# Reactions of CO$_2$ with Amines:

## The search for a sustainable route for isocyanates synthesis

Sandra Filipa Sousa da Silva

*DEQ – IST – Departamento de Engenharia Química, Instituto Superior Técnico*

**ABSTRACT**

Isocyanates are important chemical intermediates in polyurethanes production. However, the existent production processes used at industrial scale implies the utilization of huge amounts of chlorinated species and the synthesis of harmful byproducts. The increasing importance given to the reduction of the emission of greenhouse gases, including carbon dioxide, have led to the search for new methods of utilization of this same class of compounds as reagents for the production of chemical compounds with high added value.

Previous studies showed that the carbon dioxide with amines cannot be a relatively efficient method for the synthesis of various products including, isocyanates due to high reactivity of N=C=O group. In this project, it was attempted to demonstrate the effectiveness of these methods in the synthesis of isocyanates, using Mitsunobu zwitterion ($^{i}$PrO$_2$C-N(P$^{+}$R$_3$)-N$^{-}$- $^{i}$PrO$_2$C), as well as through the use of metal complexes of magnesium (BrMg(THF)$_2$NSi(CH$_3$)$_3$Ph(CH$_3$)$_2$).

**Keywords:** isocyanate, carbon dioxide, amines, magnesium.

## 1.  Introduction

### 1.1  Isocyanates importance

Isocyanates are organic compounds with an R-N=C=O functional group. They have a low molecular weight and they are chemically very reactive. The first synthesis of this type of compounds occurred in 1848 by Wurtz from the reaction of diethyl sulfate with potassium-cyanide. The development of this type of compounds begins during the Second World War, in Germany, with the purpose of replacing natural rubber that was becoming scarce. [1-2]

### 1.2  Market Applications

The market of isocyanates has grown rapidly, both on production rates and applications [2]. The most used aromatic isocyanates are TDI (toluene diisocyanate) and MDI (methylene diphenyl diisocyanate). The first is used essentially to produce soft synthetic rubbers while the major applications of MDI are foams, hard synthetic rubbers, and coatings [3-7].

The worldwide production of isocyanates is around 3 million tons [8]. It is possible to expect that the market of isocyanates will experience a high growth due to the rising demand for more and new applications that can become significant in the future [9].

### 1.3  Synthesis Processes

*1.3.1 Phosgene Route*

There are several ways to produce isocyanates. The most common way used to produce isocyanates is known as "the phosgene route". This technique consists in doing a reaction between an amine and phosgene [10-12].

There are four major drawbacks related to the utilization of phosgene. The first is related to the extreme toxicity and flammability of phosgene and isocyanates that make these compounds difficult to handle in bulk quantities. In second place for one mole of amine group there are formed two moles of hydrochloric acid which allows the occurrence of parallel reactions and the degradation of reactors. The third aspect is related to high dilution that is needed to perform reactions of this type. Ideally,

concentrations should be high and volumes as low as possible to avoid recycling and concentration costs. For last, it is impossible not to include compounds that not contain chloride groups in the final product which can be detrimental to further processing of isocyanate [13]. The utilization of phosgene or its derivatives (diphosgene and triphosgene) [14] brings huge environment and health problems: amounts of chloro-based compounds used during the syntheses of isocyanates can cause corrosion of the equipment and the repeated exposure to phosgene can cause chronic bronchitis and emphysema. Furthermore, the availability of petrochemicals and their depletion leads to discovering of new sustainable methods of production of this type of products [15].

### 1.3.2 Other synthesis processes

Along the time, other methods were described and used to produce isocyanates [16-17;18-19]. Due to the limitations and disadvantages of all the processes listed before, it is possible to conclude that a sustainable route for isocyanates' production is highly desirable. The growing value of polyurethane into the global market and the importance of isocyanates as PU precursor led to the search for more sustainable and ecological routes for their synthesis in order to avoid phosgene and hazardous procedures [16].

### 1.3.3 Carbon dioxide utilization

In order to achieve a new safer and cleaner process, phosgene has been replaced by new eco-friendly technologies using carbon dioxide and amines as starting materials [20].

Carbon dioxide is an easily renewable carbon source with the advantages of being non-toxic, economical and abundant, although it is only used as starting material in few industrial processes [21].

