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Carbomethoxylating reactivity of methyl phenyl carbonate toward aromatic amines in the presence of group 3 metal (Sc, La) triflate catalysts

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Abstract

Methyl phenyl carbonate (MPC) has been investigated as a carbomethoxylating agent of aromatic amines in the presence of group 3 metal (Sc or La) triflate catalysts. Under mild conditions (363 K), both $Sc(OTf)_3$ and $La(OTf)_3$ ($OTf = O_3SCF_3$) can promote the carbamation of aniline and a few industrially relevant aromatic diamines, such as 4,4′-methylenedianiline (MDA) and 2,4-diaminotoluene (TDA), with MPC. Carbamate yield and selectivity are markedly affected by the experimental conditions (temperature, reaction medium, nature of the metal center). $Sc(OTf)_3$ is a more effective and selective carbamation catalyst than $La(OTf)_3$. Ad hoc experiments have shown that, in the presence of the $M(OTf)_3$ (M = Sc, La) catalysts, MPC is not only more *reactive* but also a *more selective* carbomethoxylating agent than dimethyl carbonate (DMC).

Keywords: Methyl phenyl carbonate; Dimethyl carbonate; Organic carbamates; Scandium triflate; Lanthanum triflate

1. Introduction

The substitution of hazardous reagents with innocuous or less noxious compounds in synthetic chemistry is a major target for the modern chemical industry [1]. A very risky compound is phosgene [2], which, despite its toxicity, is still being used as a starting material for the synthesis of a number of chemicals, such as, for instance, organic carbamates RR′NHC(O)OR″ (R = alkyl, aryl; R′ = H, alkyl, aryl; R″ = alkyl, aryl) [3]. Carbamate esters are very useful compounds which find wide application in several fields (pharmacology, agriculture) and also play a key role as intermediates in the chemical industry for the production of fine and commodity chemicals [3,4].

Scheme 1 shows a few synthetic ways to carbamate esters [2,5–7], potentially an alternative to the current methods based on phosgene. Among them, the reaction of amines with carbonic acid diesters [2] merits particular attention as a "green" route to organic carbamates, since innovative phosgene-free methodologies for the industrial synthesis of dimethyl carbonate (DMC)

$$2MeOH + CO + \tfrac{1}{2}O_2 \xrightarrow{Cat.} (MeO)_2CO + H_2O \quad (1)$$

and other organic carbonates

$$(MeO)_2CO + PhOH \xrightarrow{Cat.} MeOC(O)OPh + MeOH \quad (2)$$

have been implemented in the last few years [8]. DMC, especially, is widely being studied as a carbomethoxylating substrate for the carbamation of both aliphatic and aromatic amines [9–27]. This process requires a suitable catalyst. Recently, we have demonstrated that d^0 transition metal systems, such as $Sc(OTf)_3$ or $La(OTf)_3$ ($OTf = O_3SCF_3$) are active catalysts for the selective (≈ 100%) synthesis of carbamate methyl esters from primary or secondary aliphatic amines and DMC at *ambient temperature* (293 K) [25].

In this work the $M(OTf)_3$ (M = Sc, La) triflate salts have been investigated as carbamation catalysts of aromatic

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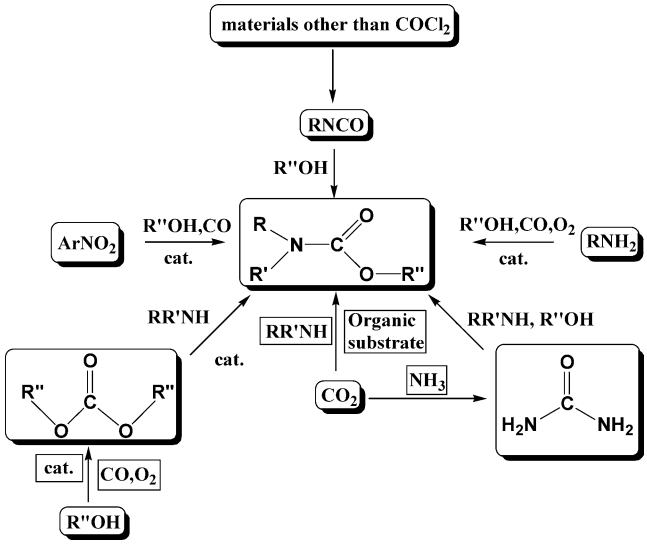


