Available online at www.sciencedirect.com
ScienceDirect
ELSEVIER
Tetrahedron 64 (2008) 1808−1812
Tetrahedron
www.elsevier.com/locate/tet

A mechanistic study on modern palladium catalyst precursors as new gateways to Pd(0) in cationic Heck reactions

Andreas Svennebring [a], Per J.R. Sjöberg [b], Mats Larhed [a], Peter Nilsson [a,*]

[a] *Organic Pharmaceutical Chemistry, Department of Medicinal Chemistry, Uppsala Biomedical Center, Uppsala University, PO Box 574, SE-751 23 Uppsala, Sweden*
[b] *Department of Physical and Analytical Chemistry, Uppsala Biomedical Center, Uppsala University, PO Box 599, SE-751 23 Uppsala, Sweden*

Received 22 August 2007; received in revised form 13 November 2007; accepted 29 November 2007
Available online 8 December 2007

Abstract

Electrospray ionization mass spectrometry (ESI-MS) was used as a means to directly identify catalytic cationic organopalladium species in ligand-controlled Heck reactions involving electron-rich olefins and different Pd-sources. In these high-temperature Heck arylations, the oxidative addition intermediates were observed as bidentate ligand chelated cationic aryl palladium species, suggesting that the used ligand attaches to the metal center at the very beginning of the catalytic cycle. This was also in agreement with the obtained regioisomeric profile of the isolated products. The investigation supports the standard Pd(0)/Pd(II) Heck mechanism and provides further insight regarding the conceivable composition of fundamental Pd(II) intermediates in an ongoing Heck reaction.

Keywords: ESI-MS; Heck; Palladium; Microwave

1. Introduction

Since its disclosure in the early seventies, the palladium(0)-catalyzed Heck reaction has enjoyed a considerable amount of interest in synthetic organic chemistry.[1−4] Originally, Pd(II) salts were used as the precatalyst which were, under standard Heck reaction conditions, believed to be rapidly reduced in situ to form Pd(0). The essential aryl/alkenyl palladium(II) intermediate was thereafter generated from Pd(0) and an organic halide by an oxidative addition process.[3,4] The recent decade has seen the introduction of a multitude of new palladium formulations/complexes to be used as precatalysts in palladium(0)-catalyzed coupling reactions. Of clear importance are the different classes of palladacycles[5,6] and palladium carbenes[7,8] as well as various polymer supported[9] palladium sources. In parallel, a debate regarding the true nature of the catalytically active palladium species has been enduring. Herrmann and Beller suggested early on that the use of palladacycles (e.g., **3a**[10]) might provide an alternative catalytic cycle, proceeding through a Pd(II)/Pd(IV) redox cycle.[11,12] A mechanistic rational for this cycle was later proposed by Shaw.[13] The good thermal stability and high recovery of the palladacycle after completion of the reaction, along with the lack of a distinct reducing agent, supported this assumption. However, several reports on the existence of highly active soluble palladium(0) colloids (nanoparticles) has established the function of palladacycles as plain Pd(0) reservoirs in high-temperature applications like Heck and Suzuki couplings.[14,15] Unfortunately, very little is known about the actual structures of catalytically active PdL_n complexes generated from modern and highly sophisticated Pd-precursors.[16] In addition, there have been few attempts to elucidate the composition of the active species present in the Heck cycle. Published studies have been limited to the use of electrochemistry,[17] anionic detection (ESI-MS, EXAFS)[18] together with detailed kinetic studies,[19−21] and catalyst poisoning experiments.[22,23] The *three-phase test* has been used to differentiate between homogeneous and heterogeneous catalysts.[24,25]

---

* Corresponding author. Tel.: +46 8 524 831 34; fax: +46 8 524 831 01.
E-mail address: peter@orgfarm.uu.se (P. Nilsson).

