

Silica Gel Confined Ionic Liquid + Metal Complexes for Oxygen-Free Carbonylation of Amines and Nitrobenzene to Ureas

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Abstract: A new kind of silica gel confined ionic liquid containing a metal complex as heterogenized catalysts was prepared for the carbonylation of amines and nitrobenzene without molecular oxygen to afford the corresponding ureas with greatly enhanced catalytic activity (TOF exceeded $11000 \text{ mol} \cdot \text{mol}^{-1} \cdot \text{h}^{-1}$), with a much lower amount of ionic liquids being needed, with easy catalyst separation and possible reusability, and avoidance of the using of explosive $\text{CO} + \text{O}_2$ gas mixtures. Such an enhancement in catalytic activity may be derived from the effect of a high concentration of ionic liquid containing a metal complex due to the confinement into the nanopores or cavities of the silica gel matrix.

Keywords: amines; carbonylation; ionic liquids; nitrobenzene; phosgene-free

Since the discovery of the carbon monoxide-induced reduction of nitro groups 30 years ago, there has been a widespread increase of interest in the application of carbon monoxide in the carbonylation of nitrogen-containing compounds because the subject is of great significance both in academia and in the chemical industry.^[1] Needless to say, the syntheses of disubstituted ureas with carbon monoxide was one of the most important aspects due to their extensive applications such as agricultural chemicals, resin precursors, dyes, polymers, drug candidates including HIV protease inhibitors, FKBP12 inhibitors, CCK-B receptor antagonists and endothelin antagonists etc.^[2] Furthermore, they could be intermediates for the phosgene-free synthesis of isocyanates.^[2] In previous studies, various of catalysts including Ru,^[3] Rh,^[4] Co,^[5] Mn,^[6] Se,^[7] Au,^[8] W^[9] and most commonly and especially reported recently by Gabriele et al., Pd,^[10] have been examined for the syntheses of ureas through oxidative carbonylation of amines with good to excellent catalytic performance. However, the explosive $\text{CO} + \text{O}_2$ gas mixture has been inevitably used for

such oxidative carbonylation processes, which may be dangerous during its application in industry. In the light of a catalytic reaction process under environmental and economic impacts, the synthesis of disubstituted ureas by “oxidative” carbonylation without using dioxygen has also been paid more and more attention. Although many catalysts have been developed for this process in recent years,^[11] the catalytic efficiency was still very low and separation of catalysts from the products has not yet been solved successfully. Therefore, the development of a highly efficient, easily separable catalyst system for the syntheses of disubstituted symmetrical or unsymmetrical ureas, especially those in which aromatic groups are contained, for an oxidative carbonylation process without molecular oxygen, was highly desired.

Room temperature ionic liquids or molten salts, especially those derived from the combination of quaternary ammonium salts and weakly coordinating anions, have been demonstrated to be ideal immobilizing agents for various “classical” transition-metal catalyst precursors with excellent catalytic performance or easy product separation for many reactions.^[12] More recently, it was exemplified that the carbonylation of aniline for the synthesis of the corresponding carbamates could proceed in ionic liquids with much higher efficiency than in traditional organic solvents using selenium or a palladium complex as catalyst.^[13] However, large amounts of ionic liquid would be used for this homogeneous catalytic process and the ionic liquids, so far, are still so expensive that they cannot be used and consumed as ordinary organic solvents. At the same time, a heterogeneous catalytic process, due to the ease of separation and the possibility to be used in a fixed-bed reactor, would be more preferred in the chemical industry. Therefore, the immobilization of an ionic liquid should be an ideal method to minimize the amount of utilized ionic liquid and facilitate product separation. A typical process for the support or immobilization of ionic liquid catalysts was reported recently,^[14] in which the ionic liquid fragment such as the dialkylimidazolium cation was covalently bonded to the silica surface. Chemical bonding of the dialkylimidazolium cation to a solid surface, how-

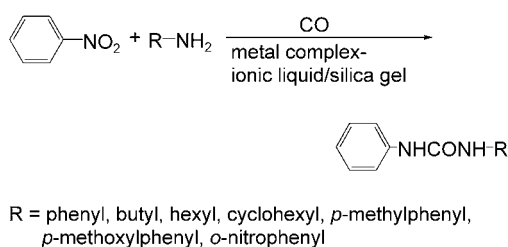
ever, may limit the free degree of dialkylimidazolium cation and even change the physicochemical properties of the ionic liquids. Another method for immobilization of ionic liquids was by dipping the porous support in an ionic liquid containing the metal complex.^[15] Due to such a physical deposition, leaching of the ionic liquid and catalyst was unavoidable if used under rigorous reaction conditions.

