

# The role of additional solvents in transition metal complex catalyzed asymmetric reductions in ionic liquid containing systems

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## Abstract

When ionic liquids (ILs) are employed as solvents for transition metal complex (TMC) catalyzed reductions, a second solvent can be added to increase the efficiency of the catalytic cycle and the solubility of the reactant in the IL phase. Two industrially relevant asymmetric hydrogenations, the enantioselective reductions of methyl 2-acetamidoacrylate with Rh-EtDuPHOS and methyl acetoacetate with Ru-BINAP, were performed in different catalytic systems including 1-butyl-3-methylimidazolium hexafluorophosphate/tetrafluoroborate as ILs. Product separation and TMC recycling was performed by extracting the product from the reaction mixture. This can be accomplished by cooling the system, by adding an excess of the second solvent or by adding a third solvent. A high solubility of the second solvent in the IL catalytic phase favors the reaction activity, but can induce leaching of the IL and TMC. © 2005 Elsevier B.V. All rights reserved.

**Keywords:** Ionic liquids; Transition metal complexes; Hydrogenation; Rh-DUPHOS; Ru-BINAP

## 1. Introduction

Ionic liquids (ILs) have gained increased attention in the past decade as an alternative green medium for organic synthesis [1]. Their unique and versatile physical and chemical properties can be tuned and tailored, thus making them very attractive solvents. Numerous catalytic and non-catalytic reactions have been successfully run already in a variety of ILs. In this respect, imidazolium based ILs and especially 1,3-dialkylimidazolium cations combined with hexafluorophosphate and tetrafluoroborate anions, are the most commonly employed [1].

When transition metal complexes (TMCs), which act as very active and selective catalysts in many reactions [2], are the catalysts of choice, employing ILs also has economical and practical benefits. Since many TMCs dissolve easily in ILs, catalytic reactions can be performed easily in this medium, while product separation can be readily accomplished by distillation or extraction with an organic solvent [1]. Moreover, the IL-phase and the catalyst can be re-used. The heterogenization of TMCs was intensely studied over the past 30 years [3]. Different heterogenization methods have been reported, including the immobilization or entrapment of TMCs in solid organic or inorganic supports, separation of the complex via membrane filtration [4], or the use of biphasic systems. Water-organic biphasic systems were traditionally employed [5], yet preliminary modification of the complex to ensure its solubility in the water phase is necessary. Modification of TMCs

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is also required when fluorinated solvents are used [6]. Supercritical fluids have also been reported as green solvents for catalysis, but the critical conditions limited their use [7].

Even though ILs have a high potential as solvents for catalytic reactions with TMCs, some issues still limit their use. The activity of many TMCs catalyzed reactions in ILs is lower than the activity of the corresponding homogeneous reaction in conventional organic solvents [1]. It can be attributed to several factors. First, in many catalytic reactions the nature of the solvent can influence catalytic performance [8]. When TMCs are employed, the organic solvent can coordinate to the complex and assist in the catalytic cycle to make it more efficient [9]. On the other hand, the coordination of the solvent might block the complex and hence decrease its activity. Lower concentration of reagents (gases, liquids and solids) in the IL catalytic phase, or mass transfer limitations in the highly viscous ILs can also occur. In addition, it should be taken into account that products with high solubility in the IL phase require large amounts of extracting solvent to ensure their recovery and to recycle the complex [1]. TMCs catalyzed hydrogenations are good examples for the above mentioned drawbacks [10]. Not only because molecular hydrogen has a relatively low solubility in ILs [11], but mainly because coordination of the solvent to the TMCs activates the catalytic cycle [9].

In this paper, we report on various IL containing catalytic systems with TMCs where the addition of a second solvent during the reaction step enhances catalytic performance, while product separation and catalyst recycling are still feasible. Two industrially relevant asymmetric hydrogenations, the enantioselective reductions of methyl 2-acetamidoacrylate (MAT) with Rh-EtDuPHOS [12] (Fig. 1(a)) and methyl acetoacetate (MAA) as representative  $\beta$ -ketoester with Ru-BINAP [9] (Fig. 1(b)), were performed in different catalytic systems including 1-butyl-3-methylimidazolium

hexafluorophosphate/tetrafluoroborate (bmimPF<sub>6</sub>/BF<sub>4</sub>) as ILs.

