Chitosan-supported ionic liquid phase: Application to organometallic catalysis

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Abstract

Supported ionic liquids for organometallic catalysis is a new exciting concept, which associates the advantages of both the ionic liquids (high solubility for the active species) and the solid supports (rapid extraction and recovering of the catalyst). The main encountered supports are silica based one and in a few exemples organic polymers. Chitosan, a polysaccharide extracted from chitin, has never been used for this purpose even if it is recognized as a valuable support for heterogeneous catalysis. We report here the preparation of original reactors based on chitosan-supported ionic liquid and their application to the palladium catalysed allylic substitution.

Introduction

Chitosan is a cationic biopolymer obtained by alkaline *N*-deacetylation of chitin, the most abundant natural biopolymer after cellulose. It ideally consists of 2-amino-2-deoxy-(1-4)-β- D-glucopyranose residues (D-glucosamine units) and can include or not a small amount of *N*-acetyl-D-glucosamine units. Chitosan and its derivatives have attracted considerable attention as polymeric supports in various fields such as enzyme immobilization, cell encapsulation and controlled release pharmaceutical applications[1]. Another field of interest which recently merged is the use of chitosan for supported catalysis (or heterogenous catalysis)[2]. The main advantages in using chitosan for supporting catalytic metals are : high sorption capacities, stability of metal anions (such as Pt and Pd) on chitosan, and physical and chemical versatility of the biopolymer.

Ionic liquids (ILs) are low melting point salts (< 100°C) that have attracted considerable attention recently as greener alternatives to classical environnementally damaging solvents[3]. This is mainly due to their peculiar properties such as the absence of flammability, the lack of measurable vapour pressure and their ability to dissolve a wide range of organic, organometallic and even some inorganic compounds. The main structures of ILs possess an ammonium, an imidazolium or a pyridinium backbone and their properties such as the melting point, the thermal stability or the solvating ability depend on both the anion and the cation parts. ILs have been shown to be suitable media for numerous catalytic reactions[4], however because of problem in product extraction and in recycling of the catalyst, heterogenisation of ionic liquids on solid support is highly desirable. Supported ionic liquids phase catalysts (SILC) were developped for this purpose. This new concept associates the advantages of both the ionic liquids (high solubility for the active species) and the solid supports (rapid extraction and recovering of the catalyst). SILC were used successfully in hydrogenations[5], hydroformylations[6] and Friedel-Crafts acylations[7]. Although the mesoporous silica is the most frequently used support, the properties of the chitosan as catalytic support renders it an attractive candidate for SILC. Our aim in this project was to developp original catalytic reactor based on chitosan-supported IL and to use them in the milestone Tsuji-Trost allylic substitution reaction

Material and Method

Morpholine and the allylic substrates were used as received from Accros (France). Palladium acetate, palladium chloride and the TPPTS (P(m-C$_6$H$_4$SO$_3$Na)$_3$) were used as received from Sigma-Aldrich (France). Cinnamyl acetate and 3-acetoxy-1,3-diphenylpropene were synthesized and purified according to a litterature procedure[8]. Butylmethylimidazolium tetrafluoroborate ([bmim][BF$_4$]) was provided by Solvionic SA (France).

Reactions were carried out under nitrogen with magnetic stirring, unless otherwise specified. Solvents were dried by distillation, prior to use. The NMR spectra were recorded in CDCl$_3$ using a Bruker DRX250. Chemical shifts (δ) are expressed in ppm relative to Me$_4$Si for ^{1}H and ^{13}C nuclei, and the coupling constants (J) are given in Hz; conventional abbreviations are used. The infrared spectra were recorded with a Perkin-Elmer Spectrum One spectrometer with the ATR accessory, and absorbances are given in υ (cm^{-1}).

Chitosan obtained from Fluka is purified before use by dissolution in aqueous hydrochloric acid (0.2 %) to get a solution with a polymer concentration of 1% (w/v) and is precipitated in aqueous NaOH solution (pH >7). After filtration, the residue is washed several times with deionized water to attain the water conductivity and finally freeze-dried. The viscosity-average molar mass ($\overline{M}_v$) is 330,000 g.mol^{-1} (determined by viscosimetry)[9] and the degree of deacetylation determined by ^{1}H NMR is 80%[10].

Preparation of reactor based on chitosan-supported ionic liquid (general procedure)

Pre-degazed [bmim][BF$_4$] (0.7 mL) was slowly added to palladium source (PdCl$_2$ or Pd(OAc)$_2$) (0.02 mmol, 0.05 eq.), TPPTS (51 mg, 0.09 mmol, 0.2 eq.) and purified chitosan (100 mg). The resulting mixture was stirred at room temperature under Ar (or N$_2$) atmosphere for 30 min. The reactor is then ready for application in catalysis.

