Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 47 (2006) 2311–2314

Tetrahedron Letters

Palladium *N*-methylimidazolium supported complexes as efficient catalysts for the Heck reaction

Belen Altava, M. Isabel Burguete, Eduardo García-Verdugo, Naima Karbass, Santiago V. Luis,* Amrit Puzary and Victor Sans

Departamento de Química Inorgánica y Orgánica, UAMOA, Universidad Jaume I/CSIC, Campus del Riu Sec,
Avenida Sos Baynat, s/n, E-12071 Castellón, Spain

Received 5 December 2005; revised 2 February 2006; accepted 3 February 2006
Available online 20 February 2006

Abstract—Different *N*-methylimidazolium supported ligands have been easily synthesized. The palladium complexes derived from those materials can be used for the catalysis of the Heck reaction giving excellent yields, selectivities and very good TON and TOF values. The supported Pd-pincer complexes show an increased stability, and provide a clear improvement in the recovery and reuse for the supported catalysts.

Soluble and insoluble polymer-supported catalysts have received much attention in organic cross-coupling reactions due to the industrial interest of the resulting products and the need for the search of recoverable catalysts with long-term stability.[1] Although homogeneous catalysts often have higher activities in such transformations, heterogeneous catalysts possess significant advantages from a practical point of view as well as in terms of sustainable green chemistry for the ease of product purification and the potential for recycling.

The Heck coupling reaction is one of the most important methods for carbon–carbon bond formation in general organic synthesis, synthesis of intermediates for pharmaceuticals and in the preparation of conducting polymers.[2] Palladium species have largely been used as catalysts for C–C bond forming reactions in allylic substitutions and Heck coupling of aryl halides with olefins.[3] In such reactions, the recovery and reuse of the catalyst is highly important from an economic point of view, due to the high cost of palladium compounds, but also for the strict limitations to the palladium content in final products, particularly for pharmaceutical applications.

Stable transition metal carbene complexes are gaining importance in organic transformations since its discovery.[4] Thus for instance, the metal complexes of N-heterocyclic carbene (NHC) have been reported as a class of moisture- and air-stable catalysts with remarkable activity in carbon–carbon bond forming reactions.[5] The strong metal–carbon bond in such complexes prevents the possible dissociation of the metal centre, thereby making them thermally and oxidatively stable. Thus the NHC complexes are potential candidates to be used as catalysts for many important coupling reactions such as the Heck and Suzuki coupling reactions.[6]

In order to provide the potential for easy recycling, the synthesis of analogous heterogeneous systems is important. Progress towards this goal include the preparation and use of NHC metal complexes supported either on inorganic or organic supports.[7–10] Here we report on the preparation of polymer-supported methylimidazolium salts prepared via the covalent anchoring of 1-methylimidazolium moieties onto PS-DVB gel type resins. The catalytic behaviour of the corresponding resin-bound Pd-complexes was investigated for the Heck reaction.

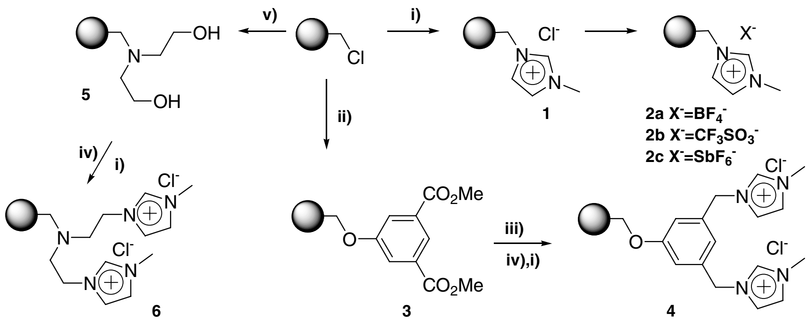
The synthesis of the supported ligands was accomplished according to Scheme 1. The reaction of a Merrifield resin (1% DVB-cross-linked, 1.19 mmol Cl/g) with neat methylimidazole led to **1** in quantitative yields. The transformation was followed using different analytical

---

Keywords: Supported catalysts; Polymer; Heck reaction; Facilitated chemical synthesis.

