

CO₂ Activation in an Ionic Liquid**Alternatives to Phosgene and Carbon Monoxide:
Synthesis of Symmetric Urea Derivatives with
Carbon Dioxide in Ionic Liquids****

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N-containing compounds such as isocyanates, carbamates, and *N,N'*-disubstituted urea derivatives are important chemicals. For example, the world production of isocyanates exceeded 5 megatons in 2001. Currently, these chemicals are mainly manufactured by the phosgenation of amines. The worldwide production of phosgene ranges from 6–8 megatons per year, which have been used mainly (>85%) for the synthesis of isocyanates and their derivatives. Therefore, as a first step, the use of an alternative to phosgene in the synthesis of isocyanates should be found to help eliminate the use of phosgene altogether.^[1–2]

Many strategies for nonphosgene routes, including reductive carbonylation^[3] and oxidative carbonylation^[4] by using CO as carbonyl source, and the use of Pd,^[5] Ru,^[6] Rh,^[7] Fe,^[8] Ni,^[9] Co,^[10] Mn,^[11] Se,^[12] Au,^[13] and W^[14] catalysts, have been extensively studied. The progress in this field of research, however, is relatively slow. Carbon monoxide is also poisonous and the mixing of CO and O₂ for oxidative carbonylation is potentially explosive. As an alternative, the use of dimethyl carbonate or dimethyl sulfate as phosgene substitutes are relatively expensive for commercial applications.^[15] Therefore, the most desirable option to avoid phosgene is to replace it with CO₂ directly. Besides the abundance of CO₂ and its environmentally benign nature, a process that uses CO₂ has the benefit of recycling carbon from the atmosphere when its use is linked with other processes that emit CO₂. The detrimental influence of CO₂ as a “green house” gas has

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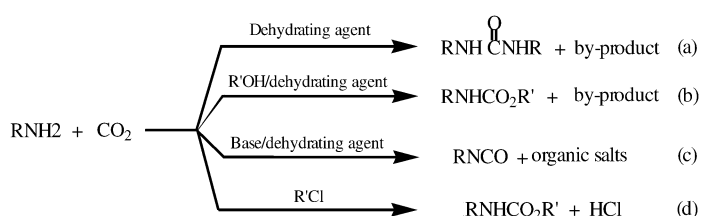
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received more and more attention, so its use as raw material for basic chemical production is an attractive subject. Until now, the studies of carbonylation reactions of nitrogen containing compounds by using CO_2 are relatively few in comparison with those that make use of CO , probably because of the chemical inertness of CO_2 . Nevertheless, only four kinds of carbonylations of N-containing compounds that make use of CO_2 as the carbonyl source have been reported^[16] (Scheme 1).

Although the desired products are obtained in good yields by these routes (ca. 60–90%), large amounts of dehydrating agents, such as PCl_5 , POCl_3 , dicyclohexylcarbodiimide (reactions a, b and c) and/or an appropriate base, such as Et_3N (reaction c), or relatively expensive alkyl chlorides, $\text{R}'\text{Cl}$ (reaction d) are needed. Furthermore, large amounts of by-products, such as Et_3NHCl , Et_3NHPOCl , HCl are inevitably formed. Although CO_2 was used as a carbonyl source as an alternative to phosgene in the synthesis of isocyanate and its derivatives, this route was not only more expensive but also environmentally less friendly.

Recently, room-temperature ionic liquids, a reaction media with very low vapor pressure, peculiar physicochemical properties, and selective solubility towards many organic and inorganic substances, have attracted growing interest. Many catalytic reactions that proceed in ionic liquids were reported, with satisfactory performances in many cases.^[17] The combination of ionic liquids as versatile and novel reaction media with a suitable catalyst, such as acid, base, nanostructures, or metal-complex, may result in a more diverse and flexible “platform” to establish a highly effective and easily separable catalytic system.