Synthesis of 4-cinnamylmorpholine

Cinnamyl acetate (0.09 mL, 0.5 mmol, 1 eq.) and morpholine (0.04 mL, 0.5 mmol, 1 eq.) were successively added to the reactor, which was stirred at room temperature under Ar for 20 h. The solution was then extracted with diethyl ether (monitored by TLC). The combined diethyl ether extracts were washed with water (1 mL), dried over MgSO$_4$ and filtered. Evaporation of the solvent gave a residue, which was purified by column chromatography on silica gel (petroleum ether 40/60 /ether : 8/2) affording 4-cinnamylmorpholine in 92% yield. Oil. **^{1}H NMR** (250 MHz, CDCl$_3$,) δ 2.51 (t, J = 4.3 Hz, 4H); 3.15 (d, J = 6.8 Hz, 2H) ; 3.73 (t, J = 4.3 Hz, 4H) ; 6.25 (dt, J = 15.8 Hz, J = 6.8 Hz, 1H) ; 6.53 (d, J = 15.8 Hz, 1H) ; 7.19-7.38 (m, 5H). **^{13}C RMN** (CDCl$_3$, 62.5 MHz) δ 52.91 (2*CH$_2$) ; 60.72 (CH$_2$) ; 66.20 (2*CH$_2$) ; 125.03 (CH) ; 125.50 (2*CH) ; 126.38 (CH) ; 127.85 (2*CH) ; 132.98 (CH) ; 136.00 (Cq).

Synthesis of (E)-3-morpholino-1,3-diphenylprop-1-ene

(E)-1,3-diphenyl-3-acetoxyprop-1-ene (105 mg, 0.4 mmol, 1 eq.) and morpholine (0.05 mL, 0.6 mmol, 1.4 eq.) were successively added to the reactor, which was stirred at room temperature under Ar for 20 h. The solution was then extracted with diethyl ether (monitored by TLC). The combined diethyl ether extracts were washed with water (1 mL), dried over MgSO$_4$ and filtered. Evaporation of the solvent gave a residue, which was purified by column chromatography on silica gel (petroleum ether 40/60 /ether : 8/2) to give the product in 80.5% (using Pd(OAc)$_2$) and 89.5% (using PdCl$_2$). **mp** (DSC) 64-65°C. **^{1}H NMR** (250 MHz, CDCl$_3$,) δ 2.21-2.33 (m, 2H) ; 2.39-2.47 (m, 2H) ; 3.58 (m, 4H) ; 3.65 (d, J = 8.8 Hz, 1H) ; 6.16 (dd, J = 15.8 Hz, J = 8.8 Hz, 1H) ; 6.44 (d, J = 15.8 Hz, 1H) ; 7.03-7.37 (m, 10H). **^{13}C RMN** (CDCl$_3$, 62.5 MHz) δ 52.7 (2*CH$_2$) ; 67.6 (2*CH$_2$) ; 75.3 (CH) ; 126.9 (2*CH) ; 127.5 (CH) ; 128.1 (CH) ; 128.5 (2*CH) ; 129.1 (2*CH) ; 129.5 (2*CH) ; 131.4 (CH) ; 132.1 (CH) ; 137.3 (C$_q$) ; 142.1 (C$_q$). υ_{max} (CHCl$_3$/cm^{-1}) : 3025.8 ; 2955.6 ; 2851.3 ; 2803.6 ; 1493.6 ;1449.5 ; 1270.0 ; 1114.9 ; 1005.1 ; 965.6 ; 879.6 ; 743.1 ; 692.1. **Elemental analysis** theo 81.68 (C) 7.58 (H) 5.01 (N) found 81.39 (C) 7.77 (H) 4.78 (N). **HRMS (EI)** calculated for C$_{19}$H$_{22}$NO requires 280.1701, found 280.1712.

Results and Discussion

The new catalytic reactor was constituted of chitosan and [bmim][BF$_4$]. The choice of this latter was based on its melting point (-75°C), its hydrophobic/hydrophilic balance and its commercially availability. The palladium source and the TPPTS were dissolved in [bmim][BF$_4$]. Addition of chitosan beads gave an oily-solid. In these reactors, the homogeneous catalyst is dissolved in the layer of IL, which is confined on the surface of chitosan (Figure 1).
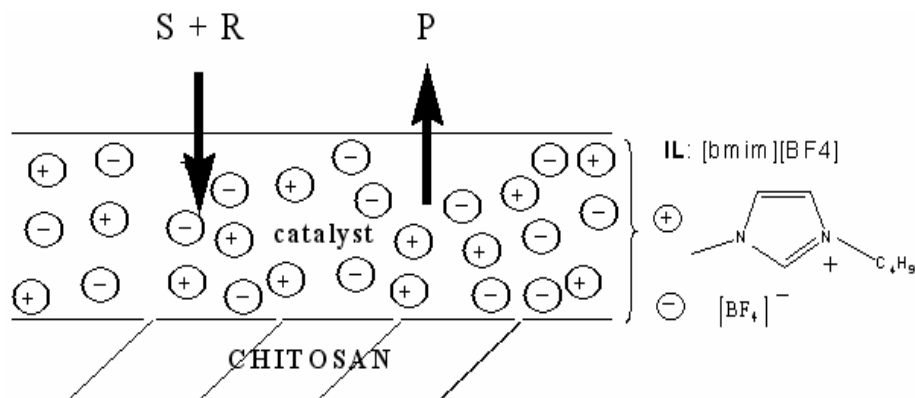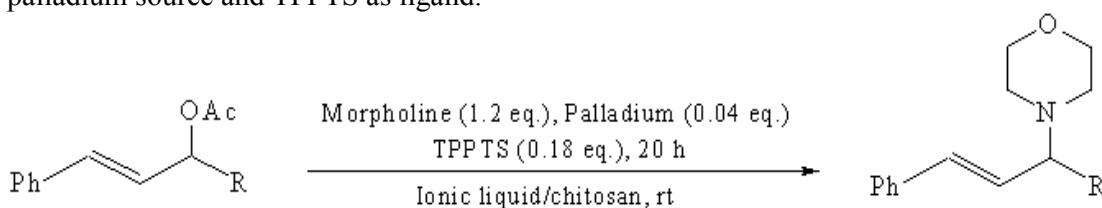