The replacement of phosgene by $CO_2$ strives many obstacles related to the catalytic activation of $CO_2$

due to its thermodynamic stability and inert kinetics, and so it's potential is not totally explored. The electronic deficiency of carbonyl carbons leads to a strong affinity for nucleophiles and electron-donating reagents [21]. The main difficulty for using carbon dioxide is how is possible to achieve a new clean and selective route for the production of high value-added products. [21]

### 1.3.4 New Processes Development

There is a considerable amount of research aiming at the development of new commercial and environmental routes to produce isocyanates.

A procedure that has been investigated for alkyl and hindered aryl isocyanate synthesis is Mitsunobu technology [20]. This system involves the reaction of primary aliphatic or hindered aromatic amines, reaction of the amines in dichloromethane with $CO_2$ at -5° to -10°C to form the carbamate salts. Then, the solution is treated with $POCl_3$ to form the carbamic acid species [20]. Lastly, the Mitsunobu zwitterion, which is obtained by diisopropylazodicarboxylate (DIAD) with a solution of tri-*n*-butyl phosphine or triphenylphosphine in dichloromethane, is added to the reaction system, forming the isocyanate in the sequential dehydration process [20].

### 1.3.5 Organometallic catalysis

Due to the thermodynamic stability of $CO_2$, the process of its fixation and activation to produce high-value products is a field of investigation. The most important research in the activation of carbon dioxide is centered in transition metals systems, however, main group metal complexes have been studied already [23].

An example of metal transition complex utilization is described by [24]. It was proven that the use of metal catalysts coupled with reducing agents was an effective way to reduce carbon dioxide and had resulted in activation and incorporation of $CO_2$ into

larger molecules yielding functionalized products. The metals with a low valence of *d*-block are especially interesting for carbon dioxide reduction and activation because they are highly reducing oxophilic metals that can mediate redox processes with one electron or more [24].

Usage of main group metals for reactions with carbon dioxide are described by [25]. The majority of previous studies are related to the use of transition metals. However, some studies on the interaction of carbon dioxide with main group compounds has also been investigated. Main group elements are more available and inexpensive relative to most transition metals.

### 1.4 Aim of the project

The aim of this project is the search for a sustainable route for the synthesis of aryl isocyanates starting with $CO_2$ and amines.

Many conventional industrial and laboratory processes are not environmentally friendly or atom efficient. One of the major advantages of using organometallic compounds as catalysts or reagents in organic synthesis is their high reactivity. Some typical reactions that not occur with the usual organic reaction can be easily done using a variety of organometallics. Another advantage is related to the high reaction selectivity obtained by using organometallics catalysts. The stability and the capacity to recover pure metals are other advantages of using organometallics compounds.

Developing new methods based on the mentioned properties of organometallic compounds can lead to a change in organic synthesis: new efficient and environmental safer processes producing fewer by-products can discard other methods used until now [43-44].

### 2. Results and Discussion

**2.1 Reactions with wet CO₂**

### 2.1.1 Reaction of 2,6-dimethylphenyl-N-trimethylsilyl-bromomagnesium amide (1)

Carbon dioxide was bubbled through a crude solution of (1) for 5 minutes at room temperature and 0.5 bar. ^{1}H and ^{13}C NMR spectra of the solution were made in order to characterize the product. Later, the solvent was removed under reduced pressure. By the spectrum analysis for the reaction of solution of (1) with bubbled carbon dioxide and peak integration and comparison with the spectrum of the starting material and the spectrum of the free amine is possible to conclude that it corresponds to a mixture of bromo magnesium amide starting material and free amine which leads to the conclusion that could be occurred a hydrolysis reaction. Relatively to ^{13}C NMR spectra, this confirm the previous conclusion. The peak at 17.74 ppm belongs to 2,6-dimethyl-N-trimethylsilylaniline and the peak at 25.27 ppm can be assigned to the bromo magnesium starting material. An IR spectrum for the yielded mixture from the reaction of the magnesium amide with carbon dioxide was also made and it is possible to confirm the existence of free amine by the presence of a broad band corresponding to the –N-H bond at around 3300 cm^{-1}. However, the existence of a band at around 1670 cm^{-1} can be assigned to the existence of a specie with a C=O bond [28-30]. Even so, there is no formation of the pretended isocyanate, by absence of a band in the characteristic region of N=C=O bond.

**2.2 Reactions with dry CO₂**

### 2.2.1 Experimental conditions

In order to avoid the hydrolysis reaction, a column filled with a gas dryer agent [26] and molecular sieves [27] was added to the experimental installation.