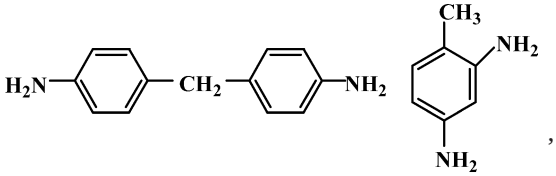
Scheme 1. Phosgene-free synthetic routes to carbamate esters.

amines. We have focused also on methyl phenyl carbonate (MPC) as a potential carbomethoxylating substrate:

$$ArNH_2 + MeOC(O)OPh \rightarrow ArNHC(O)OMe + PhOH \quad (3)$$

Growing attention, in fact, is currently devoted to the study of alternative carbomethoxy or, more generally, carboalkoxylating substrates [28–32], able to react selectively, under not drastic conditions.

The use of MPC in carbamation reactions of amines has been scarcely studied in the past [29–32]. In a previous study, we have shown that organo-phosphorous Brønsted acids $X_2P(O)OH$ (X = Ph, OPh, OBu) can selectively catalyze the synthesis of methylcarbamates from MPC and 4,4′-methylenedianiline (**1**, MDA) or 2,4-diaminotoluene (**2**, TDA) [32]. Also organic bases have been used to promote the carbamation of aromatic amines,



1 **2**

with MPC [30,31]. To date, metal salts or complexes have been poorly investigated as catalysts in this reaction [Eq. (3)]. Herein, for the first time, we fully report on the activity of a few metal systems, such as $Sc(OTf)_3$ and $La(OTf)_3$ [25,33] as catalysts in this process. We also compare the carbomethoxylating properties of MPC and DMC toward $PhNH_2$. We show that, in the presence of the above catalysts, MPC is not only more reactive, but also a more selective carbomethoxylating agent than DMC.

2. Experimental

2.1. General

Unless otherwise stated, all reactions and manipulations were conducted under a dinitrogen atmosphere, by using vacuum line techniques. All solvents were dried according to literature methods [34] and stored under N_2. DMC (Fluka) was dried over 5A molecular sieves for 24 h, filtered, distilled, and stored under N_2. MPC was prepared as described in the literature [35]. The amines were Fluka or Aldrich products. $PhNH_2$ was dried over KOH, distilled, and stored under N_2. $M(OTf)_3$ (M = Sc, La) salts (Fluka, Aldrich) were used as received and manipulated under an inert gas atmosphere.

IR spectra were obtained with a Perkin–Elmer 883 spectrophotometer or with a Perkin–Elmer FTIR 1710 instrument. NMR spectra (chemical shift in ppm vs TMS) were run on a Varian XL-200 or a Bruker AM 500 instrument and referenced to the solvent peak. GC-MS analyses were carried out with a Shimadzu GC-17A linked to a Shimadzu GCMS-QP5050 selective mass detector (capillary column: Supelco MDN-5S, 30 m × 0.25 mm, 0.25 μm film thickness). GC analyses were performed with a HP 5890 Series II gas chromatograph (capillary column: Heliflex AT-5, 30 m × 0.25 mm, 0.25 μm film thickness). HPLC analyses were carried out with a Perkin–Elmer Series 4 LC liquid chromatograph connected with a LC 290 UV/vis detector.

2.2. Reaction of $PhNH_2$ with MPC in the presence of $M(OTf)_3$ (M = Sc, La) salts

2.2.1. General procedure

Into a 10-mL tube, containing the catalyst $M(OTf)_3$ (M = Sc or La), the reactants (MPC and aniline), the solvent (THF), and the internal standard (*n*-dodecane) were introduced. The tube was closed with a screw cap equipped with a silicon septum through which the reaction mixture could be sampled using a GC syringe. The reaction mixture was then allowed to react at the working temperature. At measured intervals of time, heating was stopped, and the reaction mixture was cooled to room temperature and analyzed by GC.

