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Catalyst retention utilizing a novel fluorinated phosphonium ionic liquid in Heck reactions under fluorous biphasic conditions

Daniel Rauber[a,*], Frederik Philippi[a], Rolf Hempelmann[a,b]

[a] *Institute of Physical Chemistry, Saarland University, Campus B 2.2, 66123 Saarbrücken, Germany*
[b] *Korea Institute of Science and Technology Europe, Campus E 7.1, 66123 Saarbrücken, Germany*

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ABSTRACT

A novel ionic liquid based on a highly fluorinated phosphonium cation was synthesized and its physicochemical properties were compared to its semi- and non-fluorinated analogue. The fluorinated ionic liquid was found to show a thermomorphic mixing behavior with organic solvents so that it could be applied as a substitute for volatile perfluorinated solvents in fluorous biphasic catalysis to achieve the recovery of perfluoro-tagged catalysts. Efficient immobilization of a perfluoro-tagged palladium catalyst in the fluorous ionic liquid phase was demonstrated for the Heck reaction as a model reaction of the widely applied Pd-catalysed C−C coupling reactions. The reaction of iodobenzene and methyl acrylate resulted in 83% yield after 20 runs proofing the efficient immobilization in the fluorophilic ionic liquid.

1. Introduction

Ionic liquids (ILs) and fluorous solvents are both regarded as “neoteric solvents” in the context of a greener, more sustainable chemistry since they share the potential to facilitate recycling procedures and reduce waste material as well as energy consumption [1–4]. However their physicochemical properties vary considerably. While ionic liquids have a negligible vapor pressure, polar structural motifs and are often hydrophilic, fluorous solvents show a significant vapor pressure and are highly apolar. Furthermore perfluoroalkyl groups show an even greater hydrophobicity than hydrocarbons through the reduced polarizability resulting from the high electronegativity of the fluorine atoms. The behavior of the perfluorocarbons of being hydro- and lipophobic at the same time is referred to as flurorophilicity [5]. Many fluorous and organic solvents are known to show a thermomorphic mixing behavior, forming a biphasic system at room temperature and a homogenous phase at elevated temperatures. This thermoregulated effect allows the specific separation and immobilization of components in liquid–liquid multiphasic systems and orthogonal chemistry in the separated phases [6]. A famous concept for thermoregulated chemistry is the fluorous biphasic catalysis (FBC) to achieve the recovery of perfluoro-tagged transition metal catalysts [7–10]. Important drawbacks of conventional fluorous solvents are their limited tuneability and relatively high vapor pressure, which restricts the useable temperature range. Furthermore bioaccumulation, persistence and the global warming potential of the volatile fluorous solvents can pose serious environmental problems [11,12]. The use of highly fluorinated ionic liquids [13] combines the advantages of fluorous solvents for efficient extraction and immobilization with non-volatility and a high degree of flexibility (through the task-specific and tailored designs) of ionic liquids. In this way it is possible to combine the benefits of these two neoteric solvents classes for effective and environmentally friendly reagent immobilization strategies. The use of fluorous groups in ionic liquids allows the implementation of fluorophilicity to the broad field of possible modifications beside the choices for anion and cation. This task-specific tuning allows new possible applications or the improvement of existing techniques [14]. It thus becomes feasible to modify the properties of liquid multiphasic systems in a wide range using non-volatile, modifiable fluorinated ILs as fluorous phase. The search for effective and reusable catalyst systems for multiphasic homogenous catalysis is an important issue in green chemistry since it saves energetic and chemical input [15,16]. ILs with perfluoroalkyl substituents have found numerous applications in many scientific fields like the use as surfactants [17], coating material [18] or liquid crystals [19,20], highly hydrophobic extraction agents [21], as well as for gas separation and gas dissolution [22,23] to name only a few. Furthermore fluorinated ILs are intensively investigated because of their unique microscopic heterogeneous structuring leading to a triphilic organization in ionic, hydrocarbon and fluorous domains driven by solvophobic interactions comparable to the macroscopic solvent behavior observed in limited miscibility and phase separation [24–27].