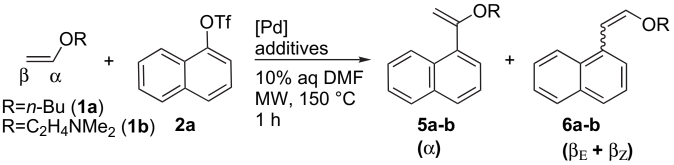
0040-4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.11.111

We have recently reported on the use of ESI-MS to monitor cationic reaction intermediates in a Pd(II)-catalyzed and ligand-promoted oxidative Heck reaction.[26,27] These studies indicate a strong chelating effect from bidentate ligands (1,3-bis-(diphenylphosphino)propane (dppp), and 2,9-dimethyl-1,10-phenanthroline (dmphen)). Thus, we decided to utilize ESI-MS detection with the addition of chelating ligands to search for mechanistic information regarding Pd(0)-catalyzed Heck reactions. Herein we present an investigation on the ability of selected catalyst precursors to act as Pd(0)-sources in ligand-controlled Heck reactions with electron-rich alkenes proceeding via charged intermediates.

2. Results and discussion

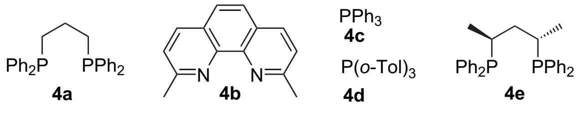
2.1. Preparative results from vinyl ether Heck arylations

Electron-rich heteroatom-substituted linear olefins (e.g., vinyl ether **1a**) often furnish low regioselectivities under standard (neutral) reaction conditions. To overcome the poor regioselectivity with non-functionalized acyclic electron-rich olefins in Heck chemistry,[28,29] Cabri introduced the use of chelating ligands and cationic reaction conditions to obtain internal (α)-substitutions of vinyl ethers.[30,31] Furthermore, arylation of the Ar–Pd presenting *N*,*N*-dimethylamino substituted vinyl ether **1b** has been shown to result in the terminal β-product in the presence of monodentate ligands, and in the internal product with bidentate ligands.[32–34] Accordingly, we selected **1a** and **1b** as model substrates in our studies (Scheme 1).



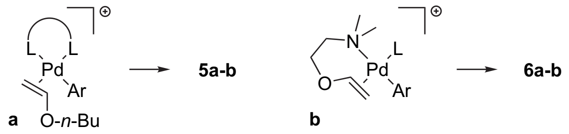
Scheme 1. Preparative model reaction using different Pd-sources and additives (ligands **4a**–**e** or LiCl).

To unambiguously assign the metal oxidation state during catalysis we utilized external mono- and bidentate ligands as mechanistic tools (Scheme 2).

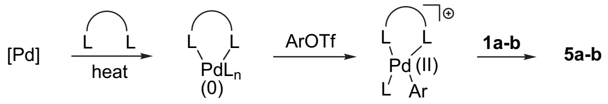


Scheme 2. Mono- and bidentate ligands employed in the study.

If the arylation of butyl vinyl ether (**1a**) with 1-naphthyl triflate **2a** using a palladium source and dppp/dmphen as precatalytic system would produce a selective α-arylation, this would support the hypothesis that liberated Pd(0) was trapped by chelating bidentate ligands (Schemes 3 and 4). In addition, if a Pd(II)/Pd(IV)-pathway[35] was active, and not the more widely recognized Pd(0)/Pd(II)-route, some difference in regioselectivity would be expected. Moreover, Herrmann has reported a similar distribution of isomers in the Heck arylation of non-chelating **1a** with both phosphopalladacycle **3a** and with classic Pd(OAc)$_2$.[36] Performing the reactions with **2a**, under microwave high-temperature conditions, using standard Pd(OAc)$_2$ and Pd$_2$dba$_3$ based systems did not give any substantial difference in the expected regioselectivity outcome but only in conversion and yield (Table 1).[34] Thus, olefin **1a** underwent internal α-arylation with dppp (**4a**), but only non-selective arylation under chloride containing neutral conditions (entries 5 and 7).