In a few experiments MPC was used both as solvent and reactant. In this case, at measured intervals of time, heating was stopped, and 5 μL of reaction solution was sampled, diluted with THF (0.1 mL), and, after addition of *n*-dodecane, analyzed by GC.

2.2.2. Isolation of $(PhNH_3)(OTf)$ and PhNHC(O)OMe

To the solution of $Sc(OTf)_3$ (0.08850 g, 0.179 mmol) in THF (1.3 mL), MPC and aniline were added. The reaction solution was stirred at 363 K for 24 h, cooled to 293 K, and evaporated in vacuo. The residue was extracted with diethyl ether. A white solid, poorly soluble in ether, was recovered and identified as $(PhNH_3)(OTf)$ (42.6 mg, 0.174 mmol). Anal. Calcd. for $C_7H_8SNO_3F_3$: C, 34.57; H, 3.32; N, 5.76.

Table 1
Reaction of $PhNH_2$ with DMC in the presence of $M(OTf)_3$ (M = Sc, La) salts, under solvent-free conditions

Entry	$PhNH_2$ (mmol)	DMC (mmol)	$M(OTf)_3$[a]		T (K)	Time (h)	GC yield vs $PhNH_2$[b] (%)		
			M = Sc	M = La			$PhNHCO_2Me$	Ph(Me)NH	$PhNMe_2$
1	5.48	59.35	–	–	363	96	–	[c]	[c]
2	0.823	9.03	6.4	–	363	24	8	25	10
3	2.192	5.46	3.0	–	363	26	5	19	4
4	1.096	11.87	–	5.6	368	24	3	20	5

[a] (mol M/mol $PhNH_2$)%.
[b] Under the working conditions, the formation of other by-products, such as diphenylurea and Ph(Me)NCO(O)Me, was not observed.
[c] The total yield of *N*-methylation products was less than 2%.

Table 2
MPC vs DMC reactivity toward $PhNH_2$ in the presence of $M(OTf)_3$ (M = Sc, La) salts (363 K)[a]

$PhNH_2$ (mmol)	MPC (mmol)	DMC (mmol)	$M(OTf)_3$ (mmol)		Time (h)	GC yield vs $PhNH_2$ (%)		
			M = Sc	M = La		$PhNHCO_2Me$	Ph(Me)NH	$PhNMe_2$
1.096	1.109	–	0.073	–	2	38	3	Traces
1.096	1.109	–	0.073	–	24	72	5	< 1
1.096	–	1.128	0.072	–	27	18	20	2
1.096	1.109	–	–	0.064	25	25	5	< 1
1.096	–	1.128	–	0.064	26	7	26	5

[a] THF (0.5 mL) was the solvent, in all the runs.

Found: C, 35.08; H, 3.65; N, 5.97. IR (Nujol, cm^{-1}): 3180, 1636, 1621, 1587, 1538, 1498, 1284 (vs, br), 1238 (vs, br), 1197, 1174, 1159, 1141, 1108, 1094, 1044 (s), 1026, 973, 764, 744, 688, 650, 618, 588, 575.

The washing solutions, collected together, were extracted with water, NaOH 0.6 M (4 × 25 mL), and again with water. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo. Upon addition of *n*-hexane and cooling to 273 K, a white solid separated and was isolated by filtration and identified as PhNHC(O)OMe (60%). Anal. Calcd. for $C_8H_9NO_2$: C, 63.57; H, 6.00; N, 9.26. Found: C, 63.93; H, 6.04; N, 9.33. The IR, MS, ^1H and ^{13}C NMR spectra of the isolated product fully agree with those of an authentic sample of PhNHC(O)OMe prepared by another route [13]. No attempt was made to recover minor amounts of product from the mother solution.

