Ionic Liquids

Transition-Metal-Catalyzed Reactions Involving Imidazolium Salt/N-Heterocyclic Carbene Couples as Substrates**

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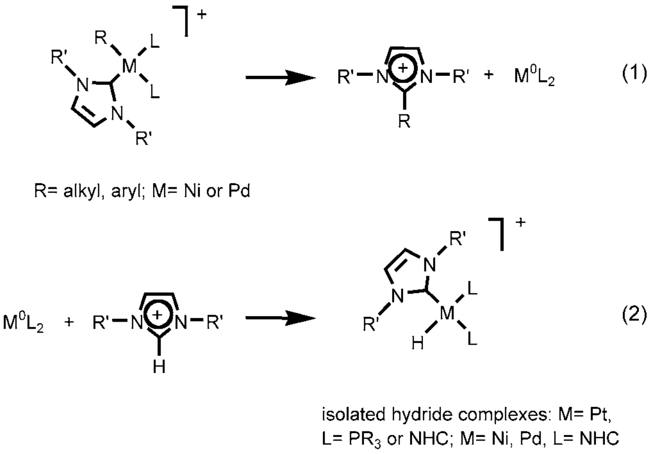
In previous studies we demonstrated that hydrocarbyl–M–carbene complexes (M = Group 10 metal) readily undergo reductive elimination to give M^0 and C2-substituted imidazolium salts (Scheme 1, Equation (1)).[1] As this presents a potential impediment for the use of N-heterocyclic carbene (NHC) complexes in catalysis, we investigated methods for controlling or restricting the reaction. Subsequently, we were able to show that this reductive elimination reaction could be "reversed". Reaction of imidazolium salts with Pt^0 species gave carbene–Pt–hydride complexes,[2] and very recently we reported that the reaction of imidazolium salts (ionic liquids) with low-valent M^0 (M = Pd, Ni) bearing strong σ-donor ligands can be a facile process for the generation of surprisingly stable carbene–M–hydride complexes (Scheme 1, Equation (2)).[3] One notable feature of this study is that direct formation of a carbene-—M–H provides an atom-efficient, in situ route to an active catalytic species. NHCs have found application in a wide range of catalytic reactions (such as the Heck, Kumada, Stille, Suzuki-Miyaura, and Sonogashira coupling reactions, amination reactions, hydrosilylation, olefin metathesis, hydroformylation, polymerization, etc.),[4] and metal hydrides are implicated in a number of these catalytic processes.

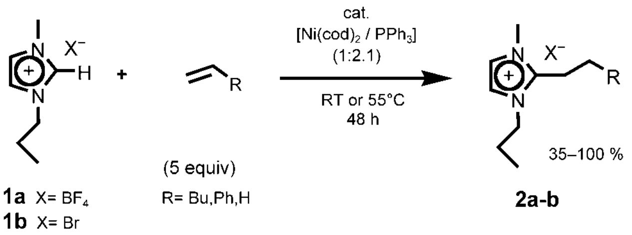


Scheme 1. Redox processes undergone by the carbene/imidazolium couple.

Furthermore, 1,3-dialkyl imidazolium salts have been extensively employed as ionic-liquid solvents, potentially valuable alternatives to non-aqueous solvents for biphasic catalysis.[5] Although commonly considered as inert solvents, a number of reports have suggested their possible participation during catalysis, forming strong σ-donor carbene ligands with the metal center under basic conditions, and the generation of carbene complexes from imidazolium salts has frequently been observed in the presence of base.[6] Our studies demonstrate that basic conditions are unnecessary and that imidazolium-based ionic liquids can react with low-valent metal complexes of Group 10 through C2–H oxidative addition.[2,3]

Herein we report on the continuation of our studies in which the unusual chemical reactivity of imidazolium salts/NHC couples with transition metals is examined, and the potential applications of this chemistry are explored. We describe a C–C coupling reaction in which imidazolium salts act as substrates in a novel catalytic reaction that proceeds through a redox process involving a carbene intermediate. Combining the two "half-reactions" described in Equations (1) and (2) (Scheme 1) in the presence of an alkene establishes a unique catalytic process.

On stirring a solution of imidazolium salts **1a**,**b** in acetone/thf with various alkenes in the presence of a Ni^0 catalyst, the salts are progressively converted into the C2-alkylated products **2a**,**b** (Scheme 2; Table 1).



Scheme 2. Imidazolium C–H/alkene coupling reaction.

