

CARBON DIOXIDE CATALYSIS IN TRANS-ESTERIFICATION REACTION FOR THE CARBAMATION OF AMINES OF INDUSTRIAL INTEREST

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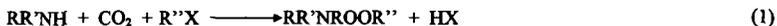
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Abstract: Developing clean synthetic methodology for the production of carbamates, avoiding phosgene, is a very attractive perspective. In this paper, the reactivity of industrially relevant amines, aliphatic and aromatic, towards CO₂ and alkylating agents, or dialkyl/aryl-carbonates, is discussed. We also describe the catalytic role of carbon dioxide in the carbamation of aliphatic amines and that of P-acids in the reaction of aromatic amines towards carbonates. The reaction mechanism is discussed.

Keywords: carbon dioxide, organic carbamates, amines.

Introduction

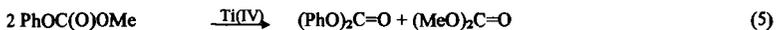
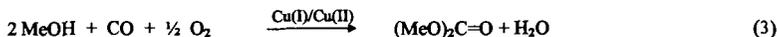
Organic carbamates are compounds of great interest used in pharmacology, agriculture, and chemical industry.¹ Their conventional syntheses are based on the use of phosgene, a chemical difficult to handle because of its toxicity. The substitution of phosgene with less noxious starting materials represents a very important target of "green chemistry" for the future. Carbon dioxide and organic carbonates are good candidates as succedaneous for phosgene.² Utilisation of carbon dioxide in the synthesis of carbonate esters has been investigated for long time. We have reported about their selective synthesis from amines, CO₂ and alkylating agents³ [Eq. 1]:



Aminolysis of organic carbonates [Eq. 2] is another attractive synthetic route to carbamates, since non-phosgene routes to carbonic acid diesters are now available.



In fact, dimethylcarbonate (DMC) is produced on large-scale by oxidative carbonylation of methanol [Eq. 3], and other organic carbonates can be prepared by transesterification of DMC with phenols or long chain alcohols [Eq. 4, 5]



Carboalkoxylation of aliphatic amines requires suitable catalysts in order to observe high conversion rate and good selectivity. Lewis acids, such as AlCl₃, SnCl₂, ZnCl₂, FeCl₃, or metal (Rh, Ru) complexes, can catalytically promote the carboalkoxylation of aliphatic amines with carbonates. A major drawback is the methylation of the amine.

Recently, we have shown that carbon dioxide is an efficient catalyst for the synthesis of organic carbonates from aliphatic amines and DMC.⁴ As this synthetic approach requires mild conditions, we have extended our studies to aminofunctional silanes. The corresponding carbamates are used as modulators of physico-mechanical properties of polymeric materials.⁵ CO₂ plays again a quite interesting catalytic role.

The conventional carboalkoxylation/arylation of aromatic amines, obtained using Zn, Co, Sn, Al, Ti catalyst, has again as major drawback the alkylation/arylation of the amines. We have found that in this case organophosphorous acids can be advantageously used as very selective catalysts avoiding the alkylation/arylation process.

Experimental

All reaction and manipulation were carried out under the specified atmosphere, by using vacuum line techniques. All solvents were dried as described in literature⁶, and they were stored under dinitrogen.

Synthesis of RNHC(O)OCH₃ from aliphatic amines or aminofunctional silanes and DMC in the presence of CO₂

A solution of amine (9.15 · 10⁻³ mmol) in DMC (10 mL) was prepared under dinitrogen in an appropriate flask and, then, saturated with CO₂ (P_{CO₂} = 0.1 MPa) to give (RCH₂)₃NH₃⁺O₂CNH(CH₂R) as white microcrystalline solid which was poorly soluble in the reaction solvent. The system was heated to 343 K for 5-7 h. After cooling to room temperatures

the reaction mixture was filtered. A small amount of unreacted $(\text{RCH}_2)_3\text{NH}_3^+\text{O}_2\text{CNH}(\text{CH}_2\text{R})$ was recovered. The solution was evaporated in vacuo and the residue fractionated on a silica gel column using a diethyl ether/hexane (2:1 v/v) eluent mixture. Solvent was evaporated from the eluted fractions and pure carbamate obtained.

When the reaction mixture was heated at 363 K, an increase of the yield (Table 1) was observed.

