Palladium-Nanoparticle-Catalysed Ullmann Reactions in Ionic Liquids with Aldehydes as the Reductants: Scope and Mechanism

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Abstract: An efficient Ullmann-type reductive homocoupling of aryl, vinyl and heteroaryl halides can be promoted by an aldehyde in tetraalkylammonium ionic liquids under very mild reaction conditions. This simple procedure generates symmetrical biaryls under relatively mild conditions. The ionic liquid is crucial for this process because it behaves simultaneously as a base, ligand and reaction medium. The role of the aldehyde is also discussed and a general mechanism for this unusual reaction is proposed. These results open the way to a new efficient method of Pd-catalysed dehydrogenation of carbonyl compounds.

Keywords: biaryls · ionic liquids · nanoparticles · palladium · Ullmann reactions

Introduction

Biaryls are useful compounds: their skeleton is commonly found in a variety of bioactive natural substances[1] and they are key building blocks for the synthesis of pharmaceuticals,[2] conducting materials,[3] agrochemicals, supramolecules[4] and ligands for asymmetric catalysis.[5]

Several modern methods for the preparation of biaryls are available, such as the Suzuki, Stille, Negishi, Kumada and Hiyama cross-coupling reactions, which involve the palladium- or nickel-catalysed coupling of aryl halides with an aryl organometallic reagent.[6] Alternatively, the direct catalytic arylation of simple arenes[7] is another useful route for the construction of aryl–aryl bonds. However, most of these methodologies suffer the two major drawbacks of requiring the preparation of the aryl metal nucleophiles and the use of these nucleophiles in stoichiometric amounts.

As a consequence, the direct dimerisation of aryl halides is considered to be a more convenient and straightforward method for the synthesis of biaryls. In this context, the well-known Ullmann[8] reaction is a useful process, but it requires an excess of copper[9] and harsh reaction conditions ($T > 200\,°C$). A valuable and milder catalytic alternative is the palladium-catalysed reductive coupling of haloarenes, which affords symmetrical biaryls and usually requires the presence of reducing agents such as amines,[10] zinc dust,[11] molecular hydrogen,[12] hydroquinone,[13] alcohols,[14] carbon monoxide,[15] ascorbic acid[16] or formic acid salts.[17]

Besides being performed in traditional solvents, these reactions have also been carried out in environmentally compatible solvents, such as water,[18] poly(ethylene glycol)[19] and supercritical CO_2.[20] In this context, little attention has been paid to ionic liquids (ILs)[21] as the reaction media, with a few exceptions.[22]

ILs are more and more frequently suggested as ideal substitutes for traditional solvents in catalysis, due to their ability in the immobilisation of transition-metal catalysts. They are also suitable media for the dissolution of ionic complexes because ILs are capable of retaining these complexes in a polar state and thus providing remarkable advantages in terms of activity and selectivity. In addition, ILs open the route to multiphase processes and easier catalyst recovery.[23]

During the last five years, we have shown that a number of well-known Pd-catalysed reactions, such as Heck, Suzuki and Stille cross-couplings or hydro-dechlorinations of chloroarenes, can be performed with excellent yields and under mild conditions by using tetrabutylammonium salt ILs as the reaction media with Pd colloids as the catalysts.[24] Indeed, these solvents provide a special colloid stabilisation by surrounding the Pd nanoparticles with a protecting shell

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that impedes them from aggregating. This type of "ligand-free" catalysis is gaining considerable importance because it avoids the use of toxic or expensive phosphane ligands and allows catalyst recycling.

In addition, we have recently found that both the catalyst activity and the selectivity are strictly dependent on the nature of the anion of the tetraalkylammonium salt in these IL media. A clear example was provided by us in the Heck arylations of allyl alcohols,[24b] in which the regioselectivity totally changed according to whether tetrabutylammonium bromide (TBAB) or tetrabutylammonium acetate (TBAA) was used as the reaction medium.

When extending our protocol to the α arylation of aldehydes, we noted that the catalyst behaviour in the latter two ionic media was so different as to switch the reaction mechanism from the Heck arylation to a reductive homocoupling. We report here that, in a reaction unprecedented in the literature, under typical Heck conditions with TBAA as the medium, aldehydes promoted a very convenient homocoupling of aryl halides under relatively mild reaction conditions.

