



Aerobic oxidation of alcohols with ruthenium catalysts in ionic liquids

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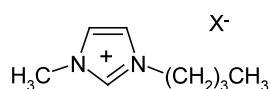
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Abstract—The aerobic oxidations of aliphatic and aromatic alcohols into the corresponding aldehydes and ketones have been efficiently performed with several ruthenium catalysts in various ammonium salts under low oxygen pressure and without any co-catalyst. © 2002 Elsevier Science Ltd. All rights reserved.

Whereas the oxidation of primary and secondary alcohols into the corresponding aldehydes and ketones is a fundamental reaction in organic synthesis,¹ still many oxidation processes use non-environmentally friendly oxidants. The search for catalytic oxidations with inexpensive green oxidants, such as molecular oxygen or hydrogen peroxide, still plays a key role in the development of industrial processes.² The oxidation of alcohols with ruthenium catalysts using a variety of oxidants^{3–7} or molecular oxygen^{6,8} has been investigated previously. While activated allylic or benzylic alcohols have been successfully oxidized with oxygen, few aerobic oxida-

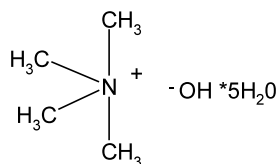
tions of non-activated aliphatic alcohols are known and all of them require co-catalysts or other additives.^{5–11} Though tetrapropylammonium perruthenate (TPAP) in conjunction with *N*-methylmorpholine-*N*-oxide or molecular oxygen as a co-oxidant resulted in high product yields, rather high catalyst loadings (usually 10%) were used and deactivation of the catalyst was always observed.

In the past decade, ionic liquids (ILs) have been extensively tested as environmentally friendly solvents for a large variety of reactions.^{12–14} Besides their low vapor

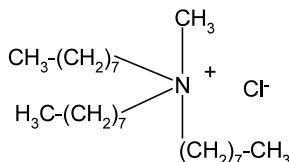


1-Butyl-3-methyl-imidazolium=**bimim**⁺

X= (a): PF₆, (b): BF₄ (c): Cl



Tetramethylammonium hydroxide pentahydrate (**d**)



Aliquat^(R) 336 (**e**)

Figure 1. Commercially available ILs.

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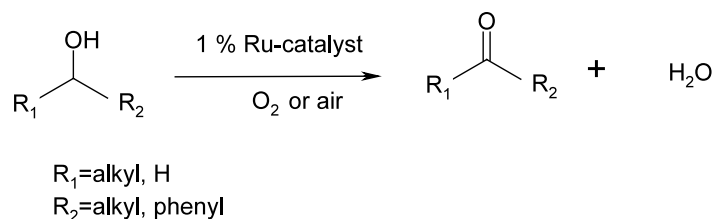


Figure 2. Aerobic oxidation of alcohols.

pressure and good thermal stability, their high polarity makes them even more attractive as solvents for catalytic reactions with transition metal complexes (TMCs). Since the miscibility of ILs with different organic solvents is tunable, it is possible to perform catalytic reactions in monophasic IL^{15,16} or (IL/solvent)-biphasic systems,¹⁷ followed by recycling of the complex and isolation of the product. Although many organic cations can be used, such as ammonium, sulfonium, phosphonium, and pyridinium, room temperature ILs (RTILs) based on *N,N'*-dialkylimidazolium cations coupled with anions such as tetrafluoroborate and hexafluorophosphate are the most commonly used (Fig. 1a and b, respectively).

Many hydrogenation, hydroformylation, dimerization and C–C coupling reactions have been successfully performed in ILs, but only few oxidation reactions in ILs have been reported.^{18–22} The catalytic aerobic oxidation of aromatic aldehydes to the corresponding carboxylic acids with Ni(acac)₂ in IL was the first example of an aerobic oxidation in IL.¹⁸ More recently, the aerobic oxidation of aromatic and aliphatic alcohols with TPAP/CuCl²⁰ and CuCl/TEMPO²¹ in RTILs was published. Rather high amounts of catalyst (5–10%) and the need for additives make these reactions less attractive. Ley et al.¹⁹ added ILs to the homogeneous oxidation of alcohols in dichloromethane with TPAP as catalyst and *N*-methylmorpholine-*N*-oxide as co-oxidant. The addition of large amounts of ether after reaction allowed the precipitation of the ILs and the recovery of the catalyst, which was re-used with partial loss of activity. However, the aerobic catalytic oxidation of 1-phenylethanol in such systems required high oxygen pressure (30–40 bar) and long reaction times. Some other examples of epoxidation with Jacobsen's catalyst²² and methyltrioxorhenium²³ have also been demonstrated in RTILs.