Scheme 3. Cationic π-complexes affording internal α-arylation (a) and terminal β-arylation (b); L=neutral ligand.

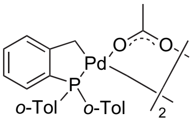
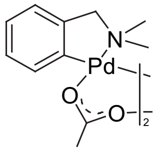
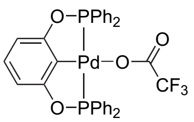


Scheme 4. Mechanistic hypothesis; L=neutral ligand.

With olefin **1b**, β-arylation predominated, delivering **6b** unless a bidentate ligand was added. Using cationic conditions and **3a**, an excellent α-selectivity was experienced with both olefins, providing **5**[37] and the corresponding methyl ketone **7a** (via direct hydrolysis). Thus supporting a reaction mechanism similar to traditional catalysts, such as Pd(OAc)$_2$ and Pd$_2$(dba)$_3$ (comparing entries 20,21 with 3,4 and 13,14). Similarly, in the presence of dppp both the charcoal-supported catalyst (Pd/C) and the recently marketed encapsulated polyurea-supported palladium catalysts (Pd EnCat 30) showed complete α-selectivity (entries 28, 33 and 34, 38 and 39). In contrast, olefin **1a** failed to give any product with Pd/C. A possible explanation might be that olefin **1b**, via the dimethylamino group, can more efficiently trap the presumably very low concentration of solubilized palladium, furnishing improved conversion and yield (c.f. entries 27 and 28).[33]

The oxidatively more stable di-nitrogen ligand dmphen (**4b**) provided full α-selectivity using **1a**, but failed to fully displace the internal nitrogen of olefin **1b** in chelating the palladium metal, resulting in poor regioselectivity (entries 9 and 10, 25 and 26). Control experiments, using LiCl and/or a monodentate ligand, PPh$_3$ (**4c**), afforded regioisomeric mixtures regardless of catalyst precursor confirming that an external bidentate ligand is necessary to obtain regioselective reactions. Employing amino palladacycle **3b**[38] and pincer complex **3c**[39,40] gave a preparative outcome perfectly consistent with Pd(0)-catalysis under both cationic and neutral conditions (entries 40–46). Overall, bidentate ligands gave more productive reactions. A result, which is in agreement with the hypothesis that electron-rich alkenes (good σ-donors) react more smoothly under cationic conditions for electronic reasons. The emerging picture from the preparative investigation reveals that none of the investigated Pd-sources influenced the regioisomeric outcome. Instead it was the choice between neutral or cationic conditions, which indicated that a normal Pd(0)/Pd(II)-cycle was prevailing.

Table 1
Microwave-assisted reactions employing different Pd-catalyst precursors and additives for the reaction with **2a** as depicted in Scheme 1