Results and Discussion

As part of our program aimed at developing powerful catalytic methods in ILs, we were initially interested in the Heck α arylation of aldehydes, a process that provides very useful synthons for organic chemistry, such as the α-aryl carbonyl compounds, but that has remained relatively unexplored.[25]

Following a protocol we have previously reported,[24b] we were studying Pd-catalysed substitution with bromobenzene at the α position via the enolate of heptanal (1a). The reactions were carried out by treating aldehyde (1 mmol) with bromobenzene (1 mmol) in TBAB (1 g) under nitrogen at 130 °C for 2 h in the presence of Pd colloids (1.5 mol %) and a base (2 mmol).

As already reported by Miura and co-workers,[25b] the reactions reached complete conversion in the presence of inorganic bases such as potassium, sodium and cesium carbonate and afforded mixtures of the α-phenylated aldehyde (2-phenylheptanal, 1b), the aldol condensation compound ((E)-2-pentyl-2-nonenal, 1c) and its γ-phenylated derivative ((E)-2-pentyl-4-phenyl-2-nonenal, 1d) as the main products (Table 1, entries 1–3). Besides these products, small amounts of biphenyl (2) were also detected.

With weaker bases, such as sodium bicarbonate, tributylamine and potassium acetate, low conversions were observed (Table 1, entries 4–6). With imidazolium- and pyridinium-based ILs, the bromobenzene was almost unreactive and the aldol condensation process was mainly observed (Table 1, entries 7 and 8). These latter results confirmed the need for the tetraalkylammonium cation to stabilise the Pd colloids.[24c]

Interestingly, when tetrabutylammonium acetate was used as the base, the selectivity proved to be strictly dependent on the TBAB:TBAA ratio. Indeed, with an increase in that ratio up to 5:1 (w/w), the selectivity in favour of the Heck product 1b was improved to 75 % (Table 1, entry 9), although all attempts aimed at totally suppressing the by-products failed.

Conversely, when the TBAB:TBAA ratio was inverted in favour of the latter or was 1:1, a remarkable increase in the biphenyl yields was observed (Table 1, entries 10–12). In these cases, the bromobenzene was completely converted, while the initial aldehyde was partially recovered (20–40 %). In addition, besides the expected products 1b–d, small amounts of a great number of by-products were also detected (10–15 % of the overall peaks). When TBAA was used as both base and reaction medium, the homocoupling product became predominant (Table 1, entry 12).

Due to the synthetic importance of biaryls, we decided to investigate this process in more depth with the aim of developing a new method for the synthesis of biaryls by using aldehydes as sacrificial reagents. As it is known that during the reductive homocoupling of aryl halides, Pd^{2+} is generated and reduced back to Pd^0 by using an external reducing agent and that, in principle, this process requires only two electrons to close the catalytic cycle,[26] we thought, based on

Table 1. Pd-colloid-catalysed arylation of heptanal (1a) in ionic liquids.[a]

Entry	IL	Base	Conversion [%][b]		Product ratio [%][c]				
			1a	PhBr	1b	1c	1d	2	other by-products
1	TBAB	K₂CO₃	>99	95	47	25	21	7	–
2	TBAB	Na₂CO₃	>99	95	43	36	18	3	–
3	TBAB	Cs₂CO₃	>99	95	38	35	23	4	–
4	TBAB	NaHCO₃	14	7	32	53	–	15	–
5	TBAB	Bu₃N	21	4	29	71	–	–	–
6	TBAB	KOAc	46	3	–	95	–	2	3
7	BmimBr[d]	K₂CO₃	70	–	–	100	–	–	–
8	BupyBr[e]	K₂CO₃	>99	5	–	85	–	5	5
9[f]	TBAB	TBAA	>99	>99	75	10	8	7	–
10[g]	TBAB	TBAA	75	>99	34	13	3	36	14
11[h]	TBAB	TBAA	70	>99	22	15	5	43	15
12	TBAA	–	60	>99	7	–	5	78	10

[a] General conditions: IL (1 g), aryl halide (1 mmol), heptanal (1a; 1 mmol), Pd(OAc)₂ (1.5 mol %) and base (2 mmol) stirred under an inert atmosphere at 130 °C. [b] Conversions of both 1a and bromobenzene were evaluated by GLC with decane as an internal standard. [c] Ratios evaluated on the basis of the GLC peak areas of all of the products detected. [d] BmimBr: 1-butyl-3-methylimidazolium bromide. [e] BupyBr: N-butylpyridinium bromide. [f] TBAB:TBAA ratio of 5:1 (w/w). [g] TBAB:TBAA ratio of 1:1 (w/w). [h] TBAB:TBAA ratio of 1:3 (w/w).

the data in Table 1, that the aldehyde could behave as the reductant.