## 2. Results and discussion

### 2.1. Homogeneous reference reactions

As a reference, both hydrogenations were performed in ILs under the typical conditions reported in literature [9,12]. Although both TMCs and substrates dissolved in the both ILs easily, no reaction took place (Table 1, entries 1 and 2). As stated previously, the hydrogen solubility in the two selected ILs is rather low [11], but even a higher hydrogen pressure for several hours did not trigger the reaction. Hence, it was considered whether the absence of reaction in pure ILs could be ascribed to the absence of organic solvent in the catalytic cycle of the reaction. It would thus mean that, in order to perform the reaction, another solvent apart from the IL is necessary (hereafter called reaction solvent, RS).

According to the literature, the homogeneous asymmetric hydrogenation of MAT with Rh-EtDuPHOS can be performed with high enantiomeric excess (ee) in several solvents, with alcohols inducing the highest activities [12]. The best reaction rates for the enantioselective reduction of MAA with Ru-BINAP have also been reported in short chain alcohols [9]. For the latter, the alcohol was actually participating in the reaction as a proton donor [9b]. The homogeneous reference reactions of both hydrogenations were thus performed in methanol, ethanol, and isopropanol (IPA) (Table 1, entries 3–5). Methanol yielded the highest performance for both hydrogenations. Since methanol is miscible in both ILs, the monophasic hydrogenations in mixtures of ILs + methanol (RS/IL = 1/1 v/v) were examined (entries 8 and 9). It yielded activities and selectivities equal to those of the homogeneous systems. This ‘homogeneous-like’ performance can be explained by (1) the

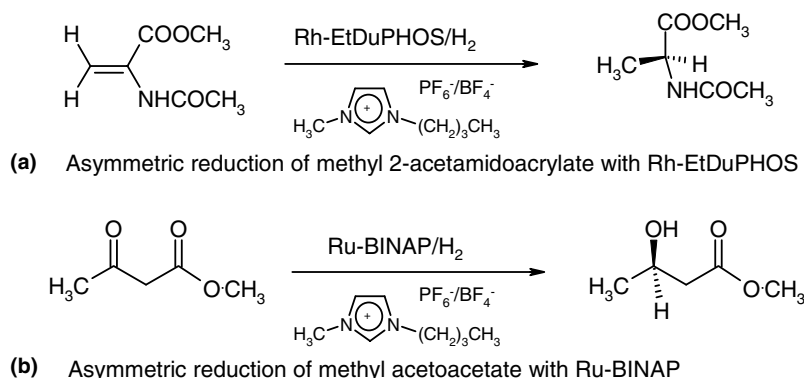


Fig. 1. Representative asymmetric reduction with TMCs in ILs.

Table 1  
Asymmetric reductions with TMCs in ionic liquid containing systems

Entry	Solvent(s)	Rh-EtDuPHOS <sup>a</sup>		Ru-BINAP <sup>b</sup>		
		TOF (h <sup>-1</sup> ) (Re-use)	ee (%) (Re-use)	TOF (h <sup>-1</sup> ) (Re-use)	ee (%) (Re-use)	Selec. (%) <sup>c</sup> (Re-use)
<i>Homogeneous<sup>d</sup></i>						
1	bmimPF <sub>6</sub>	0	0	0	0	0
2	bmimBF <sub>4</sub>	0	0	0	0	0
3	Methanol	3225	97	105	99	85
4	Ethanol	3220	98	92	99	87
5	IPA	2950	96	71	99	93
6	Methanol + water <sup>e</sup>	2560	97	7	21	100
7	Methanol + hexane <sup>e</sup>	1352	97	60	99	89
<i>Monophasic: dilution/extraction<sup>e</sup></i>						
8	bmimPF <sub>6</sub> /methanol	3012 (2953)	97 (98)	99	99	91
9	bmimBF <sub>4</sub> /methanol	2605	93	86	84	93
10	bmimBF <sub>4</sub> /water	1601	92	–	–	–
<i>Biphasic<sup>f</sup></i>						
11	bmimPF <sub>6</sub> /hexane	0	0	0	0	0
12	bmimPF <sub>6</sub> /ether	179 (180)	96 (96)	0	0	0
13	bmimPF <sub>6</sub> /IPA	460 (453)	95 (94)	21 (20)	97 (96)	83 (84)
14	bmimPF <sub>6</sub> /water	1025 (998)	96 (97)	1.9	93	100
<i>Reversible phase</i>						
15	BmimPF <sub>6</sub> /ethanol <sup>g</sup>	758 (755)	98 (99)	63 (65)	95 (96)	93 (93)
16	BmimBF <sub>4</sub> /2-propanol <sup>h</sup>	–	–	32 (32)	89 (88)	91 (91)

<sup>a</sup> 1 μmol Rh-EtDuPHOS, substrate over catalyst molar ratio of 500, hydrogen pressure of 5 bar, reaction temperature of 20 °C.