Figure 1: Chitosan-supported ionic liquid in catalytic reactions

The new reactors was tested in a model reaction: the allylic substitution between morpholine and allyl acetates (Scheme 1). The reactions were conducting using either PdCl$_2$ or Pd(OAc)$_2$ as palladium source and TPPTS as ligand.

**Scheme 1:** coupling of different allyl acetate substrates with morpholine

For comparison with another heterogeneous catalytic system, the reaction was also investigated in the chitosan-supported aqueous phase (SAP) catalysis (Table 1).

R	Supported liquid phase	Palladium	Time (h)	Isolated yield (%)
Ph	[bmim][BF$_4$]	PdCl$_2$	20	89.5
Ph	[bmim][BF$_4$]	Pd(OAc)$_2$	20	80.5
H	[bmim][BF$_4$]	Pd(OAc)$_2$	20	92
Ph	H$_2$O	PdCl$_2$	60	20

Table 1: Allylic substitution reaction carried out with chitosan-supported ionic liquid reactors and homogeneous catalyst systems

An enhanced activity for the chitosan-supported ionic liquid system in comparison to the chitosan-SAP system was clearly observed (89.5% compared to 20%). The low activity for the chitosan-SAP catalysis was already reported in previous work[10]. The increase in the catalytic activity for the chitosan-SILC can be correlated to a higher mobility of the organometallic complex in the IL layer than in the water layer. As shown in table 1, different palladium sources such as PdCl$_2$ and Pd(OAc)$_2$ can be used successfully with these new reactors. Moreover the reactions were also conducted successfully using different allylic substrates (R= H or Ph).

Another advantage of the chitosan-SILC concerns the ease of product extraction as illustrated by the reaction of (E)-1,3-diphenyl-3-acetoxyprop-1-ene with morpholine using Pd(OAc)$_2$ and TPPTS (Scheme 2).
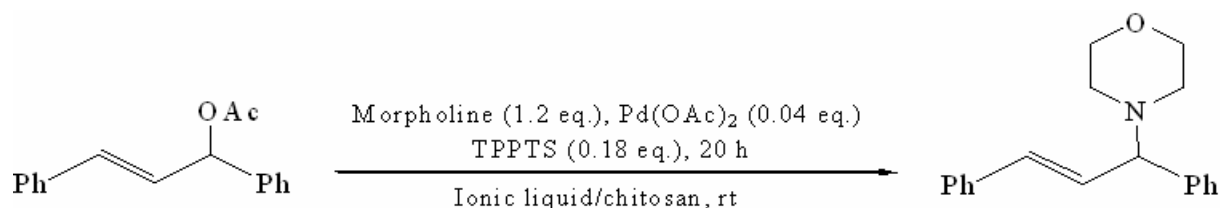
Scheme 2: coupling of (E)-1,3-diphenyl-3-acetoxyprop-1-ene with morpholine

For comparison, the reaction was also investigated in the free [bmim][BF$_4$]. In the case of the chitosan-SILC, after nine extractions with 1 mL of ether, the crude yield in product amounted to 100% corresponding to an isolated yield of 81% whereas in the case of the homogeneous system, at least twenty extractions were required for a complete extraction

We then turned our attention to the recovering and the recycling of the palladium catalyst. After extraction of the product using ether, the reactor was successfully reused in three other runs without a decrease of the activity.

In summary, these new reactors were successfully applied to the allylic substitution reaction. They allowed to obtain very good yields and allowed the easy extraction of product. Moreover, with these reactors, the palladium catalyst can be recycling. Another advantages of using these new systems is that they require a small amount of IL and the reactions were carried out successfully without any organic solvent. That lead us to expect their use in the fixed-bed technology.

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