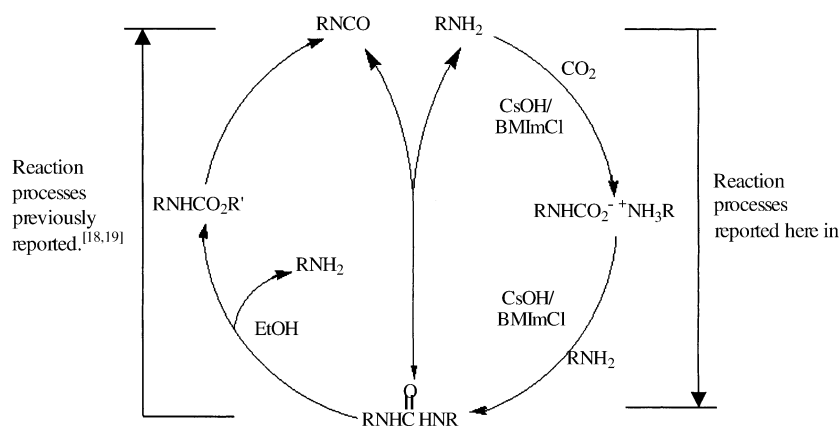
Herein, we report an effective process for the direct synthesis and separation of symmetric urea derivatives in good yield from amines by using CO_2 as the carbonyl source. The recyclable catalytic system consists of an ionic liquid and base and avoids the need for stoichiometric quantities of dehydrating agent. As it was demonstrated that N,N' -disubstituted urea derivatives could easily be converted into the corresponding carbamates,^[18] and the carbamates can be thermally decomposed to form isocyanates,^[19] thus, the breakthrough in the synthesis of N,N' -disubstituted urea derivatives in the absence of stoichiometric



Scheme 1. Carbonylations of N-containing compounds with CO_2 as the carbonyl source.

quantities of dehydrating agents should imply a breakthrough in the synthesis of isocyanates with CO_2 and amine without the need of stoichiometric quantities dehydrating agent. These processes are illustrated in Scheme 2.

A series of aliphatic amines, and even aromatic amines, react with CO_2 to afford corresponding urea derivatives with moderate to high yields in the presence of the CsOH /ionic-liquid catalyst system (Table 1).^[20] The type of cations and anions of the ionic liquids have a strong impact on the



Scheme 2. The transformations between urea, carbamate, and isocyanate derived from amine and CO_2 .

Table 1: Results for synthesis of symmetric urea derivatives with carbon dioxide.

Entry	Substrates	Ionic liquid	Catalysts	t [h]	Product	Yield [%, isolated]
1		BMIImBF ₄	CsOH	4		84.5
2		BMIImPF ₆	CsOH	4		56.6
3		BMIImCl	CsOH	4		98
4 ^[a]		BMIImCl	CsOH	4		93
5		CMIImCl	CsOH	4		–
6		BMIImCl	KOH	4		53.5
7		BMIImCl	CsOH	6		93
8		BMIImCl	CsOH	6		86
9		BMIImCl	CsOH	36		27
10		BMIImCl	CsOH	36		33

[a] The catalyst system had been twice recovered and used for a third time.

formation of urea derivatives when cyclohexylamine is the substrate (Table 1 entries 1–6).^[21] If the conversion is sufficiently high, the desired product precipitates on adding about 10 mL water into the reaction mixture as urea is insoluble in water,^[22] whereas CsOH and the ionic liquid are water-soluble (Figure 1). The solid product could be recovered by filtration and dried. A yield of 98% was obtained when BMImCl ionic liquid containing CsOH was employed (Table 1 entry 3).