<sup>b</sup> 2 μmol Ru-BINAP, substrate over catalyst molar ratio of 140, hydrogen pressure of 40 bar, reaction temperature of 60 °C.

<sup>c</sup> Selectivity to methyl hydroxybutyrate.

<sup>d</sup> 2 mL solvent, 5 min.

<sup>e</sup> 1 mL of each solvent, 5 min.

<sup>f</sup> 2 mL IL and 2 mL solvent, 20 min. Re-use of the catalyst was done by addition of fresh substrate after extraction of the IL with 6 mL of the solvent.

<sup>g</sup> 1.1 mL bmimPF<sub>6</sub> and 0.9 mL ethanol (33 wt% ethanol). Re-use of the catalyst phase after addition of 3.2 mL ethanol to extract.

<sup>h</sup> 0.8 mL bmimBF<sub>4</sub> and 1.2 mL 2-propanol (50 wt% 2-propanol). Re-use of the catalyst phase after adding 3.2 mL 2-propanol to extract.

presence of a solvent that can participate in the catalytic cycle during the reaction, and (2) by the increased hydrogen solubility in the ILs + methanol mixtures. The reactions in bmimBF<sub>4</sub> showed lower activities and selectivities, probably due to impurities left from the synthesis of this particular IL [1b].

## 2.2. Extractions from IL phase

When a miscible solvent is added as a RS to the IL catalytic phase, product separation and recycling of the IL phase and the catalyst within look at first sight complicated. However, it will be shown below that some elegant methods exist due to some particularities of the investigated ILs.

Since distillation is limited to compounds with relatively low boiling point, extraction of the products from the IL + RS system with a third solvent (hereafter: extraction solvent, ES) was investigated. Depending on their mutual miscibility, the RS could be co-extracted by the ES (Fig. 2(a), type A) or not (type B), while the three solvents formed one-phase in still other cases (type C). Both the extraction yields of the organic compounds

as well as the losses of IL and complex to the extracting phase should be considered when selecting a combination of IL + RS + ES. Thus, several representative polar and non-polar solvents were tested as ES and combined with several RS + IL couples (ES/(RS + IL) = 1/1 v/v) (Table 2). Methanol, which is fully miscible in both ILs (entries 1–8), and water, which is miscible in bmimBF<sub>4</sub> (entries 9 and 10), were added as RS. Two combinations with ESs that mix partly or fully with the IL, such as IPA and water in bmimBF<sub>4</sub> (entries 2 and 8), resulted in type C systems. Obviously, this type of system is non-practical for extraction. However, employing hydrophobic solvents which are immiscible with the ILs, yielded type B systems with methanol preferably dissolved in the polar IL phase (entries 3 and 4). Still other ESs co-extracted the RS, resulting in type A systems (entries 1, 5–7, 9–10).

The leaching of both complexes in the various (IL/RS/ES)-combinations as well as the extraction yields of MAA in one extraction step are also summarized in Table 2. It should be considered that MAA is a representative organic compound, but one with a high solubility in both ILs, and thus very challenging to