2.3. Reaction of aromatic diamines (MDA, TDA) with MPC in the presence of $M(OTf)_3$ (M = Sc, La) salts

Into a 10-mL tube containing the catalyst $M(OTf)_3$, THF, MPC, and the diamine (MDA or TDA) were introduced. After sealing the tube, the reaction mixture was heated to 363 K for about 24 h and, after cooling to 293 K, diluted with THF (2.5 mL) and analyzed by HPLC (see Table 4).

For the reaction with MDA, the conditions are as follows: internal standard, mesitylene; column, Supelcosil LC-DP, 5 μm, 250 × 4.6 mm; mobile phase, CH_3CN/H_2O (35/65 v/v); flow, 1.5 mL/min.

For the reaction with TDA, the conditions are as follows: internal standard, benzene; column, Supelcosil LC8, 5 μm, 250 × 4.6 mm; mobile phase, CH_3CN/H_2O (30/70 v/v); flow, 1.5 mL/min.

2.4. Reaction of $PhNH_2$ with DMC in the presence of $M(OTf)_3$ (M = Sc, La) salts

Into a 10-mL tube, containing the catalyst $M(OTf)_3$ and anhydrous DMC, aniline and THF (if used) were introduced. After the tube was sealed, the reaction mixture was allowed to react at the working temperature for a variable time (see Tables 1 and 2) and, after cooling to ambient temperature, analyzed by GC (internal standard: *n*-dodecane).

2.5. Reaction of MPC (or DMC) with $PhCH_2NH_2$ in the absence of any catalyst

To a MPC (0.100 mL, 0.822 mmol) solution in THF (0.5 mL) an excess of $PhCH_2NH_2$ (0.250 mL, 2.291 mmol; amine/MPC = 2.8 (mol/mol)) was added. The reaction mixture was allowed to react at 293 K and periodically monitored by GC-MS. The GC-MS analysis of the reaction solution showed that the conversion of MPC into $PhCH_2NHC(O)OMe$ was quantitative within 24 h.

A smooth reaction was observed also when an equimolar amine/carbonate ratio was used ($PhCH_2NH_2$, 0.090 mL, 0.825 mmol; MPC, 0.100 mL, 0.822 mmol; THF, 0.5 mL). Under the latter conditions (293 K), the conversion of the reactants was found to be complete within 55 h.

In both cases, no evidence of the formation of *N*-methylation by-products was found by GC-MS.

Similar experiments carried out with DMC afforded, after comparable times, $PhCH_2NC(O)OMe$ in much lower yield (13 and 8%, respectively).

3. Results

3.1. Carbomethoxylation of aniline in the presence of $M(OTf)_3$ (M = Sc, La) salts: MPC vs DMC carbomethoxylating behavior

In this study aniline was chosen as model compound for aromatic amines. Under the experimental conditions (293 K) employed for the aliphatic ones [25], less reactive $PhNH_2$ did no react with DMC in the presence of the $M(OTf)_3$ (Sc, La) salts, even after very long reaction times (4 days). At 363 K, both $Sc(OTf)_3$ and La $(OTf)_3$ (3–6% (mol/mol) vs $PhNH_2$) can promote the formation of PhNHC(O)OMe from aniline and DMC (see Table 1), but slowly, with low yield (< 10% after 24 h) and selectivity, because of the predominant formation of *N*-alkylation products (Ph(Me)NH, $PhNMe_2$).

However, a drastic change of reactivity was observed by suitably changing carbomethoxylating agent. In fact, at 363 K, in THF, the $M(OTf)_3$ salts (M = Sc, La; 3–6% (mol/mol) vs $PhNH_2$) catalyzed the carbamation of $PhNH_2$ with MPC to give PhNHC(O)OMe with higher yield and selectivity. This is clearly emphasized in Table 2, where the carbomethoxylating properties of MPC and DMC toward $PhNH_2$, in the presence of the $M(OTf)_3$ (Sc, La) salts (under otherwise analogous reaction conditions: solvent, catalyst concentration, reactants concentration, etc.), are compared. The data in Table 2 clearly demonstrate that MPC is, not only more *reactive*, but also a more *selective* carbomethoxylating agent than DMC.