In this work, we report a new concept for synthesizing silica gel-immobilized ionic liquids containing a metal complex as heterogenized catalysts for the carbonylation of amines and nitrobenzene to afford ureas with unexpectedly high catalytic activity.

The key innovation of such a catalyst involves the physical confinement of a dialkylimidazolium ionic liquid containing a metal complex into the pores or cavities of silica gel through one-pot assembly of the ionic liquid, the metal complex and the silica gel by a modified traditional sol-gel process. This process is different from the so-called “ship in a bottle” method,^[16] because it uses ready-made “ships” and then tailor-making of a “bottle” (Figure 1).

Two ionic liquids, DMImBF₄ (1-decyl-3-methylimidazolium tetrafluoroborate, relatively larger in size) and EMImBF₄ (1-ethyl-3-methylimidazolium tetrafluoroborate), and four metal complexes, including HRu(PPh₃)₂Cl₂, Rh(PPh₃)₃Cl, Pd(PPh₃)₂Cl₂ and Co(PPh₃)₃Cl₂, were employed. A series of silica gel-confined ionic liquid-metal complexes were prepared (denoted as M-ionic liquid/silica gel) and dry, solid and porous samples were obtained (Figure 2).

Firstly, the synthesis of symmetrical diphenylureas from nitrobenzene and aniline over these catalysts were tested, see Table 1. The carbonylations of aniline and nitrobenzene proceeded efficiently, and the best result was obtained over the catalyst Rh-DMImBF₄/silica gel with a conversion of 93% and a selectivity of 92%



Scheme 1.

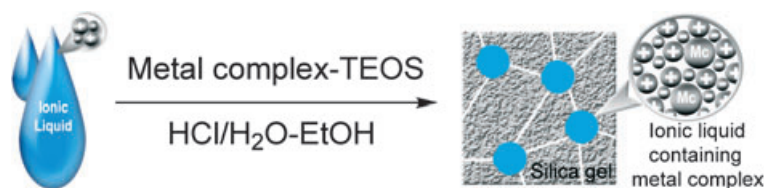


Figure 1. One-pot assembly of silica gel confined ionic liquid-metal complexes with a modified sol-gel process.

(entries 1–4). The corresponding TOF exceeded 11000 mol·mol⁻¹·h⁻¹, which should be unprecedented in comparison with previous homogeneous ionic liquid carbonylation systems.^[13b] It could be conjectured that better conversion would be achieved if, for example, the amount of nitrobenzene added was stoichiometrically in excess of that of aniline. After the reaction, the desired dry and crystallized product mixed with the cata-

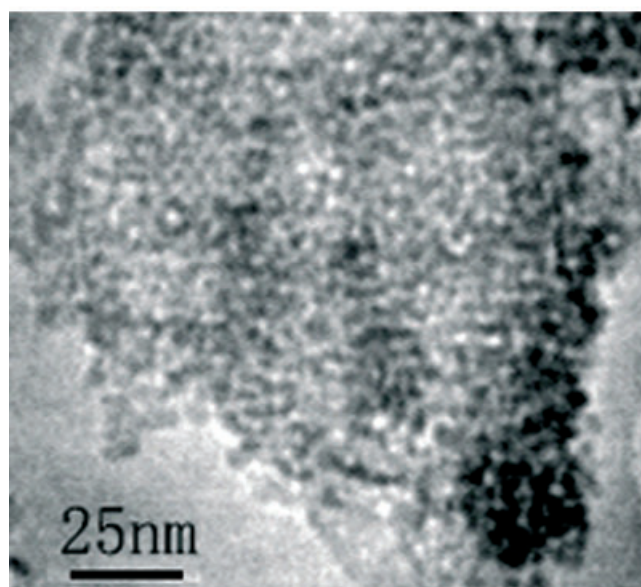
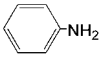
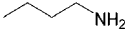
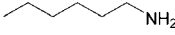
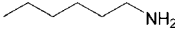
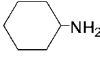
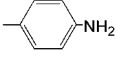
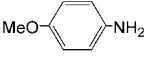
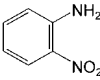


Figure 2. Picture of the prepared solid sample (Rh-DMImBF₄/silica gel (top) and HRTEM (JEOL JEM 2010) picture of the sample (bottom).