No	Palladium source	Additive	Olefin	Yield[a] $(\alpha/\beta_E/\beta_Z)$
1	$Pd(OAc)_2$	—	**1a**	6:7:3
2		—	**1b**	0:22:30
3		**4a**	**1a**	87:0:0
4		**4a**	**1b**	62:0:0
5		LiCl, **4c**	**1a**	32:12:4
6		LiCl, **4c**	**1b**	11:52:21
7		LiCl	**1a**	3:6:4
8		LiCl	**1b**	6:13:53
9		**4b**	**1a**	39:0:0
10		**4b**	**1b**	42:19:15
11	$Pd_2(dba)_3$	—	**1a**	17:17:9
12		—	**1b**	0:29:24
13		**4a**	**1a**	71:0:0
14		**4a**	**1b**	66:0:0
15		LiCl, **4c**	**1a**	19:10:3
16		LiCl, **4c**	**1b**	8:43:18
17		LiCl	**1b**	6:15:57
18	 **3a**	—	**1a**	17:17:9
19		—	**1b**	0:29:24
20		**4a**	**1a**	71:0:0
21		**4a**	**1b**	66:0:0
22		LiCl, **4c**	**1b**	4:17:5
23		LiCl	**1a**	15:18:4
24		LiCl	**1b**	13:11:42
25		**4b**	**1a**	72:0:0
26		**4b**	**1b**	50:16:10
27	Pd/C	**4a**	**1a**	0:0:0
28		**4a**	**1b**	41:0:0
29		LiCl, **4c**	**1a**	27:14:3
30		LiCl, **4c**	**1b**	8:38: 23
31		LiCl	**1b**	9:10:13[b]
32	EnCat 30	—	**1b**	0:11:49
33		**4a**	**1a**	82:0:0
34		**4a**	**1b**	70:0:0
35		LiCl, **4c**	**1a**	12:9:3
36		LiCl, **4c**	**1b**	9:36:11
37	EnCat Pd(0)	LiCl	**1b**	0:13:50
38		**4a**	**1a**	67:0:0
39		**4a**	**1b**	71:0:0
40	 **3b**	—	**1b**	0:21:28
41		**4a**	**1a**	82:0:0
42		**4a**	**1b**	63:0:0
43		LiCl	**1b**	5:13:40
44	 **3c**	**4a**	**1a**	67:0:0
45		**4a**	**1b**	68:0:0
46		LiCl, **4c**	**1a**	27:16:4

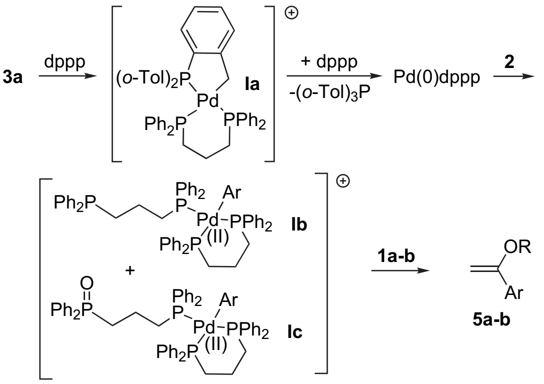
---

[a] Conditions: **2a** (0.4 mmol), **1** (1.0 mmol), DMF (1.8 mL), water (0.2 mL), additive (**4a** (7.5 mol %) or **4b** (7.5 mol %) or **4c** (7.5 mol %)+LiCl (1 mmol), or LiCl (4 mmol)+triethylamine (0.5 mmol), and palladium source (2.5 mol % Pd) were mixed and microwave heated at 150 °C for 1 h in a sealed vessel. The products were isolated after column purification. The α-product **5** was isolated as 1-naphthyl methyl ketone **7a** after acidic hydrolysis (>95% by GC–MS).

[b] Reaction time (3 h).

2.2. ESI-MS investigation

ESI-MS has become an increasingly valuable method for investigating the composition of charged organometallic species. This so-called ion-fishing method provides the ability to detect, directly from the reaction cocktail, existing intermediates due to the very mild desolvation technique involved.[41] ESI-MS analysis of a reaction using the conditions in entry 20, Table 1 at 120 °C revealed three important signals exhibiting the characteristic Pd isotopic distribution (**Ia**, *m*/*z*=821; **Ib**, *m*/*z*=1057; **Ic**, *m*/*z*=1073; based on ^{106}Pd) (Scheme 5 and entry 1, Table 2). The cation complex corresponding to **Ia** was subjected to MS–MS analysis and showed the collision-induced elimination of tri-*o*-tolyl phosphine (**4d**) and dppp (**4a**). Interestingly, adding **4d** together with **4a** and $Pd(OAc)_2$ again produced intermediate **Ia** along with mono-oxidated class **Ic** complex (Table 2, entry 2). Substitution of the arylating agent to 4-cyanophenyl triflate **2b** allowed, at 70 °C, mainly detection of the analogous intermediate of type **Ic** (*m*/*z*=1048) with **4a** and $Pd(OAc)_2$ (entry 3). Exchanging dppp with the commercially available and related (2*S*,4*S*)-(−)-2,4-bis(diphenylphosphino)pentane ligand[42] (**4e**) generated the corresponding cation analogous to class **Ic** (*m*/*z*=1104) using $Pd(OAc)_2$ (Table 2, entry 4).