Carbamate yield and selectivity depend on the catalyst used and the experimental conditions. Table 3 summarizes the results obtained by using $Sc(OTf)_3$) (≈ 6% (mol/mol) vs $PhNH_2$). At 363 K, in THF (Entry 2, Table 3), the carbamation reaction was, by far, the favored process (selectivity ≈ 92%). The formation of *N*-methylation by-products (mainly Ph(Me)NH) was very modest, but tended to be more significant at higher temperatures, as observed, for example, at 393 K (Entry 3, Table 3).

La$(OTf)_3$ also promotes aniline carbomethoxylation by reaction with MPC, but it shows a lower catalytic activity than $Sc(OTf)_3$. Fig. 1 shows the catalytic activities of $Sc(OTf)_3$ and La$(OTf)_3$ in the carbomethoxylation of aniline

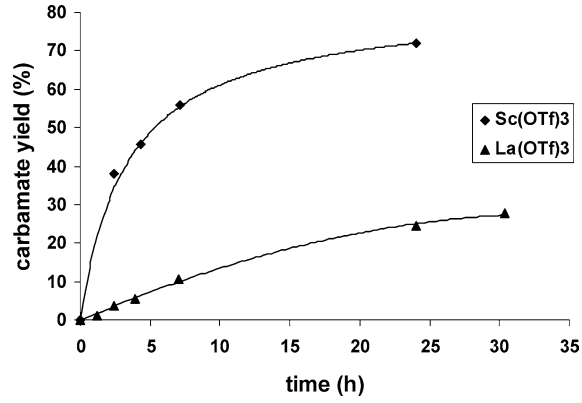


Fig. 1. Carbomethoxylation of $PhNH_2$ (0.100 mL, 1.096 mmol) with MPC (0.135 mL, 1.109 mmol) in the presence of $Sc(OTf)_3$ (0.03550 g, 0.073 mmol) or La$(OTf)_3$ (0.03735 g, 0.064 mmol), at 363 K. Solvent: THF (0.5 mL).

with MPC, at 363 K, under otherwise analogous reaction conditions. In the presence of the La salt, the carbamation reaction occurred more slowly, with lower selectivity (82%, after 30.4 h). In the case of $Sc(OTf)_3$ more than 56% of aniline was selectively (93%) converted into carbamate in less than 7.5 h. Afterward, the carbamation proceeded at a lower rate, with a slower increase of the conversion of the amine, until a plateau was reached corresponding to a yield close to 70% after about 24 h. If the fresh reactants (both $PhNH_2$ and MPC) are added to the reaction solution at the plateau (Fig. 2), the reaction restarted with a noticeable formation of more product (PhNHC(O)OMe). This proves that, at the plateau, the catalyst is still active, although not so effective as at the beginning.

This issue was studied in greater detail (see Section 2.2.2). We have found that aniline can undergo protonation and convert into the corresponding phenylammonium cation $PhNH_3^+$. This species is not reactive toward MPC and can be recovered at the end of the catalytic run as $(PhNH_3)OTf$. The formation of this salt may be explained according to

$$\begin{aligned} &L_nSc(OTf)_3 + x\,PhOH + x\,PhNH_2 \\ &\quad\rightarrow L_nSc(OPh)_x(OTf)_{3-x} + x(PhNH_3)OTf \\ &\quad L = \text{ligand} \end{aligned} \tag{4}$$

which suggests that the starting catalyst modifies during the catalytic run. We have tried to isolate Sc-phenoxy derivatives

Table 3
Reaction of $PhNH_2$ with MPC in the presence of $Sc(OTf)_3$[a]