Table 1. Results of the synthesis of disubstituted ureas from nitrobenzene and amines.

Entry	Amine	Catalyst	Conversion [%]		Selectivity [%]	TOF ^[a]
			NB	AM		
1		Co-DMImBF ₄ /silica gel	19	18	> 98	2140
2		Ru-DMImBF ₄ /silica gel	37	39	> 98	1760
3		Rh-DMImBF ₄ /silica gel	93	92	> 98	11548
4		Pd-DMImBF ₄ /silica gel	81	79	> 98	7440
5		Rh-EMImBF ₄ /silica gel	85	84	> 98	10550
6 ^[b]		Rh-DMImBF ₄ /silica gel	83	81	> 98	10800
7 ^[b]		Rh-EMImBF ₄ /silica gel	16	16	> 98	9987
8 ^[c]		Rh(PPh ₃) ₃ Cl	8	9	> 95	1586
9 ^[d]		silica gel + DMImBF ₄	–	–	–	–
10 ^[e]		silica gel + DMImBF ₄ + Rh(PPh ₃) ₃ Cl	41	39	> 98	7463
11		Rh-DMImBF ₄ /silica gel	86	94	> 94	11818
12		Rh-DMImBF ₄ /silica gel	85	97	> 96	11943
13		Rh-DMImBF ₄ /silica gel	87	93	> 92	11818
14		Rh-DMImBF ₄ /silica gel	78	81	> 98	9890
15		Rh-DMImBF ₄ /silica gel	88	87	> 98	10884
16		Rh-DMImBF ₄ /silica gel	–	–	–	–

^[a] TOF = mol substrates converted per mol metal complexes per hour.

^[b] The catalyst system had been recovered and reused for the second time.

^[c] 1 mg of Rh(PPh₃)₃Cl was used.

^[d] 0.1 g of silica gel and 0.2 g of DMImBF₄ were used.

^[e] 1 mg of Rh(PPh₃)₃Cl, 0.1 g of silica gel and 0.2 g of DMImBF₄ were used.

lyst was obtained, and the supported catalyst could be separated from the product after methanol had been added to the resultant solid mixture (catalyst deposits on the bottom of the reactor). An 81% aniline conversion and > 98% selectivity were maintained when Rh-DMImBF₄/silica gel was reused for the second time, entry 5. Over Rh-EMImBF₄/silica gel, a slightly lower activity was observed and the catalytic activity was greatly reduced when it was reused for the second time, entries 6 and 7. Analyses of rhodium contents in Rh-DMImBF₄/silica gel and Rh-EMImBF₄/silica gel before and after reaction were 0.11 wt %, 0.13 wt % and 0.09 wt %, 0.10 wt %. DRIFTS (diffuse reflectance infrared Fourier transform spectroscopy, Nexus 870) characterization of the bulk ionic liquids and silica gel-confined ionic liquid catalysts indicated that the characteristic peak of EMImBF₄ (1580 cm⁻¹) almost disappeared while the

similar peak of DMImBF₄ (1581 cm⁻¹) could be observed clearly even without any weakening after the catalysts were reused (Figure 3).^[17] New peaks for the diphenylurea, 1701 cm⁻¹ and 1699 cm⁻¹, were also observed in the spectra of used catalysts (Figures 3c and f). These results suggested that the deactivation of Rh-EMImBF₄/silica gel was mainly attributable to EMImBF₄ leaching from silica gel, probably due to its relatively smaller molecular in size, while DMImBF₄ could be confined into the pores of silica gel in a relatively more stable manner due to its larger molecular size.

