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Editor's choice paper

High catalytic and recyclable systems for heck reactions in biosourced ionic liquids

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ABSTRACT

Tetrabutylammoniums (TBA) and tetrabutylphosphoniums (TBP) ionic liquids (ILs) comporting a biosourced anion were easily synthesized by an acido-basic method. These ILS were then used as solvent for Heck reaction between iodoarene or halogenoaromatics with *tert*-butylacrylate in presence of $PdCl_2$ as catalyst and a base. With $NaHCO_3$, good conversion and selectivity were obtained; however the catalytic system could not be recycled. Use of triethylamine as base permitted good efficiency of the reaction, with the advantage to have the possibility to recycle the catalytic system without loss of reactivity, especially with TBA L-lactate **1a**, TBP L-lactate **2a** and TBP L-malate **2b**.

1. Introduction

Ionic liquids (ILs) are ionic, salt-like materials which are liquid below 100 °C. Their numerous properties (high solubility power, high stability, non volatility, . . .) make them an attractive choice of solvent in many important chemical processes [1]. Many examples are reported in (bio)catalysis [2], in organic synthesis [3], in electrochemistry [4] or in extraction [5]. Recently, appropriate reviews detailed the advantages of using ILs as new solvents in various fields [6].

Considering the use of ILs in metallo-catalyzed reactions, the most significant developments in palladium-catalyzed cross-coupling (Heck, Suzuki-Miyaura, Stille, Sonogashira, Ullman, and Negishi) have been recently reviewed by Mastrorilli et al. [7]. Beneficials effects of the used of ILs were described in terms of activity, of selectivity through the formation of metallic nanoparticles leading to a ligand free system and being most of the time more active on aryle bromide or chloride; furthermore the use of ILs can allow the possibility to recyclable catalytic systems. This work was in the continuity of previously reported works of Bellina and Chiappe [8a], Wu and al. [8b], Welton and Smith [8c] and Beller and Bölm [8d]. S-arylation coupling was also performed using ionic liquid framework (Pd@IL-PMO) as an efficient green catalyst [8e] and efficient tandem aqueous room temperature oxidative amidations were realized in the presence of supported Pd nanoparticles on graphene oxide and ammonium salts as surfactant [8f].

For the Heck reaction, ILs as solvents play in general an important role for the formation on Pd nanoparticles, and as stabilizers or promoters of ligand-assisted or phosphine-free reactions [9]. This role was well described by Trzeciak et al. with imidazolium halides [10a] and Calo et al. with imidazolium or pyridinium derivatives [10b]. Supported ionic liquid layer catalysts (SILCs) or supported ionic liquid phase catalyst (SILPC) have been also largely described in the recent literature and proved the increasing interest of this kind of catalyst for many metal-induced processes, among them the Heck reactions [11]; homogeneous catalysts are by this way immobilized and can be recovered by simple filtration to be reused. Heck reaction employing simple ILs as tetrabutylammonium bromide (TBA Br), was reported by Böhm and Herrmann in 2000 [12a]. A wide range of phosphonium based room temperature ionic liquids (RTILs) have been used for the Heck reaction and allowed a ligand free approach for this reaction leading to a very attractive interest for purification, costs, and reaction scale up [12b].

However, it is clear today that ILs are nor green solvent considering thermodynamic and physical behaviours as mentioned in different publications of Marlair's group [13]. Furthermore, their low biodegradability (or the toxicity of their degradation products) and their high (eco)toxicity led the scientific community to reduce their use or to find other greener alternatives [13]. Due to their

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biodegradability and non-toxicity, the use of renewable resources such as amino acids, amino alcohols, or sugars, could improve the green character of ILs [14]. Chiappe et al. [15a] developed Heck reactions in ILs derived from natural sugars folllowing previously work of Handy et al. [15b] on fructose-based ionic liquids. These works revealed the possibility to use this kind of ionic liquids as solvents for free ligand Heck reactions. Indeed, coupling between methyl cinnamate and electron-rich and electron-deficient compounds aryle iodide and bromide worked well and the catalyst/RTIL layer could be recycled three or four times with no detectable loss in activity.

Our group developed a few years ago various ILs based on ammonium or phosphonium with anions from natural acids (L-lactic, L-tartaric, pyruvic, malic, malonic, succinic and osidic acids), but also L-proline and its derivatives. Even if they were not readily biodegradable, these compounds showed in general lower toxicity towards various organisms than usual chlorinated and commercial ILs [16a,b,c]. These ILs were used as solvents and showed good performance and recyclability (until 10 runs without loss of activity) in catalytic selective hydrogenation of 1,5-cyclooctadiene and linoleic acid at room temperature under atmospheric H_2 pressure [16a,b]. The proline-based ILs were also used as co-solvent with *iso* propanol for the enantioselective hydrogenation of double carbon–carbon bonds of α,β-unsaturated ketones still under mild conditions with $PdCl_2$ [16c].