* Corresponding author. Tel.: +34 964728239; fax: +34 964728214; e-mail: luiss@qio.uji.es

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.02.023



Scheme 1. Reagents and conditions: (i) methylimidazole, 90 °C; (ii) dimethyl 5-hydroxyisophthalate NaH, ^{t}Bu$_4$NI, THF, reflux, 48 h; (iii) LiBH$_4$ in THF, B(OMe)$_3$, THF, reflux, 24 h; (iv) SOCl$_2$, CH$_2$Cl$_2$, reflux, 3.5 h; (v) diethanolamine, DMF, Et$_3$N.

tools, in particular, FT-Raman spectroscopy and the NBP test.[11,12] The combined use of both techniques allowed us to observe that the reaction time required to achieve a quantitative conversion of the C–Cl groups is much shorter than previously reported for related systems (30 min vs 12–78 h).[9] Polymers **2a**–**c** were prepared by exchange of the chloride anion with NaBF$_4$, CF$_3$SO$_3$H and NaSbF$_6$, respectively.[13] The pincer ligands were obtained by initial reaction of a Merrifield resin with dimethyl 5-hydroxyisophthalate or diethanolamine to give **3** and **5**, respectively. The diester **3** was converted into the corresponding diol by treatment with lithium borohydride and the diol was easily transformed into the dichloride by reaction with thionyl chloride. The reaction of dichloride with *N*-methyl imidazole afforded the di-imidazolium salt **4**. A similar procedure allowed us to prepare the modified resin **6**. The polymer-supported Pd species were synthesized according to the literature procedures by heating the corresponding resin-bound imidazolium salt with Pd(OAc)$_2$ in the presence of sodium carbonate for 2 h in DMF/H$_2$O (1:1, v/v) at 50 °C.[9a,10] Table 1 summarizes the functionalization degrees either for the imidazolium salts (EA) or the Pd complexes (ICP-MS). The pincer ligand showed a ratio NHC/Pd of ca. 2:1, while monodentate ligands led to ratios ranging from 2 to 8 depending on the nature of the anions.

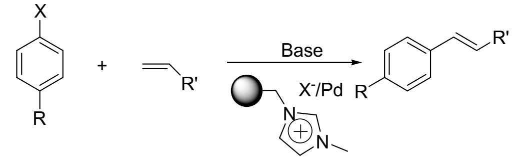
The reaction of iodobenzene with methyl acrylate (Scheme 2, R = H, R′ = CO$_2$Me) was selected as the benchmark Heck reaction to be tested with the different Pd-supported systems.[14] The reactions were initially performed at two different temperatures, 90 and 130 °C, in the presence of air and without prior solvent distillation.

Table 1. Functionalization degrees of the supported ligands and catalysts

Entry	Polymer	meq. NHC/g[a]	meq. Pd/g[b]	meq. NHC/ meq. Pd
1	**1**	0.93	0.17	5.5
2	**2a**	0.89	0.30	3.0
3	**2b**	0.84	0.40	2.1
4	**2c**	0.83	0.10	8.3
5	**4**	0.84	0.41	2.0
6	**6**	1.40	0.71	1.9

[a] Determined by elemental analysis.

[b] Determined by ICP-MS.



Scheme 2.

At 130 °C the conversion is complete within 15–20 min with only 0.02 mol % of catalyst loading, while the reaction at 90 °C needs relatively longer reaction times for completion using the same substrate/catalyst ratio. No other differences related to the change in temperature were found.

Figure 1 shows a graph of the yield versus time for the reactions catalyzed by the corresponding Pd-supported complexes (0.02 mol %) derived from **1**, **2a**–**c** and Pd(OAc)$_2$ at 90 °C in DMF using NEt$_3$ as the base. The reaction was highly selective for all the catalysts, leading to the *trans*-methyl cinnamate isomer exclusively. The reaction rates for the supported catalysts were slower than that of the homogeneous reaction catalyzed by Pd(OAc)$_2$. One of the most notable features observed was the strong influence of the nature of the anion (see Fig. 1). The reaction rates for Pd-polymers

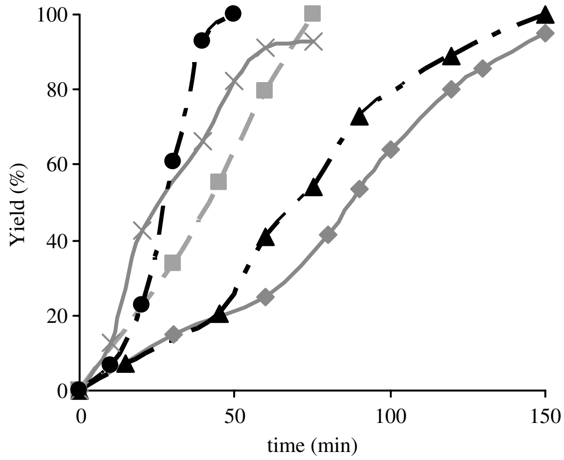


Figure 1. Yields of *trans*-methylcinnamate obtained for catalysts derived from —◆— **1**, —■— **2a**, —▲— **2b**, —×— **2c**, —●— Pd(OAc)$_2$ (0.02%).

