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Metal catalysed Michael additions in ionic liquids

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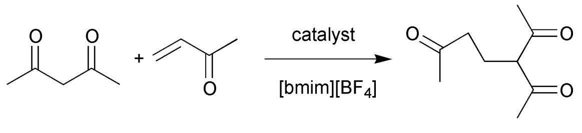
The ionic liquid [bmim][BF$_4$] (1-*n*-butyl-3-methylimidazolium tetrafluoroborate) was used as innovative solvent for a recyclable catalytic system active in metal promoted Michael additions employing Ni(acac)$_2$ as catalyst.

Ionic liquids (ILs) are attracting increasing interest as environmentally benign solvents, because they possess a number of interesting properties. Among these, one of the most important is their virtually non existent vapour pressure, which makes them easily confinable, and also enables an easy recyclability of catalytic systems after distillation of volatile products. The solvation strength of ILs can also be easily fine-tuned for optimization of catalyst retention, and allows the choice of suitable solvents for product extraction, both crucial factors for potential technological applications. The above-mentioned features and the state of the art of the research in this area have been highlighted by several reviews[1] from which it is evident how ILs are now ubiquitously being used as solvents for a wide range of catalytic reactions. Interesting results have been obtained especially in carbon–carbon bond forming reactions. Very recent work on the topic accounts ILs use as solvents for the Robinson annulation and the Knoevenagel reaction,[2] the palladium catalysed allylic alkylation[3] and Suzuki cross-coupling,[4] and the Rh(I) catalysed polymerization of phenylacetylene.[5]

In this framework, the Michael addition is among the most useful carbon–carbon bond forming reaction and has wide synthetic application in organic synthesis.[6] It has received great attention in recent years, especially in view of the advantages in terms of chemoselectivity and activity that can be achieved using a transition metal complex instead of the traditional basic catalysts. The metal catalysis approach prevents in fact the formation of undesirable side-products by polymerisation, bis-addition and self-condensation. Many homogeneous catalysts[7] have been employed successfully for this reaction, after the systematic work of Nelson,[8] and heterogeneous approaches have also been tried.[9] Recently, different attempts were made to apply a 'green' approach to this reaction. For example Yb(TfO)$_3$ proved to be an active catalyst in water[10] and Eu^{3+} facilitated solvent-free reaction under microwave irradiation was also reported.[11] So far, no alternative solvents have been tested for the Ni(acac)$_2$ catalysed reaction. In this perspective we undertook an investigation on the metal catalysed Michael addition in ionic liquids. Ni(acac)$_2$, Yb(TfO)$_3$ and FeCl$_3$·6H$_2$O have been studied in 1-*n*-butyl-3-methylimidazolium tetrafluoroborate [bmim][BF$_4$], focusing on the addition of acetylacetone (Hacac) to methylvinylketone (mvk) as a model reaction (Scheme 1). Given that Ni(acac)$_2$ is a typical catalyst for the title reaction,[8] preliminary tests were devoted to exploring the catalytic activity of Ni(acac)$_2$ in [bmim][BF$_4$]. The results, reported in Table 1, have been compared with those obtained using dioxane as solvent or carring out the reaction without solvent.†



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Scheme 1

In all reactions reported in Table 1, the selectivity towards the Michael adduct 3-acetyl-2,6-heptanedione (**1**, Scheme 1) was higher than 98%. In agreement with literature data[8] by carrying out the reaction in dioxane at 85 °C (entry 1), a 31% isolated yield in **1** was obtained after 5 h. When [bmim][BF$_4$] was used as solvent at 85 °C, a 94% yield in **1** was obtained after 5 h (entry 2). By performing the reaction in solvent-free conditions (entry 3) the yield was 88%. At 25 °C and 96 h reaction, a 73% yield in **1** was obtained when the reaction was carried out in [bmim][BF$_4$] (entry 4), and only a 21% yield in **1** was obtained when the reaction was carried out in solvent-free conditions (entry 5). These data point out an accelerating effect of the ionic solvent.

Next the recyclability of the catalytic system in IL was studied. The results are reported in Fig. 1 and reveal that the catalyst is recyclable at least 7 times. After each cycle the product was directly isolated by distillation under reduced pressure.

Also the catalyst recovered after reactions carried out in solvent free conditions at 85 °C gave a comparable catalytic activity when repeatedly recycled. However, a drop in selectivity towards **1** observed after the second recycle seems to point out a slow decomposition of the active Ni(II) species.

Table 1 Ni(acac)$_2$ catalysed Michael additions[a]

Entry	Solvent	T /°C	Time [h]	Isolated yield in **1** [%]
1	Dioxane	85	5	31
2	[bmim][BF$_4$]	85	5	94
3	None	85	5	88
4	[bmim][BF$_4$]	25	96	73
5	None	25	96	21

[a] Reaction conditions: Ni(acac)$_2$: 0.025 mmol; Hacac/Ni(acac)$_2$ = 100 mol/mol; mvk/Hacac = 1.2 mol/mol; solvent mass: 2.0 g.