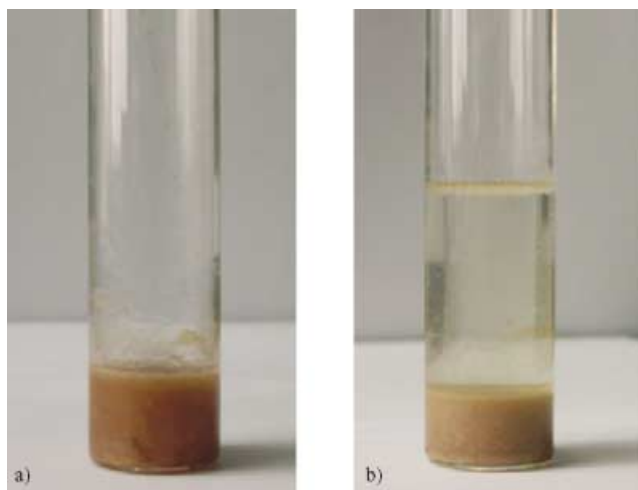


Figure 1. a) The resulting liquid mixture after the reaction of cyclohexylamine with CO₂. b) The reaction mixture with added water, the ionic liquid and base dissolved in the water layer and the crystallized product precipitated.

The use of a weaker base was found to disfavor the formation of urea derivatives; a yield of only 53.5% was obtained when CsOH was replaced with KOH, a relatively weak base. The ionic liquid was indispensable for the formation of the desired product as the yield of dicyclohexyl urea was almost zero in the absence of ionic liquid.

As to primary amines with a linear chain, a longer reaction time was needed to obtain similar yields to those of cyclohexylamine, (Table 1 entries 7, 8).

Surprisingly, good results were also achieved with aromatic amines, which have never been effectively carbonylated directly by carbon dioxide, although longer reaction times were required. Yields of 27% and 33% were obtained with aniline and *p*-methoxyaniline, respectively, (Table 1 entries 9, 10). No urea derivative was afforded with *m*-nitroaniline, which may be attributed to the strong electron-withdrawing property of the nitro group.

The recycling of BMImCl/CsOH catalyst system was also tested. Ionic liquid containing CsOH could be recovered and reused after it was distilled to remove water, and a yield of 93% of urea was obtained when CsOH/BMImCl system was used for a third time.

In summary, the organic-solvent- and dehydrating-agent-free process for carbonylation of both aliphatic and aromatic amines with carbon dioxide to afford urea derivatives is simple, clean, safe, reproducible, and even practical. Furthermore, urea derivatives are potential precursors for the phosgene- and carbon monoxide-free synthesis of isocya-

nates. The concept of reaction and separation has been fulfilled with a simple CsOH/ionic liquid catalyst system that takes advantage of the nonvolatility and selective solubility of the ionic liquid. This concept may be expanded to other catalysis systems.

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- [20] The ionic liquids were synthesized according to reported procedures (P. Bonhote, A. P. Dias, N. Papageorgiou, K. Kalyanasundaram, M. Grätzel, *Inorg. Chem.* **1996**, *35*, 1168) with slight modifications. The following ionic liquids were synthesized: 1-*n*-butyl-3-methyl imidazolium tetrafluoroborate (BMImBF₄), 1-*n*-butyl-3-methyl imidazolium hexafluorophosphate (BMImPF₆), 1-*n*-butyl-3-methyl imidazolium chloride (BMImCl) and 1-*n*-cetic-3-methyl imidazolium chloride (CMImCl). A typical procedure for the carbonylation of amines with CO₂ is as follows. 2 ml (or 2 g) of amine, 3 ml of ionic liquid and 0.05 g of base were put into an autoclave (100 ml) with a magnetic stirring bar. Carbon dioxide (60 atm, purity > 99 %) was introduced into the reactor, and the reaction was stirred and heated at 170 °C for 4–36 h. Water (10 mL) was added into the resulting reaction mixture, and the desired resulted product precipitated out. The solid product was recovered by filtration, washing and drying. Ionic liquid containing CsOH could also be recovered and reused after the filtrate was distilled to remove water. All products were qualitatively analyzed with a HP 6890/5973 GC–MS and quantitatively analyzed with HP 1790GC (flame ion detector).
- [21] When using CsOH/CMImCl, a foamy mixture resulted that could not be separated effectively, although the conversion of cyclohexylamine was analyzed by GC and found to be > 95 %.
- [22] The by-products formed in the reactions were only carbamic salts, which readily dissolved in water.