Inhibition of Catalytic Activity in Ionic Liquids: Implications for Catalyst Design and the Effect of Cosolvents

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Summary: As a consequence of inherently weak interactions between the chloride anion and the 1-butyl-3-methylimidazolium cation (ca. 15 kJ/mol), chloride dissociation from a transition-metal complex can be thermodynamically disfavored in ionic liquids. Therefore, when chloride dissociation is a crucial step for the formation of the active catalytic species, the activity of the catalyst precursor might be completely inhibited in ionic liquids.

With the aim of improving the efficiency of homogeneous catalytic processes, as well as being environmentally responsible, ionic liquids have become popular solvents in which to conduct catalytic experiments.[1] The ease of product separation and catalyst recycling has allowed many transition-metal-catalyzed reactions, e.g. hydrogenations, to be carried out in ionic liquids.[2] Besides the advantage of recycling, catalytic activity in ionic liquids has sometimes been shown to be superior to that observed in other solvents.[3] However, ionic liquids, made via the classic metathesis route, usually contain halide impurities,[4] which may result in catalyst poisoning and consequently decrease activity.[5] Hence, considerable effort has been focused on the development of new synthetic methods that provide halide-free ionic liquids.[6]

We believe that the strong coordinating nature of the chloride anion in 1-butyl-3-methylimidazolium (bmim) molten salts is related to the low solvation enthalpy of chloride in such ionic liquids. Therefore, in this study, the enthalpy of interaction between chloride and 1-butyl-3-methylimidazolium was estimated by variable-temperature ^{1}H NMR measurements. On the basis of this estimation, it is suggested herein that chloride dissociation from a transition-metal complex might be inhibited in ionic liquids. As an illustration of this phenomenon, the catalytic activity of ruthenium(II) complexes, which require a ligand dissociation step (normally chloride dissociation) to enter the catalytic cycle, were screened in bmim-based ionic liquids.

The existence of a hydrogen bond between the proton H^2 of the imidazolium ring and the chloride, as illustrated in Scheme 1, is the strongest in such cations.[7] The formation of this hydrogen bond was found to be highly influenced by the concentration of the imidazolium chloride and, consequently, provided a substantial change in the ^{1}H NMR chemical shift of H^2, as the concentration was varied (see Supporting Information).[7] Accordingly, the H^2 proton chemical shifts, $\delta(B^+)$ and $\delta(B^+Cl^-)$, of 0.034 and 1.0 *m* solutions of [bmim]Cl in CD_3CN were assumed to correspond to the chemical shifts for the totally dissociated and the fully H bonded ion pair, respectively. The H^2 chemical shift, δ(obsd), of a 0.18 *m* (c_{BCl}) solution of [bmim]Cl in CD_3CN, which involves the two types of imidazolium species in equilibrium (Scheme 1), represents the population-weighted mean of the chemical shifts of each species. Thus, the equilibrium constant *K* for the H-bond dissociation can be determined by measuring the proton H^2 chemical shift for the three solutions of [bmim]Cl and is expressed in eq 1 (for details, see the Supporting Information):

$$K = \frac{c_{BCl}}{D(D+1)} \tag{1}$$

where

$$D = \frac{\delta(\mathrm{obsd}) - \delta(\mathrm{B}^+)}{\delta(\mathrm{B}^+\mathrm{Cl}^-) - \delta(\mathrm{obsd})}$$

Variable-temperature ^{1}H NMR measurements enabled the determination of the reaction parameters,

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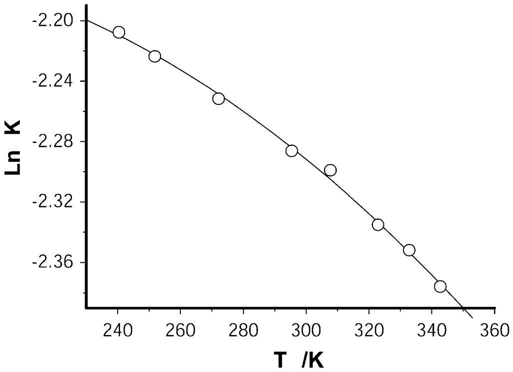

Figure 1. Determination of the reaction parameters by a least-squares fitting procedure using the Ives and Pryor equation.