Searching for evidence to support this hypothesis, we carried out a series of reactions for the homocoupling of halobenzenes, with TBAA as the solvent and with variations in the structure of the aldehyde (Table 2). After optimisation of the reaction conditions, we established that by-product formation was limited by performing the reaction at 90°C[27] with 3 mol% of catalyst and with the minimum amount of aldehyde required by stoichiometry (0.5 equiv relative to the aryl halide).

Under these conditions, the homocoupling of bromobenzene was totally inhibited in the absence of aldehyde (Table 2, entry 1), whereas it proceeded smoothly in the presence of the linear aldehydes **1a** and **3a–5a** (Table 2, entries 2–5). However, in these cases variable amounts of by-products were detected. Careful GC–MS analyses of the reaction mixtures allowed the identification of the by-products as coming from three main reactions that occur randomly on the initial aldehydes: Heck arylation, aldol condensation and palladium(II)-catalysed dehydrogenation. Plausible reaction pathways for the formation of most of detected by-products are given in Scheme 1 for 3-phenylpropanal (**5a**). Studies are in progress to ascertain the exact mechanisms.
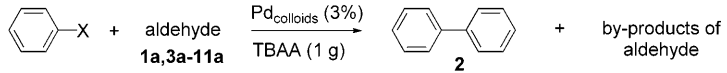
Of fundamental importance in understanding the mechanism was the fact that, among the three processes mentioned, only the palladium(II)-catalysed dehydrogenation is suitable to reduce Pd^{2+} to Pd^0 and close the cycle of homocoupling. It is also noteworthy that the efficiency of this catalyst system proved to be so high that multiple dehydrogenations occurred and afforded, at first, polyunsaturated aldehydes (products **5d** and **5e**) and then, after cyclising condensation (product **5g**), very intriguing polysubstituted aromatic compounds (product **5h**).[28]

Very interesting from the synthetic point of view was the

fact that by using aldehydes with short alkyl chains, such as propanal (**6a**), the process proved to be highly selective, with only trace amounts of cinnamic aldehyde as the sole by-product (Table 2, entry 6). In addition, reactions on iodobenzene occurred under very mild conditions (even at 40°C), whereas chlorobenzene proved to be unreactive (Table 2, entries 7–9).

Further mechanistic insights were obtained by using an α-substituted aldehyde such as 2-phenylpropanal (**7a**; Table 2, entry 10). As expected, because the aldol condensation reaction is inhibited in this case, two main by-products, **7b** and

Table 2. Pd-catalysed homocoupling of aryl halides with aldehydes as reductants in TBAA.[a]

Entry	X	Aldehyde	T [°C]	t [h]	Yields [%] of: biphenyl[b]	by-products of aldehyde[c]
1	Br	–	90	14	–	–
2	Br	heptanal (**1a**)	90	2	88	22[d]
3	Br	nonanal (**3a**)	90	2	91	14[d]
4	Br	tetradecanal (**4a**)	90	5	86	41[d]
5	Br	3-phenylpropanal (**5a**)	90	3	75	37
6	Br	propanal (**6a**)	90	2	95	traces[e]
7	I	propanal (**6a**)	70	4	90	traces[e]
8	I	propanal (**6a**)	40	6	85	5[e]
9	Cl	propanal (**6a**)	90	14	–	–
10	Br	2-phenylpropanal (**7a**)	90	1	80	17
11	Br	benzaldehyde (**8a**)	90	14	–	–
12	Br	pivalaldehyde (**9a**)	90	14	–	–
13	Br	acetaldehyde (**10a**)	90	14	–	15[f]
14	Br	diphenylacetaldehyde (**11a**)	90	14	–	–
15[g]	Br	diphenylacetaldehyde (**11a**)	90	14	78	60

