{-1}): 3255 (CONH), 1647 (C=O); ESI-MS (m/z): $(M + H)^+$ = 587; HRMS (m/z): calcd for $C_{28}H_{29}N_6O_2Pd$ $(M + H)^+$ = 587.1386, found: 587.1369.

*4.2.2. Complex **2b***

Mp: decomposed to black metal at 194 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + CD_3OD, TMS) δ 3.87 (s, 6H), 4.61 (d, J = 16.1 Hz, 2H), 5.35 (d, J = 16.8 Hz, 2H), 6.68 (d, J = 8.8 Hz, 4H), 7.13 (d, J = 8.8 Hz, 4H), 7.30–7.35 (m, 2H), 7.59 (d, J = 8.1, Hz, 2H), 7.88 (t, J = 8.1 Hz, 2H), 8.12 (d, J = 5.1 Hz, 2H), 8.78 (s, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ 55.2, 56.3, 113.8, 120.2, 121.5, 123.5, 133.6, 139.3, 147.9, 154.4, 163.2, 166.7; IR (KBr, cm^{-1}): 3257 (CONH), 1643 (C=O); ESI-MS (m/z): $(M + H)^+$ = 619; HRMS (m/z): calcd for $C_{28}H_{29}N_6O_4Pd$ $(M + H)^+$ = 619.1285, found: 619.1287.

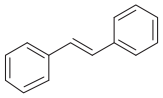
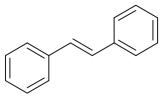
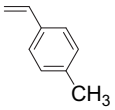
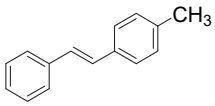
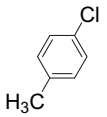
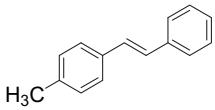
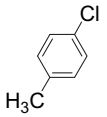
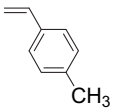
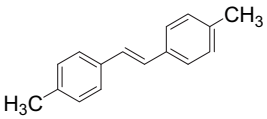
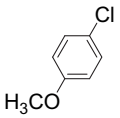
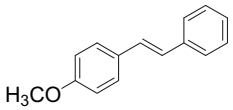
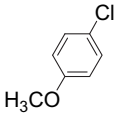
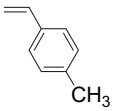
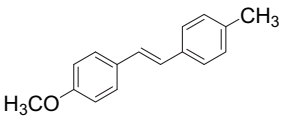
*4.2.3. Complex **2c***

Mp: decomposed to black metal at 204 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6, TMS) δ 4.74 (s, 2H), 5.42 (s, 2H), 7.19 (s, 2H), 7.43 (t, J = 5.9 Hz, 2H), 7.69 (d, J = 7.3 Hz, 2H), 7.77 (s, 4H), 7.97 (t, J = 7.3 Hz, 2H), 8.22 (d, J = 5.9 Hz, 2H), 9.32 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 54.9, 112.0, 115.7, 120.4, 122.9, 123.4, 129.7, 129.8, 130.1, 130.5, 138.6, 141.4, 147.4, 160.7, 164.8; IR (KBr, cm^{-1}): 3285 (CONH), 1657 (C=O); ESI-MS (m/z): $(M + H)^+$ = 831; HRMS (m/z): calcd for $C_{30}H_{21}F_{12}N_6O_2Pd$ $(M + H)^+$ = 831.0569, found: 831.0558.

4.3. Typical procedure for the Heck reaction of aryl bromides

A 100 mL RB-flask was charged with aryl bromide (30 mmol), alkene (60 mmol), $LiOH\cdot H_2O$ (36 mmol) and catalyst (**2c**) (0.001 mol%). *N*,*N*-Dimethylformamide (50 mL) was added and the

Table 4
Heck reaction of aryl chlorides and olefins[a].

Entry	Arylhalide	Olefin	Product	Yield (%)[b]
1				0[c]
2				42
3				28
4				15
5				26
6				8
7				21

[a] Reaction conditions: aryl chloride (1 mmol), olefin (2 mmol), **2c** (1 mol%), $LiOH \cdot H_2O$ (1.2 mmol), DMA (2 mL) at 160 °C for 20 h.
[b] Isolated yields.
[c] Using the reaction conditions described in Table 2.

reaction mixture was heated to 145 °C for 10 h and the progress of the reaction was monitored by GC. Upon the completion of the reaction, the mixture was cooled to room temperature, diluted with EtOAc (200 mL) and the solution washed successively with 1 N aq. HCl and water. The combined organic phases were dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was subjected to column chromatography on silica gel (ethyl acetate and hexane 5:95) to afford the Heck product in high purity.