In this work we describe a new highly fluorinated phosphonium

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[*] Corresponding author.
E-mail address: daniel.rauber@uni-saarland.de (D. Rauber).

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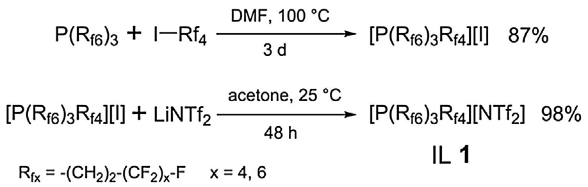
ionic liquid $[P(R_{f6})_3R_{f4}][NTf_2]$ (**1**) having four perfluoroalkyl chains ($R_{fx} = (CH_2)_2(CF_2)_xF$; x = 4, 6) in the cation combined with the bis(trifluoromethanesulfonyl)imide (NTf_2^-) anion. The application of this “building-block”-approach [28] for the synthesis of perfluoroalkyl substituted ILs allows the synthesis under laboratory conditions with easily adjustable structures. To investigate the effect of fluorination on important physicochemical properties and mixing behavior with organic solvents, IL **1** was compared to the non-fluorinated analogues hexyltrioctylphosphonium bis(trifluoromethanesulfonyl)imide $[P(oct)_3hex][NTf_2]$, the semifluorinated IL $[P(oct)_3R_{f4}][NTf_2]$ and the commonly

used 1-butyl-3-methyl-imidazolium bis(trifluoromethanesulfonyl)imide $[BMIM][NTf_2]$. The highly fluorinated IL **1** shows a low solubility and thermomorphic phase-mixing behavior with many organic solvents as it is commonly found for perfluorinated molecular solvents. The combination of the perfluorinated IL **1** and DMF was found to be an effective liquid–liquid system for immobilization of a palladium catalyst with highly fluorinated ligands [29] in Heck reactions [30]. Van Koten and coworkers already reported the use of a highly fluorinated IL for the retention of a perfluoro-tagged rhodium catalyst in a hydrosilylation [13]. Since the palladium catalyzed C—C bond formation is of high interest for laboratory and industrial preparations we wanted to demonstrate the application of this concept to the cross coupling reactions utilizing a Pd-catalyst immobilized in a fluorous ionic liquid phase. As a model reaction for palladium catalysis we chose the widely used Heck reaction for the cross coupling reaction of iodobenzene with either methyl acrylate or styrene. The Heck reaction is one of the most important reactions for C-C-bond formation, but in most reports the catalyst is lost during work-up and cannot be recovered. Creating an efficient recycling protocol for the Heck cross coupling is found to be a tough challenge because of the instable catalytic cycle and the use of multiple reagents and products which are changing the system properties and may have a disturbing or inactivating effect on the catalyst [31].

2. Experimental

2.1. Synthesis of the ionic liquids

The investigated ILs were synthesized by modified quaternization reactions of the corresponding phosphines with 1-bromohexane or 1*H*,1*H*,2*H*,2*H*-perfluorohexyl iodide in acetonitrile or DMF under inert gas atmosphere at elevated temperatures [32]. Tris(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)phosphine was synthesized following literature protocols [18,33]. The halide ILs were then converted to the corresponding NTf_2-ILs by anion metathesis reaction with $LiNTf_2$ in acetone. The exemplary synthesis of the fluorous IL **1** via quarternization of the fluorinated phosphine followed by anion metathesis is sketched in Scheme 1. Purity of the obtained ILs was checked by multinuclear NMR-spectroscopy and ESI–MS. The absence of halide ions was confirmed using methanolic $AgNO_3$ solution. Further details about the applied materials, synthesis conditions and multinuclear NMR-spectra are given in the Supporting information. $[BMIM][NTf_2]$ was prepared following literature reports [34].