[a] General conditions: TBAA (1 g), aryl halide (1 mmol), aldehyde (0.5 mmol), and Pd(OAc)$_2$ (3 mol%) stirred under an inert atmosphere at the stated reaction temperature. [b] Reactions were monitored for a maximum of 14 h. Yields of biphenyl were evaluated by GLC with decane as an internal standard. [c] By-products yields were evaluated on the basis of their GLC peak areas with respect to that of the standard. [d] In these cases, up to 0.2 of an equivalent of the starting aldehyde was recovered depending on the reaction time. [e] Small amounts of cinnamic aldehyde were detected. [f] Only the aldol condensation compound was detected. [g] In a reaction carried out under air, benzophenone was the sole by-product.
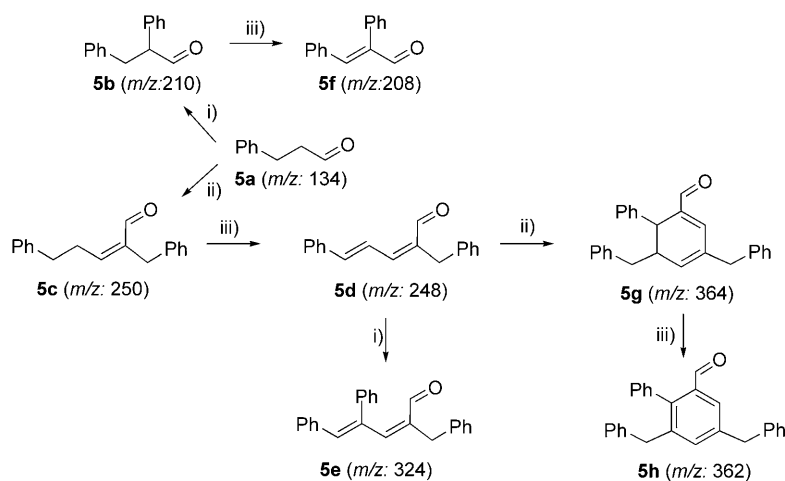
Scheme 1. Possible reaction pathways in the presence of 3-phenylpropanal (**5a**): i) PhPdX (Heck reaction); ii) aldol condensation with **5a**; iii) Pd^{II}-catalysed dehydrogenation.

5 f, were detected to arise from the Pd-catalysed dehydrogenation of the initial aldehyde, followed by the Heck arylation (Scheme 2).
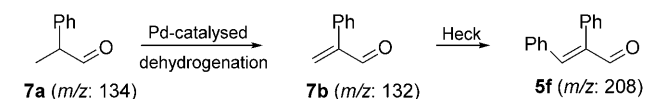
Scheme 2. Major by-products of 2-phenylpropanal (**7a**).

Conclusive confirmation of our hypothesis was found by using aldehydes **8a–10a**, which are totally devoid of protons at either the α or β position. Indeed, these types of compounds were unable to promote the coupling (Table 2, entries 11–13).

Based on these data, we proposed the general mechanism depicted in Scheme 3, whereby the generic aldehyde **12**, which must possess at least one proton on both the α and the β positions, undergoes a fast enolisation equilibrium under the basic conditions furnished by TBAA[29] to afford high amounts of enolate **13**.

The latter compound enters the catalytic cycle by being coordinated by palladium centre of the Ar−Pd−X intermediate **14** to provide the π complex **15**.[30] Next, the palladium atom gives rise to the addition on the double bond (σ complex **16**) followed by the β-hydride elimination, which releases both the α,β-unsaturated carbonyl compound **17** and the Pd hydride species **18**.[31] The involvement of the TBAA as a base provides the anionic σ-aryl palladium(0) complex **19**,[32] which in turn furnishes the bisaryl palladium(II) species **20** by means of oxidative addition to Ar−X. Finally, reductive elimination to form the biaryl compound (Ar−Ar) closes the cycle.
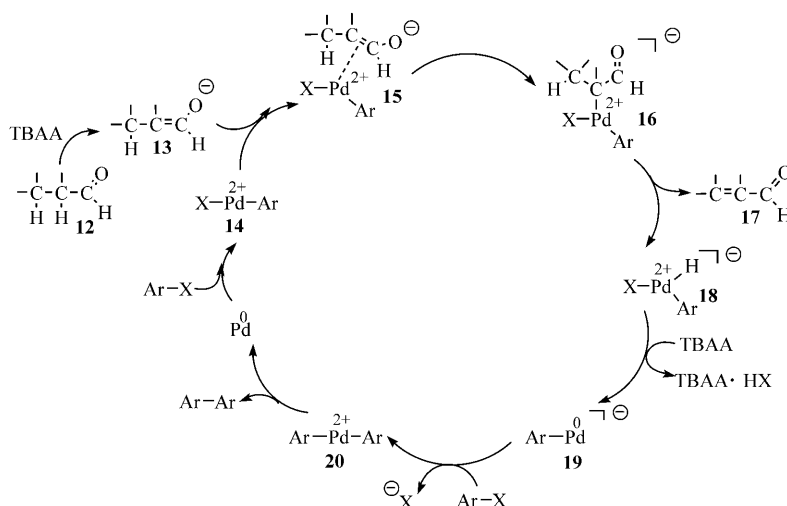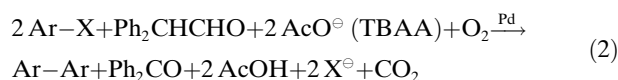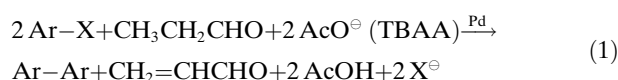
A special trend was observed in the case of diphenylacetaldehyde (**11a**; Table 2, entries 14 and 15). As expected, this compound proved to be unable to promote the coupling, due to the absence of protons at the β position. However, when the reaction was carried out under air, biphenyl was slowly formed and the initial aldehyde was stoichiometrically converted into benzophenone.