4.4. Typical procedure for the Heck reaction of aryl chlorides

The reaction vessel was charged with aryl chloride (1 mmol), alkene (2 mmol), $LiOH \cdot H_2O$ (1.2 mmol) catalyst (**2c**) (1 mol%) and *N*,*N*-dimethylacetamide (3 mL). The reaction mixture was heated to 160 °C for 20 h and the progress of reaction was monitored by GC. At the end of the reaction, the reaction mixture was cooled to room temperature, diluted with EtOAc (20 mL) and washed successively with 1 N aq. HCl and water. The combined organic phases were dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was subjected to column chromatography on silica gel (ethyl acetate and hexane 5:95) to afford the Heck product in high purity.

4.5. Analytical data for the products of the Heck reaction

4.5.1. trans-Stilbene (Table 3, entry 1)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.05 (s, 2H), 7.17–7.22 (m, 2H), 7.30 (t, J = 7.5 Hz, 4H), 7.46 (d, J = 7.5 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 126.5, 127.6, 128.6, 137.3; IR (KBr, cm^{-1}) 3021, 2925, 1593, 1445, 958, 687; EI-MS (m/z) $(M)^+$ = 180.

4.5.2. 4-Methyl-trans-stilbene (Table 3, entry 4)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.35 (s, 3H), 7.01 (s, 2H), 7.11 (d, J = 8.3 Hz, 2H), 7.16–7.22 (m,1H), 7.29 (t, J = 7.5 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 126.3, 126.4, 127.3, 127.7, 128.6, 129.3, 134.5, 137.4, 137.5; IR (KBr, cm^{-1}) 3021, 2917, 2855, 1589, 1506, 967, 804, 527; EI-MS (m/z) $(M)^+$ = 194.

4.5.3. 4,4′-Dimethyl-trans-stilbene (Table 3, entry 6)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.34 (s, 6H), 6.97 (s, 2H), 7.09 (d, J = 7.9 Hz, 4H), 7.33 (d, J = 7.9 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 126.3, 127.6, 129.4, 134.8, 137.3; IR (KBr, cm^{-1}) 3017, 2920, 2854, 1511, 1111, 969, 818; EI-MS (m/z) $(M)^+$ = 208.

4.5.4. 4-Methoxy-trans-stilbene (Table 3, entry 7)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 3.80 (s, 3H), 6.83 (d, J = 8.3 Hz, 2H), 6.90 (d, J = 15.9 Hz, 1H), 7.01 (d, J = 16.6 Hz, 1H), 7.15–7.31 (m, 4H), 7.38–7.44 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.3, 114.1, 126.3, 126.7, 127.2, 127.7, 128.2, 128.7, 130.2, 137.7, 159.3; IR (KBr, cm^{-1}) 3015, 2920, 2847, 1602, 1511, 1250, 1030, 826, 538; EI-MS (m/z) $(M)^+$ = 210.

4.5.5. 4-Methoxy-4′-methyl-trans-stilbene (Table 3, entry 8)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.34 (s, 3H), 3.80 (s, 3H), 6.82 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 16.2 Hz, 1H), 6.95 (d, J = 16.4 Hz, 1H), 7.09 (d, J = 7.9 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 55.3, 114.1, 126.1, 126.5, 127.2, 127.5, 129.3, 130.3, 134.8, 137.0, 159.1; IR (KBr, cm^{-1}) 3015, 2920, 2847, 1602, 1511, 1250, 1030, 826, 538; EI-MS (m/z) $(M)^+$ = 224.

4.5.6. 2-Methoxy-trans-stilbene (Table 3, entry 9)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 3.88 (s, 3H), 6.84 (d, J = 8.3 Hz, 1H), 6.91 (t, J = 7.5 Hz, 1H), 7.04 (d, J = 16.6 Hz, 1H), 7.18 (t, J = 7.5 Hz, 2H), 7.30 (t, J = 7.5 Hz, 2H), 7.42 (d, J = 16.6 Hz, 1H), 7.49 (d, J = 7.5 Hz, 2H), 7.55 (d, J = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.5, 110.9, 120.7, 123.5, 126.4, 126.5, 127.3, 128.5, 128.6, 129.1, 137.9, 156.9; IR (KBr, cm^{-1}) 3023, 2936, 1593, 1483, 1244, 1027, 750, 691; EI-MS (m/z) $(M)^+$ = 210.