Scheme 1

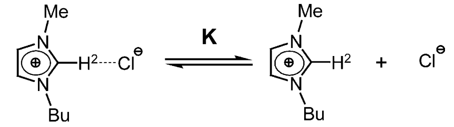

Table 1. Enthalpy and Entropy of the Ionic Dissociation of [bmim]Cl in Acetonitrile and Hydration Enthalpy of the Chloride Anion at 298 K

$\Delta_r H$, kJ/mol	−1.24
$\Delta_r S$, J/mol K	−23.2
$\Delta_r H_T$, kJ/mol	15.4
$-\Delta H_{Cl^-}(H_2O)$,[a] kJ/mol	54.8, 62.4

[a] From ref 13.

which provided information about the strength of the interaction between the imidazolium cation and the chloride counteranion (H^2 chemical shifts at different temperatures are given in the Supporting Information). In a recent article, the thermodynamics of the ion-pair association for a related imidazolium salt, which displayed two different sets of ^1H NMR signals for the dissociated and the ion-paired species, respectively, was also described using NMR spectroscopy.[8] Herein, the dependence of ln K versus T, shown in Figure 1, was treated using the Ives and Pryor equation,[9] which is based on an assumption about the isobaric reaction heat capacity; i.e. the second differential, $\partial^2 \Delta_r C_p^\infty / \partial T^2$, is a constant.[10] The reaction parameters $\Delta_r H^{298}$ and $\Delta_r S^{298}$ were then determined by a least-squares fit of the data using the quadratic equation (2) as a model (see Supporting Information for the details of the equations).

$$\ln K(T) = \ln K(\theta = 1) + \frac{1}{2R}\left(\frac{\partial \Delta_r C_p}{\partial T}\right)_{\theta=1} T + \frac{1}{12R}\left(\frac{\partial^2 \Delta_r C_p}{\partial T^2}\right)_{\theta=1} T^2 \quad (2)$$

The values of the reaction enthalpy and entropy at 298 K are collected in Table 1. It was surprising to observe negative values for both enthalpy and entropy, but this is due to solvent effects. The integral thermodynamic characteristics, which were fitted with the Ives and Pryor equation, can be divided into two components, namely, a van't Hoff component, $\Delta_r H_T$, which directly describes the bonds involved in the equilibrium, and a dielectric component, $\Delta_r H_\epsilon$, related to the solvent effects.[11,12] The determination of the van't Hoff component, previously reported for various ionic association equilibria in acetonitrile, was performed through the calculation of the dielectric contribution using Ebeling's equation.[12] Accordingly, for the dissociation of [bmim]-Cl in acetonitrile, using a dielectric contribution, $\Delta_r H_\epsilon$, of −16.6 kJ/mol at 298 K, the van't Hoff component, $\Delta_r H_T$, was found to be equal to 15.4 kJ/mol, which is an estimation of the H-bond dissociation enthalpy.

The crystal structure of [bmim]Cl reveals that each chloride interacts with three imidazolium cations through H-bonds involving H^2, providing the smallest H−Cl⁻ distance, and methylene protons from the butyl group adjacent to the ring.[14] At the same time, Rodgers and co-workers published the crystal structure of two polymorphs of [bmim]Cl, in which each ion is in close contact with four and six counterions, respectively.[15] The number of cations surrounding the chloride in solution should not be very different from that in the solid state, as has been demonstrated by neutron diffraction for 1,3-dimethylimidazolium chloride.[16] Therefore, the solvation enthalpy of the chloride anion in a 1-butyl-3-methylimidazlium salt can be considered between 3 and 6 times the negative value of the H-bond dissociation enthalpy determined above: i.e., ΔH_{solv} is between −46.2 and −92.4 kJ/mol. However, the coordination of the chloride to a metal complex, or another molecule, is achieved after partial desolvation of the anion. The energy required for this process can be correlated with the nucleophilicity of the chloride, the removal of a water molecule in the coordination sphere of the chloride requires an energy which is 3.5−4 times higher than for the removal of a bmim cation solvating the chloride (see Table 1). The higher nucleophilicity of the chloride anion in imidazolium-based ionic liquids, compared to water, is thus rationalized. Furthermore, it is reasonable to assume that chloride dissociation from a transition-metal complex will be thermodynamically less favored in such ionic liquids than in water. As a consequence, metal complexes involving chloride dissociation, either for the formation of the active catalyst or in a step in the catalytic cycle, may not be active in imidazolium-based ionic liquids, although they may demonstrate high activity in water.

