DOI: 10.1002/ejoc.200600045

Effects of Ionic Liquids on Pd-Catalysed Carbon–Carbon Bond Formation

Vincenzo Calò,*[a] Angelo Nacci,[a] and Antonio Monopoli[b]

Keywords: Carbene ligands / Carbonylation / Heck reaction / Ionic liquids / Palladium / Suzuki reaction

A comparative study of the effects exerted by different ionic liquids on catalyst stability, reaction rates and regio- and stereoselectivity in carbon–carbon coupling reactions points to the superiority of the quaternary ammonium halides over pyridinium- and imidazolium-derived ionic liquids. The influence of ionic liquids on the Heck and Suzuki reactions emerges as being associated with the Coulombic interaction between the cations and anions in ILs as well as the nucleophilicity of the anions. In the tetraalkylammonium halides and acetate, the bulkiness of tetrahedral tetraalkylammonium cations, which forces the anions away from the cation, renders these anions available for a good activity and stability of the palladium catalysts. On the contrary, the planar structures of imidazolium and pyridinium cations, due to a strong Coulombic interaction that binds the anions tightly, decrease their availability for stabilisation and activity of the catalysts.

Introduction

A problem has emerged in today's environmentally conscious world, namely that many of the solvents traditionally used in organic reactions, such as chlorinated hydrocarbons, acetonitrile, DMF, DMA and NMP, to name but a few, are currently on the "environmental blacklist". Furthermore, toxic and air-sensitive phosphanes are commonly used as ligands in transition-metal-catalysed reactions, therefore most industrial organic syntheses need rethinking. An approach to resolve these drawbacks may be the replacement of traditional solvents with ionic liquids (ILs), together with the discovery of new ligands for the metals. The advantages of using ILs would be manifold: in addition to facilitating recovery of the catalyst and reaction products, they exhibit high thermal and air stability and have a negligible vapour pressure. For these reasons, ILs are nowadays finding an increasing use for different reactions.[1] However, few studies have been dedicated to exploring the influence of different ILs on the rate and selectivity of organic reactions.

The objective of our research concerns the study of the effects exerted by ILs on the rate and selectivity of C–C coupling reactions.

The Mizoroki–Heck Reaction

The carbon–carbon bond formation reaction of aryl halides with olefins, known as the Mizoroki–Heck reaction,[2,3] was a milestone in the field of organic synthesis and has since attracted a growing interest, as evidenced by the publication of more than a thousand papers on this topic in the last five years. Although some mechanistic features of the Heck reaction are still under debate,[4] many Pd-based catalysts with phosphanes as ligands have been proposed as well as different bases and solvents, both under homogeneous and heterogeneous conditions. Generally, the solvents are DMF or DMA while, to activate the less reactive aryl chlorides, tertiary phosphanes ligands, cesium carbonate or sterically hindered amines are the bases of choice.[4d,5]

In view of the well-known[6] degradation of phosphanes by C–P bond cleavage, and the sensibility of such species to air and moisture, they have been replaced by nucleophilic carbenes of imidazole and triazole (N-heterocyclic carbenes, NHCs) as ligands for palladium.[7] Curiously, although the first synthesis of the Pd–benzothiazol-2-ylidene complex was reported early-on,[8] it did not find any applications as a catalyst for the Heck reaction. Therefore, we synthesised complex **1** (Figure 1) by reaction of 3-methylbenzothiazolium iodide with palladium acetate in THF.[9]

This complex, which is very stable to air and moisture, was found to efficiently catalyse the Heck reaction of iodobenzene and activated aryl bromides in DMF and DMA,

---

[a] Department of Chemistry, University of Bari,
Via Orabona 4, 70126 Bari, Italy
[b] Lab. for Repressione frodi alimentari,
Via Cavedone, 18, 41100 Modena, Italy
E-mail: calo@chimica.uniba.it

MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

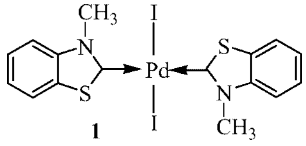
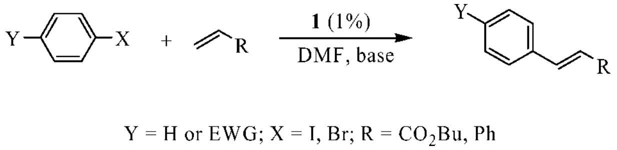


Figure 1. Pd–benzothiazole carbene complex.

with turnover numbers (TONs) of up to a million and with a higher rate than those observed with the corresponding NHC complexes,[10] although it was ineffective in catalysing the reactions of the less-reactive bromo and chloro derivatives (Scheme 1).

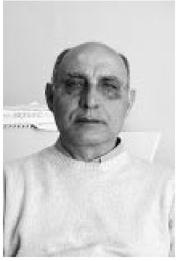


Scheme 1.

Since it was found, following the discovery by Jeffery,[11] that the addition of quaternary ammonium and phosphonium salts to conventional solvents in the Heck reaction led to higher catalytic activity,[10,12–15] we decided to perform this reaction in tetrabutylammonium bromide (TBAB) as solvent.[16] The coupling reactions in this solvent are very fast at 130 °C. For example, bromobenzene reacts with butyl acrylate in only 10 min in the presence of sodium carbonate as base. This latter was subsequently replaced with a cheap and eco-friendly base such as sodium hydrogen carbonate as TBAB undergoes a partial Hoffmann elimination with strong bases at this temperature. Under these conditions, bromobenzene and *p*-nitrochlorobenzene react in less than 1 h. Catalyst **1** is more efficient than a palladacycle. Indeed, with the latter catalyst, bromobenzene requires 48 h at 140 °C to obtain good conversions.[17] In addition, TBAB appeared to be more efficient as a solvent than the imidazolium [bmim] and pyridinium ILs in reactions catalysed by different catalysts, including palladium imidazol-2-ylidenes. It has been reported[18] that only aryl iodides react with high conversions in [bmim]s, whereas the less-reactive aryl bromides require both higher temperatures and catalyst concentrations.[19] Therefore, the addition of phosphanes was considered to be necessary to activate aryl bromides in these ILs.[20]

Few examples have been reported dealing with the Heck reaction of methacrylates as olefin acceptors.[21,22] It has been reported[23] that the reaction of 3-hydroxy-2-methylenealkanoates **2** with aryl halides affords β-oxoalkanoates **4** (Scheme 2).

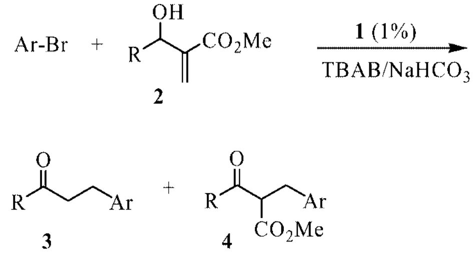
Generally, when this reaction is performed in conventional solvents it requires harsh reaction conditions and suffers from both a competitive retro-Baylis–Hillman process and a further arylation of the β-oxoalkanoate end-product.[24–26] These side reactions did not occur in TBAB, where **1** is very stable and catalyses the reactions of both electron-rich and electron-poor aryl bromides to afford only β-aryl ketones **3** and not the expected keto ester **4** (Scheme 2).[27] It is noteworthy that these reactions are inhibited upon replacing TBAB with a different IL such as



Vincenzo Calò, born in Martina Franca, Italy, graduated from the University of Bari in 1964 under the guidance of Professor G. Modena. In 1970 he joined Professor Todesco's team to study the factors influencing the regioselectivity in electrophilic aromatic substitutions. In 1980 he was appointed Full Professor in organic chemistry and joined the Department of Chemistry at the University of Bari, where he actually teaches organic chemistry. During the 1980ies his research focused on the field of organocopper chemistry. His research interests are currently focused on the chemistry of metal nanocolloids in ionic liquids for eco-friendly chemical reactions.

Angelo Nacci received his PhD degree in 1993 from the University of Bari, where in 1994 he became Assistant Professor. In 2001 he spent a period at the Technische Universität, München (Munich, Germany) in the group of Professor W. A. Herrmann. In 2004 he became Associate Professor at the University of Bari, where he currently works in the field of organic synthesis in ionic liquids. Other research interests are focussed on green chemistry, organometallic chemistry and organic transformations promoted by monoelectronic oxidants.

Antonio Monopoli graduated in 1998 from the University of Bari. He received his PhD degree from the same university in 2001 with a thesis on organic and organometallic reactions in ionic liquids. In 2001 he spent a short period in Ottawa, Canada, studying the reactivity of rhodium catalysts under the guidance of Prof. H. Alper. His research interests are focused on the use of ionic liquids as "greener solvents" and as alternative reaction media in catalysis.



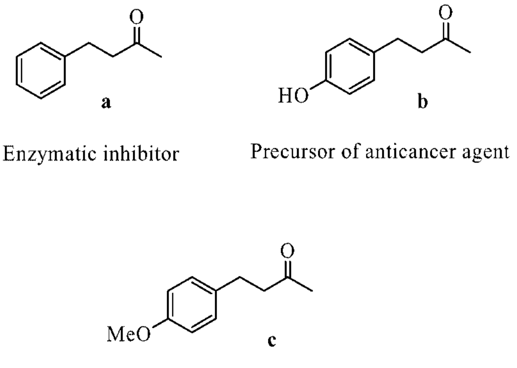
Ar = p-MeC$_6$H$_4$, p-MeOC$_6$H$_4$, p-MeCOC$_6$H$_4$,

2-naphthyl, R = Ph, Me, isopropyl, n-propyl, n-octyl

Scheme 2.