Compounds **2a**,**b** were isolated and characterized by NMR spectroscopy. The imidazolium C–H/alkene coupling reaction occurs under very mild conditions in the presence of the commonly employed $Ni(cod)_2/PPh_3$ (cod = 1,5-cyclooctadiene) catalyst system. The addition of 2 equivalents of PPh_3 is essential for the effective catalytic performance of the system. Use of $Ni(cod)_2$ on its own quickly leads to decomposition of the catalyst, resulting in poor reaction yields (Table 1, entry 1). Increasing or decreasing the PPh_3/Ni ratio gives lower conversions. We found that the addition of 2.1 equivalents of PPh_3/Ni gives the best overall catalytic results. The reactions could also be conducted in the ionic liquid itself, although conversions were considerably lower

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Supporting information for this article (catalytic procedure, separation method and spectroscopic data for compounds **2a**,**b**) is available on the WWW under http://www.angewandte.org or from the author.

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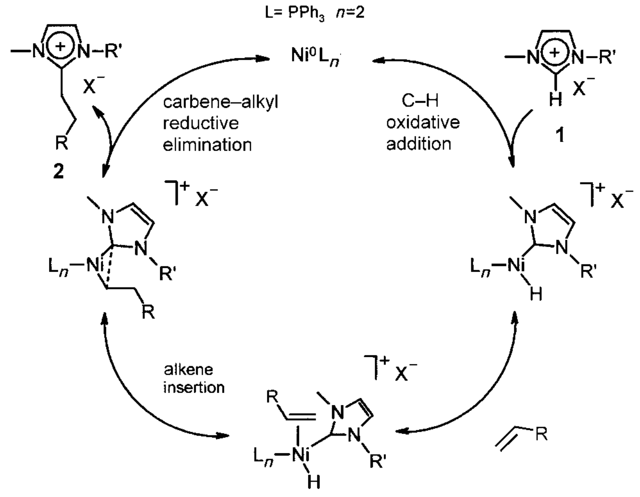
Table 1: Catalytic coupling results.[a]

Entry	Ionic Liquid	Alkene	T [°C]	Yield [%][b]
1	**1a,b**		55, RT	< 15[c]
2	**1a**		55	56
3	**1b**		55	51
4	**1b**		RT	64
5	**1b**		55	39[d]
6	**1a**	 [e]	55	100;[a] 72[f]
7	**1b**	 [e]	55	100;[a] 95[g]
8	**1b**	 [e]	RT	35

[a] Conditions: Catalyst [$Ni(cod)_2/PPh_3$ (1:2.1)] (10 mol%); acetone/THF (3:1); reaction stopped after 48 h. [b] Determined by ^{1}H NMR spectroscopy, average of two runs or more. [c] Catalytic [$Ni(cod)_2$] only. [d] Mixture of linear and branched product (4:1). [e] Pressure: 1 bar. [f] Catalyst (5 mol%). [g] Catalyst (3 mol%).



Scheme 3. Proposed catalytic cycle for imidazolium/alkene coupling reaction.

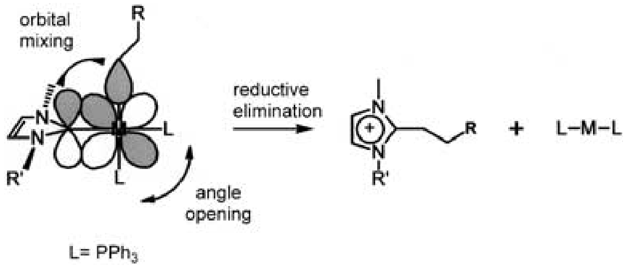


Figure 1. Proposed mechanism for carbene–alkyl reductive elimination.

(yields < 10%). The various 1-alkenes (1-hexene, ethylene) and styrene undergo coupling with the imidazolium salts to varying extents (Table 1).

Not surprisingly, ethylene (1 bar) couples more readily with imidazolium salts than does 1-hexene (Table 1, entries 6,7 and 2,3). This follows the expected reactivity pattern for alkenes (ethylene > propylene > butene ~ higher alkenes). Styrene gives lower conversions than either of the aliphatic alkenes (Table 1, entries 5 and 2–4/6–7); steric elements may be a factor in this observed behavior. Interestingly, styrene uniquely gives rise to linear and branched isomers — the branched isomer has a chiral center linking the imidazolium ring to the benzene ring. Both the tetrafluoroborate **1a** and bromide **1b** salts react with the different alkenes tested, especially with ethylene for which complete or nearly complete conversions were observed (Table 1, entries 6–7). With ionic liquid **1b** at 55 °C, almost complete conversion was observed even with a lower catalyst loading of 3%. (Table 1, entry 7).