Scheme 5. Catalytic Heck reaction pathway supported by detected ESI-MS signals; Ar=1-naphthyl (**2a**) or 4-CN–Ph (**2b**).

Two experiments were performed to further establish the composition of metal containing **Ia** and **Ic**, which included

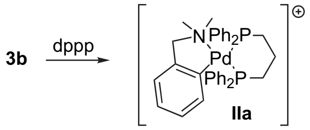
Table 2
Detected cationic intermediates from ESI-MS analysis using various substrates and catalysts for the microwave-assisted Heck coupling

Entry[a]	Catalyst	Reaction time (min)	Aryl triflate	Ligand	Detected intermediate
1	**3a**	10	**2a**	**4a**	**Ia**, **Ib**, **Ic**
2	$Pd(OAc)_2$	10	**2a**	**4d**, **4a**	**Ia**, **Ic**
3	$Pd(OAc)_2$	20[b]	**2b**	**4a**	**Ic**
4	$Pd(OAc)_2$	5	**2b**	**4e**	**Ic**
5	Pd EnCat 30	5	**2b**	**4a**	**Ic**
6	**3a**	5	**2b**	**4a**	**Ia**, **Ic**
7	**3a**	20[b]	**2b**	**4a**	**Ia**
8	**3b**	10	**2b**	**4a**	**IIa**, **Ic**
9	**3c**	5	**2b**	**4a**	**Ic**

[a] Conditions: **2** (0.4 mmol), **1a** (1.0 mmol), DMF (1.8 mL), water (0.2 mL), ligand (7.5 mol %), K_2CO_3 (0.5 mmol), and palladium source (2.5 mol % Pd) were mixed and heated at 120 °C in a sealed vessel. After the indicated time an aliquot was taken, diluted, and injected to the ESI-MS.

[b] 70 °C.

the interpretation of the corresponding MS−MS fragmentations (entries 6 and 7). Employing Pd EnCat 30 as Pd source with **2b** gave a signal (*m*/*z*=1048) in agreement with intermediate **Ic**, indicating the function of this polyurea encapsulated Pd(II) as a source of plain Pd(0) in our high-temperature system (entry 5). Using palladacycle **3a** with the electron-deficient **2b**, produced the oxidative addition intermediate **Ic**, although at lower temperature (70 °C) only intermediate **Ia** was detectable. This result implies that ligand exchange to furnish **Ia** should be considered a facile process. Moreover, performing preparative reactions at 150 °C over 15 min using **1a** and **2b** with **4a** furnished selectively 4-cyanoacetophenone **7b** in 66% yield using **3a**, and 84% yield with $Pd(OAc)_2$.[43] Using the dimethylamino palladacycle **3b** as precursor produced two key signals with *m*/*z*=652 and 1048, corresponding to intermediates of type **IIa** and **Ic** (entry 8). The depicted structures in Scheme 6 were further supported by MS−MS fragmentation analysis.



Scheme 6. Plausible reaction pathway using **3b**, as indicated by detected ESI-MS signals.

The pincer complex **3c** did not give any detectable signal from a ligand exchange complex similar to **Ia**, providing only a **Ic** signal (entry 9).

Regrettably, no cationic complexes containing Pd-associated olefin **1a** could be detected in this study, suggesting that such complexes are either present in very low concentrations, or just too unstable, and therefore not to be considered as resting states for the catalytic cycle.