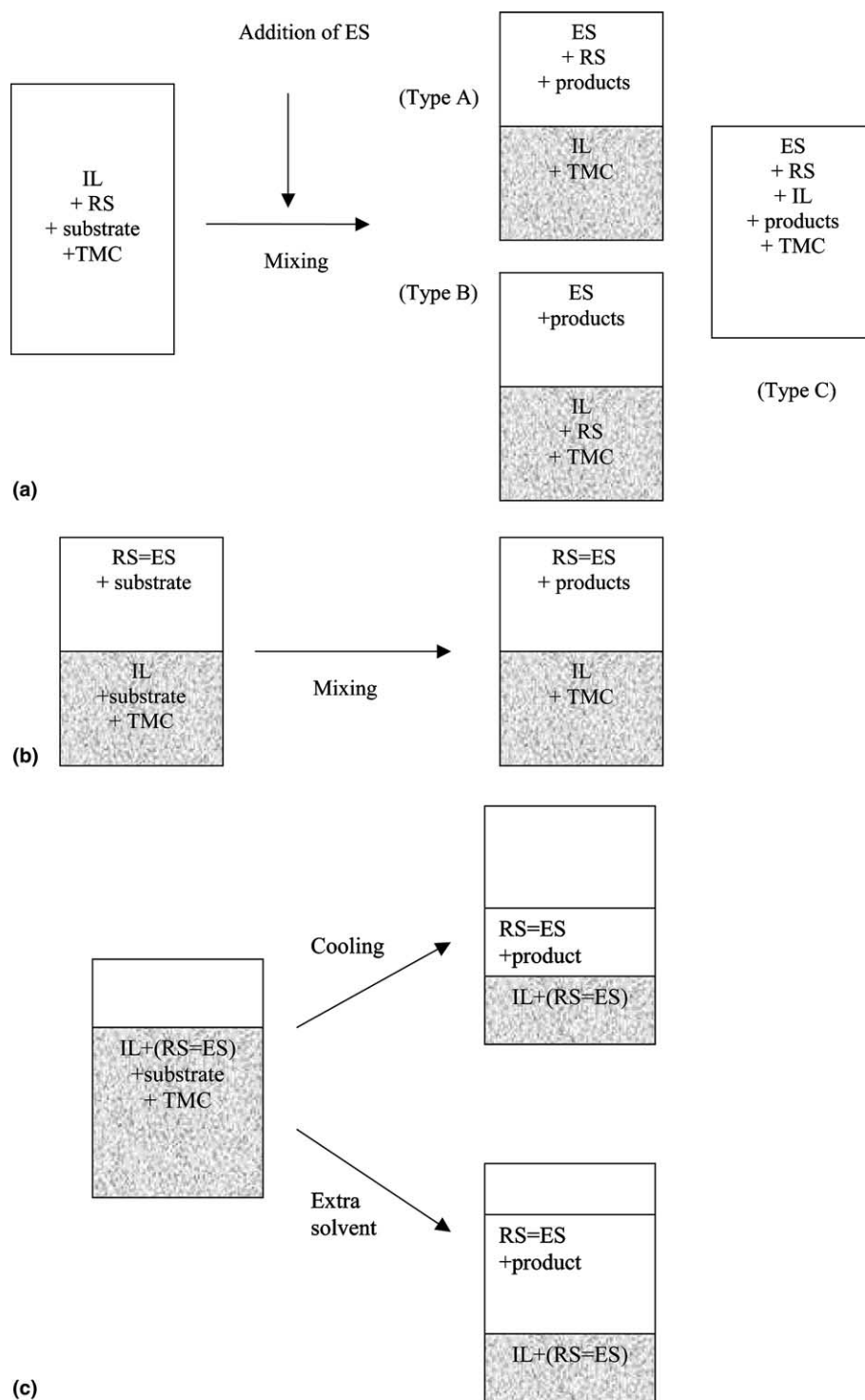


Fig. 2. IL containing catalytic systems: (a) monophasic system: dilution/extraction concept; (b) biphasic system; (c) reversible phase system.

recover. It can be concluded in general that when type A systems are formed, the extraction yields are full, yet there is often some leaching of the complexes. On the other hand, type B systems resulted in lower extraction yields, but negligible TMC leaching. It thus seems that co-extracting the RS (type A) efficiently extracts the

product from the IL, but it also extracts some of the IL and hence the complex within. On the contrary, systems that do not co-extract the RS (type B), do not extract the IL and the complex either. However, the extraction yields of the organic compounds from the IL phase are lowered.

Table 2

The type of system formed by adding an ES to the (IL + RS) mixture and the extraction yield with such system for MAA and leaching for the two selected TMCs<sup>a</sup>

Entry	IL anion	Reaction solvent	Extraction solvent	System type	Extraction yield (%) <sup>b</sup>	Leaching of Ru-BINAP (%) <sup>c</sup>	Leaching of Rh-DuPHOS (%) <sup>d</sup>
1	PF <sub>6</sub>	Methanol	IPA	A	100	1 (8) <sup>c</sup>	7
2	BF <sub>4</sub>	Methanol	IPA	C	–	–	–
3	PF <sub>6</sub>	Methanol	Hexane	B	6	0 (0)	0
4	BF <sub>4</sub>	Methanol	Hexane	B	5	0	0
5	PF <sub>6</sub>	Methanol	Ether	A	100	0	0
6	BF <sub>4</sub>	Methanol	Ether	A	100	1	4
7	PF <sub>6</sub>	Methanol	Water	A	100	1 (3)	2
8	BF <sub>4</sub>	Methanol	Water	C	–	–	–
9	BF <sub>4</sub>	Water	Hexane	B	0	0	0
10	BF <sub>4</sub>	Water	Ether	B	31	0	0

<sup>a</sup> 1 mL IL and 1 mL reaction solvent, 2 mL extraction solvent.