Entry	MPC (mmol)	$Sc(OTf)_3$ (mmol)	Solvent[b] (mL)	*T* (K)	Time (h)	GC yield vs $PhNH_2$ (%)		
						PhNHC(O)OMe	Ph(Me)NH	$PhNMe_2$
1	1.109	–	0.5	363	23	< 1	< 1	Traces
2	1.109	0.073	0.5	363	24	72	5	< 1
3[c]	1.109	0.081	0.5	393	25	16	25	13
4	4.437	0.068	No solv.	363	22	52	7	12

[a] $PhNH_2$: 0.100 mL (1.096 mmol) in all the runs.
[b] Solvent: THF.
[c] At the working temperature (393 K), the selectivity of the carbamation process was very low. The GC-MS analysis of the reaction mixture revealed the formation of a few other by-products, whose identification and characterization are in progress.

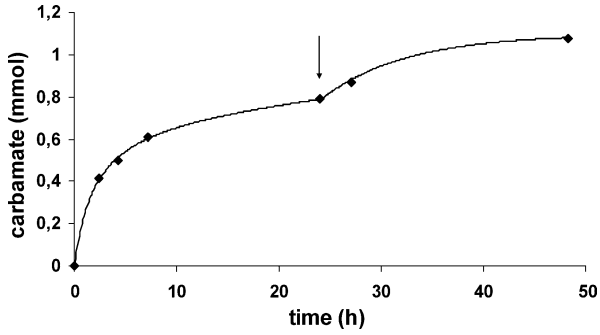


Fig. 2. Carbomethoxylation of $PhNH_2$ with MPC in the presence of $Sc(OTf)_3$ at 363 K: effect of further addition of the fresh reactants ($PhNH_2$ and MPC) at the plateau. Experimental conditions: MPC (0.135 mL, 1.109 mmol); $PhNH_2$ (0.100 mL, 1.096 mmol); $Sc(OTf)_3$ (0.03550 g, 0.073 mmol); solvent THF (0.5 mL). After 24 h, 0.100 mL (1.096 mmol) of $PhNH_2$ and 0.135 mL (1.109 mmol) of MPC were added.

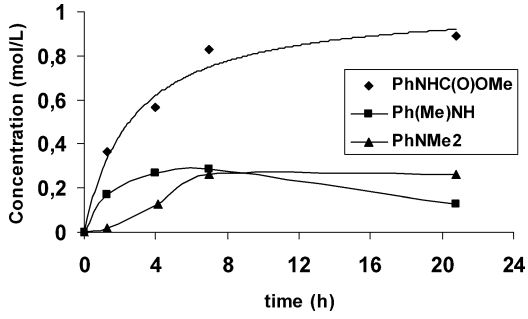


Fig. 3. Reaction of $PhNH_2$ (0.100 mL, 1.096 mmol) with MPC (0.540 mL, 4.437 mmol), used both as reagent and solvent, in the presence of $La(OTf)_3$ (0.03935 g, 0.067 mmol), at 363 K.

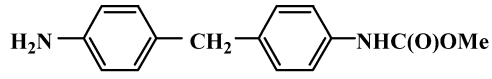
[36,37] from the reaction mixture. However, in no case such species could be obtained in a pure form.

The carbomethoxylation reaction was investigated, at 363 K, under solvent-free conditions, employing an excess of MPC (Entry 4 in Table 3 (Sc) and Fig. 3 (La)). Under these conditions, a marked decrease of both carbamate yield and selectivity was observed as a result of the increased incidence of the *N*-methylation reaction. In both cases (Entry 4 in Table 3 (Sc) and Fig. 3 (La)), after prolonged reaction times (> 20 h), the formation of $PhNMe_2$ was found to prevail significantly over that of Ph(Me)NH.

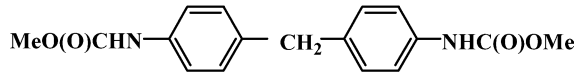
3.2. Carbomethoxylation of aromatic diamines with MPC in the presence of M(OTf)$_3$ (M = Sc, La) salts

We have extended the study also to a few industrially relevant aromatic diamines, such as MDA and TDA [32].