3. Conclusion

The findings from the ESI-MS analyses of ongoing bidentate-controlled Heck reactions support the following mechanistic hypothesis. The palladacycles/pincer undergoes a structural cleavage upon metal coordination to the bidentate ligand followed by a reduction to 'Pd(0)'.[44,45] Subsequent ligand-exchange forms the crucial Pd(0)−dppp (or dmphen) complex. Oxidative addition and regioselective insertion deliver the internally arylated α-product according to the cationic route depicted in Scheme 4. The Pd(II) catalyst Pd EnCat 30 show similar behavior as standard $Pd(OAc)_2$, both in preparative experiments and in ESI-MS investigations. Based on ESI-MS detected charged intermediates and measured product regioselectivities, we conclude that it is unlikely that the investigated reactions are catalyzed via Pd(IV)-intermediates.[44−46]

4. Experimental

4.1. General procedure for the preparative Table 1

The following chemicals were added to a 5-mL process vial: palladium precatalyst (0.01 mmol [Pd]) according to entry, either of **4a** (0.03 mmol, 12.4 mg) or **4b** (0.03 mmol, 6.2 mg) or **4c** (0.03 mmol, 7.9 mg) and LiCl (1 mmol, 42 mg) or LiCl (4 mmol, 168 mg). To the mixture were added DMF (1.8 mL), water (0.2 mL), **2a** (0.4 mmol, 110 mg), Et_3N (0.5 mmol, 70 μL), and either of **1a** (1 mmol, 129 μL) or **1b** (1 mmol, 140 μL). The vial was sealed under air and the contents were magnetically stirred and microwave heated for 1 h at 150 °C. After cooling, the reaction mixture was extracted (0.1 M NaOH, ether), washed (water), dried (K_2CO_3), and the solvent was removed under reduced pressure. The compounds were purified by chromatography on aluminum oxide (reactions starting from **1a**, 0−20% ether/isohexane) or silica (reactions starting from **1b**, 0−20% ether/isohexane with 1% Et_3N in the mobile phases). Any contamination of remaining **2a** in the product was removed by bulb-to-bulb distillation (1.5 mmHg, 130 °C).

4.2. Preparative reactions employing aryl triflate 2b

The following chemicals were added to a 5-mL process vial: $Pd(OAc)_2$ (0.01 mmol, 2.2 mg) or **3a** (0.01 mmol [Pd], 4.7 mg), dppp (0.03 mmol, 12.4 mg), K_2CO_3 (0.5 mmol, 66 mg), **2b** (0.4 mmol, 100 mg), 10% aqueous DMF (2 mL), **1a** (1 mmol, 129 μL) or **1b** (1 mmol, 140 μL). The vial was sealed under air and the contents were magnetically stirred and microwave heated for 15 min at 150 °C. After cooling to ambient temperature, 12 M (aq) HCl (1 mL) was added and the reaction mixture was magnetically stirred for 1 h, diluted with water (20 mL), extracted with ether, washed (water), dried ($MgSO_4$), and the solvent was removed at reduced pressure. The crude product was purified by chromatography on silica to give pure **7b**.

4.3. Mass spectrometric investigations (Table 2)

The following chemicals were added to a 5-mL process vial according to entry: either of $Pd(OAc)_2$ (0.01 mmol, 2.2 mg), **3a** (0.01 mmol [Pd], 4.7 mg), Pd EnCat 30 (0.01 mmol [Pd], 25.0 mg) or **3b** (0.01 mmol [Pd], 3.0 mg), **3c** (0.01 mmol [Pd], 7.0 mg); either of **4a** (0.03 mmol, 12.4 mg) or **4d** (0.01 mmol, 3.0 mg) or **4e** (0.03 mmol, 13.3 mg). To the same vial was added: K_2CO_3 (0.5 mmol, 66 mg), DMF (1.8 mL), water (0.2 mL) and either of **2a** (0.4 mmol, 110 mg) or **2b** (0.4 mmol, 100 mg). The reactions were microwave or metal block heated in sealed vessels at 120 °C for 5−20 min according to Table 2 after which a sample of 100 μL were taken from the hot reaction mixture and pipetted into 5 mL of cold (−78 °C) methanol and stored at −78 °C until injection. Before injection, the samples were again diluted ten times with methanol stored at ambient temperature. An API III+ triple-quadrupole mass spectrometer equipped with an articulated IonSpray interface was used in this study. The samples were introduced by continuous infusion with the aid of a syringe pump at a flow rate of 5 μL/min through a fused silica capillary (50 μm inner diameter and 184 μm outer diameter). The fused silica capillary was centered in a stainless steel capillary counter assembly, which also served as the