In order to understand the contribution of each metal complex, ionic liquid and silica gel to the reaction, the metal complex only or physical mixtures of the ionic liquid + pure silica gel, and metal complex + ionic liquid + silica gel were also examined and showed poor catalytic performance, entries 8–10, and even more metal com-

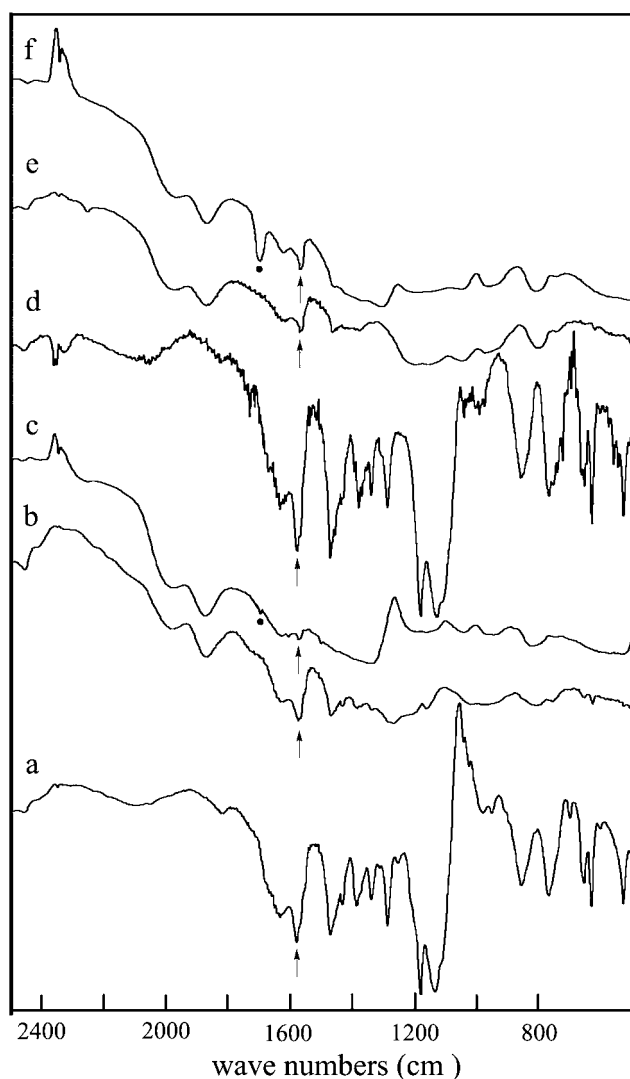


Figure 3. DRIFTS spectra of (a) pure bulk EMImBF₄, (b) Rh-EMImBF₄/silica gel, (c) Rh-EMImBF₄/silica gel after reacting for one time, (d) pure bulk DMImBF₄, (e) Rh-DMImBF₄/silica gel, and (f) Rh-DMImBF₄/silica gel after use.

plex or ionic liquid were charged in comparison with that present in the silica gel-confined ionic liquid containing metal complex catalyst. This means that a major

enhancement in catalytic activity was exhibited when the ionic liquid containing the metal complex was physically confined into the pores or cavities of the silica gel matrix, and such an enhancement in catalytic activity may be derived from the effect of the high concentration of ionic liquid containing the metal complex due to this confinement (Figure 4a), and such an effect would disappear when the bulk ionic liquid and metal complexes were completely diluted with large amounts of the reactant molecules, thus resulting in poor catalytic performance (Figure 4b).

Syntheses of asymmetric ureas were also tested when aniline was replaced with *n*-butylamine, *n*-hexylamine and cyclohexylamine, entries 11–13. The corresponding asymmetrical ureas were also formed with high conversion and selectivity, and relatively higher conversions of alkylamines (93–97%) were observed compared with that of nitrobenzene (85–87%). This means that direct carbonylation between alkylamines occurred since some dialkylureas (2–3%) were also detected on GC/MS. Finally, several other aromatic amines, i.e., *p*-methylaniline and *p*-methoxyaniline, were subjected to the reaction, entries 14 and 15, with sufficient high catalytic performance. No reaction occurred on using *o*-nitroaniline as substrate, entry 16, suggesting that the presence of the electron-attracting NO₂ severely weakened the activity of the NH₂.

In summary, a new kind of silica gel-confined ionic liquid containing a metal complex as heterogenized catalysts for the carbonylation of amines and nitrobenzene without molecular oxygen to afford the corresponding ureas has successfully been developed with the following advantages: (1) greatly enhanced catalytic activity with TOF exceeded 11000 mol·mol⁻¹·h⁻¹; (2) much lower amount of ionic liquids needed; (3) easy separation and reusability of catalyst are possible; (4) the use of explosive CO + O₂ gas mixtures is avoided. Such an enhancement in catalytic activity may be attributed to the effect of the high concentration of ionic liquid containing the metal complex due to its confinement in the pores or cavities of the silica gel matrix. The concept of such a catalyst system may be universal, and could be expanded to other catalysis fields.