We now report the aerobic oxidation of aliphatic and aromatic alcohols (Fig. 2) with different recyclable ruthenium catalysts (Fig. 3) in various commercially available ILs (Fig. 1) without any co-catalyst or additive. Besides separation of the product and recycling of the catalyst, the use of ILs as solvents for catalytic aerobic oxidation allows replacement of the hazardous organic solvents with ILs, enabling work to proceed at a wider range of temperatures and oxygen pressures.

The aerobic oxidation of 1-phenylethanol with several ruthenium complexes was chosen as a representative oxidation reaction to study the scope and limitations of

the new catalytic system (Table 1). The two most commonly used RTILs (Fig. 1a and b) were first tested (entries 1–2).²⁴ Unfortunately, no reaction took place even after 24 h. The low solubility of oxygen in these ILs²⁵ might be the explanation.

The aerobic oxidation of various alcohols with RuCl₂(PPh₃)₃ combined with TEMPO has been reported to be very efficient.^{10,11} Although the reaction can proceed without TEMPO, it was found that TEMPO tremendously increased reaction activities and selectivities. It was proposed that the active complex is the ruthenium-dihydride, similar to the active species in ruthenium-catalyzed transfer hydrogenation and racemization of chiral alcohols.^{26,27} The active catalyst can be formed by the dissociation of the chloro ligand in the presence of base²³ or TEMPO^{10,11} and the coordination of the formed alkoxide, followed by β-hydride elimination. In the oxidation of alcohols, the TEMPO co-catalyst also assists in the hydride transfer from the active complex to molecular oxygen which allows the initiation of a new catalytic cycle.¹¹ We suspected that the high concentration of the RTIL anion might prevent the dissociation of the chloro ligand or even replace it, and thus prevent reaction. On the other hand, the imidazolium cation can also coordinate to the complex via the protonation of its acidic C(2) proton²⁸ resulting in a 18e⁻ ruthenium complex which is completely unreactive towards oxidation.¹¹ To clarify the role of the cation and anion of the IL on reactivity, the reaction was performed in other ILs (Table 1 and Fig. 1). When the PF₆⁻ and BF₄⁻ anions were replaced by chloride, the moderate reactivities (entry 3) proved that the PF₆⁻ and BF₄⁻ anions indeed prevent the reaction. Moreover, performing the reaction in Aliquat[®] 336 (tricaprylylmethylammonium chloride, Fig. 1d) as an alternative

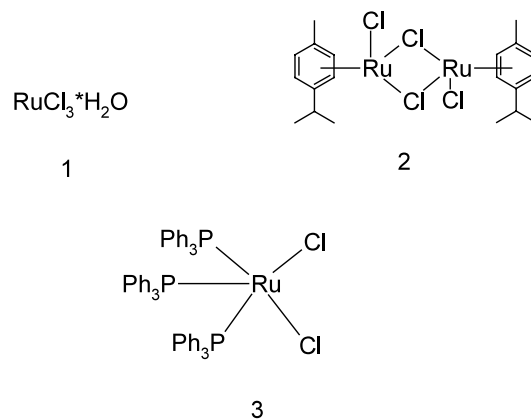


Figure 3. Ruthenium catalysts for oxidation.

Table 1. Aerobic oxidation of 1-phenylethanol into acetophenone with several ruthenium catalysts in different ILs^a

Entry	Catalyst	IL	% Conversion		
			RuCl ₃	Ru-Cy	RuCl ₂ (PPh ₃) ₃
1		BmimPF ₆	0	0	0 ^b
2		BmimBF ₄	0	0	0 ^b
3		BmimCl	17	20	15
4		Aliquat	–	–	99
5		BmimPF ₆ +KOH ^c	–	–	4
6		BmimCl+KOH ^c	–	–	30
7		Tetramethyl ammonium hydroxide	63	65	95
8		BmimCl+water ^d	–	–	2

^a 80°C, 1.5 g IL, 0.32 mmol 1-phenyl ethanol, 1 mol% ruthenium catalyst, 1 atm O₂, 5 h.

^b 24 h.

^c 200 mg KOH.

^d 400 mg water.