4.5.7. 2-Methoxy-4′-methyl-trans-stilbene (Table 3, entry 10)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.35 (s, 3H), 3.88 (s, 3H), 6.83 (d, J = 8.3 Hz, 1H), 6.90 (t, J = 7.5 Hz, 1H), 7.00 (d, J = 16.6 Hz, 1H), 7.09 (d, J = 8.3 Hz, 2H), 7.16 (t, J = 8.3 Hz, 1H), 7.33–7.39 (m, 3H), 7.53 (d, J = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.8, 55.5, 110.9, 120.8, 122.5, 126.3, 126.5, 128.5, 129.0, 129.3, 137.2, 156.9; IR (KBr, cm^{-1}) 2922, 2851, 1602, 1511, 1249, 1029, 826, 537; EI-MS (m/z) $(M)^+$ = 224.

4.5.8. 3-Methoxy-4′-methyl-trans-stilbene (Table 3, entry 11)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.35 (s, 3H), 3.82 (s, 3H), 6.72 (d, J = 7.9, 1H), 7.25–6.97 (m,7H), 7.35 (d, J = 7.9, 2H); 13C NMR (75

MHz CDCl3) δ 21.2, 55.1, 111.5, 113.0, 119.0, 126.4, 127.5, 128.8, 129.3, 134.3, 137.5, 138.9, 159.7; IR (KBr, cm^{-1}) 3013, 2924, 2840, 1586, 1478, 1256, 1045, 807, 684; EI-MS (*m*/*z*) $(M)^+ = 224$.

4.5.9. n-Butyl cinnamate (Table 3, entry 12)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.97 (t, $J = 7.30$ Hz, 3H), 1.44 (m, 2H), 1.69 (m, 2H), 4.18 (t, $J = 6.61$ Hz, 2H), 6.39 (d, $J = 16.05$ Hz, 1H), 7.34 (m, 3H), 7.49 (m, 2H), 7.64 (d, $J = 16.05$ Hz, 1H); ^{13}C NMR (75 MHz CDCl3) δ 13.6, 19.1, 30.6, 64.3, 118.1, 127.9, 128.7, 130.0, 134.3, 144.4, 166.9; IR (KBr, cm^{-1}) 2959, 1713, 1638, 1310, 1172, 1066, 981, 767; EI-MS (*m*/*z*) $(M)^+ = 204$.

4.5.10. n-Butyl-4-methyl cinnamate (Table 3, entry 13)

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.97 (t, 3H), 1.43 (m, 2H), 1.66 (m, 2H), 2.37 (s, 3H), 4.17 (t, $J = 6.90$ Hz, 2H), 6.34 (d, $J = 16.05$ Hz, 1H), 7.19 (d, $J = 7.93$ Hz, 2H), 7.39 (d, $J = 8.12$ Hz, 2H),7.60 (d, $J = 15.86$ Hz, 1H); ^{13}C NMR (50 MHz CDCl3) δ 13.7, 19.2, 21.3, 30.8, 64.2, 117.1, 127.9, 129.5, 131.7, 140.4, 144.5,167.1; IR (KBr, cm^{-1})2925, 2855, 1715, 1637, 1311, 1168, 1060, 938, 813; EI-MS (*m*/*z*) $(M)^+ = 218$.

4.5.11. n-Butyl-4-methoxy cinnamate (Table 3, entry 14)

^{1}H NMR (300 MHz, $CDCl_3$, TMS)δ 0.97 (t, 3H), 1.43 (m, 2H), 1.66 (m, 2H), 3.82 (s, 3H),4.16 (t, $J = 6.61$ Hz, 2H), 6.25 (d, $J = 15.86$ Hz, 1H), 6.85 (d, $J = 8.68$ Hz, 2H), 7.43 (d, $J = 8.68$ Hz, 2H), 7.57 (d, $J = 15.86$ Hz, 1H); ^{13}C NMR (75 MHz CDCl3) δ 13.6, 19.1, 30.7, 55.2, 64.2, 114.1, 115.6, 127.0, 129.5, 144.1, 161.2, 167.4; IR (KBr, cm^{-1}) 2959, 1708, 1603, 1253, 1169, 1029, 829; EI-MS (*m*/*z*) $(M)^+ = 234$.