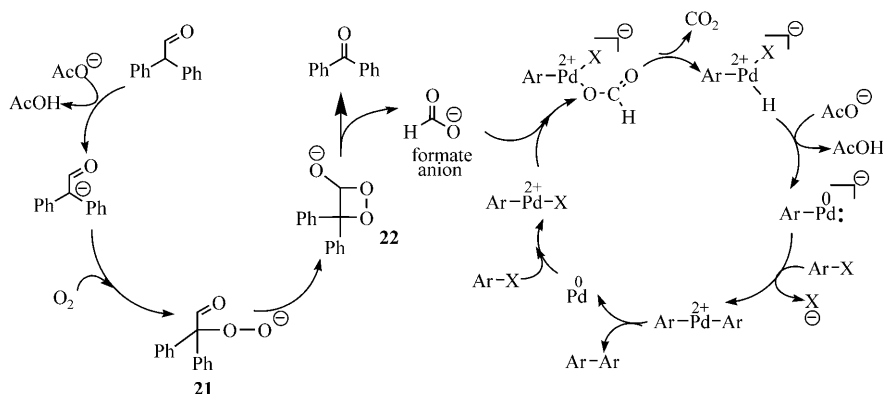The singular behaviour observed in this case is related to the particular reactivity of that aldehyde. It is known[33] that the base-catalysed autoxidation of diphenylacetaldehyde can release formate anions; therefore, it can be assumed that these latter ions can take the place of enolate **13** as the reducing agent for palladium,[17] as depicted in Scheme 4. It is noteworthy that the air oxidation of the enolate ion of diphenylacetaldehyde most probably proceeds via the dioxetane intermediate **22**.[34]

A number of proofs supporting the mechanisms in Scheme 3 and Scheme 4 are given below:

1) Experimental evidence established that homocoupling was complete with reagents in the following stoichiometric ratios: ArX:Aldehyde:TBAA = 1:0.5:1. This confirms the mass balance shown in the mechanisms of Scheme 3 and Scheme 4 and reported in Equations (1) and (2) in

$$2\,Ar-X+CH_3CH_2CHO+2\,AcO^{\ominus}\,(TBAA)\xrightarrow{Pd}$$
$$Ar-Ar+CH_2=CHCHO+2\,AcOH+2\,X^{\ominus} \quad (1)$$

$$2\,Ar-X+Ph_2CHCHO+2\,AcO^{\ominus}\,(TBAA)+O_2\xrightarrow{Pd}$$
$$Ar-Ar+Ph_2CO+2\,AcOH+2\,X^{\ominus}+CO_2 \quad (2)$$

Scheme 3. The general mechanism, illustrated with propanal.

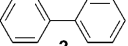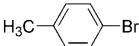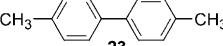Scheme 4. The reductive homocoupling with formate anions promoted by diphenylacetaldehyde.
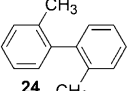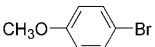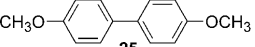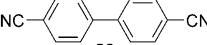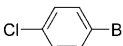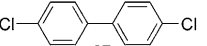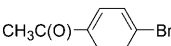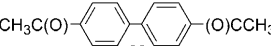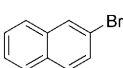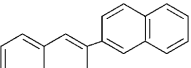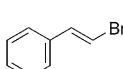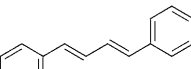
the case of propanal and diphenylacetaldehyde, respectively.

2) In the cases with aldehydes bearing long alkyl chains, less than 0.5 of an equivalent of the carbonyl reagents is needed because of the possibility of multiple dehydrogenations (Scheme 1, Table 2).

3) Related to the mechanism depicted in Scheme 4, the reaction carried out by replacing aldehyde with sodium formate occurred in TBAA in a similar way, although with some minor selectivity due to the formation of noticeable amounts of hydro-dehalogenation product (Ar–H).[35]

4) The air oxidation of diphenylacetaldehyde in TBAA at 90 °C furnishes, after neutralisation of the reaction mixture with HCl (6N), 1 equivalent of formic acid, as quantitatively determined by GC–MS.[36]

5) The formation of carbon dioxide was confirmed by a positive test with barium hydroxide that was carried out on the gaseous mixture released during the reaction.