<sup>b</sup> 0.014 g MAA.

<sup>c</sup> 1 μmol Ru-BINAP.

<sup>d</sup> 1 μmol Rh-EtDuPHOS.

### 2.3. Monophasic reactions, followed by extraction

All the above findings were finally combined in the two representative hydrogenations with both ILs under monophasic reaction conditions, followed by extraction (Table 1 (entries 8–10)). As previously mentioned, when methanol was employed as the RS, the activity of Rh-EtDuPHOS in MAT hydrogenation was comparable to those of the best homogeneous system (entries 8 and 9). The ES was chosen so that the methanol would not be co-extracted, since this would cause complex and IL leaching. Hexane clearly fulfilled these requirements (Type B system). However, only 7 wt% of the reaction product could be extracted by hexane in one step. In order to increase the extraction yield, an alternative monophasic-IL system was tested with bmimBF<sub>4</sub> as IL, water as RS and ether as ES (Table 1, entry 10). Indeed, the product extraction yield could be increased now to 19% in one step without complex or IL leaching, but this took place at the expense of a lower activity and slightly decreased ee. The former is probably due to the fact that methanol is a better solvent for this reaction than water, the latter to the fact that bmimBF<sub>4</sub> had to be used here and possible chlorine leftovers from the IL synthesis might harm the Rh-EtDuPHOS performance [1b]. Re-use of the IL-containing Rh-DuPHOS phase after five sequential extraction steps and addition of extra MAT was successful (entry 8, numbers between brackets).

In the asymmetric reduction of MAA with Ru-BINAP, the choice of reaction solvent is even more crucial, and thus limited [9b]. Homogeneous reactions can only be performed in alcoholic or chlorinated solvents, but the alcoholic solvents yield much higher activities, due to the participation of the alcoholic solvent in the catalytic cycle. Furthermore, addition of high amounts of water severely decreases the catalyst performance. Therefore, only methanol could be selected as the RS,

allowing hexane for the subsequent extraction. A similar system was studied by Ngo and co-authors using a phosphinic acid derived Ru-BINAP [13]. In agreement with this report, the activity of the asymmetric reduction of MAA with Ru-BINAP in the (bmimPF<sub>6</sub>/methanol) mixture was again comparable to the best homogeneous activity (Table 1, entries 8 and 3, respectively). Addition of 2 mL hexane to the reaction mixture resulted in the extraction of 8% of the product in the first step.

### 2.4. Biphasic reactions

Another approach commonly used in the literature, is performing the reaction in a biphasic system [10]. Guernik et al. studied the asymmetric reduction of MAT with Rh-MeDuPHOS in bmimPF<sub>6</sub>/IPA biphasic system and the activity in the biphasic system was 4–5 times lower than the activity of the homogeneous reaction in IPA [10c]. In such a system, the RS and ES are the same solvent with a low miscibility in the IL. It can thus both activate the reaction and extract the product at the end of the reaction (Fig. 2(b)). Various representative solvents were thus combined with the two selected ILs in the two asymmetric hydrogenations (Table 1). While hexane as RS did not allow any reaction in the asymmetric reduction of MAT with Rh-EtDuPHOS (entry 11), combining bmimPF<sub>6</sub> with ether, IPA or water yielded activities (entries 12–14) that were lower than the activity of the homogeneous reactions in alcohols (entries 3–5). The absence of reaction with hexane illustrates that hexane cannot participate in the catalytic cycle (entry 7). The lower activities in the biphasic systems can be attributed to the low concentration of the RS in the IL catalytic phase, but also to the distribution of the substrate between the two phases present during reaction. The amount of MAT in the catalyst containing IL phase was determined by extraction of the IL phase with the

Table 3  
The effect of solvent type in the (bmimPF<sub>6</sub> + solvent)-biphasic systems on the extraction yields of MAT and MAA and on TMCs leaching<sup>a</sup>

Entry	Solvent	MAA extraction yield (%) <sup>b</sup>	MAT extraction yield (%) <sup>c</sup>	Leaching of Ru-BINAP (%) <sup>d</sup>	Leaching of Rh-DuPHOS (%) <sup>e</sup>
1	IPA	24	38	0	0
2	Water	23	27	1	1
3	Ether	19	19	0	0

<sup>a</sup> 1 mL bmimPF<sub>6</sub>, 1 mL solvent, room temperature.