ESI high voltage contact. The nebulizer gas flow was set to 0.5 L/min. The flow rate of dry nitrogen counter-current curtain gas (heated to 60 °C) was 1.2 L/min over the sampling orifice. The mass spectrometric parameters were as follows: ion spray voltage (ISV) 3500 V, interface plate voltage (IN) 650 V, orifice lens voltage (OR) 50 V, and AC entrance rod (R0) 30 V. Mass spectral data were typically recorded by scanning the 100–1200 u region with a dwell time of 1–2 ms and a step size of 0.1 u in multi channel acquisition mode (MCA summation of 10–20 scans). Mass scale calibration was performed using polypropylene glycol solution (PPG). During the MS–MS experiments the collision energy was set to 20 eV. The collision gas was argon with 99.9999% purity. The collision gas thickness was 2×10^{15} molecules/cm^2.

Acknowledgements

We would like to thank Knut and Alice Wallenberg's Foundation and the Swedish Research Council for generous support. We also thank Dr. Luke Odell for linguistic advice and Prof. Anders Hallberg for fruitful discussions.

Supplementary data

Experimental procedures of the synthetic reactions and the ESI-MS analyses. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.11.111.

References and notes

1. Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581.
2. Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320–2322.
3. Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009–3066.
4. Heck, R. F. *Org. React.* **1982**, *27*, 345–390.
5. Herrmann, W. A.; Brossmer, C.; Reisinger, C. P.; Riermeier, T. H.; Ofele, K.; Beller, M. *Chem.—Eur. J.* **1997**, *3*, 1357–1364.
6. Herrmann, W. A.; Bohm, V. P. W. *J. Organomet. Chem.* **1999**, *572*, 141–145.
7. Xu, L.; Chen, W.; Xiao, J. *Organometallics* **2000**, *19*, 1123–1127.
8. Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290–1309.
9. Alonso, F.; Beletskaya, I. P.; Yus, M. *Tetrahedron* **2005**, *61*, 11771–11835.
10. Herrmann's catalyst (*trans*-di-(μ-acetato)-bis[*o*-(di-*o*-tolylphosphino)-benzyl]dipalladium(II)).
11. Herrmann, W. A.; Brossmer, C.; Oefele, K.; Reisinger, C.-P.; Priermeier, T.; Beller, M.; Fischer, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1844–1847.
12. Campo, M. A.; Zhang, H.; Yao, T.; Ibdah, A.; McCulla, R. D.; Huang, Q.; Zhao, J.; Jenks, W. S.; Larock, R. C. *J. Am. Chem. Soc.* **2007**, *129*, 6298–6307.
13. Shaw, B. L. *New J. Chem.* **1998**, *22*, 77–79.
14. Beletskaya, I. P.; Cheprakov, A. V. *J. Organomet. Chem.* **2004**, *689*, 4055–4082.
15. Notable exception is e.g., certain low temperature allylic transformations, using pincer complexes, where the +2 oxidation state of Pd seem to be preserved throughout the catalytic cycle, see: Solin, N.; Kjellgren, J.; Szabo, K. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 3656–3658.
16. Sabino, A. A.; Machado, A. H. L.; Correia, C. R. D.; Eberlin, M. N. *Angew. Chem., Int. Ed.* **2004**, *43*, 2514–2518.
17. d'Orlye, F.; Jutand, A. *Tetrahedron* **2005**, *61*, 9670–9678.