2c and **2a** (SbF_6^- and BF_4^-) were faster than those observed for **Pd-1** and **Pd-2b**. This can be related to the relative coordination ability of the different anions and with the formation and stability of diverse complex forms in the presence of these contraanions. Similar effects have been reported for homogeneous carbene complexes in ionic liquids.[16] The presence of different anions could either stabilize the complex or give rise to the formation of precipitated palladium particles.

The influence of the catalyst/substrate ratio was also studied (Table 2). Polymer **2c** proved to be an efficient catalysts leading to good TON (11,600) and TOF (12,000) values even for very low catalysts/substrate ratio (0.005 mol % Pd). The participation of Pd species in a solution is revealed by the significant leaching observed when the reactions were carried out at 90 °C. For polymer **2c** (see Table 3) the first and second run produced a quantitative transformation of the substrates, but conversion decreased dramatically after the third use.

Table 2. Effect of catalyst/substrate ratio

Entry	Polymer	Pd (mol %)	TON[a]	TOF[b]
1	**2c**	0.02	4550	4800
2	**2c**	0.008	9750	9750
3	**2c**	0.005	11600	12000

[a] TON after 1 h, all experiments were carried out in parallel, using three different new flasks and stir bars.

[b] TOF calculated for 80% conversion.

Table 3. Stability study for supported Pd catalysts

Entry	Polymer	Yield (%)				
		Run 1	Run 2	Run 3	Run 4	Run 5
1	**2c**[a]	99	99	20	12	—
2	**6**[b]	99	99	51	—	—
3	**4**[b]	99	99	99	99	99

[a] 90 °C.

[b] 130 °C.

Polymers **4** and **6** were designed to form more stable and robust Pd-pincer complexes.[15] Catalysts derived from bi-dentate ligands **4** and **6** showed lower reaction rates than the **Pd-1** catalyst and longer induction periods (Fig. 2). Nevertheless, a significant improvement in stability was achieved with the catalyst derived from **4**. This catalyst was effective for at least five cycles without losing any activity and leading to a TON value of 25,000 (Table 3).

The study of the Pd complex prepared from the supported pincer ligand **4** as a catalyst for the Heck reaction was extended to include different substrates. Results are summarized in Table 4. The reaction of iodobenzene with different alkenes led to excellent yields in all cases (see entries 1–3 in Table 4) using Et_3N as the base and DMF as the solvent. A much lower reaction rate was observed in the absence of DMF, using a solventless Et_3N/PhI (2:1) medium (see entry 11).

Reaction of *p*-bromoacetophenone and *p*-nitrobromobenzene with methyl acrylate gave the corresponding product in 66% and 100% yield, respectively (entries 9

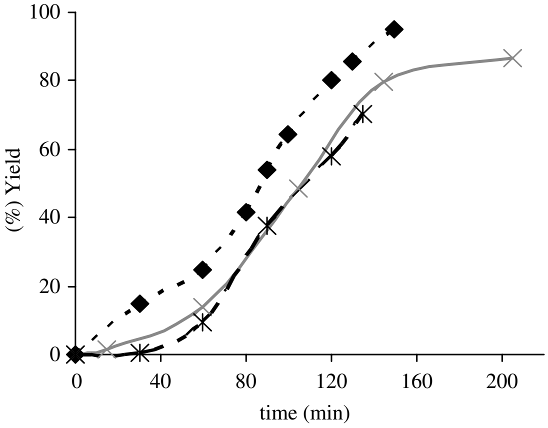


Figure 2. Yield (%) for *trans*-methylcinnamate obtained using catalysts derived from resins - -◆ - **1**, ——✕—— **4**, —✳— **6**.