<sup>b</sup> 140 mg MAA.

<sup>c</sup> 45 mg MAT.

<sup>d</sup> 1 μmol Ru-BINAP.

<sup>e</sup> 1 μmol Rh-EtDuPHOS.

three solvents (Table 3). It was found to increase in the order ether > water > IPA, as expressed by the decrease of the amount of MAT extracted from the IL phase from IPA to diethyl ether. Hence, if a higher concentration of the substrate in the IL catalytic phase would have been the only reason for the higher reaction rate, the reaction should have proceeded faster in ether than in water, which is clearly not the case. In the enantioselective reduction of MAA with Ru-BINAP, IPA was the only solvent that could work (entry 13), as expected, but the activity was only 20% of the best homogeneous system in methanol (entry 3) and about 30% of the homogeneous reaction in IPA (entry 5).

The superior reaction rate of the (bmimPF<sub>6</sub>/water) biphasic system can be thus mainly attributed to the excellent mixing in this system. In fact, visual observations supported this suggestion (Fig. 3). The combination of bmimPF<sub>6</sub> with hexane or IPA resulted in visibly big droplets of the organic solvent in the IL-continuous phase. The addition of water to bmimPF<sub>6</sub> on the other hand, resulted in a much better dispersed system, as reflected in the turbid aspect of the mixture, indicating the presence of smaller droplets. The different mixing of the various IL-biphasic systems can be explained by the difference in their mutual solubility with bmimPF<sub>6</sub> [14a]. While hexane has negligible solubility in the IL due to its insignificant polarity and hydrogen bonding character, IPA has a higher solubility in bmimPF<sub>6</sub> and water the highest solubility. The solubility of water in bmimPF<sub>6</sub> and of bmimPF<sub>6</sub> in water were found to be around 2 wt% [14b].

Although the conversions of the biphasic systems were lower than the conversion of the homogeneous and monophasic reactions, the products could be fully extracted after three sequential extractions with 2 mL of the corresponding solvent. The leaching of both complexes from the IL phase was negligible, except for a small loss of complex when water was used as RS due to some leaching of the IL to the water (Table 3). The IL catalytic phase was thus successfully re-used after re-

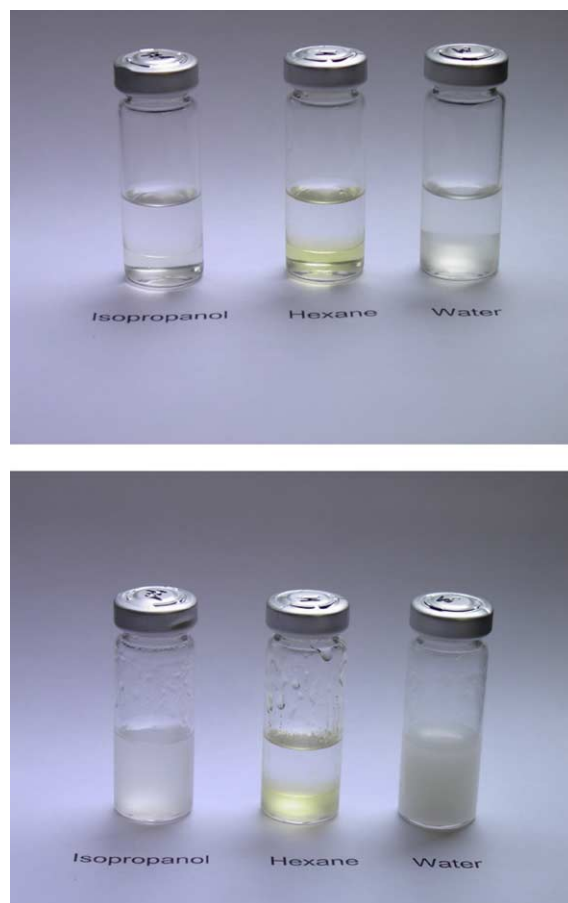


Fig. 3. Biphasic systems with bmimPF<sub>6</sub> before mixing (top picture) and a few seconds after mixing (bottom picture).

moval of the products by extraction with extra amounts of the RS and showed similar performance as in the first run (Table 1, values between brackets in entries 9–11). The small decrease in the activity of the re-use of the (bmimPF<sub>6</sub>/water) system is probably due to the loss of some IL and catalyst during extraction (Table 1, entry 14).