Acknowledgements

P.S. thanks UGC and K.S. thank CSIR, India for their fellowships.

Appendix. Supplementary material

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.jorganchem.2010.09.075.

References

[1] (a) T. Mizoroki, K. Mori, A. Ozaki, Bull. Chem. Soc. Jpn. 44 (1971) 581;
(b) R.F. Heck, J.P. Nolley Jr., J. Org. Chem 37 (1972) 2320.
[2] For reviews of the Heck reaction: (a) R.F. Heck, Org. React. 27 (1982) 345;
(b) A. Spencer, J. Organomet. Chem 258 (1983) 101;
(c) W. Cabri, I. Candiani, Acc. Chem. Res. 28 (1995) 2;
(d) R.F. Heck, in: B.M. Trost (Ed.), Comprehensive Organic Synthesis, Pergamon, New York, 1991 vol. 4(Chapter 4.3);
(e) G.T. Crisp, Chem. Soc. Rev. 27 (1998) 427;
(f) I.P. Beletskaya, A.V. Cheprakov, Chem. Rev. 100 (2000) 3009.
[3] (a) R.F. Heck, Acc. Chem. Res. 12 (1979) 146;
(b) L.F. Overman, D.J. Ricca, V.D. Tran, J. Am. Chem. Soc. 115 (1993) 2042;
(c) K.C. Nicolaou, E.J. Sorensen, Classics in Total Synthesis. VCH, New York, 1996, (Chapter 31);
(d) R.A. de Vries, P.C. Vosejpka, M.L. Ash, in: F.E. Herkes (Ed.), Catalysis of Organic Reactions, Marcel Dekker, New York, 1998 (Chapter 37);
(e) L.F. Tietze, G. Kettschau, U. Heuschert, G. Nordmann, Chem. Eur. J. 7 (2001) 368.
[4] (a) Y. Ben-David, M. Portnoy, M. Gozin, D. Milstein, Organometallics 11 (1992) 1995;
(b) M. Portnoy, Y. Ben-David, D. Milstein, Organometallics 12 (1993) 4734;
(c) A.F. Littke, G.C. Fu, J. Org. Chem 64 (1999) 10;
(d) K.H. Shaughnessy, P. Kim, J.F. Hartwig, J. Am. Chem. Soc. 121 (1999) 2123;
(e) A. Ehrentraut, A. Zapf, M. Beller, Synlett (2000) 1589;
(f) V.P.W. Bohm, W.A. Herrmann, Chem. Eur. J. 6 (2000) 1017;
(g) A.F. Littke, G.C. Fu, J. Am. Chem. Soc. 123 (2001) 6989.
[5] (a) V.V. Grushin, H. Alper, Chem. Rev. 94 (1994) 1047;
(b) M. Beller, A. Zapf, Synlett (1998) 792.
[6] (a) M.T. Reetz, E. Westermann, R. Lohmer, G. Lohmer, Tetrahedron Lett. 39 (1998) 8449;
(b) W.A. Herrmann, Angew. Chem. Int. Ed. 41 (2002) 1290;
(c) B.S. Yong, S.P. Nolan, Chemtracts: Org. Chem. (2003) 205.
[7] (a) W.A. Herrmann, C. Brossmer, K. Ofele, C.-P. Reisinger, T. Priermeier, M. Beller, H. Fisher, Angew. Chem., Int. Ed. Engl. 34 (1995) 1844;
(b) W.A. Herrmann, C. Brossmer, C.-P. Reisinger, T. Priermeier, K. Ofele, M. Beller, Chem. Eur. J. 3 (1997) 1357;
(c) X. Gai, R. Grigg, M.I. Ramzan, V. Sridharan, S. Collard, J.E. Muir, Chem. Commun. (2000) 2053;
(d) A.S. Gruber, D.Z. Zim, G. Ebeling, A.L. Monteriro, J. Dupont, Org. Lett. 2 (2000) 1287;
(e) S. Gibson, D.F. Foster, G.R. Eastam, R.P. Tooze, D.J. Cole-Hamilton, Chem. Commun. (2001) 779;
(f) C.S. Consorti, M.L. Zanini, S. Leal, G. Ebeling, J. Dupont, Org. Lett. 5 (2003) 983;