Previously described works in the literature proved the real improvement of ILs as solvent for Heck reaction. With our expertise in the use of biosourced ILs as solvents in hydrogenation processes, we wanted to explore the potentialities of these biosourced ILs in Heck reaction. The present paper describes the development of a new methodology for Heck coupling using bioderived ILs with $PdCl_2$ in presence of a base.

2. Experimental

2.1. Materials

All materials were analytical grade and used as received from Strem Chemicals (Palladium (II) chloride) and Alfa-Aesar (trimethylamine, *tert*-Butyl acrylate and all substrates). Ionic liquids were all known and prepared by previously described methods [16a,b].

2.2. Characterization

NMR spectroscopy was performed at 500 MHz with Bruker Avance III spectrometer equipped with a BBFO$^+$ probe and at 600 MHz with Bruker Avance III spectrometer equipped with a CPTCI cryoprobe. The sample was dissolved in MeOD-d_4 and the resulting solution was placed in a 5 mm diameter NMR tube. 1H NMR spectra were taken with 30° pulse angle, 10 s relaxation delay and 16 scans.

GC analyses were recorded on a Hewlett–Packard HP-6890 gas chromatograph, fitted with DB-1 capillary column (25 m, 0.32 mm), a flame ionization detector and HP-3395 integrator under the following conditions: helium as vector gas (5.10^4 Pa), temperature of injector: 250 °C, temperature of the oven: isotherm 150 °C, 5 min, then 150–300 °C (10 °C/min) and isotherm 300 °C, 5 min. GC/MS analyses were recorded on a THERMOQUEST Draw GC on 2000 Series by using the techniques of chemical ionization under the following conditions: capillary column DB1 (length: 25 m, diameter: 0.32 mm), vector gas: helium (0.5 bar), temperature injector: 250 °C.

2.3. General procedure for the Heck reaction with $NaHCO_3$ as base

$PdCl_2$ (4.3 mg, 0.024 mmol, 0.02 eq) and $NaHCO_3$ (121 mg, 1.44 mmol, 1.2 eq) were introduced in a Schlenk tube containing 600 mg of ionic liquid. The resulting mixture was dried for 2 h at 100 °C under vacuum. The halogenoarene (1.2 mmol) and the *tert*-butylacrylate (210 µL, 1.45 mmol, 1.2 eq) were introduced under inert atmosphere. The system was closed and heating for 24 h at 100 °C.

After cooling, the reacting mixture was extracted four times with 5 mL of diethylether. The reacting phase was kept and dried. The different organic phases were assembled, filtered through cotton. 1 µL was injected in GC to determine conversion and selectivity. The organic phase was then concentrated and dried for NMR analysis if necessary.

2.4. Recycling/reuse of catalytic system

After extraction with diethylether, the ionic liquid phase was kept in the Schlenk tube and dried at reduced pressure. $NaHCO_3$ (121 mg, 1.44 mmol, 1.2 eq.) was added, then halogenoarene (1.2 mmol) and *tert*-butylacrylate (210 µL, 1.45 mmol, 1.2 eq.) were introduced under inert atmosphere. Reaction was then performed again at 100 °C for 24 h. Same work-up as for the first cycle was then realized and the liquid ionic phase re-used as necessary.

2.5. General procedures for the Heck reaction with NEt_3 as base

Under argon atmosphere, the substrate (bromobenzene, chlorobenzene or iodoarenes, 1.2 mmol), *tert*-butyl acrylate (210 µL, 1.45 mmol, 1.2 eq.) and triethylamine (200 µL, 1.44 mmol, 1.2 eq.) were mixed in a Schlenk tube containing 600 mg of ionic liquid and $PdCl_2$ (4.3 mg, 0.024 mmol, 0.02 eq.). The resulting mixture was stirred for 24 h at the desired temperature (60 or 100 °C). Once the reaction was completed, the crude product was extracted four times with 5 mL of diethyl ether, combined, filtered through cotton and then concentrated under reduced pressure. 1 µL of the organic phase was injected in a gas chromatography (GC end GC/MS) to determine the conversion. The ratio *E*/*Z* was determined with ^{1}H NMR.

2.6. Recycling

After the diethylether extraction, drying and a short vacuum/argon sequence, the respective substrates in similar ratios as before were added into the precedent ionic liquid phase in the Schlenk tube. The mixture was stirred vigorously for 24 h at the desired temperature under argon atmosphere. Same treatment as previously described was then employed for the separation and the analysis of the coupling product.

3. Results and discussion

3.1. Synthesis of bio-derived ionic liquids

The ionic liquids (ILs) were easily synthesized using an acid-base method [16]. Tetrabutylammonium hydroxide (TBA OH) was reacted in water at reflux with an excess of a biobased acids (Table 1) [16a]. The acids (L-lactic, L-malic acid, pyruvic acid, malonic acid and succinic acid) were chosen for their low cost, their non–toxicity and high availability. ILs **1a-1f** were obtained with quantitative yields.

Same method was used to prepare phosphonium ILs with L-lactic acid (**2a**) and L-malic acid (**2b**) (Table 2) [16b], this time using tetrabutylphosphonium hydroxide (TBP OH). Again, ILs were easily