### 2.5. Reversible phase catalytic systems

Finally, it was found that the phase behavior of the two selected ILs with some alcohols could combine the advantages of homogeneous and heterogeneous catalysis. These solvent combinations showed a temperature and concentration dependent reversible phase behavior, as can be seen in Table 4. While methanol was miscible with both ILs over the full temperature range, longer alcohols like pentanol showed poor miscibility in the same ILs. However, ethanol, IPA and 2-butanol displayed solubility at the two selected temperatures which are suitable for catalytic applications. By increasing the temperature from 20 to 60 °C, the solubility of ethanol in bmimPF<sub>6</sub> doubled, while the solubility of IPA and 2-butanol in bmimBF<sub>4</sub> increased 5- and 8-fold,



Table 4  
Solubilities of alcohols in the two selected RTILs at different temperatures<sup>a</sup>

IL	Alcohol	wt% (20 °C) <sup>b</sup>	wt.% (60 °C) <sup>b</sup>
BmimPF <sub>6</sub>	Methanol	Full	Full
	Ethanol	17	35
	2-butanol	Negligible	Negligible
BmimBF <sub>4</sub>	Methanol	Full	Full
	Ethanol	Full	Full
		15	75
	2-butanol	5	40
	<i>n</i> -Pentanol	Negligible	Negligible

<sup>a</sup> Measured by addition of the alcohol to the IL under stirring, until phase separation was observed.

<sup>b</sup> Weight of alcohol/weight of alcohol and IL.

respectively. This behavior would allow the use of these alcohols for the two representative reactions as both the RS and ES. It means that a partially miscible solvent can be added to the IL already during reaction and allow catalysis to take place under 'homogeneous-like' conditions, while a simple decrease in temperature or further increase of the dilution degree with the same solvent allows easy separation of the catalyst from the product (Fig. 2(c)). Similar phase behavior of IL with supercritical carbon dioxide was employed to recycle several TMCs [15].

The two selected enantioselective hydrogenations were run in (bmimPF<sub>6</sub>/ethanol) and (bmimBF<sub>4</sub>/IPA) (Table 1, entries 15 and 16). As previously shown, the BF<sub>4</sub>-system yielded a lower activity and enantioselectivity (entry 16). Addition of an extra 2 mL of ethanol to the monophasic hydrogenation of MAT with Rh-EtDuPHOS in (bmimPF<sub>6</sub>/ethanol) resulted in a 36 wt% product extraction yield. The complex of entry 15 was successfully recycled after three successive extractions of the IL phase adding such excess of ethanol. Alternatively, Ru-BINAP was successfully recycled (Table 1, entry 15) with removal of the methyl hydroxybutyrate saturated top layer after simple cooling to room temperature. This yielded 13% of the product. Combining excess solvent addition with cooling via the addition of 2 mL of cold ethanol to the reaction mixture, increased the extraction yield to 46%. A similar successful extraction and re-use procedure was also done with the (bmimBF<sub>4</sub>/IPA) system. The activities and selectivities during the second run in both reactions were found to be equal to those of the first one. This proved already the negligible TMC leaching during the extraction procedure, as could be confirmed by direct ICP-analysis of the ethanol phase for Ru and Rh (<2% leaching). Only ~1 wt% of the IL was detected in the extractant phase.

This remarkable reversible phase behavior of mixtures of certain ionic liquids and organic solvents thus allows to perform reactions under homogeneous condi-

tions, followed by a straightforward phase separation induced by either cooling or by addition of excess solvent or by a combination of both. After fast phase separation the formed products can be easily extracted, while the TMCs could be recycled without loss of activity.