Table 1. Yield of carbamate esters from aliphatic amines or aminofunctional silanes and DMC in the presence of carbon dioxide

Amine	Yield (%)	Yield (%)
$(\text{PhCH}_2)_3\text{NH}_2$	50 (343 K)	92 (363 K)
$\text{C}_6\text{H}_{11}\text{NH}_2$	27 (343 K)	45 (363 K)
$\text{CH}_2=\text{CHCH}_2\text{NH}_2$	44 (343 K)	70 (363 K)
$\text{H}_2\text{N}(\text{CH}_2)_3\text{Si}(\text{OMe})_3$	70-80 (348 K)	/
$\text{H}_2\text{N}(\text{CH}_2)_3\text{Si}(\text{OEt})_3$	70-80 (348 K)	/
$\text{H}_2\text{N}(\text{CH}_2)_2\text{NH}(\text{CH}_2)_3\text{Si}(\text{OMe})_3$	100 (348 K)	/

Synthesis of mono- and di-carbamates, from aromatic di-amines and 1) diphenylcarbonate (DPC) or 2) methylphenylcarbonate (MPC), in the presence of phosphorous acids

1) A mixture of DPC (26.1 mmol), di-amine (1.35 mmol) and phosphorous acid (0.135 mmol) was heated at 363 K under stirring for 4 h. The mixture was cooled to room temperature (293 K) and the solid was extracted with diethyl ether. The white residue was analysed as pure di-carbamate. By reducing the reaction time to 30 min, it was possible to isolate the mono-carbamate (Table 2) by using the same purification procedure.

2) A mixture of MPC (6.9 mmol), di-amine (3.45 mmol) and phosphorous acid (0.347 mmol) in THF (10 mL) was stirred at 363 K for 10 h, then cooled to room temperature and the solid that precipitated was isolated by filtration and identified as $(\text{ArH}_2)(\text{O}_2\text{PPh}_2)_2$. The solution was fractionated on a silica gel column using diethyl ether/toluene for MDA and diethyl ether/hexane for TDA as eluent. Methylphenylcarbonate afforded very selectively the methylcarbamate without production of neither phenyl carbamate nor methyl-amine.

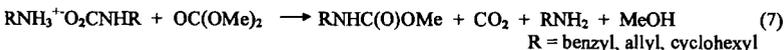
Table 2. Yield of mono- and di-carbamate synthesised from di-amines and carbonates in the presence of phosphorous acids.

Di-amine	Yield (%) of Mono-carbamate	Yield (%) of Di-carbamate	Phosphorous acid
$\text{H}_2\text{NPh}(\text{CH}_2)\text{PhNH}_2$	50 (DPC)	100 (DPC)	$\text{Ph}_2\text{P}(\text{O})\text{OH}$
$\text{H}_2\text{NPh}(\text{CH}_2)_2\text{PhNH}_2$	35 (MPC)	32 (MPC)	$\text{Ph}_2\text{P}(\text{O})\text{OH}$
$\text{H}_2\text{NPh}(\text{CH}_3)\text{NH}_2$	42 (DPC)	84 (DPC)	$\text{Ph}_2\text{P}(\text{O})\text{OH}$
$\text{H}_2\text{NPh}(\text{CH}_3)\text{NH}_2$	51 (MPC)	66 (MPC)	$\text{Ph}_2\text{P}(\text{O})\text{OH}$

Results

Reactivity of aliphatic amines towards DMC in the presence of carbon dioxide

Saturation of an amine solution in DMC with carbon dioxide gives the corresponding alkylammonium N-alkylcarbamate that reacts with DMC to afford N-alkylmethylcarbamates [Eq. 6, 7].



The alkylammonium N-alkylcarbamate was prepared *in situ* and, after its precipitation, the reaction mixture was heated to the required temperature. The reaction was carried out in conventional solvents as THF, CH_2Cl_2 , and aromatics. Interestingly, the organic carbonate (DMC) could be used as reaction solvent. In order to ameliorate the reaction rate and selectivity, we have tested different reaction conditions and established that working at temperature higher than 343 K and pressure of $\text{CO}_2 = 0.1 - 0.2$ MPa produces best results. In all cases, the products have been completely characterised. By-products as ureas, N,N-substituted carbamates, secondary and tertiary amines were formed in very low yield (< 1%), if not absent.