Based on previous detailed theoretical and experimental studies on the mechanism of individual reaction steps,[1–3] the following catalytic cycle is proposed (Scheme 3) and described below.

Imidazolium salts **1a**,**b** oxidatively add to low-valent, [$Ni(PPh_3)_n$] generated in situ to form a carbene–Ni–hydrido species. C–H oxidative addition of imidazolium salts has been shown to be facile with low-valent Ni complexes, in particular with coordinatively unsaturated complexes bearing σ-donor ligands.[3] Alkene insertion into the ensuing M–H bond produces an alkyl–Ni intermediate that subsequently undergoes reductive elimination with the carbene ligand to produce 2-alkyl imidazolium salts **2a**,**b** and re-form M^0L_n. Kinetic and density functional studies have shown that reductive elimination from NHC–alkyl complexes proceeds in a concerted fashion.[1] The reductive elimination effectively involves orbital overlap between the carbene carbon p(π) orbital, the alkyl sp^3 orbital, and the metal d orbital, which occurs with concurrent opening of the angle between the two nonparticipating ligands L (Figure 1).

For the alkenes studied, only the monoinsertion product is observed (i.e. for ethylene, only the 2-ethyl product is formed), which suggests that under the conditions employed the rate of carbene–alkyl reductive elimination is faster than the rate of alkene insertion into the Ni–alkyl bond. Consistent with this proposal, in earlier studies with Ni–carbene complexes as catalysts for alkene dimerization, effective catalysis was only observed in ionic liquid solvents.[7] In toluene the predominant reaction was reductive elimination to give imidazolium salts and Ni^0. In studies pertinent to our investigations, Bergman, Ellman, and co-workers have recently used a Rh^I complex to catalyze the conversion of benzimidazoles, thiazoles, and oxazoles into 2-substituted azole rings and also into fused azole-based heterocyclic compounds.[8] Rh–carbene complexes have been isolated from the reaction mixture, indicating that these may be intermediates in the catalytic reaction. On first consideration the reaction appears similar to that reported herein. However, the mechanism proposed by Bergman, Ullman and co-workers consists of an initial H-atom shift on the imidazole substrate to generate a Rh^I-NHC complex. This is then followed by the insertion of the coordinated alkene into the Rh–carbene bond to form a zwitterionic intermediate and generate the C–C bond. An intramolecular proton transfer, C–H reductive elimination, and product displacement complete the catalytic cycle.[8b]

Our study represents the first example in which the imidazolium oxidative addition and carbene reductive elimination processes have been combined into the same catalytic cycle, and the first demonstration that the imidazolium C–H activation step can be used to generate an active catalyst. These results also illustrate the ease with which interconversion between imidazolium salts and NHC–transition-metal complexes occur even under very mild conditions, particularly under conditions where low-valent, unsaturated metal species are generated.

These results have important catalytic implications. First, this reaction represents a unique example of Ni^0-catalyzed C–H activation/C–C bond-formation reactions under mild conditions.[9] Second, the results also provide a catalytic methodology for producing 2-alkyl imidazolium-type salts through a coupling reaction. Third and most importantly, these results have direct ramifications for the use of imidazolium-based ionic liquids as solvents in transition-metal catalysis. It is clear that imidazolium salts can form carbene–hydrido species in the presence of a M^0 source, or when M^0 species are generated in situ during a reaction. Generation of carbene—-M–hydrido species would have a major impact on catalysis reactions in ionic-liquid media. This study, when considered in conjunction with our earlier investigations on imidazolium-based ionic-liquid solvents in catalysis,[7] demonstrates the unique potential for employing ionic liquids concomitantly as solvent and activator, generating long-lived (stabilized) active catalyst sites for a range of catalytic processes.

In conclusion we have demonstrated a new type of Ni^0-catalyzed C–H activation/C–C bond-forming reaction to produce 2-alkyl imidazolium-type salts under mild conditions. These results illustrate the facile redox processes associated with these salts, commonly used as ionic liquids. Of significance is the generation of (carbene)metal-hydride species in situ that may be employed in catalytic processes using the ionic liquid as both solvent and activator. The optimization and extension of the methodology described herein is currently under investigation.

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