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Ionophilic Phosphines: Versatile Ligands for Ionic Liquid Biphasic Catalysis

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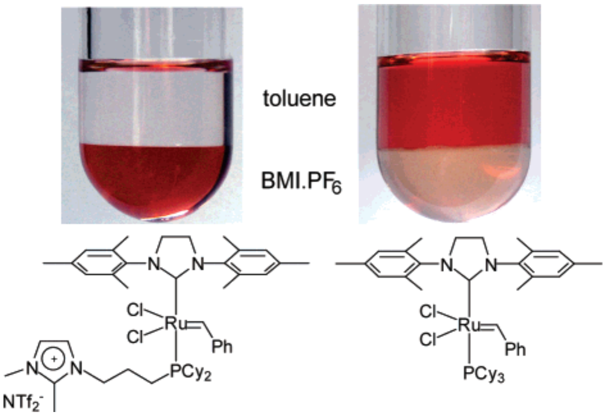
ABSTRACT



Phosphine ligands bearing an imidazolium fragment were easily prepared by one-step radical chain addition of secondary phosphines to allyl or vinyl imidazolium salts. These ligands were used to prepare new ionophilic second generation Grubbs-type catalysts. The catalyst immobilized in 1-butyl-3-methyl imidazolium ILs shows good catalytic activity in RCM reactions of several substrates and, depending on the media employed, is stable up to eight cycles.

Multiphase organometallic catalysis, in particular, liquid−liquid biphasic catalysis involving two immiscible phases, may offer the possibility of circumventing the problems associated with the homogeneous process such as product separation, catalyst recycling, and the use of organic solvents. Nowadays, there are several alternatives under investigation as fluids for multiphase catalysis for ring-closing metathesis reactions including the resurgence of water,[1−3] perfluorinated hydrocarbons,[4−6] and supercritical fluids, in particular CO_2.[7,8] Indeed, the advent of water-soluble organometallic complexes, especially those based on sulfonated phosphorus-containing ligands, has enabled various biphasic catalytic reactions to be conducted on an industrial scale. However, the use of water as a catalyst immobilizing phase has its limitations: (i) it is a highly polar and coordinating protic solvent, (ii) it is reactive toward many organometallic complexes and substrates, (iii) from an environmental perspective, trace amounts of organic compounds in water are notoriously difficult to remove, and (iv) the synthesis of

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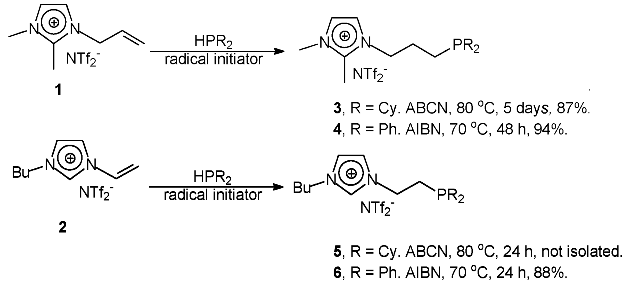
specially designed water-soluble ligands/organometallic complexes is essential for its use.

Classical transition-metal catalyst precursors are, in many cases, “soluble” in imidazolium ILs and are not removed from the ionic solution by the majority of organic compounds. Indeed various catalytic processes can be “directly” transposed in ionic liquids, such as those based on homogeneous transition-metal catalyst precursors and colloids, with great advantages compared with those performed in organic solvents or in water.[9,10] This is one of the great advantages of ILs in organometallic catalysis, that is, they allow the direct transposition of well-known homogeneous processes for liquid−liquid biphasic conditions without the use of specially designed ligands/complexes that are necessary for aqueous, perfluorinated, or supercritical fluid-based catalytic processes. However, in some cases classical metal catalysts are removed from the ionic liquid by the products formed, and ionic modified ligands such as phosphines should be used to minimize catalyst leaching.[11] This is the case in the hydroformylation reactions for which mono- and diphosphine ligands containing the imidazolium moiety have been developed[12] or for the hydrogen transfer reactions for which imidazolium containing η^6-arene ligands have been used.[13] Ring-closing metathesis reactions[14−16] can be performed by simple dissolution of Grubbs first or second generation catalysts,[17,18] allenylidene ruthenium precursors[19] or Hoveyda type catalysts bearing imidazolium fragments[20] dissolved in ionic liquids. However, no simple ionophilic ruthenium−phosphine catalysts precursors for ring-closing metathesis in ILs have been reported so far.

We report herein the synthesis of a new family of phosphine ligands that bear an imidazolium fragment and consist of a versatile ligand class for IL biphasic catalysis. We also report the syntheses of a second generation Grubbs type compound with high IL affinity and with potential for RCM reaction in ionic media.

