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Ruthenium-catalyzed allylation reaction in ionic liquid

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Abstract

Ruthenium-catalyzed allylic substitution reactions from unsymmetrical allylic carbonates have been demonstrated to proceed in the ionic liquid 1-hexyl-2,3-dimethylimidazolium hexafluorophosphate ([hdmim][PF_6]) under neutral conditions with very good conversion and regioselectivity, and high level of recyclability of the solvent/catalyst system.
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1. Introduction

Homogeneous catalysis is an efficient method for the formation of new C–H, C–C, C–O or C–N bonds [1]. Some of those reactions have gained wide acceptance because of their efficiency and/or selectivity. However, the high cost of catalysts can restrain their industrial use. Driven by economical considerations, significant progress were made to immobilize the catalysts, in order to facilitate their recovery and recycling. Among the known methodologies, ionic liquids have attracted a growing interest in the last few years [2–5]. They offer an interesting alternative to organic solvents as they have negligible vapor pressure and non-flammable nature, and are easy to recycle. Due to their low miscibility with many organic solvent, they also have a potential for catalyst/product separation. Some transition metal-catalyzed reactions have already been described in ionic liquid [4–6], among them, metathesis [7] and hydrogenation [8–10] reactions are the two most significant examples with ruthenium catalysts.

Allylic substitution represents a very useful reaction in organic chemistry [11,12], and to the best of our knowledge, only neutral palladium complexes were reported in the literature to perform allylic alkylations in the presence of a base in ionic liquid ([bmim][PF_6] or [bmim][BF_4]) [13–15]. Following our studies on ruthenium-catalyzed allylic substitution (Scheme 1) [16–19], we now report the first examples of allylic alkylation and etherification reactions in the ionic liquid [hdmim][PF_6] using the complex [Cp^*Ru(4,4′-*t*Bu-bipyridine)(CH$_3$CN)][PF_6] (Cp^* = pentamethylcyclopentadienyl) as catalyst under neutral conditions.

2. Experimental

2.1. Materials

The allylic carbonate **1**, the ruthenium catalyst [Cp^*Ru(4,4′-*t*Bu-bipy)(CH$_3$CN)][PF_6] [19], and the ionic liquid [20] were prepared according to literature procedures. Dimethylmalonate **2b**, acetylacetone **2a** and phenol **2c** were purchased from Aldrich or Acros.

2.2. 1-Hexyl-2,3-dimethylimidazolium hexafluorophosphate

A two-neck flask was charged with 5.55 ml (62.4 mmol, 1 eq.) of 1,2-dimethylimidazole and 9.17 ml (65 mmol, 1.05 eq.) of *n*-hexylbromide, and the reaction mixture heated

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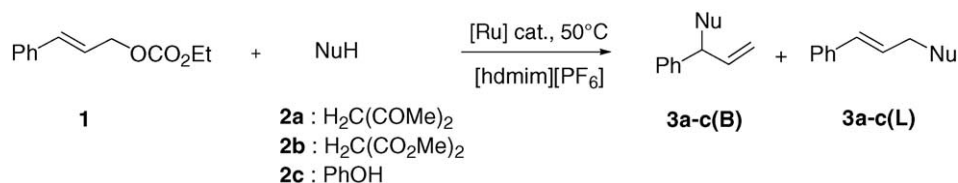
Scheme 1. Allylation of nucleophiles catalyzed by a cationic ruthenium complex in ionic liquid.

at 70 °C for 24 h. A beige solid formed upon cooling. The *n*-hexylbromide in excess was evaporated under vacuum and the flask was directly loaded with 11.48 g of potassium hexafluorophosphate (62.4 mmol, 1 eq.) in 50 ml of degassed acetone. The reaction mixture was stirred at 30 °C for 40 h. Filtration over alumina and evaporation of acetone afforded a white/brown solid, which was dissolved in 100 ml of dichloromethane and washed by 5×20 ml of water.[1] The organic phase was dried over sodium sulfate and passed on an alumina/MgSO$_4$ plug. Evaporation of the solvent gave 15 g (75% yield) of a whitish solid. Melting point of [hdmim][PF$_6$]: mp = 60 °C.

^{1}H NMR (acetone-d6, δ ppm): 0.87 (m, 3H, CH$_2$C*H*$_3$), 1.22–1.39 (m, 6H, C*H*$_2$), 1.76–1.87 (m, 2H, C*H*$_2$), 2.74 (s, 3H, NC(C*H*$_3$)N), 3.90 (s, 3H, NC*H*$_3$), 4.24 (t, 8 Hz, 2H, NC*H*$_2$), 7.53 (d, 2 Hz, 1H, C*H*), 7.57 (d, 2 Hz, 1H, C*H*).
^{31}P NMR (acetone-d6, δ ppm): −143.02.