N-butylpyridinium tosylate. The exclusive formation of **3** is due to a fast decarbomethoxylation, which is favoured by TBAB, of the β-oxoalkanoate **4**. Indeed, when using a *tert*-butyl ester of **2** we obtained, besides **3**, a 30% yield of the corresponding β-oxoalkanoate, which slowly undergoes decarbobutoxylation to afford the corresponding ketone. The stability of **1** in TBAB makes a recycling process feasible. For example, in only 3 g of TBAB, after three cycles, 8 g of bromobenzene were processed with a total TON of a very decent 1720, thus making a synthesis of the active anti-inflammatory drug Nabumetone c economically viable.

Some β-aryl ketones, such as **a**–**c** (Figure 2), are useful intermediates for the synthesis of medicinal products[28,29] and therefore the development of efficient synthetic methods would be of significant utility.



a Enzymatic inhibitor

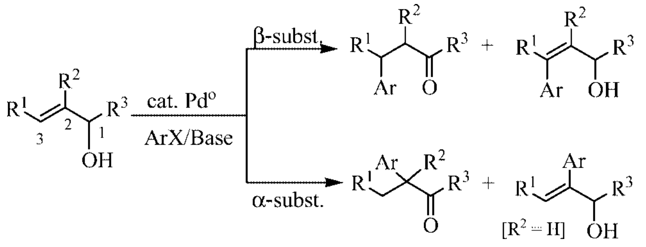
b Precursor of anticancer agent

c Nabumetone, anti-inflammatory drug

Figure 2. Biologically active β-aryl ketones.

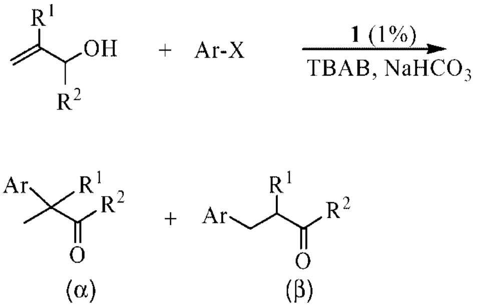
The Pd-catalysed arylation of allylic alcohols has been applied by various authors for the synthesis of these compounds.[30–32] However, this arylation was found to be barely regioselective (Scheme 3) as the reaction afforded a mixture of carbonyl compounds and substituted allylic alcohols.[33]

Beside this drawback, the choice of aryl substrates and bases was limited to aryl iodides,[30,31] triflates[33b] and weak bases since aryl bromides, which require more harsh reaction conditions, led, in the arylation of primary allylic alcohols, to aldol reaction of the formed aldehydes. Moreover, toxic solvents such as DMF or HMPA, phosphanes and high palladium concentrations[31] have been found to be necessary.



Scheme 3.

Catalyst **1**, in TBAB as solvent and with sodium hydrogen carbonate as base (Scheme 4), catalyses the coupling of aryl bromides and activated aryl chlorides with allylic alcohols to afford the β-aryl ketones efficiently and regioselectively, together with a small quantity of the positional α-isomers.[34,35]



R^1 = H, Me; R^2 = Me, Et; Ar = Ph, p-CH$_3$C$_6$H$_4$,

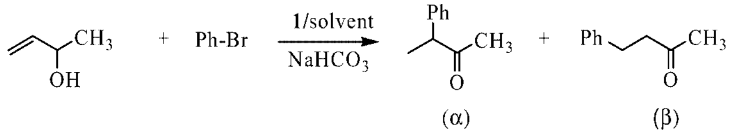
p-CH$_3$OC$_6$H$_4$, p-CH$_3$COC$_6$H$_4$; X = Br, Cl

Scheme 4.

Once more, TBAB is a more efficient solvent than [bmim]Br and DMA for these reactions. Selected examples for the reactions of bromobenzene with 1-buten-3-ol are reported in Scheme 5.

This procedure was subsequently extended to an efficient synthesis of compounds **a**–**c** by reaction of 1-buten-3-ol with the appropriate aryl bromide. However, the regioselectivity decreased when β-alkyl- or aryl-substituted allylic alcohols were used. For example, the reaction of cinnamic alcohol with p-bromotoluene gave an equal mixture of 3,3- and 2,3-diphenylpropanal.

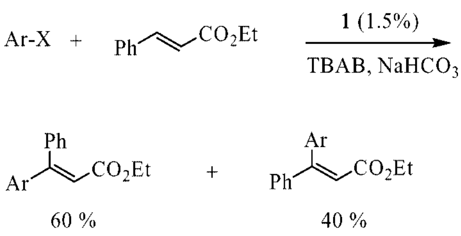
Of the papers dedicated to the Heck reaction, only a few examples describe its use for the synthesis of trisubstituted olefins.[36–39] As some β,β-diaryl acrylates are useful intermediates for the synthesis of angiotensin II antagonist,[40] platelet activating factors antagonist,[41] and SRS-A antagonists (slow-reacting substance of anaphylaxis),[42] the development of an efficient process for the Heck arylation of β-substituted acrylates would be of significant utility. Arylation of β-substituted α,β-unsaturated esters requires harsh reaction conditions, cyclopalladated phosphanes[37,38] or palladium acetate as catalysts, sterically hindered tertiary



	(α)	(β)
TBAB 5h, 99%	5	95
[bmim]Br 24 h, 50 %	10	90
DMA 22 h, 20 %	10	90

Scheme 5.

amines as bases and quaternary ammonium salts as phase-transfer agents in DMF or DMA as solvents.[13] In addition, this reaction lacks stereoselectivity as a mixture of stereoisomers is obtained. Catalyst **1**, although efficient in catalyzing this reaction,[43] did not lead to a better control of the stereoselectivity (Scheme 6).



Ar = p-$CH_3C_6H_4$, p-$CH_3OC_6H_4$, p-$CH_3COC_6H_4$,

α-naphthyl, p-$O_2NC_6H_4$, p-NCC_6H_4; X = Br, Cl

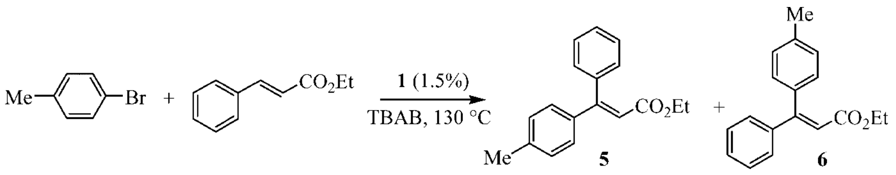
Scheme 6.

This finding is of considerable interest since the generally accepted mechanism for the Heck arylation of disubstituted alkenes predicts that the trisubstituted alkene should be formed in a stereospecific manner. The observed lack of stereoselectivity may be explained[4,21] either as base-catalysed isomerisation of products, leading to the accumulation of the more thermodynamically favourable isomer, or by re-addition of PdH to the reaction products if the hydride is not neutralised rapidly by a base. This latter process is well known as it leads to the isomerisation of alkenes, which results in the formation of isomeric Heck products with the wrong stereochemistry. Therefore, the stereochemistry of these reactions is likely to be defined by the base-catalysed isomerisation of the products. This is not surprising as the olefins with such a substitution pattern should be susceptible to base-catalysed (E)/(Z)-isomerisation.[4,44,45]

To verify the latter hypothesis, since it was known[13,46–48] that a small difference in basicity of bases can exert a dramatic influence on the regio- and stereoselectivity in the arylation of disubstituted olefins, we examined the influence of bases on the reaction between 4-bromotoluene and *trans*-ethyl cinnamate catalysed by **1** in TBAB.[49] As previously reported,[43] however, whatever the base, these reactions were devoid of stereoselectivity (Table 1, entries 1–8), and, yet again, [bmim]Br was less efficient than TBAB (Table 1, entry 8).

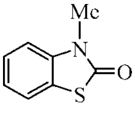
The addition of inorganic or organic bases to either of the stereoisomers in TBAB at 130 °C to verify a post-reaction isomerisation did not cause any change. Therefore, by exclusion, these results can be explained either by the Curtin–Hammet kinetic control principle,[50] with the ratio of (E)- and (Z)-isomers reflecting the relative energy of the respective transition states, or by PdH isomerisation of the reaction products. The latter hypothesis implies that, if a base does not neutralise the PdH rapidly, isomerisation of the reaction products to a thermodynamically controlled mixture of isomers should occur. As the addition of amines, sodium acetate and other inorganic bases did not improve

Table 1. Base effect on the reaction of 4-bromotoluene with *trans*-ethyl cinnamate.