Table 2. The oxidation of various alcohols into the corresponding aldehydes and ketones with Ru(PPh₃)₃Cl₂ in two different ILs^a

Entry	Substrate	Tetramethyl ammonium hydroxide		Aliquat	
		Time (h)	% Conversion	Time (h)	% Conversion
1	1-Phenylethanol	5	95	5	99
2	Benzyl alcohol	5	91	5	58
3	3-Methyl-1-butanol	5	3	5	9
4	Cycloheptanol	5	30	5	46
5	Cycloheptanol	11	61	11	92
6	2-Octanol	5	11	5	22
7	2-Octanol	25	43	25	81

^a 80°C, 1.5 g IL, 0.32 mmol alcohol, 1 mol% Ru(PPh₃)₃Cl₂, 1 atm O₂, 5 h.

RTIL with a chloride anion, resulted in a very high activity (entry 4) thus confirming the effect of the cation on reaction activity. Using Aliquat requires isolation of the product by distillation²¹ since this IL dissolves in most organic solvents to a high extent. Water can be used as extracting solvent, but it forms an emulsion with this particular IL.

Since the addition of strong base is essential to obtain transfer hydrogenation or racemization activity with different ruthenium catalysts,^{25,27} KOH was added to both bmimPF₆ and bmimCl (entries 5, 6). As previously explained, the base assists in the dissociation of the chloro ligand and coordination of the alcohol. Although the solubility of the base in the IL is not high, part of the RTIL bmimPF₆ solidified, probably due to anion exchange between the PF₆ and the hydroxide. Indeed, some reaction took place in bmimPF₆ with addition of KOH and the activity in bmimCl was clearly higher than without the addition of base. Addition of base might favor the necessary deprotonation of the hydroxyl group of the substrate and dissociation of the chloro ligand.

Alternatively, different tetraalkylammonium hydroxides with melting point around room temperature were used (Fig. 1e). This type of IL is cheaper than the more common imidazolium ILs but could also have other

advantages. The solubility of aliphatic alcohols in bmimPF₆ and bmimBF₄ is very low while the solubility of ketones is high. This implies that the reaction may be controlled by mass transfer limitations, while the extraction of the product would need an excess of extraction solvent. Indeed, using tetramethylammonium hydroxide as a representative IL of this class resulted in a high activity in the presence of the three kinds of ruthenium catalysts, even with ruthenium(III) chloride (entry 7). The high activity observed with the RuCl₂(PPh₃)₃ complex was only slightly lower than the activity of the same complex in Aliquat. Whereas this difference might be explained by the different anion, the presence of a high amount of water in the tetraalkylammonium hydroxide can decrease the activity. Addition of some water to bmimCl decreased the activity (entry 8). Performing the reaction with atmospheric air instead of oxygen yielded lower conversions.

Re-use of the catalyst was done with 10% decrease in activity for the tetramethylammonium hydroxide/RuCl₂(PPh₃)₃ system (entry 7) after full extraction of the product at 80°C with three times 5 mL *n*-octane.

In order to expand the scope of the new catalytic system for aerobic alcohol oxidation, the oxidation of some primary and secondary aliphatic alcohols with both tetramethylammonium hydroxide and aliquat as

ILs with $\text{RuCl}_2(\text{PPh}_3)_3$ complex was also tested (Table 2). Though expectedly¹⁰ the reactivity of aliphatic alcohols was lower than that of aromatic alcohols, the reaction was performed successfully without any over-oxidation of the formed aldehyde to the corresponding acid. It is clear that the reaction in Aliquat is faster than in tetramethylammonium hydroxide, except for the oxidation of benzyl alcohol. The difference in activity between the two ILs is more pronounced in the oxidation of aliphatic alcohols.

The aerobic oxidation of several aliphatic and aromatic alcohols into the corresponding aldehydes and ketones with ruthenium catalysts has been successfully demonstrated in commercially available ILs. The reaction is fast and selective under mild conditions and does not require the addition of co-catalyst, while allowing facile isolation of the product and re-use of the complex. The activity in the oxidation of several alcohols in the presently reported catalytic systems is much higher than that of other aerobic oxidations in ILs, even with lower catalyst loading and devoid of any additive. Even when compared with the highly efficient catalytic oxidation of alcohols with the combination of a $\text{RuCl}_2(\text{PPh}_3)_3$ complex and TEMPO, the activity of the new catalytic system is very high.

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- Typical reaction procedure: 0.3 mmol substrate and 3 μmol catalyst were added to a glass vial with 1.5 g IL. The mixture was stirred at 80°C for 5 min and then flushed with oxygen for 2 min. The product was extracted by addition of 3 \times 5 mL *n*-octane and mixing at 80°C for 5 min.
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