The synthesis of the imidazolium phosphine ligands is shown in Scheme 1. In the presence of catalytic amounts of the appropriate radical initiator, the radical chain addition of secondary phosphines to allyl or vinyl imidazolium salts was easily performed.[21] The addition of $HPPh_2$ to the allyl imidazolium salt **1**[22] and vinyl imidazolium salt **2**[22] is straightforward, and almost quantitative conversions are attained with the mild radical initiator azobis(isobutyronitrile) (AIBN). Ligands **4** and **6** were isolated as colorless oils in 94% and 88% yields. Radical addition of the bulkier $HPCy_2$ fails with AIBN, and with the high-temperature radical initiator dicumyl peroxide, a complex mixture of products was obtained. The target ligand **3** was successfully synthesized in 87% yield as a white solid by using the radical initiator azobis(cyclohexanecarbonitrile) (ABCN). The reaction of the vinylimidazolium salt **2** with $HPCy_2$ promoted by ABCN gives the target ligand **5** together with byproducts which could not be separated. Despite the low reactivity of the allyl group toward secondary aliphatic phosphine addition, the method described offers a simple, single-step strategy for the synthesis of phosphine ligands bearing an ionic fragment. This methodology was succinctly mentioned but not exploited in earlier literature.[23]

Scheme 1. Synthesis of Phosphine Ligands



In particular this method has several advantages over others reported so far such as those based on base-catalyzed addition of primary or secondary phosphines to 1-vinylimidazole,[24] alkylation of imidazoles with bromoalkyl(diphenylphosphine) oxides folowed by phosphine reduction,[25,26] or nucleophilic substitution using bromo-alkyl-1-methylimidazolium salts.[27] However, the phosphines are prepared in four steps in the case of base-catalyzed method and the

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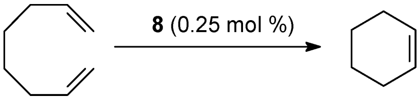
Table 1. Optimization in the 1,7-Octadiene RCM with Catalyst Precursor **8**[a]



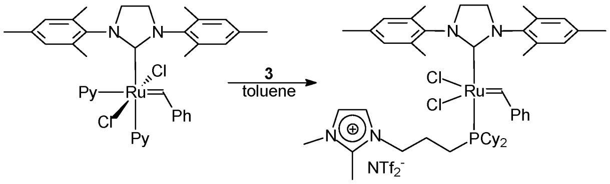
entry	solvent	cycle/yield (%)[b] (time (min))							
		1	2	3	4	5	6	7	8
1	BMI.NTf$_2$/toluene	98(80)	95(90)	96(90)	81(120)	-			
2	BMI.PF$_6$/toluene	98(70)	98(50)	99(40)	99(40)	92(60)	98(80)	94(90)	88(90)
3	BMI.FAP[c]/toluene	-							
4	BMI.PF$_6$/toluene[d]	99(10)	99(25)	86(90)	95(180)	-			
5	BMI.NTf$_2$/toluene[d]	99(10)	99(30)	90(60)	89(180)	-			

[a] Reaction conditions: 1,7-octadiene (2.0 mmol), toluene (4 mL), IL (1.5 g), catalyst (0.0050 mmol), 45 °C. [b] GC yield. [c] FAP = tris(perfluoroethyl)-trifluorophosphate. [d] Reaction performed with the second-generation Grubbs catalyst.

phosphorus center must be protected and deprotected. In the case of the nucleophilic substitution method only ionophilic ligands containing the diphenyl phosphine moiety have been reported so far. The radical chain addition method reported herein allows the one-step generation of diphenyl and dicyclohexyl ionophilic phosphine ligands.

Next, **7**[28] and the phosphine ligand **3** were reacted in toluene, according to known methodology, affording the Grubbs catalyst analogue **8** as a pink powder in 75% yield (Scheme 2). For toluene-IL biphasic systems, compound **8** presents a high IL phase affinity with undetectable Ru amounts (measured by atomic absorption for BMI.NTf$_2$/toluene biphasic system at room temperature) in toluene. It is worth noting that for the same biphasic system, the conventional second-generation Grubbs catalyst[29] has a very low IL phase affinity and is mainly present in the toluene phase.

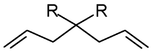
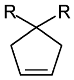
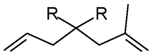
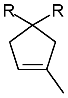
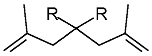
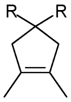
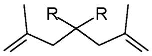
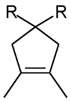
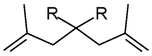
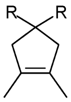
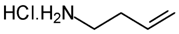
Scheme 2. Synthesis of Grubbs Catalyst Analogue **8**



7 **8**

The catalytic activity of the catalyst precursor **8** was first evaluated in the ring closing metathesis reaction of 1,7-octadiene yielding cyclohexene in IL/toluene biphasic media (Table 1). Three different hydrophobic ILs (BMI.NTf$_2$, BMI.PF$_6$, and BMI.FAP (FAP = (tris(perfluoroethyl)trifluorophosphate))) in the presence of toluene as cosolvent were employed for this study. We found that the concentration of compound **8** could be lowered from 5 to 0.25 mol % without a significant reduction in catalytic activity. This may be ascribed to the catalytic activity being mainly controlled by diffusion of the substrate into the ionic phase on this scale. Although excellent RCM yields are obtained for the first three cycles in BMI.NTf$_2$ (entry 1, Table 1), a noticeable IL phase color change from pinkish to brown is observed after the first cycle. Solutions of compound **8** in BMI.FAP (entry 3, Table 1) turn immediately colorless with a complete lack of catalytic activity. The use of BMI.PF$_6$ (entry 2, Table 1) improves both catalytic activity and recyclability of compound **8**. In BMI.PF$_6$/toluene media, compound **8** can be recycled up to eight times with virtually no loss of catalytic activity. Atomic absorption analysis of the toluene phase after each recycling revealed a ruthenium content below the detection limits of the technique (<2 ppm, i.e., less than 1.5% of the initial Ru content).