Conversely, if aliphatic amines were reacted with DMC under N_2 atmosphere the formation of carbamate esters was completely suppressed and methylation products were formed.

Reactivity of aminofunctional silanes towards DMC in the presence of carbon dioxide

Under mild condition (348 K), aminofunctional silanes as $\text{H}_2\text{N}(\text{CH}_2)_3\text{Si}(\text{OMe})_3$ (I), $\text{H}_2\text{N}(\text{CH}_2)_3\text{Si}(\text{OEt})_3$ (II), $\text{H}_2\text{N}(\text{CH}_2)_2\text{NH}(\text{CH}_2)_3\text{Si}(\text{OMe})_3$ (III) react with DMC in the presence of carbon dioxide to give the corresponding carbamate esters $\text{MeO}(\text{O})\text{CNH}(\text{CH}_2)_3\text{Si}(\text{OMe})_3$, $\text{MeO}(\text{O})\text{CNH}(\text{CH}_2)_3\text{Si}(\text{OEt})_3$, $\text{MeO}(\text{O})\text{CNH}(\text{CH}_2)_2\text{NH}(\text{CH}_2)_3\text{Si}(\text{OMe})_3$, respectively.

The carbamation reaction is very selective⁷; no formation of N-mono- or N,N'-di-methylated derivatives as by-products has been observed.

The reactivity of the di-amine (III) was higher than that of amines (I) and (II). In fact, the conversion of (III) into the corresponding carbamate was complete in less than 7 hours.

When the reactivity of silyl amines towards DMC, at 348 K, was investigated in a dinitrogen atmosphere the carbamation reaction was not observed: the formation of N-methylated species was the main process.

The development of new clean methodologies for these products is required by the fact that silyl carbamates are more and more used as silane coupling agents and as source of isocyanates, largely used in the chemical industry.

Reactivity of 4,4'-methylenedianiline (MDA) and 2,4-diaminotoluene (TDA) towards DPC or MPC in the presence of P-acids

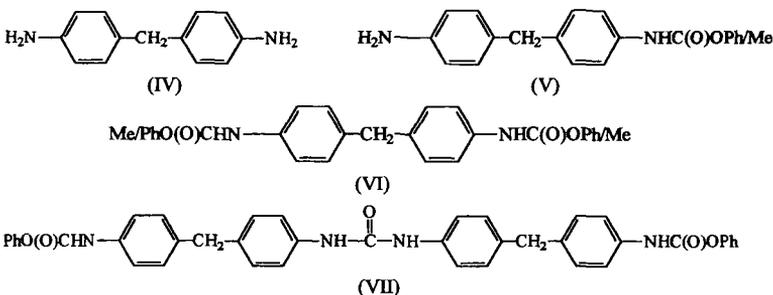
Aromatic amines show a poorer reactivity towards DPC or MPC in the presence of CO₂ with respect to aliphatic ones. This behaviour is most probably due to their low nucleophilicity. In the presence of catalysts such as Ph₂P(O)OH, (PhO)₂P(O)OH, (BuO)₂P(O)OH, (BuO)P(O)(OH)₂ aromatic mono-⁸ and di-amines^{9,10} react with DPC and DMC to give the corresponding carbamate esters with high yield and selectivity. DPC affords the phenyl carbamate, while MPC¹⁰ affords selectively the methyl carbamate and results to be a much better carboxymethylating agent than DMC.

In order to gather information about the reaction mechanism of mono- and di-carbamate of MDA (IV) with either DPC or MPC, we have carried out a kinetic study. At 363 K, mono-carbamate (V) was formed followed by di-carbamate (VI), in very good yield. In absence of the catalyst, no reaction was observed. The kinetics is first order in the amine and first order in the carbamate.¹¹

Carrying out the reaction in THF as solvent, at different temperatures (393, 363, 323 K) it was possible to establish the better reaction conditions for addressing the reaction towards the preferential formation of mono- or di-carbamate.

The temperature affects the selectivity of the reaction. In fact at 393 K, when DPC is used, the formation of urea (VII) is observed, produced by reaction of the di-carbamate with mono-carbamate. At 363 K, urea is not observed.