Entry	Base	Solvent	t [h]	Conv. [%]	**5**:**6** ratio
1	$NaHCO_3$	TBAB	7	100	59:41
2	K_3PO_4	TBAB	4	75	61:39
3	Spartein	TBAB	3	95	60:40
4	DABCO	TBAB	5	85	62:38
5	Na_2CO_3	TBAB	5	74	59:41
6	Bu_3N	TBAB	8	94	60:40
7	NaOAc	TBAB	8	92	64:36
8	$NaHCO_3$	[bmim]Br	24	22	65:35
9	TBAA	TBAB	1	100	>99:1

the stereoselectivity, we replaced these bases with tetrabutylammonium acetate (TBAA). Upon addition of TBAA, the red colour of the solution faded rapidly to give, in addition to a dark suspension, an increase of both reaction rate and stereoselectivity, with the almost exclusive formation of the *trans* isomer **5** (Table 1, entry 9). The same increase in stereoselectivity was observed using different aryl bromides and *p*-substituted *trans*-cinnamates as acceptors. Therefore, depending on the structure of both the reaction partners, we have realized a selective synthesis of *trans*- or *cis*-β-arylcinnamates. However, catalyst **1** decomposed under these conditions to afford 3-methyl-2-oxobenzothiazole (**7**; Figure 3) due to deligation of the benzothiazolidene ligand.



7

Figure 3. 3-Methyl-2-oxobenzothiazole, a product deriving from the decomposition of catalyst **1**.

A reaction sample deposited on carbon-coated TEM grids revealed the presence of Pd nanoparticles with a size of 2–6 nm. The formation of Pd nanocolloids upon treatment of **1** with TBAA is conceivable since Reetz[51] has demonstrated that Pd nanoparticles[52–57] stabilized by alkylammonium alkanoates are formed upon heating Pd salts in the presence of tetraalkylammonium alkanoates. Dupont[52a] has reported that tributylamine, which is formed by partial decomposition of TBAB, may also be a reducing agent for Pd^{II} to give Pd colloids. However, TBAA appears to be more efficient than the amine as the reaction starts immediately without an induction period.

Almost the same results were obtained with palladium acetate as catalyst dissolved in TBAB and TBAA as base. The stereospecificity of these reactions is thermodynamic in origin and two possible explanations of the effect exerted by TBAA could be proposed: firstly, the acetate, which, for steric reasons, is distant from the bulky tetraalkylammonium cation, is poorly solvated and therefore exhibits a higher basicity than in water, and secondly, an intramolecular neutralisation of PdH, which is still bound to the olefin, by an acetate ion in the metal coordination shell may operate (Figure 4).[58] This implies that TBAA not only affords Pd nanocolloids but also efficiently neutralises the PdH.

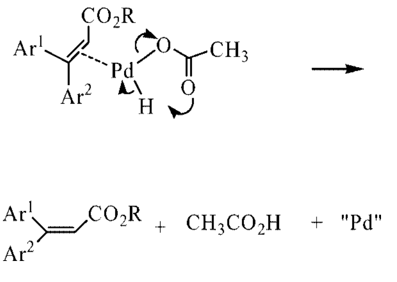
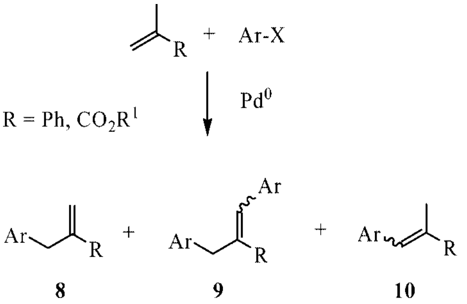


Figure 4. Intramolecular neutralisation mechanism of Pd–H by an acetate ion.

Another problem arose in the arylation of 1,1-disubstituted olefins, such as methacrylates and α-methylstyrene, where two pathways are possible, one leading to the 1,1-disubstituted terminal olefin **8**, which is susceptible to further arylation to **9**, and another that leads to the internal regioisomer **10**, for which there is an (*E*)/(*Z*) stereochemical issue (Scheme 7).



Scheme 7.

As reported above for the arylation of cinnamates, the regioisomeric ratio is either thermodynamic in origin (base-catalysed isomerisation of product leading to the accumulation of the more thermodynamically favourable internal isomer)[13,27,48] or follows the Curtin–Hammet kinetic control principle. Since the Heck reactions of aryl halides with methacrylates and α-methylstyrene allow the synthesis of medicinally interesting products,[59] the search for control of the regiochemistry has been targeted by some authors. Beller[22,47] has reported that, in the arylation of these olefins catalysed by Herrmann's palladacycle,[60–62] the control of the regioselectivity depends on the choice of the base. Inorganic bases such as sodium acetate led to the formation of a mixture of **8** and **10**, whereas the internal olefin **10** was favoured by organic bases, such as sterically hindered tertiary amines. Buchwald[13] and Fu[48] have obtained a good regioisomeric control using the above mentioned amines and a Pd catalyst with sterically hindered phosphanes, whereas Jensen[63] has reported that in similar reactions catalysed by a phosphinitopalladium complex at 180 °C in DMF both the inorganic and organic bases are equally effective in giving the internal olefins. From these data it is difficult to see which of the two regioisomers represents the kinetically favoured one or whether, in contrast, the observed ratio between the two olefins is due to a PdH equilibration and/or to a base-catalysed isomerisation of the reaction products.

Recently, palladium nanoparticles of different origin have been utilized in the Heck arylation of unsubstituted acrylates[55–57,64–67] and styrene[68–70] with variable degrees of success although, to the best of our knowledge, none of these catalysts was applied to a selective synthesis of 1,1-disubstituited and trisubstituted olefins. Therefore, it was of interest to study the influence exerted on the regiochemistry by TBAA as base and TBAB as solvent in the Heck reactions of butyl methacrylate and α-methylstyrene with aryl halides catalysed by Pd nanoparticles. Under these reaction conditions, Pd nanoparticles (1.5–6 nm), prepared simply by adding Pd acetate to a mixture of TBAB and TBAA at 120 °C, catalyze the coupling of aryl bromides with butyl methacrylate with an astonishingly high reaction rate (less than 15 min; Table 2).[71] Clearly, as reported above,[49] as PdH is efficiently neutralised by TBAA, it should be possible to distinguish the effect of the base, including TBAA, on the regiochemistry of the coupling process. To do this, we examined reaction samples taken at low conversion values (Table 2, entry 1) for the reaction of bromobenzene with the methacrylate. At low conversion values the terminal olefin **11** was the major isomer, and its concentration decreased in favour of the doubly arylated product **12** while the internal isomer **13** remained constant (Table 2, entry 2). After 6 min **11** begun to decrease in favour of **13** (entry 3).

In contrast, *p*-bromoacetophenone (entry 6) afforded almost exclusively the internal isomer **13**, with complete conversion in less than 15 min and without the doubly arylated product **12**. To explain this contradictory regiochemical course, this reaction was monitored at lower conversion values and with a Pd concentration of 0.1 mol-% (entry 7). We found a larger concentration of the terminal isomer **11**, which was converted into **13** in only four minutes.[72] In the reaction of bromobenzene, the replacement of TBAA with tetrabutylammonium pivalate (TBAP) as base gave a major selectivity in favour of the internal isomer **13** (entry 8). As far as TBAB is concerned, it contributes to the stabilisation of Pd nanoparticles but is not responsible for the regiochemical results. Indeed, the replacement of TBAA with tributylamine or sodium acetate (entries 9 and 10) led to the same isomeric ratios as observed by Beller in organic solvents.[22,47] As found in the arylation of cinnamates,[49] no reaction occurred if [bmim]Br was utilized as solvent in place of TBAB (entry 11).

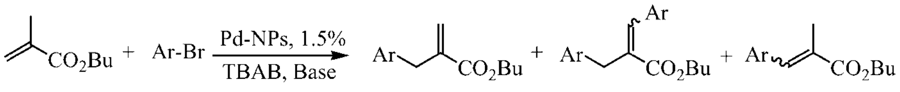
The isomerisation of the reaction products suggested that, besides a fast PdH neutralisation, TBAA isomerizes the two regioisomeric olefins, albeit slowly, in favour of the internal isomer. Moreover, a faster isomerisation was achieved by replacing TBAA with tetrabutylammonium pivalate, which is manifestly more basic than TBAA. Indeed, a mixture of the two regioisomeric olefins derived from the reaction of bromobenzene, in TBAB, isomerized completely in less than four hours into the internal olefin **13** upon addition of TBAP. The fast neutralisation of PdH could be due to an improved basicity of the acetate ion in TBAA. This is plausible and may be ascribed to the bulkiness of the tetrahedral ammonium cation, which, by forcing the acetate away from the cation, should decrease the Coulombic force between the ions, thus improving both the basicity and nucleophilicity of this anion for palladium.[73] The latter concept was supported by the enhanced ability of the TBAP to isomerize the regioisomers. Indeed, the pivalate ion, which is bulkier than acetate, is more distant from the cation and therefore more basic. These results are important from a synthetic point of view since by using these bases it is possible to obtain a full control of the regioselectivity in the Heck reaction of such olefins. The 3:1 ratio observed for the regioisomers, as measured at low conversion values (Table 2, entry 1), suggests that the terminal isomer is the kinetically favoured one. This preference for the terminal isomer may be merely statistical as all three hydrogens are equally available for a *syn* elimination of PdH (Scheme 8). In contrast, the two hydrogens at the internal position are not equal, as the respective conformations are different in energy due to Pd–Ar, Ar–R and Ar–Me eclipsing.

In addition, the statistical weights of the two routes leading to (*E*) and (*Z*) olefins are not equal, as the route leading to the (*Z*) isomer can be neglected. Indeed, the (*E*) isomer is derived from the less sterically hindered conformer.