At 363 K, in THF as solvent, $Sc(OTf)_3$ (6% (mol/mol) vs diamine) effectively promotes the carbomethoxylation of MDA (1 eq) with MPC (2 eq), which react to give monocarbamate **1a** and dicarbamate **1b**,



1a



1b

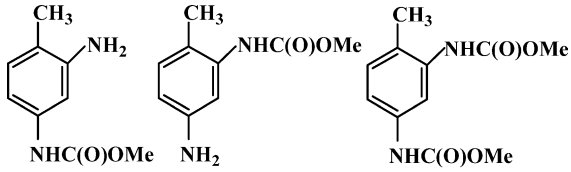
After 24 h, the overall carbamation yield was close to 80% with a selectivity as high as 94% (Entry 2, Table 4). Under these conditions the incidence of the *N*-methylation reaction was very modest as (4-methylaminophenyl)-4-aminophenylmethane (*m*/*z*: 212) and dimethylated MDA derivatives (*m*/*z*: 226) were formed with an overall yield not higher than 5%. *N*-Methyl monocarbamates (*m*/*z*: 270) were found only in trace amounts. Under comparable conditions, $La(OTf)_3$ (Entry 3, Table 4) proved to be a less effective and selective catalyst than $Sc(OTf)_3$. After 26 h at 363 K, the overall carbamate yield did not exceed 16%, with the almost exclusive formation of monocarbamate **1a**. Also the selectivity of the carbamation process was not so satisfactory (67%) as found for the Sc catalyst because of the relevant formation of *N*-methylated amines.

Under conditions analogous to those employed above for MDA, TDA showed quite a different behavior. As a matter of fact, in the presence of $Sc(OTf)_3$, the reaction of TDA with MPC, in THF, at 363 K, afforded monocarbamate **2a** as the major product (Entry 5, Table 4).

Table 4
Reactivity of MDA or TDA with MPC in the presence of $M(OTf)_3$ (M = Sc, La) salts, at 363 K

Entry	mmol of					THF[a] (mL)	Time (h)	Carbamate yield (%)[b]	
	MDA	TDA	MPC	$Sc(OTf)_3$	$La(OTf)_3$			Mono-	Di-
1	0.154	–	0.308	–	–	0.5	24	[c]	[c]
2	1.083	–	2.136	0.072	–	2	24	50	30
3	0.951	–	1.889	–	0.063	2	26	15	1
4	–	0.332	0.664	–	–	1	6	<1[d]	[c]
5	–	1.148	2.136	0.071	–	2	25	31[d]	1

[a] THF was the solvent.
[b] HPLC yield vs diamine.
[c] Not formed.
[d] Monocarbamate **2a**.



Regio-isomer **2a′** was formed only in very small amounts, most probably because carbomethoxylation of the vicinal amino group experiences steric constraints due to the proximity of the methyl group. This fact can also explain why dicarbamate **2b** formed much more slowly (1% yield, after 25 h) than **2a**. Nevertheless, the carbomethoxylation reaction was still the favored process, although selectivity toward carbamation (78%) was not so high as in the case of the corresponding reaction with MDA (94%).

In the experiments discussed above for both diamines (MDA or TDA) we found no experimental evidence for the formation of mono- and diphenyl carbamate esters or ureas. Accordingly, in the case of $PhNH_2$, by-products such as PhNHC(O)OPh or PhNHC(O)NHPh were found to form only in trace amounts. These features find an explanation in the different properties of phenoxy and methoxy groups as leaving groups, and considering the fact that urea formation usually requires more drastic conditions of temperature than those used in this work [13].