2.3. Allylic substitution in [hdmim][PF$_6$]

In a Schlenk tube, 0.015 mmol of [Cp*Ru(4,4′-*t*Bubipy)(CH$_3$CN)][PF$_6$] (**I**) was dissolved in 1 g of ionic liquid at 60 °C. When an homogeneous red phase was observed, 0.6 mmol of nucleophile **2a**–**b** and 0.5 mmol of cinnamyl carbonate **1** were added. The mixture was stirred at 50 °C for 16 h. The solution was then extracted with 4×10 ml of heptane. The ionic liquid phase was dried under vacuum and used in the next run. The heptane phase was evaporated and the crude product thus obtained was analyzed by ^{1}H NMR and purified on silica gel.

In a recycling experiment, 0.6 mmol of nucleophile **2a**–**b** and 0.5 mmol of cinnamyl carbonate **1** were added to the ionic liquid layer from the above experiment. The mixture was stirred at 50 °C for 16 h and worked up as described above.

3. Results and discussion

As the catalyst precursor is cationic and as we previously demonstrated that the key intermediate is a dicationic ruthenium(IV) species [17], we expected that the immobilization of the catalytic species would be favoured and that this catalytic system would be very well adapted for a transfer into an ionic liquid as solvent.

Several criteria were taken into account for the choice of the anionic as well as the cationic part of the ionic liquid. The [PF$_6$] anion was chosen as [PF$_6$]-containing ionic liquids are usually hydrophobic and they allow the dissolution of ruthenium salts. Moreover, the use of the same counteranion as that of the catalyst is always preferable as it prevents anion metathesis between the solvent and the catalytic species, which can modify the catalytic properties of the initial precatalyst. Concerning the cation, an important criteria to consider is the possible oxidative addition to the metal centre as reported for nickel, platinum and palladium [21], and the possibility to generate diaminocarbenes via hydrogen abstraction [22], which can coordinate the metal centre as suggested in some ruthenium-catalyzed metathesis reactions [23,24]. The presence of the ethylate anion generated in situ from carbonate **1** during the catalytic process might favour the latter transformation. To avoid these processes the [hdmim] (1-hexyl-2,3-dimethylimidazolium) cation, in which the 2-position is substituted by a methyl group was selected (Fig. 1).

The only limitation of using [hdmim][PF$_6$] is its melting point over room temperature (60 °C), thus requiring a slight heating of the reaction mixture. Typically, our experiments were carried out at 50 °C.

The allylation of acetylacetone **2a** by cinnamyl carbonate **1** was first investigated. The catalyst [Cp*Ru(4,4′-*t*Bubipy)(CH$_3$CN)][PF$_6$] (**I**) (3 mol% based on cinnamyl carbonate) was dissolved by heating in [hdmim][PF$_6$] at 60 °C. The reactions were then carried out using 0.5 mmol of carbonate **1** and 0.6 mmol of acetylacetone **2a** at 50 °C for 16 h. Analysis of the crude mixture, after extraction with diethylether, showed that the reaction was almost complete and proceeded under neutral conditions. It has to be pointed out that the regioselectivity was excellent (run 1, Scheme 1 and Table 1) and, even if the temperature was higher than that
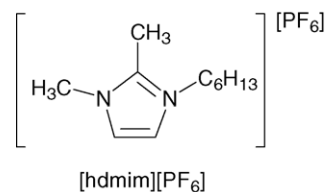
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[1] The same procedure was used for the synthesis of parent ionic liquids starting from imidazole derivatives and *n*-butyl chloride and five washings with water proved to be sufficient to remove chloride anions according to AgNO$_3$ testing.

Fig. 1.

Table 1
Alkylation of **1** with **2a** or **2b** in [hdmim][PF$_6$][a]

Run	Nucleophile	Conversion (%)[b]	Regioselectivity 3a–b(B/L)[b]
1	**2a**	80	97/3
2	**2a**	72	93/7
3	**2a**	68	96/4
4	**2a**	32	97/3
5	**2a**	11	94/6
1	**2b**	100	91/9
2	**2b**	47	94/6
3	**2b**	16	95/5
4	**2b**	15	97/3
5	**2b**	9	95/5

[a] Conditions: 0.6 mmol of nucleophile **2a–b**, 0.5 mmol of cinnamyl carbonate **1**, 0.015 mmol of [Cp*Ru(4,4′-tBu-bipy)(CH$_3$CN)][PF$_6$] (**I**) in 1 g of ionic liquid, 50 °C, 16 h.