Table 4. Results obtained for the Heck reaction (Scheme 2) with different substrates using the Pd catalyst derived from **4**

Entry	R	X	R′	Polymer	Solvent	Base	*T* (°C)	Time (h)	Yield (%)
1	H	I	Ph	**4**	DMF	Et_3N	90	24	100[a]
2	H	I	CO_2Me	**4**	DMF	Et_3N	90	2.5	100[a]
3	H	I	CN	**4**	DMF	Et_3N	90	24	70[a,b]
4	OCH_3	Br	CO_2Me	**4**	DMF/H_2O (5:1)	NaOAc	130	48	0
5	NO_2	Br	CO_2Me	**4**	DMF/H_2O (5:1)	NaOAc	130	18	100[c]
6	NO_2	Br	CO_2Me	**4**	DMF/H_2O (5:1)	NaOAc	130	2.5	100[c,d]
7	NO_2	Br	Ph	**4**	DMF/H_2O (5:1)	NaOAc	130	24	100[c]
8	$COCH_3$	Br	CO_2Me	**4**	DMF/H_2O (5:1)	NaOAc	130	24	28[c]
9	$COCH_3$	Br	CO_2Me	**4**	DMF/H_2O (8:1)	NaOAc	130	24	66[e]
10	H	Br	CO_2Me	**4**	DMF/H_2O (5:1)	NaOAc	130	24	0
11	H	I	CO_2Me	**4**	—	Et_3N	90	2.5	10[f]

[a] Yields calculated by GC and ^1H NMR.

[b] Selectivity 85:15 trans/cis.

[c] Yield calculated by ^1H NMR.

[d] 0.2% catalyst was used.

[e] Isolated yield.

[f] Solventless reaction 2:1 Et_3N/PhI.

and 5). A quantitative transformation was also achieved with *p*-nitrobromobenzene and styrene (entry 7). When the less active bromobenzene and *p*-metoxybromobenzene were used as the substrates, only traces of product were observed (entries 4 and 9).

In summary, we have prepared polymer-supported methyl imidazolium salts that can be used as efficient recoverable Pd-supported catalysts for the Heck reaction. The product recovery and purification is simple. Furthermore, dry solvents or inert atmosphere were not required to achieve excellent TON and TOF values. The supported pincer complex derived from **4** showed a very good activity being recyclable without any loss of activity for at least five catalytic cycles.

Acknowledgements

Financial support from the Spanish Ministerio de Ciencia y Tecnología (CTQ 2005-08016) Bancaixa-UJI (P1B2004-13) and Generalitat Valenciana (GRUPOS 04/031) is gratefully acknowledged. E.G. and V.S. thank MCYT for personal financial support (Ramón y Cajal and PPQ programs).