The above processes can be catalytically promoted also by nonmetal catalysts such as organo-phosphorous Brønsted acids $X_2P(O)OH$ [32]. With both classes of catalysts [the $M(OTf)_3$ (M = Sc, La) salts and $X_2P(O)OH$ acids], the carbamation of both diamines occurs under relatively mild temperature conditions (363 K), by far less severe than those required ($\geqslant$ 453 K) for the carbomethoxylation of the same systems with DMC in the presence of other catalysts [24]. The most efficient catalyst, among the organo-phosphorous acids investigated, was shown to be diphenylphosphinic acid $Ph_2P(O)OH$. Despite the lower catalyst loadings used in the present study (max 6% (mol/mol) of $M(OTf)_3$ vs diamine), $Sc(OTf)_3$ compares well, as carbomethoxylation catalyst, with $Ph_2P(O)OH$, which was used in higher catalytic amounts, up to 20% (mol/mol) vs diamine, in order to make up for its tendency to deactivate.

4. Discussion

In the presence of the same catalysts [$M(OTf)_3$ (M = Sc, La)] we effectively used for the carbamation of aliphatic amines [25], aromatic amines react with DMC in a different way from the aliphatic ones. Nevertheless, aniline, for instance, can be converted into methyl carbamate ester with good yield and selectivity, under not severe conditions, by employing a different substrate such as MPC, which has been shown to act as a carbomethoxylating agent, which is not only more reactive but also more selective than DMC. The latter features deserve attention as they can make attractive, from the applicative point of view, the use of MPC as carbomethoxylating agent in place of DMC, if they are usefully exploited to set up selective, high yield, non-energy-intensive, MPC-based carbamation processes.

The higher reactivity of MPC vs DMC as carbomethoxylating agent can be related, at least partly, to the different structures of the two substrates. This is clearly supported by a few experiments carried out with aliphatic amines in the absence of any added catalyst (see Section 2.5) and suggests that electronic effects rather than steric factors control the addition of the nucleophile (amine) to the carbonyl group [38]. The different chemical environments around the carbonyl group of MPC and DMC, by influencing the carbomethoxylating power of both substrates, can affect also the selectivity of these species as carbomethoxylating agents. In this regard, we note, also, that *N*-methylation, involving amine attack to MPC or DMC methyl group, is an irreversible process because the formed ROC(O)OH decomposes to ROH (R = Me or Ph) and CO_2 [39]. Conversely, amine attack to the carbonyl carbon atom of either MPC or DMC may take place, in principle, reversibly [40], and, in the case of MPC, subsequent conversion of the resulting tetrahedral intermediate into the carbamate product is greatly facilitated by the presence of a leaving group, such as phenoxide, better than methoxide. Nevertheless (see Table 2), a crucial role may also be played by the catalyst used, as the latter, by interacting with the substrate (DMC or MPC), can modify the substrate reactivity and affect the rates of the competitive processes (carbomethoxylation and *N*-methylation).

The nature of the metal center markedly influences the catalytic processes described above, as supported by the fact that $Sc(OTf)_3$ is a more effective and selective catalyst of reaction (3) than the homologue La salt. An analogous order of catalytic activity was previously found by us for the carbomethoxylation of aliphatic amines with DMC at room temperature [25]. The order observed in both cases matches well the relative oxophilicities of Sc^{3+} and La^{3+} as recently evaluated by tandem mass spectrometry [41], and can be related with the marked difference between the ionic radii of the two metal cations (Sc^{3+}, 0.89 Å; La^{3+}, 1.17 Å) [42]. In fact, the higher the Lewis acidity of the metal center, the more effective the activation of the substrate (MPC), which will exhibit enhanced electrophilic reactivity at the carbonyl group.

5. Conclusions

In the presence of $M(OTf)_3$ (M = Sc, La) salts, MPC can act as a carbomethoxylating agent of aromatic amines, which is not only more reactive but also more selective than DMC. In THF, under not severe conditions (363 K), both scandium and lanthanum triflate promote the carbamation of aromatic mono- and diamines by reaction with MPC, used as carbomethoxylating agent in place of DMC. Yield and se-

lectivity of the carbamation process are markedly influenced by the experimental conditions. $Sc(OTf)_3$ is a more effective and selective catalyst than the homologue La salt. Higher temperatures (> 363 K), or the use of MPC as both solvent and reactant, lower carbamate yield and selectivity, because of the higher incidence of *N*-methylation processes.

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