[b] As determined by ^{1}H NMR spectroscopy. **3a–b** extracted with diethyl ether.

Table 2
Alkylation of carbonate **1** with **2a** or **2b** in [hdmim][PF$_6$][a]

Run	Nucleophile	Conversion (%)[b]	Regioselectivity (3a–b(B)/3a–b(L))[b]
1	**2a**	100	97/3
2	**2a**	100	96/4
3	**2a**	100	98/2
4	**2a**	100	99/1
5	**2a**	100	98/2
6	**2a**	85	97/3
1	**2b**	100	96/4
2	**2b**	90	96/4
3	**2b**	90	96/4

[a] Conditions: 0.6 mmol of nucleophile **2a** or **2b**, 0.5 mmol of cinnamyl carbonate **1**, 0.015 mmol of [Cp*Ru(4,4′-tBu-bipy)(CH$_3$CN)][PF$_6$] (**I**) in 1 g of ionic liquid, 50 °C, 16 h.

[b] As determined by ^{1}H NMR spectroscopy. **3a–b** extracted with heptane.

Table 3
Etherification of **1** with phenol **2c** in [hdmim][PF$_6$][a]

Run	Conversion (%)	Selectivity (3c(B)/3c(L))[b]
1	96	52/48
2	84	50/50
3	100	53/47
4	92	47/53

[a] Conditions: 0.6 mmol of phenol, 0.5 mmol of cinnamyl carbonate **1**, 0.015 mmol of [Cp*Ru(4,4′-tBu-bipy)(CH$_3$CN)][PF$_6$] (**I**) in 1 g of ionic liquid, 50 °C, 16 h.

[b] As determined by ^{1}H NMR spectroscopy. **3c** extracted with heptane.

used in organic solvent (50 °C versus room temperature), was comparable to our previous results (conversion: 100% and branched/linear ratio: **3a(B)**/**3a(L)**: 95/5 in acetonitrile [17]). These results clearly demonstrated that the behaviour of the catalyst (**I**) was similar in both media. Catalyst recycling appeared to be more challenging as the extraction of the products with solvents of various polarities (diethyl ether, toluene) resulted either in some leaching of ruthenium species out of the ionic liquid (with diethyl ether) or in degradation of the ruthenium complex [25]. However, as depicted in Table 1, even if the activity decreased with the number of recyclings, the regioselectivity remained high and almost unchanged.

Using the procedure developed for acetylacetone **2a** and cinnamyl carbonate **1**, the alkylation was extended to dimethylmalonate **2b**. The results are summarized in Table 1. As previously observed, the reactivity regularly decreased but the regioselectivity remained high in favour of the branched isomer and comparable to that observed during the reaction in acetonitrile at room temperature (98/2 for the alkylation of **1** with **2b** [17]).

As the regioselectivity was retained cycle after cycle, improvement of the catalyst recycling by using a less polar solvent (heptane) for the extraction of compounds **3** was attempted. Then, carrying out the reaction in the [hdmim][PF$_6$] ionic liquid at 50 °C and extracting products with heptane, an excellent regioselectivity and an active catalyst were maintained for at least six runs (Table 2).

Heptane thus appeared to be a solvent of choice, which made possible an efficient extraction of the organic compounds, keeping the catalyst intact and active in the ionic liquid phase.

To extend the range of nucleophiles and the potential of this ruthenium complex (**I**)/ionic liquid system, we tested the etherification of cinnamyl carbonate **1** with phenol (Table 3). As it was the case with the soft carbonucleophiles **2a–b**, no additional base was required to perform this reaction. The reactivity did not decrease with the number of cycles (for at least four cycles), and the selectivity was still unchanged and comparable to that obtained in acetonitrile (branched/linear ratio: 53/47) at room temperature.

4. Conclusion

We report here the first allylic alkylation and etherification of cinnamyl carbonate catalyzed by the ruthenium complex [Cp*Ru(tBu-bipy)(CH$_3$CN)][PF$_6$] (**I**) in the [hdmim][PF$_6$] ionic liquid at 50 °C. We show that the catalyst is safely immobilized in this ionic solvent and can be reused several times without loss of activity and regioselectivity. Tuning the nature of the extraction solvent is crucial in the design of an effective recyclable catalytic system.

With these remarkable properties, the ionic liquid appears to be an attractive alternative to organic solvents, with which no recovery and no recycling of the catalytic system were possible.

Acknowledgments

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