18. de Vries, J. G. *Dalton Trans.* **2006**, 421–429.
19. Rosner, T.; Pfaltz, A.; Blackmond, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 4621–4622.
20. Rosner, T.; Le Bars, J.; Pfaltz, A.; Blackmond, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 1848–1855.
21. Mathew, J. S.; Klussmann, M.; Iwamura, H.; Valera, F.; Futran, A.; Emanuelsson, E. A. C.; Blackmond, D. G. *J. Org. Chem.* **2006**, *71*, 4711–4722.
22. Consorti, C. S.; Zanini, M. L.; Leal, S.; Ebeling, G.; Dupont, J. *Org. Lett.* **2003**, *5*, 983–986.
23. Eberhard, M. R. *Org. Lett.* **2004**, *6*, 2125–2128.
24. Davies, I. W.; Matty, L.; Hughes, D. L.; Reider, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 10139–10140.
25. Broadwater, S. J.; McQuade, D. T. *J. Org. Chem.* **2006**, *71*, 2131–2134.
26. Enquist, P. A.; Nilsson, P.; Sjöberg, P.; Larhed, M. *J. Org. Chem.* **2006**, *71*, 8779–8786.
27. Enquist, P. A.; Lindh, J.; Nilsson, P.; Larhed, M. *Green Chem.* **2006**, *8*, 338–343.
28. Andersson, C. M.; Hallberg, A.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 3529–3536.
29. Daves, G. D., Jr.; Hallberg, A. *Chem. Rev.* **1989**, *89*, 1433–1445.
30. Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2–7.
31. Cabri, W.; Candiani, I.; Bedeschi, A.; Penco, S.; Santi, R. *J. Org. Chem.* **1992**, *57*, 1481–1486.
32. Larhed, M.; Andersson, C. M.; Hallberg, A. *Tetrahedron* **1994**, *50*, 285–304.
33. Nilsson, P.; Larhed, M.; Hallberg, A. *J. Am. Chem. Soc.* **2001**, *123*, 8217–8225.
34. Svennebring, A.; Nilsson, P.; Larhed, M. *J. Org. Chem.* **2004**, *69*, 3345–3349.
35. Dick, A. R.; Kampf, J. W.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 12790–12791.
36. Herrmann, W. A.; Bohm, V. P. W.; Reisinger, C.-P. *J. Organomet. Chem.* **1999**, *576*, 23–41.
37. Using the same conditions as in entry 4, Table 1, afforded **5b** in 48% isolated yield compared to 62% of **7a** if additional hydrolysis was performed.
38. Thompson, J. M.; Heck, R. F. *J. Org. Chem.* **1975**, *40*, 2667–2674.
39. Bedford, R. B.; Draper, S. M.; Noelle Scully, P.; Welch, S. L. *New J. Chem.* **2000**, *24*, 745–747.
40. Yu, K.; Sommer, W.; Weck, M.; Jones, C. W. *J. Catal.* **2004**, *226*, 101–110.
41. Santos, L. S.; Knaack, L.; Metzger, J. O. *Int. J. Mass Spectrom.* **2005**, *246*, 84–104.
42. Liu, S. F.; Berry, N.; Thomson, N.; Pettman, A.; Hyder, Z.; Mo, J.; Xiao, J. L. *J. Org. Chem.* **2006**, *71*, 7467–7470.
43. Trifluoro-methanesulfonic acid 3,4-dicyano-phenylester and trifluoro-methanesulfonic acid 6-cyanonaphthyl-2-ester were also tested as arylating agents, giving strong ESI-MS peaks but unfortunately sluggish and irreproducible preparative results were obtained. These triflates were therefore discarded.
44. Beller, M.; Riermeier, T. H. *Eur. J. Inorg. Chem.* **1998**, 29–35.
45. Bohm, V. P. W.; Herrmann, W. A. *Chem.—Eur. J.* **2001**, *7*, 4191–4197.
46. For an ESI-MS study of Pd(IV) species see: Canty, A. J.; Traill, P. R.; Colton, R.; Thomas, I. M. *Inorg. Chim. Acta* **1993**, *210*, 91–97.