An almost parallel situation was observed in the arylation of α-methylstyrene, although with reaction rates slower than those observed for the methacrylate and an (*E*)/(*Z*) ratio for the internal olefin of 30:1 at low conversion. Once more, TBAP converted the terminal olefins into the internal isomers in only six hours at 120 °C in TBAB, with a final (*E*)/(*Z*) ratio of about 9:1.

In the last few years Pd catalysts deposited on inorganic and organic supports have gained in popularity because of the necessity to recycle the expensive metal catalyst and to

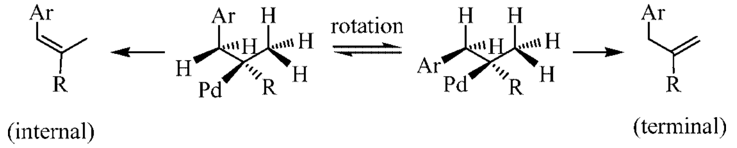
Table 2. Pd nanoparticle catalysed Heck reaction of *n*-butyl methacrylate in TBAB.



11 **12** **13**

Entry	Ar	Base	t [min]	Conv. [%]	**11**:**13**	**12**
1	C_6H_5	TBAA	1	10	74:26	–
2	C_6H_5	TBAA	6	99	65:26	9
3	C_6H_5	TBAA	30	99	46:45	9
4	p-$CH_3C_6H_4$	TBAA	15	99	59:30	11
5	p-$CH_3OC_6H_4$	TBAA	15	99	63:30	7
6	p-$CH_3COC_6H_4$	TBAA	15	99	4:96	–
7[a]	p-$CH_3COC_6H_4$	TBAA	1	45	28:72	–
8	C_6H_5	TBAP	15	59	36:64	–
9	C_6H_5	NaOAc	60	99	44:49	7
10	C_6H_5	Bu_3N	60	99	44:49	7
11[b]	C_6H_5	TBAA	18 h		n.r.	

[a] 0.1 mol-% of catalyst. [b] [bmim]Br as solvent.



Scheme 8.

avoid, especially in the pharmaceutical industry, the contamination of the products by the toxic metal.[74,75] However, these catalysts have proved useful in the Heck reaction mainly for aryl iodides because the bromides, which are practically unreactive, require elevated temperatures and high catalyst concentrations.[18a,19] In addition, the recovery of the spent catalyst from these supports has proved to be difficult. To overcome these inconveniences we synthesised Pd nanoparticles supported on a cheap and optically active matrix (chitosan). Chitosan, or poly[β-(1–4)-2-amino-2-deoxy-D-glucal], is a cheap, natural polymer that is widely utilized in biology, medicine and the food industries.[76] However, it has been little utilized as a support or supramolecular ligand for catalysts, even though its clean elimination from the metal entity makes the recovery of the precious metals easy.[77] We synthesised Pd nanoparticles on chitosan by a sacrificial anode electrolysis, carried out in acetonitrile, in the presence of the polymer and TBAB.[78] The electrolysis of palladium affords core–shell Pd nanoparticles whose metallic core is surrounded by a stabilizing shell composed of bromide, tetrabutylammonium ions and $[PdBr_4]^{2-}$, which counterbalance the positive charges in the shell[52] (Figure 5).

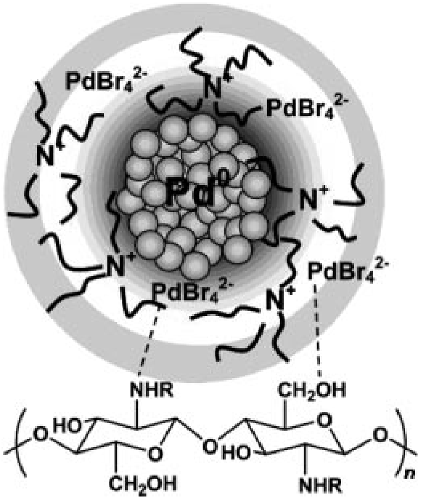


Figure 5. Core–shell structure of Pd nanocolloids supported on chitosan.

This catalyst offers several advantages over other supported Pd catalysts, such as high catalytic efficiency and stability. For example, 2-bromo-6-methoxynaphthalene, dissolved in TBAB and with TBAA as base, reacts with butyl acrylate in only 15 min with more than 99% conversion with a composite containing only 0.004% of Pd.[79,80] Under these conditions, both aryl bromides and activated chlorides reacted with high reaction rates. In addition, the stability of this catalyst allowed several recycles without significant decomposition. As reported above, the structure of the IL plays an important role in influencing reaction rates and conversions here as well. Table 3 reports some selected results concerning this influence.

Table 3. Pd-NPs/chitosan-catalysed Heck arylation of *n*-butyl acrylate in ILs.

Entry	Ionic liquid	Base	Time	Conv. [%]
1	TBAB	TBAA	15 min	>99
2	TBAB	$NaHCO_3$	2.5 h	75
3	TBAB	Bu_3N	40 min	>99
4	$[bmim]BF_4$	TBAA	24 h	<1
5	[bmim]Br	TBAA	24 h	<1
6	$[bupy]BF_4$[a]	TBAA	2.5 h	76
7	TBPBr[b]	TBAA	2.5 h	95

[a] *N*-Butylpyridinium tetrafluoroborate. [b] Tetrabutylphosphonium bromide.

This Pd nanocomposite was much more efficient in TBAB than in pyridinium, phosphonium and imidazolium ILs in catalyzing the Heck reaction.

All the results reported above point out the fundamental role of TBAB as the IL in governing the catalyst activity and life by stabilising the Pd nanoparticles. This study, due to its nature, does not address the question as to whether free palladium colloids are the actual catalysts or whether the chitosan composite functions as a reservoir of smaller and probably more reactive fragments.[52] The solvent effect on the stabilisation of nanoparticles is, however, difficult to explain. Indeed, despite the observed beneficial effects exerted by quaternary ammonium salts on the Heck reaction,[81] the exact nature of this influence cannot be ascribed to a single effect such as the high polarity or phase-transfer ability, but rather to a superposition of several factors. For example, Reetz and Maase[51] have found that Pd nanocolloids are stabilized by large ammonium cations. Furthermore, Neghishi et al.[82] and Amatore and Jutand,[4c] have demonstrated that $Pd^0(PPh_3)_2$, the proposed catalyst in the Heck reaction, is unstable in the absence of halide or acetate ions, which transform this complex into a more stable and catalytically active 16-electron anionic complex such as $[Pd(PPh_3)_2X]^-$. Following these conclusions, and to elucidate the effect of the ionic liquid, we proposed some considerations that would assist in explaining our results. For example, the oxidative addition of aryl halides to Pd nanoparticles, surrounded by TBAB (Figure 5), would afford an unstable 12-electron complex (ArPdX), which could be stabilized by interaction with TBAB or TBAA to afford an anionic, and more stable, 16-electron complex $[ArPdX_3]^{2-}\cdot 2NR_4^+$ ($X = Br^-$ and/or AcO^-). This would not be surprising as the poor solvation of the nucleophilic anions (bromide and acetate) in these ILs should make them good ligands for palladium. Indeed, the high nucleophilicity of these anions was demonstrated by us in a paper dealing with the nucleophilic ring opening of epoxides by TBAB in the presence of carbon dioxide to give cyclic carbonates under very mild reaction conditions.[83] Beside this effect, the tetraalkylammonium cation could assist the polarisation or decomplexation of the halide ion from the Pd^{II} anionic complex electrostatically, which would make the latter more electrophilic for a fast olefin insertion. Furthermore, the formation of a bulky 16-electron complex should prevent clusters from growing further into metal particles by imposing a Coulombic barrier for collision.

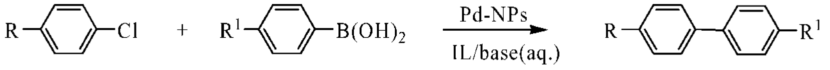
Our results reveal that, contrary to TBAB and TBAA, the effects on the catalyst formation, stability and activity are poorly or not influenced by ILs like the [bmim] salts. In our opinion, this is due to the planar structures and to an extended network of hydrogen-bonded cations and anions in which one cation is surrounded by at least three anions.[84] Therefore, these ILs decrease the availability of the anion for the formation of a stable 16-electron complex by binding it tightly. It has been reported that the availability of the anion in [bmim]Cl for coordination to a metal complex requires desolvation.[85] As a consequence, metal complexes involving halide dissociation from the imidazolium cation, either for the formation of the active catalyst or in a step in the catalytic cycle, may not be active in imidazolium ionic liquids. In addition, the ammonium cation could help the detachment of the halide from the PdHX electrostatically, thus favouring the neutralisation and reformation of the Pd^0 catalyst. Therefore, the tetrabutylammonium halides, whatever the rate-determining step in the catalytic cycle, would produce a helpful effect in each step in the catalytic cycle.