It is evident a key role is exerted by the ionic liquid in this process. As already found by us for experiments with allyl alcohols,[24b] the coordinating ability of the anion is crucial in controlling the reaction selectivity. In this regard, the decisive step can be the addition of the palladium centre to the enolate ion. Indeed, it can be assumed that the π-complex intermediate 15 (Scheme 3) can follow one of two reaction pathways according to the nature of the anion of the IL (Scheme 5). If TBAB is the reaction medium, the palladium atom will be anionic in nature and its addition will occur at the more electrophilic side of the double bond (Scheme 5; path a), which will give rise to the migratory insertion and 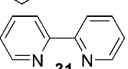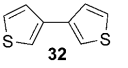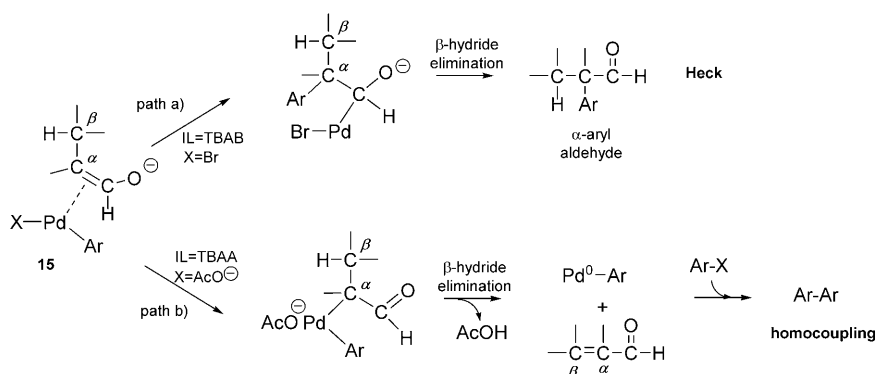consequently the Heck product (the α-aryl aldehyde). By contrast, with TBAA as the solvent, the weakly coordinating ability of the acetate ion renders the palladium atom cationic in nature, which leads to addition of the metal to the more nucleophilic position of the double bond of the enolate ion, that is, the α position (Scheme 5, path b). This could be the reason why the homocoupling process occurs in place of the classical Heck arylation in TBAA.

Finally, the scope and limitation of this methodology have been investigated by using several aryl, vinyl and heteroaryl halides as substrates with propionaldehyde as the reducing

Table 3. Pd-colloid-catalysed reductive homocoupling promoted by propionaldehyde in TBAA.[a]

$$2\ \text{R-X} \xrightarrow[\substack{\text{CH}_3\text{CH}_2\text{CHO (0.5 equiv)} \\ 90\ ^\circ\text{C}/\ \text{N}_2}]{\text{Pd}_{\text{colloids}}\ /\ \text{TBAA}} \text{R—R}$$

Entry	R–X	t [h]	Product R–R	Yield [%][b]
1	phenyl–Br	2	biphenyl **2**	90
2	H3C–phenyl–Br	4	CH3–phenyl–phenyl–CH3 **23**	88
3	2-CH3-phenyl–Br	4	2,2'-dimethylbiphenyl **24**	85
4	CH3O–phenyl–Br	7	CH3O–phenyl–phenyl–OCH3 **25**	81
5	NC–phenyl–Br	2	NC–phenyl–phenyl–CN **26**	86
6	Cl–phenyl–Br	4	Cl–phenyl–phenyl–Cl **27**	90
7	CH3C(O)–phenyl–Br	1	CH3C(O)–phenyl–phenyl–(O)CCH3 **28**	85
8	2-naphthyl–Br	1	binaphthyl **29**	90
9[c]	styryl–Br	4	diphenylbutadiene **30**	92[d]
10	2-pyridyl–Br	4	2,2'-bipyridyl **31**	89
11	3-thienyl–Br	1	bithiophene **32**	86

[a] General conditions: TBAA (1 g), aryl, vinyl or heteroaryl halide (1 mmol), proprionaldehyde (0.5 mmol) and Pd(OAc)₂ (3 mol%) stirred under an inert atmosphere at 90 °C. [b] Yields of isolated products. [c] The initial halide was used as a mixture of E/Z isomers in 85:15 ratio. [d] A mixture of E,E and E,Z dienes was obtained in a 4.3:1 ratio (see the Supporting Information).

agent (Table 3). By using this latter reagent, in fact, the reaction proved to be very clean, as very small amounts of by-products were detected (see Table 2, entry 6). This was probably due to two main reasons: 1) the low boiling point of the by-product acrolein and 2) the tendency of this latter compound to give anionic polymerisation promoted by TBAA, as also confirmed by a separate reaction carried out by dissolving pure acrolein in molten TBAA. The data in

Scheme 5. Dependence of the reaction pathway on the nature of the IL anion.

the Table 3 show that reactions proceed smoothly on bromides. Iodides and chlorides were excluded from this monitoring because the former were synthetically useless and the latter were unreactive.