Scheme 1. Synthesis of the fluorinated ionic liquid **1** via quaternization of ternary phosphine and 1*H*,1*H*,2*H*,2*H*-perfluorohexyl iodide followed by anion metathesis reaction with $LiNTf_2$.

2.2. Thermal properties

Melting, glass transition and cold crystallization points were determined by differential scanning calorimetry (DSC) using a DSC 1 STARe System (Mettler Toledo, Gießen, Germany) equipped with liquid nitrogen cooling. For the measurements about 20 mg sample were weighted into aluminum crucibles and hermetically sealed. The temperature program started with a heating rate of +5 °C/min to 100 °C followed by 30 min isothermal step at 100 °C to remove thermal history. Afterwards a dynamic step with cooling rate of −1 °C/min to -120 °C was applied. The temperature was held constant at −120 °C for 10 min, followed by a heating step (+1 °C/min) to 120 °C and then returned to the initial conditions. Decomposition temperatures were determined by thermogravimetric analysis (TGA) using a TG 209 F1 Iris (Netzsch, Selb, Germany) and Al_2O_3 crucibles. The temperature program was set from 20 °C to 600 °C applying a heating rate of 10 °C/min and a nitrogen flow of 20 mL/min. Decomposition temperatures were determined as extrapolated onset temperatures.

2.3. Polarity determination using the solvatochromic dye Nile Red

To 0.5 g of the ILs was added a solution of 0.5 mL Nile Red (NR) in acetone ($c(NR) = 3.0 \times 10^{-3}\,mol\,L^{-1}$) and stirred until the solution became homogenous. In case of IL 1 an additional milliliter acetone was added to ensure full dissolution. The solvent was then removed by drying in oil-pump vacuum for two days and the Nile Red solutions of the ILs were transferred to a quartz cuvette of 1 mm diameter to record a transmission UV/Vis spectrum. In case of 1 the UV/Vis-measurement was performed on a thin film of the sample in supercooled state as this IL showed a widely suppressed crystallization (see DCS results in Section 3.1). For each IL ten measurements were performed, the wavelength of the absorption maxima detected and the results averaged. The E_{NR} values were calculated after Eq. (1).

$$E_{NR} = hcN_A\,\lambda_{max}^{-1} \times 10^{-6} \tag{1}$$

with:

h: Planck’s constant
c: speed of light
N_A: Avogadro’s constant
λ_{max}: wavelength of the maximum absorbance (in nm)

2.4. Crystal structure determination of IL 1

Single crystal X-ray diffraction data were collected on a X8 Apex II diffractometer (Bruker AXS, Karlsruhe, Germany) at −121 °C using Mo-Kα radiation (λ = 0.71073 Å) in theta range from 0.607° to 27.811° collecting 88389 reflections in total. Crystal data: $C_{30}H_{16}F_{48}P^+$, $C_2F_6NO_4S_2^-$: $M_r = 1599.55$, triclinic, P-1, a = 9.1235(6) Å, b = 9.6920(6) Å, c = 33.677(2) Å, α = 86.357(3)°, β = 85.533(4)°, γ = 63.392(3)°, V = 2653.0(3) Å^3, Z = 2, $\rho_r = 2.002$ g cm^{-3}. The refinement using full-matrix least-squares on F^2 resulted in 12220 independent reflections, 381 restraints, 822 parameters, $R[F^2 > 2\sigma(F^2)] = 0.1245$, $wR(F^2) = 0.3897$.

2.5. Determination of ionic liquid solubility/miscibility in organic solvents

Solubilities or miscibilities of the phosphonium ILs with a range of organic solvents were determined by preparing saturated solutions of the ILs and 3.000 mL of purified and dried organic solvents under argon by stirring for at least 3 h in a thermostated bath keeping the temperature at 25 °C until a two phase system remained. Then the solution was allowed to settle for 16 h after which a completely homogenous upper phase was observed. A 2.000 mL sample of the organic phase was carefully taken and the solvent removed in oil pump vacuum by drying for at least one day until the mass remained constant. By weighting the remaining IL the solubility per liter could be calculated. If no second