Table 2. RCM of Various Dienes Promoted by **8**[a]

entry	substrate[b]/conditions	product	yield (%)[c] (time)
1	 0.25 mol % **8**		99 (1.5 h)
2	 0.25 mol % **8**		91 (7 h)
3	 0.5 mol % **8**		10 (24 h)
4[d]	 0.5 mol % **8**		7 (24 h)
5[e]	 0.5 mol %		18 (24 h)
6[f]	 0.5 mol % **8**		-

[a] Reaction conditions: substrate (2.0 mmol), toluene (4 mL), BMI.PF$_6$ (1.5 g), 45 °C. [b] R = CO_2Et. [c] GC yields. [d] No IL, homogeneous reaction in toluene. [e] Homogeneous reaction in toluene performed using the second generation Grubbs catalyst. [f] BMI.PF$_6$/H_2O biphasic system.

Comparative examples with the second-generation Grubbs catalyst were performed in both BMI.PF$_6$/toluene and BMI.NTf$_2$/toluene catalytic systems (entries 4 and 5, Table 1). Although high 1,7-octadiene conversion over a short

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reaction time was obtained in the first cycle, it decreases abruptly as can be seen by the longer reaction time required to achieve 90% conversions in subsequent cycles. This fact is not unexpected since most of the Grubbs catalyst is removed dissolved in the toluene phase, and by the fourth cycle virtually no Ru is present in the ionic phase.

Next, we decided to compare the catalytic activity of compound **8** for the RCM of several diene substrates to better assess the scope of the reaction. As summarized in Table 2, **8** proved to be effective for obtaining di- and trisubstituted olefins (entries 1 and 2, Table 2). Additionally, recycling of the ionic phase was attempted for the more reactive substrate diallyl diethylmalonate, showing a small drop in the catalytic activity after the second cycle (97% and 81% yield (1.5 h) for second and third cycles, respectively). The reaction profile for this substrate is presented in Figure 1, showing a sigmoid profile typical for catalyst precursor preactivation. In fact, after 10 to 15 min of the reaction start, an IL phase color change to orange is accompanied by copious ethene evolution. The performance of compound **8** for the RCM of the poorly reactive di(methallyl diethylmalonate) substrate gives only 10% yield of the tetra-substituted olefin product (entry 3, Table 2). Homogeneous experiments performed in toluene comparing compound **8** and the Grubbs second generation catalyst showed a slight difference in the catalytic activity (7% and 18% yields, respectively) (entries 4 and 5, Table 2). The catalyst precursor **8** was found to be completely inactive for the RCM reaction of the water-soluble substrate homopropargylamine hydrochloride in a biphasic BMI.PF_6/H_2O system (entry 6, Table 2).

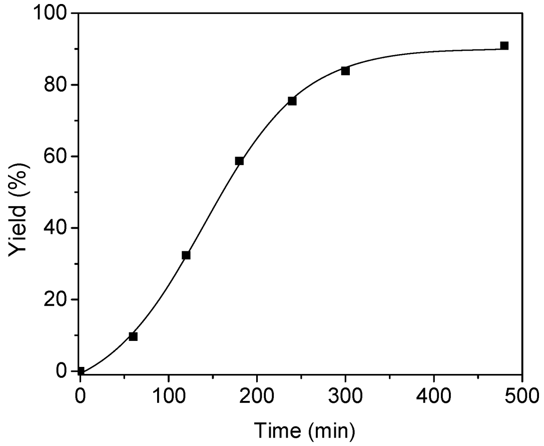

Figure 1. Conversion rate for the RCM of 2-allyl-2-methallylmalonate (reaction conditions of entry 2, Table 2).

In summary, we have designed a new class of ionophilic phosphine ligands to operate in ionic liquid media, easily attained in a one-step procedure. The proper choice of starting materials provides a versatile method to access a wide range of phosphine ligands containing imidazolium fragments. The viability of these ligands was demonstrated by employing the dicyclohexyl derivative **3** to synthesize the Grubbs type compound **8**. The catalyst precursor presents good activity for the RCM reactions performed in biphasic BMI.PF_6/toluene and good recycling properties. In particular, in this new catalytic system, the ruthenium concentration can be significantly lowered from 5 to 0.25 mol % without significant reduction of catalytic activity, as compared to other Ru-catalytic reported so far. Further work is in progress to access Grubbs-type compounds with less hindered N-heterocyclic carbene ligands in order to address the problem of less reactive substrates.

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Supporting Information Available: Full experimental details and compounds characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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