The *p*-cymene ruthenium(II) complex **1** (Chart 1), which is an active precursor for the hydrogenation of styrene in an aqueous biphase (TOF ca. 1000 h^{-1}),[17] was chosen to illustrate this point. Compound **1** was tested

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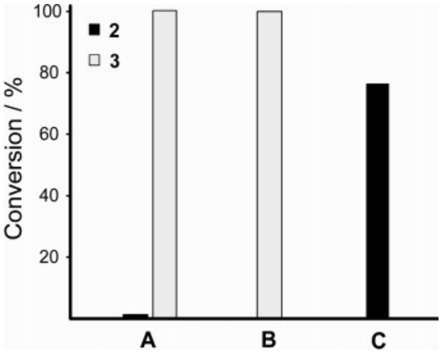
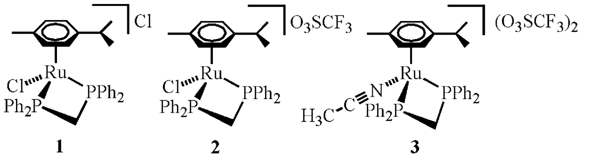


Figure 2. Catalytic activity of **2** and/or **3** for the hydrogenation of styrene in [bmim][O_3SCF_3]: (A) 15 h, **2** vs **3**; (B) 15 h, **3** with addition of mercury; (**C**) 15 h with addition of 50% v/v of water (**2** only). Conditions: 100 °C, $p(H_2)$ = 50 bar, [substrate]/[catalyst] = 2000.

Chart 1. Structure of the Ruthenium(II) η^6-*p*-Cymene dppm Derivatives 1−3



in ionic liquid, and no activity was observed. On the basis of a mechanistic study conducted in water, the formation of the catalytically active species requires the dissociation of the chloride ligand to allow the coordination of dihydrogen.[17] To rationalize the influence of chloride dissociation on the catalytic activity in an imidazolium-based ionic liquid, the triflate salt **2** was prepared, by anion exchange, as well as complex **3**, in which the coordinated chloride has been replaced by the more labile (and neutral) acetonitrile ligand, by abstraction of the chloride with silver triflate (see the Supporting Information). A comparison of **2** and **3** in the hydrogenation of styrene has been conducted in chloride-free [bmim][O_3SCF_3]. As shown in Figure 2A, a considerable difference in activity is observed between **2** and **3**, which can be related to the difference in the thermodynamics of the ligand dissociation step: i.e., chloride dissociation versus acetonitrile dissociation for **2** and **3**, respectively.

In the imidazolium salt medium, the unfavorable chloride dissociation leads to essentially complete inhibition of the catalytic activity of precursor **2**. In fact, electrospray ionization (ESI) mass spectrometry (MS), which has been previously reported to be an efficient technique to observe transition-metal complexes in ionic liquids,[18] confirms that complex **2** remains intact in the ionic liquid phase after the catalytic experiment (Figure 3a). In contrast, after catalysis was performed with **3**, the ESI mass spectrum of the ionic liquid phase shows the presence of the ruthenium(II) species [Ru(η^6-ethylbenzene)(dppm)H]$^+$ (Figure 3b). Similar species, in which arene exchange and substitution of chloride by a hydride has taken place, have been previously observed after hydrogenation of styrene, using [Ru(η^6-arene)(diphosphine)Cl]$^+$ as the precatalyst in water,[17] and combined with the mercury poisoning experiment (Figure 2B), the catalytic reaction is believed to be a homogeneous process.[19]

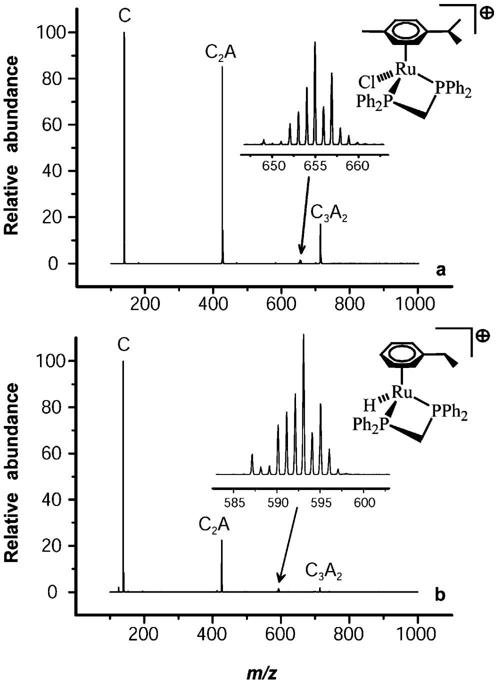


Figure 3. ESI mass spectra of the [bmim][O_3SCF_3] (CA) phase (diluted in methanol) after catalytic reaction with **2** (a) and with **3** (b), recorded in positive ion mode.