### 2.2.2 Reaction of (1) in a NMR tube

In a NMR tube, one equivalent of $CO_2$ was pressurized to a solution of (1), in deuterated toluene, for some minutes. The tube was frozen in a liquid nitrogen bath and allowed to warm at room temperature. No changes were observed. The $^1H$ NMR of this solution shows evidence of the existence of free amine in solution, but in a small quantity and the existence of to two silicium groups (0.255 ppm and 0.338 ppm). None of them can be identified as a peak of the starting material or free amine. At 1.37 ppm and 3.58 ppm it is possible to see the existence of two THF molecules. However, none of the integration for these peaks corresponds to the coordination of these molecules to the compound, but as if the molecules were free in solution. At 2.22 ppm and 2.47 ppm it is possible to conclude that are two peaks that corresponds to the methyl groups, but again none of them can be assigned to the starting materials or free amine. In the aromatic region, the attribution is more difficult to do because of its large split.

Forward, the NMR tube was heated at 50ºC overnight. A white powder was obtained and the solution was characterized by $^1H$ NMR. Comparing the obtained spectrum with the previous one it is possible to appoint some differences. First, the inversion of the two new groups of silicium groups (0.246 ppm and 0.307 ppm). The first one increases it intensity while the second peak was decreased. The methyl protons at 2.136 ppm had decreased its intensity while the peak at 2.226 ppm was increased. It is possible to see a better resolution of the aromatic protons. The peak at 6.828 ppm can be assigned to the protons in *para* position and the peak at 7.084 ppm can be attributed to the protons in *meta* position.

The NMR tube was heated at 50ºC one more day. Afterwards, the solution was characterized by $^1H$ and $^{13}C$ NMR. At 0.304 ppm, the peak from silicium group increased it intensity and the peak at 0.204 ppm decreased. The peak present at 2.226 ppm,

from the protons of one methyl group disappeared as well the peak from a proton at *para* position, at 6.871 ppm. Comparing this results with [28-30] it is possible to assume that a new specie with a -$OSiMe_3$ is formed by the reaction of the magnesium amide with carbon dioxide, as a silylcarbamate. By the analysis of $^{13}C$ NMR spectrum it is possible to confirm the existence of a carbamate specie due to the existence of peaks with a negative chemical shift (-0.48 ppm) and the existence of a peak that can be assigned to the C=O at around 150 ppm [28-30].

### 2.2.3 Reaction of (1) in a shlenck

In a shlenck, one equivalent of $CO_2$ was pressurized to a solution of (1), in toluene, for some minutes. The shlenck was frozen in a liquid nitrogen bath and allowed to warm at room temperature. Next, the solution was heated at 50ºC, for two days, yielding a white suspension. The suspension was filtered and the solid was dried under vacuum. The solvent from the solution was removed under vacuum yielding a white solid residue. This solid was characterized by IR spectrum. By the analysis of IR spectrum, it is possible to point some typical stretches as the C-H aromatic bonds and N-H bonds between 3300 and 3500 $cm^{-1}$. Si-$CH_3$ bonds appears around 1250 $cm^{-1}$, and C-N bonds appears around 1080 and 1360 $cm^{-1}$. The aromatic C=C bonds appears between 1500 $cm^{-1}$ and 1700 $cm^{-1}$. At 1655 $cm^{-1}$ it is possible to notice the presence of an intense peak. Comparing this value to the described in the literature from IR spectroscopy analysis and for other carbamate structures [28-30] it is coincident with the values for the carbamate group.

### 2.3 Mitsunobu Reaction with Isopropyl amine

Carbon dioxide was bubbled through a stirred solution between -5 and -10°C of isopropylamine in dichloromethane for 45 minutes. The Mitsunobu zwitterion was prepared by addition of diisopropyl

azodicarboxylate (DIAD) to a solution of triphenylphospine in dichloromethane at -20°C. Both solutions were cooled to -78°C and the zwitterion solution was cannulated into the carbamate containing solution. More carbon dioxide was passed into the solution after addition and the reaction mixture allowed to warm to ambient temperature and to stand overnight.

By the analysis of the IR spectrum and comparing it with [20] it is possible to conclude that there was some isocyanate formation by the existence of a band in the characteristic region of N=C=O region (2240 cm$^{-1}$).