Suzuki–Myiaura and Stille Synthesis of Biaryls

A number of papers have described the Suzuki reaction in imidazolium salts ([bmim]s) as ILs using Pd catalysts bearing phosphanes,[86] nitrogen compounds[87] or carbenes[88] as ligands or palladacycles.[89] In some cases the use of ligand-free Pd catalysts in water as solvent and tetrabutylammonium salts as phase-transfer agents has been reported.[90] Pd nanoparticles embedded into polymeric, dendritic or inorganic supports have also been utilized as catalysts for this reaction. However, harsh reaction conditions were required for aryl bromides and iodides in most of these applications, while chlorides were almost unreactive. Only a few papers report the activation of aryl chlorides and bromides by Pd nanoparticles.[75a,91]

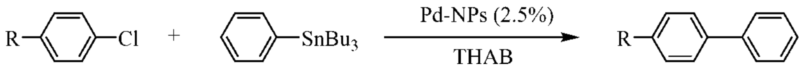
As Pd nanoparticles have proved to be very efficient catalysts in ionic liquids for the Heck reaction, it seemed to be interesting to test the effects of ILs on the Suzuki and Stille coupling of aryl chlorides. Our recent research on this subject[92] has revealed that several factors, such as the nature of the IL and base, influence the efficiency of the coupling process for aryl chlorides (Table 4). TBAB in this case appeared less efficient in catalyzing the Suzuki than the Heck reaction in the presence of inorganic bases (Table 4, entries 1 and 2). Better results were observed using a concentrated aqueous solution of tetrabutylammonium hydroxide as base, which is more soluble in TBAB. However, the presence of an aqueous base, which is necessary for the Suzuki reaction, accelerated the aggregation of Pd nanoparticles to afford catalytically inactive "Pd black", which inhibits the catalyst recycling. Good results were obtained by substituting TBAB with a more hydrophobic solvent such as tetraheptylammonium bromide (THAB) in the reaction of aryl chlorides with phenylboronic acids. Indeed, THAB was found to be far superior to TBAB as solvent (entries 3 and 4). The lipophilic character of THAB probably limits the aggregation of the Pd nanoparticles into inactive large metal particles by forming strong hydrophobic and steric interactions. In addition, the reaction rate also depends on the nucleophilicity of the anion ligated to the tetrabutylammonium cation

Table 4. The effect of base and IL on the Pd nanoparticle catalysed Suzuki reaction.



Entry	Solvent	Base (aq)	R	R^1	*T* [°C]	*t* [h]	Conv. [%]
1	TBAB	Na_2CO_3	H	H	140	16	15
2	TBAB	KOH	H	H	90	16	36
3	TBAB	NBu_4OH	H	H	60	16	<1
4	(THAB)	NBu_4OH	H	H	60	1.5	>99
5	(THAB)	NBu_4OH	CH_3CO	H	60	16	99
6	(THAB)	NBu_4OH	NO_2	H	60	3	99
7	(THAB)	NBu_4OH	CH_3CO	CH_3O	60	5	99
8	(THAB)	NBu_4OH	NO_2	CH_3O	60	5	99
9	(THAB)	NBu_4OH	CH_3O	H	110	16	55
10	(THAB)	NBu_4OH	CH_3	H	110	16	69
11	$(TBA)BF_4$	NBu_4OH	H	H	90	16	11

Table 5. The Stille cross-coupling catalysed by Pd nanoparticles.



Entry	R	T [°C]	Yield [%]
1	H	90	68
2	NO_2	90	91
3	CH_3CO	90	52
4	CH_3O	130	40

as the reaction in hydrophobic tetrabutylammonium fluoborate $(TBA)BF_4$ is slower than those in THAB (entry 11). The latter result represents additional evidence, as found for the Heck reaction, in favour of the importance of halide ions in not only stabilizing the nano-catalyst but also in assisting the transmetallation step in the Suzuki and Stille reactions, as already shown[93] for the Stille reaction in imidazolium-based ILs.

A similar behaviour was observed for the Stille reaction between aryl chlorides and tributylphenylstannanes in THAB (Table 5). Under these reaction conditions, neutral and electron-poor halides reacted with good yields at 90 °C (entries 1–3), whereas less reactive electron-rich substrates required higher temperatures (entry 4). Therefore, the latter results, as well those concerning the Suzuki reaction, emphasise the role of tetraalkylammonium bromides in stabilizing the Pd nanoparticles.

Carbonylation of Aryl Halides

The carbonylation of aryl halides (Scheme 9) was investigated by us some years ago by with catalyst **1** in order to study the effects of ILs on the parameters influencing this industrial important process.[94]

$$\text{Ar-X} \quad + \quad \text{CO} \quad + \quad \text{Nu} \quad \xrightarrow{\text{catalyst}} \quad \text{ArCONu}$$

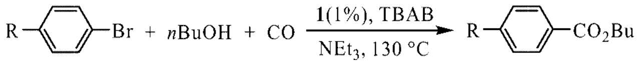
$$\text{X} = \text{Cl, Br, I;}\ \ \text{Nu} = \text{H}_2\text{O, ROH, NHR}_2$$

Scheme 9.

Among various catalysts, Pd–phosphane complexes or Pd-supported catalysts[95–98] have been widely employed mostly under homogeneous conditions in molecular solvents[99,100] but rarely in ILs.[101]

Contrary to the results and reaction rates observed in the Heck reactions catalysed by **1** in TBAB, the aryl bromides react very slowly at 130 °C under one atmosphere of CO in the presence of *n*-butanol as nucleophile and triethylamine as base. A slight increase in the conversion was observed, however, upon increasing the CO pressure (Table 6).

Table 6. IL effect on the carbonylation of aryl bromides.[a]



Entry	Catalyst	R	Il	Conv. [%]
1	**1**	H	TBAB	30
2	**1**/PPh_3	H	TBAB	96
3	**1**	CH_3CO	TBAB	78
4	**1**	CH_3CO	$[bmim]BF_4$	3
5	**1**	CH_3CO	[bmim]Cl	<1
6	**1**	CH_3CO	[bmim]Br	16
7	**1**	CH_3CO	Aliquat[b]	40
8	**1**	CH_3CO	BPT[c]	<5

[a] **1** (1%), p_{CO} = 8 atm, 14 h. [b] Tricaprylmethylammonium chloride. [c] *N*-Butylpyridinium tosylate.

Once more, the [bmim]s and pyridinium tosylate were less efficient than TBAB (Table 6, entries 4–6 and 8) in catalyzing the coupling of *p*-bromoacetophenone. Furthermore, the less activated aryl bromide bromobenzene reacted slowly, although the addition of a very small quantity of triphenylphosphane to **1** allowed an increase in the conversion rate (Table 6, entries 1 and 2).

The latter results point out the role of PPh_3 in the carbonylation of less reactive bromides such as bromobenzene. A question arises from the latter result: is the benzothiazole ligand still bonded to palladium or substituted by the phosphane to give the well-known catalyst $Pd^0(PPh_3)_2$?[4c] In order to get some insight into this we carried out the carbonylation of *p*-bromoacetophenone in the presence of palladium acetate and PPh_3 as catalyst in TBAB. Although this reaction occurred with good conversion, the catalyst rapidly deactivated to give catalytically inactive palladium metal. In contrast, the catalyst **1**/PPh_3 was more stable and was recycled more than seven times without appreciable deactivation. The latter result probably suggests an active catalyst containing both the benzothiazol-2-ylidene and phosphane ligands. This is plausible because there are several reports of characterised Pd catalysts that are active in catalyzing the cross-coupling reaction of aryl halides[102–104] and contain both imidazol-2-ylidene carbene and triphenylphosphane as ligands.

Conclusions

A comparative study on the effects exerted by different ionic liquids on catalyst stability, reaction rates and regio- and stereoselectivity in the carbon–carbon coupling reactions points out the superiority of the quaternary ammonium halides over pyridinium- and imidazolium-derived ionic liquids. The influence of the quaternary ammonium halides and acetate on the Heck and Suzuki reactions cannot be simply ascribed to their high polarity or phase-transfer properties because imidazolium and pyridinium ILs also have a high polarity comparable with those of polar aprotic solvents. It appears that the Coulombic interaction between cations and anions in ILs influences the activity and life of the palladium catalysts in the Heck reaction. In TBAB, the bulkiness of the tetrahedral ammonium cation renders this anion more nucleophilic and available for an increased activity and stability of the palladium catalysts by forcing the bromide away from the cation. In addition, the results obtained in controlling the regio- and stereoselectivity in the carbon–carbon coupling process using tetrabutylammonium acetate as base reveal that the greater efficiency of the acetate over organic bases is due to a poor solvation of this species. On the contrary, the planar structures of [bmim]s and pyridinium cations would decrease their availability for stabilisation and activity of the catalysts, due to a strong Coulombic interaction that binds the anions tightly. As a consequence, metal complexes involving halide dissociation from the imidazolium cation, either for the formation of the active catalyst or in a step in the catalytic cycle, might not be adequately active in the imidazolium ILs. This review, even though the understanding of the mechanisms of catalysis in ionic liquids is still in its infancy, is an effort to clarify the multiple effects exerted by ILs on catalytic carbon–carbon forming reactions.

Acknowledgments

This work was financially supported in part by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome, and the University of Bari (National Project: "Stereoselezione in Sintesi Organica: "Metodologie ed Applicazioni."

---

[1] Reviews for reactions in ILs: a) J. D. Holbrey, K. R. Seddon, *Clean Prod. Proc.* **1999**, *1*, 223–1346; b) T. Welton, *Chem. Rev.* **1999**, *99*, 2071–2084; c) P. Wasserscheid, W. Keim, *Angew. Chem. Int. Ed.* **2000**, *39*, 3772–3789; d) C. M. Gordon, *Appl. Catal. A* **2001**, *222*, 101–117; e) H. Oliver-Bourbigou, L. Magna, *J. Mol. Catal. A* **2002**, *182/182*, 419–437; f) J. Dupont, R. F. de Souza, P. A. Z. Suarez, *Chem. Rev.* **2002**, *102*, 3667–3692.