References and notes

1. (a) For references see the special issue: Gladysz, J. A., Ed.; Recoverable Catalyst and Reagents. *Chem. Rev.* **2002**, *102*; (b) Sherrington, D. C. *Chem. Commun.* **1998**, 2275–2286.
2. (a) Zapf, A.; Beller, M. *Top. Catal.* **2002**, *19*, 101–109; (b) de Vries, J. G.; Tucker, C. E. *Top. Catal.* **2002**, *19*, 111–118.
3. (a) Alonso, F.; Beletskaya, I. P.; Yus, M. *Tetrahedron* **2005**, *61*, 11771–11835; (b) Fairlamb, I. J. S. *Tetrahedron* **2005**, *61*, 9647–9918; (c) Gniewek, A.; Trzeciak, A. M.; Ziolkowski, J. J.; Kepinski, L.; Wrzyszcz, J.; Tylus, W. *J. Catal.* **2005**, *229*, 332–343.
4. For a recent review, see: (a) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290; (b) Öfele, K. *J. Organomet. Chem.* **1968**, *12*, 11; (c) Wanzlick, H. J.; Schönherr, H. J. *Angew. Chem.* **1968**, *80*, 154.
5. (a) *Metal Carbenes in Organic Synthesis. Topics in Organometallic Chemistry*; Dötz, K. H., Ed.; Springer: Berlin, Heidelberg, 2004; Vol. 13; (b) Herrmann, W. A.; Ofele, K.; von Preysing, D.; Schneider, S. K. *J. Organomet. Chem.* **2003**, *687*, 229; (c) Weskamp, T.; Böhm, V. P. W.; Herrmann, W. A. *J. Organomet. Chem.* **2000**, *600*, 12–22.
6. (a) Shi, M.; Qian, H.-X. *Tetrahedron* **2005**, *61*, 4949–4955; (b) Pytkowicz, J.; Roland, S.; Mangeney, P.; Meyer, G.; Jutand, A. *J. Organomet. Chem.* **2003**, *678*, 166–179.
7. (a) Papp, A.; Galbács, G.; Molnár, Á. *Tetrahedron Lett.* **2005**, *45*, 7725–7728; (b) Ozdemir, I.; Gurbuz, N.; Seckin, T.; Cetinkaya, B. *Appl. Organometal. Chem.* **2005**, *19*, 633–638; (c) Poyatos, M.; Márquez, F.; Peris, E.; Claver, C.; Fernández, E. *New J. Chem.* **2003**, *27*, 425–431.
8. (a) Schonefelder, D.; Nuyken, O.; Weberskirch, R. *J. Organomet. Chem.* **2005**, *690*, 4648–4655; (b) Kang, T. R.; Feng, Q.; Luo, M. M. *Synlett* **2005**, *15*, 2305–2308; (c) Steel, P. G.; Teasdale, C. W. T. *Tetrahedron Lett.* **2004**, *45*, 8977–8980; (d) Mayr, M.; Buchmeiser, M. R. *Macromol. Rapid Commun.* **2004**, *25*, 231–236; (e) Kim, J.-H.; Jun, B.-H.; Byun, J.-W.; Lee, Y.-S. *Tetrahedron Lett.* **2004**, *45*, 5827–5831; (f) Schwarz, J.; Böhm, V. P. W.; Gardiner, M. G.; Grosche, M.; Herrmann, W. A.; Hieringer, W.; Raudaschl-Sieber, G. *Chem. Eur. J.* **2000**, *6*, 1773–1780.
9. (a) Byun, J.-W.; Lee, Y.-S. *Tetrahedron Lett.* **2004**, *45*, 1837–1840; (b) Kim, D.-W.; Chi, D.-Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 483–485.
10. Kim, J.-H.; Kim, J.-W.; Shokouhimehr, M.; Lee, Y.-S. *J. Org. Chem.* **2005**, *70*, 6714–6720.
11. Altava, B.; Burguete, M. I.; García-Verdugo, E.; Luis, S. V.; Vicent, M. J. *Tetrahedron* **2001**, 8675–8683.
12. The NBP test is a sensitive colorimetric method developed by our group for the analysis of the presence of chlorine in chloromethylated polymers, either in gel-type (Merrifield) or monolithic resins (Macroporous). The resin is immersed in a solution of NBP [4-(4-nitrobenzyl)pyridine] in CH_2Cl_2/DMF with 5% triethylamine (TEA). Depending on the loading of the chloride in the resin, the polymer develops a colour ranging from pink to violet. Galindo, F.; Altava, B.; Burguete, M. I.; Gavara, R.; Luis, S. V. *J. Comb. Chem.* **2004**, *6*, 859–861.
13. In a typical procedure, the polymer was suspended in acetone/H_2O (for $NaBF_4$ or $NaSbF_6$) or CH_2Cl_2 (for CF_3SO_3H). Then, 3 equiv of the correspondent salt/acid were added, and the suspension was stirred for 48 h at rt. Afterwards, the polymer was filtered and thoroughly washed with water. Finally, the resulting polymer was vacuum dried.
14. General procedure for heterogeneous Heck reaction: The polymer-supported catalyst (0.02 mol % respect to the halide) was introduced in a round bottomed flask and suspended in 5 mL of DMF. Afterwards 4.5 mmol of halide, 6.75 mmol of alkene, 3 mmol of decane (internal standard) and 9 mmol of base were added. Then the flask was immersed in a thermostated oil bath. The reaction was followed by GC-FID, extracting from reaction media 30 μL of reaction mixture, and diluting it in 1 mL of MeOH. After completion of reaction, the reaction mixture was filtered to recover the catalyst. The organic phase was washed with CH_2Cl_2/H_2O and afterwards analysed by GC-FID and ^1H NMR.
15. (a) Magill, A. M.; McGuinness, D. S.; Cavell, K. J.; Britovsek, G. J. P.; Gibson, V. C.; White, A. J. P.; Williams, D. J.; White, A. H.; Skelton, B. W. *J. Organomet. Chem.* **2001**, *617*, 546; (b) Loch, J. A.; Albrecht, M.; Peris, E.; Mata, J.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2002**, *21*, 700–706.
16. Welton, T. *Coord. Chem. Rev.* **2004**, *248*, 2459–2477.