Addition of a cosolvent such as water to the ionic liquid reverses the thermodynamics of the chloride dissociation that occurs when **2** is involved in the catalysis, making dissociation feasible. As shown in Figure 2C, when the hydrogenation was carried out in a 1:1 mixture of [bmim][O_3SCF_3] and water (single phase), the activity of **2** was considerably increased. Interestingly, the application of this method (i.e. addition of 50% water) to an ionic liquid such as [bmim][BF_4], which was prepared via the metathesis route and has a maximum residual chloride content of ca. 0.4 mol/kg,[4] also results in a much higher activity of **2**. Moreover, with ionic liquid−water mixtures, the ESI-MS analyses showed that **2** was converted into the hydride [Ru(η^6-ethylbenzene)(dppm)H]$^+$, which was also retained in the ionic liquid−water phase. The extent of hydrolysis of the tetrafluoroborate anion that could occur under these experimental conditions was assessed by ^{19}F and ^{11}B NMR spectroscopy of the ionic liquid−water mixture after the reaction (see Figure S5 in the Supporting Information). The ^{19}F and ^{11}B NMR spectra respectively showed the presence of a fluoroborate species 7.6 and 1.7 ppm downfield of the BF_4^- signals and which represents ca. 0.3% of the BF_4^- signal, based on the integration of the ^{19}F spectrum. To determine whether the acidic conditions provided by the hydrolysis were responsible for chloride abstraction, the hydrogenation reaction was carried out with addition of ca. 1% of $HBF_4 \cdot Et_2O$ in [bmim][BF_4], which resulted in the polymerization of styrene and chloride abstraction from the ruthenium(II) complex was not observed. Similar

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experiments were performed using allylanisole as a substrate in neat [bmim][BF_4], [bmim][BF_4]−HBF_4·Et_2O, and [bmim][BF_4]−water, and hydrogenation into propylanisole (25% after 7 h) and the formation of [Ru(η^6-propylanisole)(dppm)H]$^+$ were only observed under the last set of conditions. The influence of added water on catalysis was also studied with the hydrogenation of benzalacetone into benzylacetone. The higher conversion, provided by the addition of larger amounts of water, may be correlated with the removal of the chloride ligand, which allows coordination of dihydrogen and yields an increased proportion of hydride species in the postreaction mixture (see Figure S6 in the Supporting Information). On the basis of these results, it seems likely that water both assists chloride dissociation and reduces the chloride nucleophilicity by facilitating the solvation of the anion. In contrast, when 2-propanol was used as a cosolvent in [bmim][BF_4], a very low activity was observed with **2** (conversion <3%), while the complex remains unchanged after the experiment, as evidenced by ESI-MS, since the solvation properties of 2-propanol are not sufficient to displace the equilibrium of chloride dissociation in the [bmim]-[BF_4] mixture. In a recent paper, mixtures of ionic liquid and water were also reported to improve the efficiency of a catalytic hydrogenation reaction.[20]

In conclusion, this study has emphasized the problematic dissociation of the chloride anion from a transition-metal complex dissolved in an imidazolium-based ionic liquid, which is thought to be associated with the low solvation enthalpy of chloride in this type of solvent. Furthermore, the inhibition of chloride dissociation has been related to the suppression of activity when such a step is involved in a homogeneous catalytic process taking place in an imidazolium-based ionic liquid. Catalytic reactions that are carried out in ionic liquids, using precatalysts in which chloride dissociation is a prerequisite to form a homogeneous active species, have to be reconsidered with some precautionary aspects that we have elucidated herein. For instance, Noyori type precatalysts for hydrogenation and transfer hydrogenation of ketones are among the complexes that require this type of catalytic step.[21] Thus, two approaches have been proposed, in this study, in an attempt to overcome this problem. The first approach directly concerns the design of the precatalyst, with the substitution of the chloride by another ligand, which is better solvated by the ionic liquid. The second approach consists of adding a cosolvent that might facilitate the solvation of the dissociated chloride, such as water.

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Supporting Information Available: Text, figures, and tables giving experimental details for the synthesis and characterization of **2** and **3**, for the hydrogenation reactions, NMR measurements, and detailed equations for the determination of the thermodynamic characteristics. This material is available free of charge via the Internet at http://pubs.acs.org.

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