[2] a) R. F. Heck, in *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), vol. 4, Pergamon, Oxford, **1991**, p. 833; b) W. A. Herrmann, in *Applied Homogeneous Catalysis with Organometallic Compounds* (Eds.: B. Cornils, W. A. Herrmann), VCH, Weinheim, **1996**, p. 712.

[3] Reviews: a) A. de Meijere, F. E. Meyer, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2379–2411; b) W. Cabri, I. Candiani, *Acc. Chem. Res.* **1995**, *28*, 2–7; c) G. T. Crisp, *Chem. Soc. Rev.* **1998**, *27*, 427–436; d) J. P. Genet, M. J. Savignac, *J. Organomet. Chem.* **1999**, *576*, 305–317; e) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009–3066; f) N. J. Whitcombe, K. K. Hii, S. E. Gibson, *Tetrahedron* **2001**, *57*, 7449–7476; g) W. A. Herrmann, K. Öfele, D. Preysing, S. K. Schneider, *J. Organomet. Chem.* **2003**, *687*, 229–248; h) H.-U. Blaser, A. Indolese, F. Naud, U. Nettekoven, A. Schnyder, *Adv. Synth. Catal.* **2004**, *346*, 1583–1598; i) U. Christmann, R. Vilar, *Angew. Chem. Int. Ed.* **2005**, *44*, 366–374.

[4] For mechanistic aspects, see: a) R. J. Deeth, A. Smith, K. K. Hii, J. M. Brown, *Tetrahedron Lett.* **1998**, *39*, 3229–3232; b) J. M. Ludwig, S. Strömberg, M. Svensson, B. Åkermark, *Organometallics* **1999**, *18*, 970–975; c) C. Amatore, A. Jutand, *J. Organomet. Chem.* **1999**, *576*, 254–278; d) H. von Schenck, B. Åkermark, M. Svensson, *J. Am. Chem. Soc.* **2003**, *125*, 3503–3508; e) I. D. Hills, G. C. Fu, *J. Am. Chem. Soc.* **2004**, *126*, 13178–13179; f) P. Fristrup, S. Le Quement, D. Tanner, P.-O. Norrby, *Organometallics* **2004**, *23*, 6160–6165.

[5] Recent examples: a) G. A. Grasa, M. S. Viciu, J. Huang, S. P. Nolan, *J. Org. Chem.* **2001**, *66*, 7729–7737; b) C. W. K. Gstöttmayr, V. P. W. Böhm, E. Herdtweck, M. Grosche, W. A. Herrmann, *Angew. Chem. Int. Ed.* **2002**, *41*, 1363–1365; c) J. Yin, M. P. Rainka, X.-X. Zhang, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 1162–1163; d) N. A. Beare, J. F. Hartwig, *J. Org. Chem.* **2002**, *67*, 541–555; e) K. Selvakumar, A. Zapf, M. Beller, *Org. Lett.* **2002**, *4*, 3031–3033.

[6] P. E. Garrou, *Chem. Rev.* **1985**, *85*, 171–185.

[7] a) S. R. Stauffer, S. Lee, J. P. Stambuli, S. I. Hauck, J. F. Hartwig, *Org. Lett.* **2000**, *2*, 1423–1426; b) H. M. Lee, C. Y. Lu, C. Y. Chen, W. L. Chen, H. C. Lin, P. L. Chiu, P. Y. Cheng, *Tetrahedron* **2004**, *60*, 5807–5825; c) W. A. Herrmann, *Angew. Chem. Int. Ed.* **2002**, *41*, 1290–1309; d) W. A. Herrmann, K. Öfele, D. von Preysing, S. K. Schneider, *J. Organomet. Chem.* **2003**, *687*, 229–248; e) J. Dupont, J. Spencer, *Angew. Chem. Int. Ed.* **2004**, *43*, 5296–5297.

[8] a) D. J. Cardin, D. Cetinkaya, E. Cetinkaya, M. F. Lappert, *J. Chem. Soc., Dalton Trans.* **1973**, 514–522; b) M. F. Lappert, *J. Organomet. Chem.* **2005**, *690*, 5467–5473.

[9] V. Calò, R. Del Sole, A. Nacci, E. Schingaro, F. Scordari, *Eur. J. Org. Chem.* **2000**, 869–871.

[10] W. A. Herrmann, $^{\mathrm{m}}$. $^{\mathrm{a}}$lison, J. Fisher, C. Köcher, G. R. J. Artus, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2371–2374.

[11] T. Jeffery, *Tetrahedron Lett.* **1994**, *35*, 3051–3054.

[12] M. T. Reetz, G. Lohmer, R. Schwickardi, *Angew. Chem. Int. Ed.* **1998**, *37*, 481.

[13] C. Gürtler, S. L. Buchwald, *Chem. Eur. J.* **1999**, *5*, 3107–3112.

[14] M. T. Reetz, E. Westermann, *Angew. Chem. Int. Ed.* **2000**, *39*, 165–168.

[15] The Heck reaction in ammonium and phosphonium salts: a) D. E. Kaufmann, M. Nourozian, H. Henze, *Synlett* **1996**, 1091–1092; b) S. Bouquillon, B. Ganghegui, B. Strine, J. Muzart, *J. Organomet. Chem.* **2001**, *634*, 153–156; c) G. Battistuzzi, S. Cacchi, G. Fabrizi, *Synlett* **2002**, 439–442; d) D. A. Gerritsma, A. Robertson, J. McNulty, A. Capretta, *Tetrahedron Lett.* **2004**, *45*, 769. See also ref.[4e]

[16] V. Calò, A. Nacci, L. Lopez, N. Mannarini, *Tetrahedron Lett.* **2000**, *41*, 8973–8976.

[17] See, for example: a) W. A. Herrmann, V. P. W. Böhm, C.-P. Reisinger, *J. Organomet. Chem.* **1999**, *576*, 23–41; b) C. S. Consorti, M. L. Zanini, S. Leal, G. Ebeling, J. Dupont, *Org. Lett.* **2003**, *5*, 983–986.

[18] a) S. B. Park, H. Alper, *Org. Lett.* **2003**, *5*, 3209–3212; b) S. Liu, T. Fukuyama, M. Sato, I. Ryu, *Synlett* **2004**, 1814–1816.

[19] a) H. Hagiwara, Y. Shimizu, T. Hoshi, T. Suzuki, M. Ando, K. Ohkubo, C. Yokoyama, *Tetrahedron Lett.* **2001**, *42*, 4349–4351; b) L. Xu, W. Chen, J. Xiao, *Organometallics* **2000**, *19*, 1123–1127; c) J. Dupont, G. S. Fonseca, A. P. Umpierre, P. F. P. Fichtner, S. R. Teixseira, *J. Am. Chem. Soc.* **2002**, *124*, 4228–4229; d) K. S. A. Vallin, P. Emilsson, M. Larhed, A. Hallberg, *J. Org. Chem.* **2002**, *67*, 6243–6246; e) G. Zou, Z. Wang, J. Zhu, J. Tang, M. J. He, *J. Mol. Catal. A* **2003**, *206*, 193–198; f) S. T. Handy, M. Okello, G. Dickenson, *Org. Lett.* **2003**, *5*, 2513–2515; g) W. Pei, J. Mo, J. Xiao, *J. Organomet. Chem.* **2005**, *690*, 3546–3551.

[20] a) A. J. Carmichael, M. J. Earle, P. B. McCormac, K. R. Seddon, *Org. Lett.* **1999**, *1*, 997–1000; b) V. P. W. Böhm, W. A. Herrmann, *Chem. Eur. J.* **2000**, *6*, 1017–1025; c) L. Xu, W. Chen, J. Xiao, *Org. Lett.* **2003**, *5*, 295–297; d) J. Schutz, E. Herdtweck, W. A. Herrmann, *Organometallics* **2004**, *23*, 6084–

6086. For the Heck coupling of electron-rich olefins, see: e) J. Mo, L. Xu, J. Xiao, *J. Am. Chem. Soc.* **2005**, *127*, 751–760; f) J. Mo, S. Liu, J. Xiao, *Tetrahedron* **2005**, *61*, 9902–9907.

[21] J. Tsuji, *Palladium Reagents and Catalysts*, Wiley, New York **1996**.

[22] M. Beller, T. H. Riermeier, *Tetrahedron Lett.* **1996**, *37*, 6535–6538.

[23] D. Basavaiah, K. Muthukumaran, *Tetrahedron* **1998**, *54*, 4943–4948.

[24] T. Satoh, Y. Kawamura, M. Miura, N. Nomura, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1740–1742.

[25] M. Palucki, S. L. Buchwald, *J. Am. Chem. Soc.* **1997**, *119*, 11108–11109.

[26] B. C. Hamann, J. F. Hartwig, *J. Am. Chem. Soc.* **1997**, *119*, 12382–12383.

[27] V. Calò, A. Nacci, L. Lopez, A. Napola, *Tetrahedron Lett.* **2001**, *42*, 4701–4703.

[28] S. Ducki, J. A. Hadfield, L. A. Hepworth, N. J. Lawrence, C.-Y. Liu, A. T. McGown, *Bioorg. Med. Chem. Lett.* **1997**, *7*, 3091–3094.