(g) G.D. Frey, C.-P. Reisinger, E. Herdtweck, W.A. Herrmann, J. Organomet. Chem. 690 (2005) 3193;
(h) K.-F. Peng, M.-T. Chen, C.-A. Huang, C.-T. Chen, Eur. J. Inorg. Chem. (2008) 2463.
[8] (a) D. Bourissou, O. Guerret, F.P. Gabbai, G. Bertrand, Chem. Rev. 100 (2000) 39;
(b) S.K. Yen, L.L. Koh, F.E. Hahn, H.V. Huynh, T.S.A. Hor, Organometallics 25 (2006) 5105;
(c) J. Ye, W. Chen, D. Wang, Dalton Trans. (2008) 4015;
(d) N. Marion, S.P. Nolan, Acc. Chem. Res. 41 (2008) 1440;
(e) X. Zhang, Z. Xi, A. Liu, W. Chen, Organometallics 27 (2008) 4401;
(f) D. Meyer, M.A. Taige, A. Zeller, K. Hohlfeld, S. Ahrens, T. Strassner, Organometallics 28 (2009) 2142;
(g) T. Tu, J. Malineni, X. Bao, K.H. Dotz, Adv. Synth. Catal. 351 (2009) 1029.
[9] (a) W.A. Herrmann, K. Ofele, S.K. Schneider, E. Herdtweck, S.D. Hoffmann, Angew. Chem., Int. Ed. 45 (2006) 3859;
(b) D.F. Wass, M.F. Haddow, T.W. Hey, A. Guy Orpen, C.A. Russell, R.L. Wingad, M. Green, Chem. Commun. (2007) 2704.
[10] (a) D. Yang, Y.-C. Chen, N.-Y. Zhu, Org. Lett. 6 (2004) 1577.
(b) T. Mino, Y. Shirae, Y. Sasai, M. Sakamoto, T. Fujita, J. Org. Chem 71 (2006) 6834;
(c) S. Lee, J. Organomet. Chem 691 (2006) 1347;
(d) X. Cui, Y. Zhou, N. Wang, L. Liu, Q.-X. Guo, Tetrahedron Lett. 48 (2007) 163;
(e) X. Cui, J. Li, Z.-P. Zhang, Y. Fu, L. Liu, Q.-X. Guo, J. Org.Chem. 72 (2007) 9342;
(f) K. Kawamura, S. Haneda, Z. Gan, K. Eda, M. Hayashi, Organometallics 27 (2008) 3748;
(g) F. Li, T.S.A. Hor, Adv. Synth. Catal. 350 (2008) 2391.
[11] (a) P. Srinivas, P.R. Likhar, H. Maheswaran, B. Sridhar, K. Ravikumar, M.L. Kantam, Chem. Eur. J. 15 (2009) 1578;
(b) M.L. Kantam, P. Srinivas, J. Yadav, P.R. Likhar, S. Bhargava, J. Org. Chem. 74 (2009) 4882.
[12] (a) R.A. Gossage, H.A. Jenkins, P.N. Yadav, Tetrahedron Lett. 45 (2004) 7689;
(b) V. Montoya, J. Pons, V. Branchadell, J. Garcia-Antón, X. Solans, M. Font-Bardía, J. Ros, Organometallics 27 (2008) 1084;
(c) C. Najera, J. Gil-Molto, S. Karlström, L.R. Falvello, Org. Lett. 5 (2003) 1451;
(d) G.A. Grasa, A.C. Hillier, S.P. Nolan, Org. Lett. 3 (2001) 1077.
[13] V. Farina, Adv. Synth. Catal. 346 (2004) 1553.
[14] (a) Q. Yao, E.P. Kinney, Z. Yang, J. Org. Chem. 68 (2003) 7528;
(b) A.H.M. de Vries, J.M.C.A. Mulders, J.H.M. Mommers, H.J.W. Henderickx, J.G. de Vries, Org. Lett. 5 (2003) 3285;
(c) M.T. Reetz, J.G. de Vries, Chem. Commun. (2004) 1559.
[15] See Ref. [7a,b] M.T. Reetz, G. Lohmer, R. Schwickardi, Angew. Chem. Int. Ed. 37 (1998) 481.
[16] See Ref. [7d]; (a) T. Kawano, T. Shinomaru, I. Ueda, Org. Lett. 4 (2002) 2545.
[17] R.B. Bedford, C.S.J. Cazin, D. Holder, Coord. Chem. Rev. 248 (2004) 2283.