Conclusion

In summary, the results presented here proved to be of particular interest for the following reasons:

1) A new method for synthesising symmetrical biaryls has been developed, by making use of Pd colloids as the catalyst, an aldehyde as the reducing agent and an ionic liquid as the reaction medium. Aryl bromides and iodides are activated without the use of special additives or ligands, under relatively mild conditions (reaction temperatures ranging from 40 to 90 °C). The procedure is very simple: the reagents and catalyst source (Pd acetate) are mixed together in the molten IL, with the latter assuring the almost immediate formation of the catalytically active species. With propanal as the reducing agent, the work-up proved to be particularly easy, due to the volatility of the reaction by-product (acrolein). In addition, the nature of the surfactant of the tetraalkylammonium IL allows the stabilisation of the Pd nanoparticles, which behave as a reservoir of catalyst.

2) The role of TBAA is crucial for this process, as this ionic liquid behaves simultaneously as a base, ligand and reaction medium.[37] Indeed, it first generates the enolate ion, which is the key intermediate for the Pd reduction (Scheme 3) and then, due to its weakly coordinating ability, renders the catalytically active palladium species cationic in nature, which definitely changes the selectivity from the expected Heck arylation to the reductive homocoupling (Scheme 5). These findings are mechanistically innovative and unprecedented in the literature, because TBAA, to our knowledge, is the one and only reaction medium in which an aldehyde gives rise, in the presence of an aryl halide, to Pd-catalysed dehydrogenation instead of an α arylation.

3) Of similar novelty are our findings on the special behaviour of diphenylacetaldehyde, which acts, in this medium, as a latent source of formate anions and, ultimately, as a reducing agent for palladium.

4) These results are innovative also from the synthetic point of view, as they open the way to a new and very efficient method of Pd-catalysed dehydrogenation of carbonyl compounds. A representative example of the dehydrogenating ability of this catalyst system has been depicted in Scheme 1. By starting from a simple commercially available aldehyde, such as 3-phenylpropanal, it is possible to obtain, in a one-pot process, a multisubstituted aromatic compound. Studies aimed at the optimisation of this protocol are in progress.

5) Finally, it is well known that, among all the features of ionic liquids, what makes them so attractive with respect to traditional solvents, is the possibility to tune their chemical properties by simply varying the nature of the cation and anion (so-called designer solvents). Our results fall in line with this principle and are in perfect accord with our previous findings on allyl alcohols[24b] in that they demonstrate, once again, the extraordinary effect exerted by the nature of ionic liquids on reaction outcomes.

Experimental Section

General procedure for the Heck phenylation of heptanal (1 a): The tetraalkylammonium salt (TBAB or TBAA, 1 g), Pd(OAc)$_2$ (6.7 mg, 0.03 mmol), heptanal (1 mmol), base (2 mmol, except for the cases with TBAA), bromobenzene (1 mmol) and an internal standard (decane, 0.5 mmol) were placed in a 25 mL three-necked flask equipped with a magnetic bar. The flask was connected with a nitrogen line to create an inert atmosphere and heated at 130 °C. The reaction mixture rapidly darkened under heating to give a dark brown suspension of very active Pd nanoparticles. Reactions were monitored by GLC and GC–MS for 2 h (Table 1).

General procedure for the homocoupling of aryl halides promoted by aldehydes in molten tetrabutylammonium acetate: Tetrabutylammonium acetate (TBAA, 1 g), Pd(OAc)$_2$ (6.7 mg, 0.03 mmol), aldehyde (0.5 mmol), an internal standard (decane, 0.5 mmol) and aryl halide (1 mmol) were placed in a 25 mL three-necked flask equipped with a magnetic bar. The flask was connected with a nitrogen line to create an inert atmosphere and heated at the reaction temperature for the appropriate time (Table 2). All reactions were monitored by GLC and GC-MS until the disappearance of the starting aldehyde.

In the case with iodobenzene described in entry 8 in Table 2, TBAA, Pd-(OAc)$_2$ and the aryl halide were added together and the mixture was melted at approximately 70 °C. Then, with vigorous stirring, the mixture was cooled to 40 °C and the aldehyde was added.