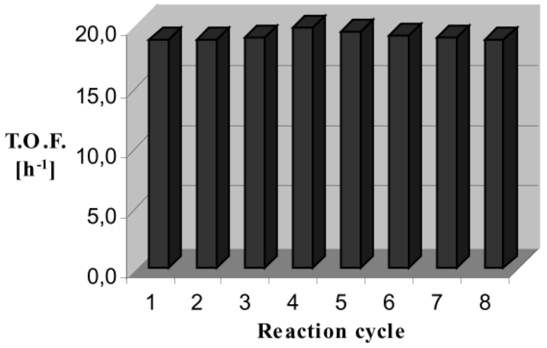

Fig. 1 Recyclability of the catalytic system in [bmim][BF$_4$]. Conditions: T = 85 °C; Ni(acac)$_2$: 0.025 mmol; Hacac/Ni(acac)$_2$ = 100 mol/mol; mvk/Hacac = 1.2 mol/mol; solvent mass: 2.0 g, time = 5h; selectivity towards **1** > 98%.

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$FeCl_3\cdot 6H_2O$[12] and $Yb(TfO)_3$[10] have been recently proposed as appealing catalysts for the Michael addition, since they are active at room temperature. Therefore, we deemed it worthwhile to test their catalytic activity in $[bmim][BF_4]$ for the title reaction.

Interestingly, $FeCl_3\cdot 6H_2O$ was much more active in solvent-free conditions than in IL (comparison of entries 1 and 2), contrary to what is observed for $Ni(acac)_2$. However considerably higher amounts of side-products were observed in solvent-free conditions: at a 94% substrate conversion the selectivity in **1** was only 60%, slightly lower than that reported by Christoffers.[13]

A similar behaviour was found using $Yb(TfO)_3$: while in $[bmim][BF_4]$ the conversion after 24 h was 24% (entry 3), a 95% conversion was obtained in the absence of solvent (entry 4). Also in this case the selectivity in **1** was poor (64%). The ytterbium catalyst is more active than the $FeCl_3\cdot 6H_2O$ based system and this was also confirmed at a higher temperature (85 °C): by fixing the reaction time at 5 h, $Yb(TfO)_3$ gave a 32% yield in **1**, to compare with a 13% yield obtained with $FeCl_3\cdot 6H_2O$ (entries 5 and 6).

Among the catalysts tested in $[bmim][BF_4]$, $Ni(acac)_2$ appears to be outstanding in terms of activity, makes up a recyclable catalytic system and affords very high selectivity in **1**. On the contrary, both catalytic systems based on ytterbium and iron are less active in IL than in solvent-free conditions. In the case of ytterbium, a strong solvent dependence of catalytic activity has already been pointed out,[10] and therefore the peculiar polarity of ionic liquid very likely depresses the dissociation of the salt and the subsequent catalytic steps. The much lower activity of $FeCl_3\cdot 6H_2O$ in IL is currently under study, as well as the activity and recyclability of the catalytic systems based on $Ni(acac)_2$ and $Yb(TfO)_3$ in different ionic liquids and, towards the Michael addition of other donors to several classes of acceptors.

Table 2 $FeCl_3\cdot 6H_2O$ and $Yb(TfO)_3$ catalysed Michael additions[a]

Entry	Catalyst	Solvent	T /°C	Time [h]	Conv. [%]	Yield[b] in **1** [%]
1	$FeCl_3\cdot 6H_2O$	$[bmim][BF_4]$	25	24	2	2
2	$FeCl_3\cdot 6H_2O$	None	25	18	94	56
3	$Yb(TfO)_3$	$[bmim][BF_4]$	25	24	24	24
4	$Yb(TfO)_3$	None	25	18	95	61
5	$FeCl_3\cdot 6H_2O$	$[bmim][BF_4]$	85	5	13	13
6	$Yb(TfO)_3$	$[bmim][BF_4]$	85	5	32	32

[a] Reaction conditions: catalyst 0.025 mmol; Hacac/catalyst = 100 mol/mol; mvk/Hacac = 1.2 mol/mol; solvent mass: 2.0 g. [b] Determined by GLC using acetophenone as internal standard.

Notes and references

† The ionic liquid $[bmim][BF_4]$ was prepared according to literature.[14] For the reactions carried out with nickel, $Ni(acac)_2\cdot 2H_2O$ (Strem Chemicals) was used. A typical Michael addition was carried out as follows: in a 10 ml Schlenk tube, 0.025 mmol of catalyst are dissolved in 2.0 g of $[bmim][BF_4]$, in which the metal complex is readily soluble by raising the temperature to about 35°C. To this solution 250.0 mg of Hacac (2.5 mmol) and 210.0 mg of methyl vinyl ketone (3.0 mmol) are added. The Schlenk is then kept under vigorous stirring and heated to the desired temperature (oil bath). In order to monitor the reaction course, at fixed times, 20 μL of the reaction mixture is withdrawn from the system, the organic phase extracted from the ionic liquid with diethyl ether and the conversion assessed by GLC. After the desired reaction time, the reaction is stopped, the excess of methyl vinyl ketone and acetylacetone removed *in vacuo* at rt. The adduct **1** is distilled at 100 °C under reduced pressure and weighed. The recycles were set up by adding fresh acetylacetone and methyl vinyl ketone to the catalyst solution after distillation. The reported turn over frequencies (T.O.F.) were calculated as (moles of **1**) per [(moles of catalyst)·(reaction time in hours)].

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