### 3. Conclusions

ILs can be employed as green solvents in heterogenization of TMCs whereas the products can be extracted by an extraction solvent which is immiscible in the IL phase. However the hydrogenations of many molecules with TMCs cannot be performed in pure IL and thus require the existence of another solvent during the reaction. The reaction solvent and the extraction solvent can be the same, partially miscible (reversible phase system) or immiscible (biphasic system) in the IL phase. Alternatively, the reaction solvent can be fully miscible in the IL while the product is extracted by another immiscible solvent (monophasic reactions, followed by extraction). In general, increasing the solubility of the reaction solvent in the IL catalytic phase increases the reaction activity. It is attributed to the activation of the catalytic cycle by the reaction solvent as well as to increase of the concentration of organic reactant and hydrogen in the IL phase. In addition, when fully or partly miscible solvents are added to the IL during the reaction, extraction of the product by the same solvent or another extracting solvent that co-extracts the reaction solvent results in high extraction yields of organic compound, yet part of the IL and catalyst within will also leach to the extraction solvent. On the other hand, employing of a second solvent which has poor miscibility with the IL, or an extracting solvent that does not co-extract the reaction solvent, yields lower extraction yield without any loss of the IL and the TMC. Hence, the combination of IL, reaction solvent and extraction solvent is primarily depending on the reaction requirements, yet it should be optimized regarding reaction activity, product extraction and catalyst recycling.

### 4. Experimental

#### 4.1. General

Rh-EtDuPHOS was purchased from Strem, while Ru-BINAP (2,2'-Bis(diphenylphosphino)-1,1'-binaphthalene]chloro(*p*-cymene)ruthenium chloride), methyl 2-acetamidoacrylate, methyl acetoacetate and ILs were purchased from Fluka. The solvents were purchased from Across. Both the homogeneous and heterogeneous reactions were performed in a 10 mL stainless steel

pressure reactor with magnetic stirring. In a typical reaction, the complex was first added to the reaction mixture under nitrogen atmosphere, followed by the addition of the substrate.

Conversion and selectivity were determined after extraction of the substrate and the product from the IL containing phase by GC analysis in a suitable column. Conversion were calculated by the amounts of substrate and product in the extracting solvent (or solvent mixture) taking into account also the different distribution constants of both substrate and product between the IL and the extracting solvent. The extractions yields were determined by calculating the amount of the substances in the extracting solvent by GC analysis (using a standard) divided by the total amount that was added to the IL phase. Leaching of the metal complexes was detected by atomic adsorption spectroscopy in accuracy of 0.05 µg/ml. In all cases, the solvent mixture was carefully evaporated and the residue was re-dissolved in 5 mL methanol.

#### 4.2. Homogenous reactions

For the asymmetric hydrogenation of MAT with Rh-EtDuPHOS, 1 µmol of the complex was added to 2 mL of solvent under nitrogen atmosphere followed by the addition of the substrate (71.5 mg). Hydrogen was fed at a pressure of 5 bar, after flushing with nitrogen and hydrogen. For the enantioselective hydrogenation of MAA with Ru-BINAP, 2 µmol of the complex was added to 2 mL of solvent under nitrogen atmosphere with 32.5 mg of substrate and the reactions proceeded at 40 bar hydrogen pressure and 60 °C.

#### 4.3. Monophasic reactions

The amount of catalysts and substrates as well as reactions procedures and conditions are the same as in the homogeneous reactions apart from the solvent which was in the monophasic reaction a mixture of 1 mL of IL and 1 mL of a solvent which is miscible in the IL. Re-use of the complex was done by extraction of the IL + RS mixture with 6 mL ES after the first run to remove the residual product and substrate. Fresh substrate was then added to the IL phase.

#### 4.4. Biphasic reactions

The amount of catalysts and substrates as well as reactions conditions is the same as in the homogeneous reactions. Both the substrate and complex were added to 2 mL of IL under nitrogen followed by addition of 2 mL of a non-miscible solvent. Re-use of this system was done after extraction of the products in three sequential extraction steps of 2 mL of the solvent that was employed during the reaction.

#### 4.5. Reversible phase reactions

The amount of catalysts and substrates as well as reactions conditions is the same as in the homogeneous reactions. The reactions in the reversible systems were performed in 1.1 mL bmimPF<sub>6</sub> and 0.9 mL ethanol (33 wt% ethanol), or 0.8 mL bmimBF<sub>4</sub> and 1.2 mL isopropanol (50 wt% isopropanol). Re-use of the catalyst phase was done by addition of 3.2 mL ethanol or isopropanol to extract the products and addition of the corresponding amount of fresh substrate and alcohol.

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