[29] V. S. N. Murthy, Y. Meah, V. Massey, *J. Am. Chem. Soc.* **1999**, *121*, 5344–5345.

[30] J. B. Melpolder, R. F. Heck, *J. Org. Chem.* **1976**, *41*, 265–272.

[31] S. Bouquillon, B. Ganchegui, B. Estrine, F. Hénin, J. Muzart, *J. Organomet. Chem.* **2001**, *634*, 153–155 and references cited therein.

[32] a) S.-K. Kang, K.-Y. Jung, C.-H. Park, E.-Y. Namkoong, *Tetrahedron Lett.* **1995**, *36*, 6287–6290; b) D. Bruyère, G. Gainard, D. Bouyssi, J. M. Lancelin, *Tetrahedron Lett.* **1997**, *38*, 827–830; c) L. Bagnell, U. Kreher, C. R. Strauss, *Chem. Commun.* **2001**, 29–30; d) T. Jeffery, *Tetrahedron Lett.* **1991**, *32*, 2121–2124; e) S. Sengupta, S. K. Sadhuikhan, *Tetrahedron Lett.* **1998**, *39*, 2291–2292; f) L. F. Tietze, J. Görlitzer, A. Schuffenhauer, M. Hübner, *Eur. J. Org. Chem.* **1999**, 1075–1084.

[33] For regioselective synthesis of aryl-substituted allylic alcohols see: a) T. Jeffery, *J. Chem. Soc., Chem. Commun.* **1991**, 324–325; b) E. Bernocchi, S. Cacchi, P. G. Ciattini, E. Morera, G. Ortar, *Tetrahedron Lett.* **1992**, *33*, 3073–3076; c) S.-K. Kang, H.-W. Lee, S.-B. Jang, T.-H. Kim, S.-J. Pyun, *J. Org. Chem.* **1996**, *61*, 2604–2605.

[34] V. Calò, A. Nacci, A. Monopoli, M. Spinelli, *Eur. J. Org. Chem.* **2003**, 1382–1385.

[35] V. Calò, A. Nacci, A. Monopoli, *J. Organomet. Chem.* **2005**, *690*, 5458–5466.

[36] A. Arcadi, S. Cacchi, G. Fabrizi, P. Pace, *Tetrahedron* **1996**, *52*, 6983–6996.

[37] M. Beller, T. H. Riermeier, *Tetrahedron Lett.* **1996**, *37*, 6535–6538.

[38] M. Moreno-Mañas, M. Pèrez, R. Pleixats, *Tetrahedron Lett.* **1996**, *37*, 7449–7452.

[39] Ref.[21].

[40] C. Almansa, L. A. Gómez, F. L. Cavalcanti, A. F. de Arriba, R. Rodríguez, E. Carceller, J. García-Rafanell, J. Forn, *J. Med. Chem.* **1996**, *39*, 2197–2206.

[41] See, for example: F. Himmelsback, H. Pieper, V. Austel, G. Linz, B. Guth, T. Mueller, J. J. Weisemberger (Dr. Karl Thomae Gmbh), Eur. Pat. EP 612,741 **1994**; *Chem. Abstr.* **1995**, *122*, 314547p.

[42] S. B. Kadin (Pfizer Inc.), U. S. Pat. US 4,342,781 **1982**; *Chem. Abstr.* **1982**, *97*, 215790w.

[43] a) V. Calò, A. Nacci, A. Monopoli, L. Lopez, A. di Cosmo, *Tetrahedron* **2001**, *57*, 6071–6077; b) V. Calò, A. Nacci, *Z. Naturforsch., Teil A* **2001**, *56*, 702–706.

[44] A. J. Spencer, *J. Organomet. Chem.* **1982**, *240*, 209–216.

[45] K. K. Hii, T. D. W. Claridge, J. M. Brown, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 984–987.

[46] L. A. Fowley, D. Michos, X.-L. Luo, R. H. Crabtree, *Tetrahedron Lett.* **1993**, *34*, 3075–3078.

[47] M. Beller, T. H. Riermeier, *Eur. J. Inorg. Chem.* **1998**, 29–35.

[48] A. F. Littke, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 6989–7000.

[49] V. Calò, A. Nacci, A. Monopoli, S. Laera, N. Cioffi, *J. Org. Chem.* **2003**, *68*, 2929–2933.

[50] L. P. Hammet, *Physical Organic Chemistry: Reaction Rates, Equilibria and Mechanisms*, 2nd ed., McGraw-Hill, New York, **1970**.

[51] M. T. Reetz, M. Maase, *Adv. Mater.* **1999**, *11*, 773–777.

[52] For Pd nanoparticles originating from palladacycles see:a) C. S. Consorti, F. R. Flores, J. Dupont, *J. Am. Chem. Soc.* **2005**, *127*, 12054–12065; b) J. G. de Vries, *Dalton Trans.* **2006**, 421.

[53] J. Le Bars, U. Specht, J. S. Bradley, D. Blackmond, *Langmuir* **1999**, *15*, 7621–7625.

[54] M. Moreno-Mañas, R. Pleixats, *Acc. Chem. Res.* **2003**, *36*, 638–643.

[55] J. A. Widegren, R. G. Finke, *J. Mol. Catal. A* **2003**, *198*, 317–341.

[56] A. H. M. de Vries, J. M. C. A. Mulders, J. H. M. Mommers, H. J. W. Henderickx, J. G. de Vries, *Org. Lett.* **2003**, *5*, 3285–3288.

[57] C. C. Cassol, A. P. Umpierre, G. Machado, S. I. Wolke, J. Dupont, *J. Am. Chem. Soc.* **2005**, *127*, 3298–3299.

[58] For the influence of acetate on the Heck reaction see ref.[4c] and C. Amatore, E. Carré, A. Jutand, M. A. M'Barki, G. Meyer, *Organometallics* **1995**, *14*, 5605–5614.

[59] A. Eisestadt, in *Catalysis of Organic Reactions* (Ed.: F. E. Herkes), Marcel Dekker, New York, **1998**, chapter 33.

[60] W. A. Herrmann, C. Brossmer, K. Öfele, C.-P. Reisinger, T. Priermeier, M. Beller, H. Fisher, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1844–1848.

[61] M. Ohff, A. Ohff, D. Milstein, *Chem. Commun.* **1999**, 357–358.

[62] I. P. Beletskaya, A. N. Kashin, N. B. Karlstedt, A. V. Mitin, A. V. Cheprakov, G. M. Kazankov, *J. Organomet. Chem.* **2001**, *622*, 89–96.

[63] D. Morales-Morales, C. Grause, K. Kasaoka, R. Redòn, R. E. Cramer, C. M. Jensen, *Inorg. Chim. Acta* **2000**, *300–302*, 958–963.

[64] M. Beller, H. Fisher, K. Kuehlein, C. P. Reisinger, W. A. Herrmann, *J. Organomet. Chem.* **1996**, *520*, 257–259.

[65] M. T. Reetz, R. Breinbauer, K. Wanninger, *Tetrahedron Lett.* **1996**, *37*, 4499–4502.

[66] M. T. Reetz, E. Westermann, *Angew. Chem. Int. Ed.* **2000**, *39*, 165–168.

[67] T. H. Galow, U. Drechsler, J. A. Hanson, V. M. Rotello, *Chem. Commun.* **2002**, 1076–1077.

[68] C. Rocaboy, J. A. Gladysz, *Org. Lett.* **2002**, *4*, 1993–1996.

[69] S. Ozkar, R. G. Finke, *J. Am. Chem. Soc.* **2002**, *124*, 5796–5810.

[70] K. R. Gopidas, J. K. Whitesell, M. A. Fox, *Nano Lett.* **2003**, *3*, 1757–1760.

[71] V. Calò, A. Nacci, A. Monopoli, A. Detomaso, P. Iliade, *Organometallics* **2003**, *22*, 4193–4197.

[72] This result is probably due to the benzylic hydrogen, whose acidity inhibits further arylation into the doubly arylated product **12** by favouring a fast isomerisation of the terminal olefin.

[73] The pK_a values of acetate and pivalate anions in TBAA and TBAP, respectively, cannot be the same as those measured in water. This is not be surprising, since the anions are poorly solvated in these ionic liquids and should therefore be both good ligands for palladium and strong bases.

[74] Selected papers for supported Pd catalysts: a) L. Djakovitch, K. Koehler, *J. Am. Chem. Soc.* **2001**, *123*, 5990–5999; b) C. Ramarao, S. V. Ley, S. C. Smith, I. M. Shirley, N. DeAlmeida, *Chem. Commun.* **2002**, 1134–1135; c) K. Mori, K. Yamaguchi, T. Hara, T. Mizugaki, K. Ebitani, K. Kaneda, *J. Am. Chem. Soc.* **2002**, *124*, 11572–11573; d) A. Dahan, M. Portnoy, *Org. Lett.* **2003**, *5*, 1197–1200; e) T. Doi, N. Fujimoto, J. Watanabe, T. Takahashi, *Tetrahedron Lett.* **2003**, *44*, 2161–2165; f) R. Akiyama, S. Kobayashi, *J. Am. Chem. Soc.* **2003**, *125*, 3412–3413; g) H. Yang, G. Zhang, X. Hong, Y. Zhu, *J. Mol. Catal. A* **2004**,

210, 143–148h) D. E. Bergbreiter, J. Li, *Chem. Commun.* **2004**, 42–43; i) D. Schonfelder, O. Nuyken, R. Weberskirch, *J. Organomet. Chem.* **2005**, *690*, 4648–4655.