### 3. Concluding Remarks

Isocyanates are important intermediate compounds for the production of PU systems. Although, the actual production processes carry huge environmental problems due to high toxicity of starting materials and formed byproducts.

Along the time, there were some attempts to synthetize isocyanates using amines and carbon dioxide. Thus, due to the environmental problems related with isocyanates production and the possibility of $CO_2$ valorization is possible to affirm that new synthesis processes are needed.

In other section of this project, it was an attempt of isocyanates synthesis using magnesium amide compounds. The study of these reactions was made by NMR and IR spectroscopy which allows verify that occurred a decomposition of the used starting materials with wet carbon dioxide. When was used a high purity carbon dioxide it is possible to assume the formation of a carbamate specie. Although none of these reactions were successful to synthetize isocyanates.

Organometallics synthesis can be a way to develop a new process for isocyanate synthesis and carbon dioxide valorization. Some work in this area have been made but it necessary more study to achieve

an efficient technique for $CO_2$ activation and insertion reaction due to several limitations of this specie.

### 4. Experimental Section

### 4.1 General Procedures

Unless stated otherwise, all manipulations were perfomed under an atmosphere of dry-oxygen-free nitrogen by means of standard Shlenck and glovebox techniques. Solvents were pre-dried using 4 A molecular sieves and collected by distillation under an atmosphere of nitrogen. Deuterated solvents were dried with a 4 A molecular sieves and freeze-pump-thaw degassed prior to use. All other reagents were commercial grade and used without further purification. Carbon dioxide were purchased from Air Liquide and used as received. NMR spectra were recorded in a Brucker AVANCE II 300 MHz and 400 MHz spectrometers, at 296 K unless stated otherwise, reference internally to residual proton-solvent ($^1$H) or solvent ($^{13}$C) resonances, and reported relative to tetramethylsilane (0 ppm). 2D NMR experiments such as $^1$H-$^{13}$C{$^1$H} HSQC, $^1$H-$^1$H NOESY, $^1$H-$^{13}$C{$^1$H} HMBC were performed to make all the assignments. FT-IR spectra were recorded in KBr using a *JASCO FT/IR-430* spectrometer.

### 4.2 Synthesis of magnesium amide

Synthesis of (1): To a stirred cold solution of EtMgBr (10 mmol, 3.34 mL) in THF was added dropwise Ph(CH$_3$)$_2$NHTMS (10 mmol, 2.04 mL). The reaction mixture was stirred overnight allowing warming up to room temperature. Solvent was removed under reduced pressure and the resulting solid was dried under vacuum. $^1$H NMR (ppm): 0.41 (9H), 1.13, 3.47 (10H), 2.53 (6H), 6.78 – 6.83 (1H), 7.12-7.15 (2H); $^{13}$C NMR (ppm): 3.77, 21.39, 24.98, 69.99, 118.92, 128.20, 134.80.

### 4.3 Reactions with wet CO$_2$

Carbon dioxide was bubbled through a crude solution of (1) for 5 minutes at room temperature and 0.5 bar. The solvent was removed under reduced pressure. The remaining mixture was dried under vacuum.

### 4.4 Reactions with dry $CO_2$

#### 4.4.1 Reaction of (1) in a NMR tube

One equivalent of carbon dioxide (0.05 mmol) was pressurized through a frozen solution of one equivalent of (1) (0.05 mmol, 0.015 g) in deuterated toluene for some minutes. After this, the solution was let too warm to room temperature.

#### 4.4.2 Reaction of (1) in a shlenck

One equivalent of carbon dioxide (1.80 mmol) was pressurized through a frozen solution of one equivalent of (1) (1.80 mmol, 0.54 g) in toluene for some minutes. After this, the solution was let too warm to room temperature and then the shlenck was heated for two days at 50ºC.

### 4.5 Mitsunobu Reaction with Isopropyl amine

Carbon dioxide was bubbled through a stirred solution at -5 to -10°C of isopropylamine (17.6 mmol, 1.5 mL) in dichloromethane for 45 minutes. The Mitsunobu zwitterion was prepared by addition of DIAD (21.3 mmol, 4.2 mL) to a solution of triphenylphospine (22.5 mmol, 5.54 g) in dichloromethane at -20°C. Both solutions were cooled to -78°C and the zwitterion solution was cannulated into the carbamate containing solution. More carbon dioxide was passed into the solution after addition and the reaction mixture allowed to warm to ambient temperature and to stand overnight.

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