In the case of coupling promoted by diphenylacetaldehyde described in entry 15 in Table 2, the reaction was conducted in the same manner but under air.

General procedure for the propanal-promoted synthesis of biaryl in molten tetrabutylammonium acetate: Tetrabutylammonium acetate (TBAA, 1 g), Pd(OAc)$_2$ (6.7 mg, 0.03 mmol), propanal (0.5 mmol), and aryl halide (1 mmol) were placed in a 25 mL 3-necked flask equipped with a magnetic bar. The flask was connected with a nitrogen line to create an inert atmosphere and heated at the reaction temperature for the appropriate time (Table 3). After completion of reaction, the mixture was washed with dilute HCl, to remove most of the tetraalkyammonium salt and trialkylamine derived from the IL decomposition, and extracted with 3×15 mL portions of ethyl acetate. After solvent removal in vacuo, the organic residue was poured over a short pad of silica gel. The yields are reported in Table 3.

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[27] 90 °C was the minimum temperature required to activate bromobenzene. Higher temperatures were avoided due to the increase in the rate of thermal degradation of TBAA. Nevertheless, we noted that the homocoupling to biphenyl also occurred in the absence of aldehyde at 120 °C. It is likely, in this case, that the ionic liquid (TBAA) takes the place of the carbonyl compound in reducing palladium (see M. T. Reetz, M. Maase, *Adv. Mater.* **1999**, *11*, 773–777). However, the redox reaction ($Pd^{II} + 2\,CH_3CO_2^- \rightarrow Pd^0 + 2\,CO_2 + CH_3^{\bullet}$) released a methyl radical, which promoted radical chain processes involving the reaction product biphenyl. As a consequence, remarkable amounts of *ortho*-, *meta*- and *para*-terphenyl and -tetraphenyl isomers were formed; this lowers the yield and selectivity of the coupling.

[28] To obtain experimental proof, we decided to use an excess of bromobenzene and prolong the reaction time for 5 h. Product **5h** was then isolated as the major by-product and was completely characterised (see the Experimental Section).

[29] As already reported by us (see reference [24b]), due to the tetrahedral structure of the tetraalkylammonium cation of TBAA, the positive charge on the nitrogen atom is shielded by the bulkiness of the butyl chains; as a consequence, the more naked acetate anions provide conditions that are more basic than those in water.

[30] The free coordination sites of palladium are presumably occupied by AcO$^-$ anions from TBAA. Their exact number is not specified; if the reaction occurs on the nanoparticle surface, it could be smaller than four due to linkage of the Pd atom to the metal bulk.

[31] Good evidence for the formation of intermediate **18** is the detection, in some cases, of small amounts (<2 %) of the reductive dehalogenation product Ar−H.

[32] Amatore et al. (see C. Amatore, E. Carré, A. Jutand, H. Tanaka, Q. Ren, S. Torii, *Chem. Eur. J.* **1996**, *2*, 957–966), as well as Rawal and co-workers (see reference [13b]), have already demonstrated the formation of this type of anionic σ-aryl Pd^0 complex.

[33] The aldehyde autoxidation usually proceeds through the formation of a free radical on the carbonyl carbon atom and, hence, to the corresponding carboxylic acid. However, the case of diphenylacetaldehyde is one of the first recognised examples of autoxidative decarbonylation affording the ketone with one less carbon atom. See: J. W. Huffman, R. P. Elliott, *Chem. Ind.* **1963**, 650–651.

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[35] As already reported by Rothenberg and co-workers (S. Mukhopadhyay, G. Rothenberg, D. Gitis, H. Wiener, Y. Sasson, *J. Chem. Soc. Perkin Trans. 2* **1999**, 2481–2484), it can be supposed that when the formate is used as the reagent, instead of being generated in situ as in this case, the side reaction of hydro-dehalogenation occurs to a greater extent.

[36] It can be supposed that this reaction can be promoted by metallic impurities (particularly copper and iron) that are present in ppm amounts in the ionic liquid. See: M. Tokunaga, Y. Shirogane, H. Aoyama, Y. Obora, Y. Tsuji, *J. Organomet. Chem.* **2005**, *690*, 5378–5382.

[37] The role played by TBAA is really unique. Indeed, the same effect on the chemoselectivity of the catalysis cannot be obtained by replacing this ionic liquid with a generic source of acetate anions. Good evidence is shown in Table 1, in which it can be seen that the use of KOAc (entry 6) in place of TBAA (entries 9–11) gives rise to quite different reaction outcomes. Two plausible explanations can be given: 1) the low solubility of KOAc in TBAB and 2) the presence of the inorganic cation (K^+), which can change the interactions between ions in the IL.