[75] Supported Pd nanocolloids: a) B. M. Choudary, S. Madhi, N. S. Chowdari, M. L. Kantam, B. Sreedhar, *J. Am. Chem. Soc.* **2002**, *124*, 14127–14136; b) I. Yuranov, P. Moeckli, E. Suvorova, P. Buffat, L. Kiwi-Minsker, A. Renken, *J. Mol. Catal. A* **2003**, *192*, 239–251; c) S. V. Ley, C. Mitchell, D. Pears, C. Ramarao, J.-Q. Yu, W. Zhou, *Org. Lett.* **2003**, *5*, 4665–4668; d) R. W. Scott, A. K. Datye, R. Crooks, *J. Am. Chem. Soc.* **2003**, *125*, 3708–3709.

[76] A. Domare, G. A. F. Roberts, *Advances in Chitin Science* (Ed.: J. André), National Taiwan Ocean University, Keelung, Taiwan **199**8.

[77] a) F. Quignard, A. Choplin, A. Domard, *Langmuir* **2000**, *16*, 9106–9108; b) A. Huang, Y. Liu, J. Hua, *J. Appl. Polym. Sci.* **2002**, *85*, 989–994; c) T. Vincent, E. Guibal, *Langmuir* **2003**, *19*, 8475–8483; d) J. Zhang, C. G. Xia, *J. Mol. Catal. A* **2003**, *206*, 59–65; e) N. V. Kramareva, A. E. Koklin, E. D. Finashina, N. S. Telegina, A. Y. Stakheev, L. M. Kustov, *Kinet. Katal.* **2004**, *45*, 784–793; f) M. Adim, M. Abu Bakar, K. Y. Liew, J. Ismail, *J. Mol. Catal. A* **2004**, *212*, 141–149; g) J. J. Hardy, S. Hubert, A. J. Wilson, *Green Chem.* **2004**, *6*, 53–56.

[78] For examples of electrochemically prepared Pd colloids, see: a) N. Cioffi, I. Losito, L. Torsi, L. Sabbatini, P. G. Zambonin, T. Bleve-Zacheo, *Electrochim. Acta* **2001**, *46*, 4205; b) M. T. Reetz, M. Winter, R. Breinbauer, T. Thurn-Albrecht, W. Vogel, *Chem. Eur. J.* **2001**, *7*, 1084–1094.

[79] V. Calò, A. Nacci, A. Monopoli, A. Fornaro, L. Sabbatini, N. Cioffi, N. Ditaranto, *Organometallics* **2004**, *23*, 5154–5158.

[80] V. Calò, A. Nacci, A. Monopoli, *J. Mol. Catal. A* **2004**, *214*, 45–56.

[81] T. Jeffery, *Tetrahedron* **1996**, *52*, 10113–10130.

[82] E.-I. Neghishi, T. Takahashi, K. Akiyoshi, *J. Chem. Soc., Chem. Commun.* **1986**, 1338–1339.

[83] V. Calò, A. Nacci, A. Monopoli, A. Fanizzi, *Org. Lett.* **2002**, *4*, 2561–2563.

[84] For structures of imidazolium ILs see: a) T. J. Gannon, G. Law, P. R. Watson, A. J. Carmichael, K. R. Seddon, *Langmuir* **1999**, *15*, 8429–8434; b) A. J. Fry, *J. Electroanal. Chem.* **2003**, *546*, 35–39; c) M. Yoshizawa, W. Xu, C. A. Angell, *J. Am. Chem. Soc.* **2003**, *125*, 15411–15419; d) J. M. Crosthwaite, S. N. V. K. Aki, E. J. Maginn, J. F. Brennecke, *J. Phys. Chem. B* **2004**, *108*, 5113–5119; e) J. D. Holbrey, W. M. Reichert, M. Nieuwenhuyzen, S. Johnston, K. R. Seddon, R. D. Rogers, *Chem. Commun.* **2003**, 1636–1637; f) C. S. Consorti, P. A. Z. Suarez, R. F. de Souza, R. A. Burrow, D. H. Farrar, A. J. Lough, W. Loh, L. H. M. da Silva, J. Dupont, *J. Phys. Chem. B* **2005**, *109*, 4341–4349. For a review on ion pairing in organometallic chemistry see: A. Macchioni, *Chem. Rev.* **2005**, *105*, 2039–2073.

[85] a) C. Daguenet, P. J. Dyson, *Organometallics* **2004**, *23*, 6080–6083; b) J.-C. Xiao, B. Twamley, J. M. Shreeve, *Org. Lett.* **2004**, *6*, 3845–3847; c) C. Chiappe, D. Pieraccini, D. Zhao, Z. Fei, P. J. Dyson, *Adv. Synth. Catal.* **2006**, *348*, 68–74.

[86] a) J. D. Revell, A. Ganesan, *Org. Lett.* **2002**, *4*, 3071–3073; b) F. McLachlan, C. J. Mathews, P. J. Smith, T. Welton, *Organometallics* **2003**, *22*, 5350–5357.

[87] C. J. Mathews, P. J. Smith, T. Welton, *J. Mol. Catal. A* **2004**, *214*, 27–32.

[88] a) R. Rajagopal, D. V. Jarikote, K. V. Srinivasan, *Chem. Commun.* **2002**, 616–617; b) S. Liu, T. Fukuyama, M. Sato, I. Ryu, *Synlett* **2004**, *10*, 1814–1816.

[89] a) D. A. Alonso, C. Najera, M. C. Pacheco, *J. Org. Chem.* **2002**, *67*, 5588–5594; b) A. Corma, H. Garcia, A. Leyva, *Tetrahedron* **2004**, *60*, 8553–8560.

[90] a) D. Zim, A. L. Monteiro, J. Dupont, *Tetrahedron Lett.* **2000**, *41*, 8199–8202; b) Y. Deng, L. Gong, A. Mi, H. Liu, Y. Yiang, *Synthesis* **2003**, 337; c) A. Arcadi, G. Cerichelli, M. Chiarini, M. Correa, D. Zorzan, *Eur. J. Org. Chem.* **2003**, 4080–4086; d) R. K. Arvela, N. E. Leadbeater, M. S. Sangri, V. A. Williams, P. Granados, R. D. Singer, *J. Org. Chem.* **2005**, *70*, 161–168.

[91] a) J. McNulty, A. Capretta, J. Wilson, J. Dyck, G. Adjabeng, A. Robertson, *Chem. Commun.* **2002**, 1986–1987; b) F. Lu, J. Ruiz, D. Astruc, *Tetrahedron Lett.* **2004**, *45*, 9443–9445.

[92] V. Calò, A. Nacci, A. Monopoli, F. Montigelli, *J. Org. Chem.* **2005**, *70*, 6040–6044.

[93] C. Chiappe, G. Imperato, E. Napoletano, D. Pieraccini, *Green Chem.* **2004**, *6*, 33–36.

[94] V. Calò, P. Giannoccaro, A. Nacci, A. Monopoli, *J. Organomet. Chem.* **2002**, *645*, 152–157.

[95] N.-F. K. Kaiser, A. Hallberg, M. Larhed, *J. Comb. Chem.* **2002**, *4*, 109–111.

[96] J. Georgsson, A. Hallberg, M. Larhed, *J. Comb. Chem.* **2003**, *5*, 350–352.

[97] M. Cai, Y. Huang, R. Hu, C. Song, *J. Mol. Catal. A* **2004**, *208*, 17–20.

[98] M. Cai, H. Zhao, Y. Huang, *J. Mol. Catal. A* **2005**, *238*, 41–45.

[99] a) V. V. Grushin, H. Alper, *J. Am. Chem. Soc.* **1995**, *117*, 4305–4315; b) A. Yamamoto, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 433–435; c) W. Mägerlein, M. Beller, A. F. Indolese, *J. Mol. Catal. A* **2000**, *156*, 213–221.

[100] a) A. V. Cheprakov, N. V. Ponomareva, I. P. Beletskaya, *J. Organomet. Chem.* **1995**, *486*, 297–300; b) B. Cornils, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1575; c) B. Jayasree, A. Seayad, R. V. Chaudhari, *Chem. Commun.* **2000**, 1239–1240; d) A. M. Trzeciak, J. J. Ziólkowsky, *J. Mol. Catal. A* **2000**, *154*, 93–101; e) Y. Huang, R. Hu, C. Song, *J. Mol. Catal. A* **2004**, *208*, 17–20.

[101] N. Karodia, S. Guise, C. Newlands, J.-A. Andersen, *Chem. Commun.* **1998**, 2341–2342.

[102] T. Weskamp, V. P. W. Böhm, W. A. Herrmann, *J. Organomet. Chem.* **1999**, *585*, 348–352.

[103] L. R. Titcomb, S. Caddick, F. G. N. Cloke, D. McKerrecher, D. J. Wilson, *Chem. Commun.* **2001**, 1388–1389.

[104] C. J. Mathews, P. J. Smith, T. Welton, A. J. P. White, D. J. Williams, *Organometallics* **2001**, *20*, 3848–3850.

Received: January 19, 2006