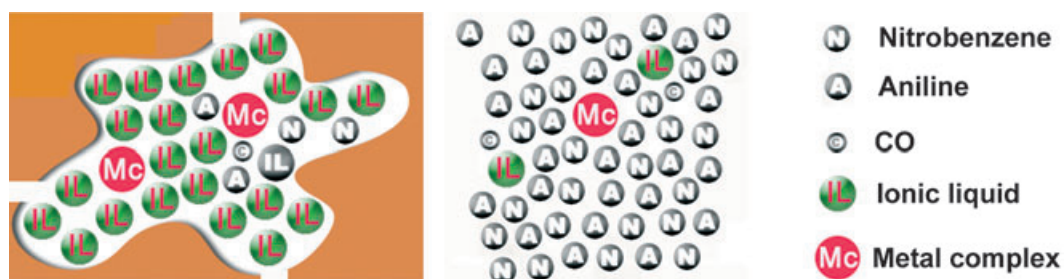


Figure 4. Reaction environment for the carbonylation of aniline and nitrobenzene in immobilized (left) and bulk (middle) ionic liquids.

Experimental Section

Synthesis of Ionic Liquids

The ionic liquids and metal complexes $\text{HRu}(\text{PPh}_3)_2\text{Cl}_2$, $\text{Rh}(\text{PPh}_3)_3\text{Cl}$, $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ and $\text{Co}(\text{PPh}_3)_3\text{Cl}_2$ were synthesized according to procedures reported previously.^[18]

Synthesis of Supported Ionic Liquids Containing Metal Complexes

Ten mL of tetraethyl silicate (TEOS), 1 mL of ionic liquid containing the metal complexes $[\text{HRu}(\text{PPh}_3)_2\text{Cl}_2]$, $[\text{Rh}(\text{PPh}_3)_3\text{Cl}]$, $[\text{Pd}(\text{PPh}_3)_2\text{Cl}_2]$ or $[\text{Co}(\text{PPh}_3)_3\text{Cl}_2]$, 7 mL of ethanol and 5 mL of hydrochloric acid (5 M) were added into a 100-mL of conical flask. After being reacted and aged at 60 °C for 12 hours, the resultant solid mixture was for 3 hours under ca. 1–5 mmHg vacuum at 150 °C and the five catalysts $\text{Ru-DMImBF}_4/\text{silica gel}$, $\text{Rh-DMImBF}_4/\text{silica gel}$, $\text{Pd-DMImBF}_4/\text{silica gel}$, $\text{Co-DMImBF}_4/\text{silica gel}$ and $\text{Rh-EMImBF}_4/\text{silica gel}$ were obtained. The contents of DMImBF_4 ionic liquid were 17–19 wt % in the different catalysts. AES analysis (ARL 3520 ICP) showed that the metal contents of the catalysts $\text{Ru-DMImBF}_4/\text{silica gel}$, $\text{Rh-DMImBF}_4/\text{silica gel}$, $\text{Pd-DMImBF}_4/\text{silica gel}$, $\text{Co-DMImBF}_4/\text{silica gel}$ and $\text{Rh-EMImBF}_4/\text{silica gel}$ were 0.14 wt %, 0.11 wt %, 0.15 wt %, 0.07 wt % and 0.13 wt % which indicated that almost all of the metal complexes were entrapped into the silica gel.

Process for the Synthesis of Ureas

All carbonylation reactions of amines were conducted in a 90-mL autoclave with a glass tube inside equipped with magnetic stirring. In each reaction, 0.1 g of catalysts, 10 mmol of nitrobenzene, 10 mmol of amines and 5.0 MPa of carbon monoxide were charged successively. The reaction proceeded at 180 °C for 1.5 hours, and after the reaction 20 mL of methanol were added to the resulting mixture which was qualitatively analyzed with HP 6890/5973 GC/MS, and quantitatively analyzed with Agilent (Shanghai) 1790 GC (FID detector) by the external standard method.

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