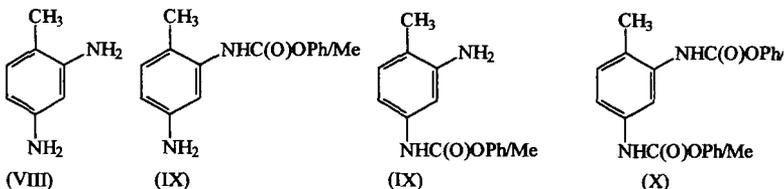
Interestingly, when MPC¹⁰ was used, urea was never detected.



The carbamation reaction was studied using solvents as diethyl ether, phenol or the carbonate itself. The use of phenol as solvent produces an inhibitory effect on the carbamation process, that results to be very selective when the carbonate is used as solvent. The conversion of the amine is quantitative.

The P-acids used as catalyst have shown a quite different activity, Ph₂P(O)OH being the most active. In the case of MPC a progressive deactivation of the catalyst was observed after sixteen hours. Further addition of catalyst results, in fact, in a significant increase of the rate of formation of both carbamates.

The P-acids show a very interesting catalytic activity also in the carbamation process of TDA (VIII). The formation of mono- (IX) and di-carbamate (X) is observed with high yield and selectivity.



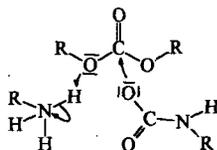
The formation of (X) involves the carbamation of two non-equivalent amino groups of the aromatic di-amine. We have demonstrated that the amino group in the *para* position is functionalised first than that in *ortho*. This is due to the hindrance of the methyl group that induces the faster reactivity of the amino group in the *para* position.

MDA and TDA carbamates have a large market as they are used as precursors of isocyanates, which are monomers for polymers.

Discussion

Carbon dioxide as catalyst

The results reported above, and the experiments carried out in absence and in presence of CO₂, clearly demonstrate that carbon dioxide plays a catalytic role in the carbamation of aliphatic amines. The kinetic study we have completed¹¹ shows that the rate determining step is the reaction of carbamate anion with the carbonate [Eq. 8], that bears to the formation of the mixed carbamic-carbonic anhydride RNHC(O)OC(O)OMe. Scheme 1 shows the reactive step.



Scheme 1.

Subsequently it is decarboxylated to form the carbamate ester.

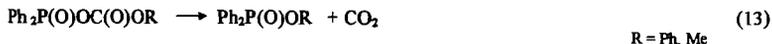
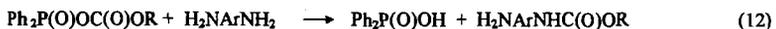
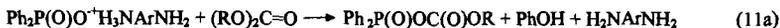
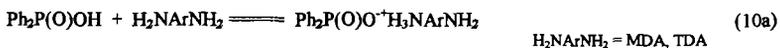


The mixed anhydride has been isolated and characterised. It is stable at low temperature and at room temperature, or higher, spontaneously converts into the carbamate with CO₂ loss. This mechanism explains why the incorporation of labelled CO₂ in the organic carbamate is not observed when RNH₃⁺O₂¹³CNHR is utilised as the starting reactant.

The reaction conditions are quite mild and selectivity is 100%.

Role of the P-acids in the carbamation process

Aromatic amines show a lower reactivity towards carbon dioxide, so the carboalkoxylation process requires suitable catalysts. Phosphorous acid can be considered as bifunctional catalysts. A plausible mechanism involves the formation of a carbonic-diphenylphosphinic mixed anhydride Ph₂P(O)OC(O)OPh, that reacts with the free aromatic amines which are converted into the carbamate esters, with regeneration of the catalyst.



The catalyst is still active at the end of the several runs if the process involves DPC. MPC can cause a progressive deactivation of the catalyst.

This could be explained considering that in the former case the starting catalyst may be converted into Ph₂P(O)OPh, that is also a catalytic species. In the latter, the catalyst converts into Ph₂P(O)OMe that has no catalytic properties.

Conclusion

In the presence of carbon dioxide, aliphatic amines and aminofunctional silanes react with carbonates (DMC) to give the corresponding carbamate esters. The carbon dioxide catalysis is a new, useful finding. The selectivity is very high.

This methodology cannot be extended to the carboalkoxylation of aromatic amines, most probably because they show a lower reactivity towards CO₂. Aromatic amines and carbonate can be converted into the corresponding carbamate esters in the presence of P-acids as catalyst.

In both cases, the carbamation reaction is very selective and no formation of N-methyl/aryl species or ureas is observed.

Acknowledgements

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