

# **Tin-Catalyzed Urea Alcoholysis With β-Citronellol: A Simple and Selective Synthesis of Carbamates**

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Abstract Tin(II) chloride is a stable and water tolerant Lewis acid, commercially available and less corrosive than Brønsted acid catalysts. Our proposal was demonstrated that SnCl<sub>2</sub> was an efficient catalyst on the urea alcoholysis with  $\beta$ -citronellol. We investigated the effects of main reaction parameters such as concentration and tin(II) catalyst nature, reagents stoichiometry and reaction temperature. In homogenous conditions with DMSO as solvent, the SnCl<sub>2</sub>-catalyzed urea alcoholysis reactions under air flux achieved high conversion and selectivity for  $\beta$ -citronellyl carbamate (ca. 90 and 95 %, respectively). Among tin(II) catalysts assessed, SnCl<sub>2</sub> was more active due to its total solubility. Possible intermediates of active Sn(II) species were discussed based on the results of catalytic runs and FT-IR spectroscopy measurements of the liquid phase after the reaction. FT-IR spectroscopy data showed that the active species could be a complex of a Sn(II) atom coordinated with N=C=O. This novel and phosgene-free selective process provide an inexpensive and attractive route to synthesize terpenic carbamates through inexpensive and renewable reactant (i.e. urea). Moreover, SnCl<sub>2</sub> was also an efficient catalyst on synthesis of  $\beta$ -citronellyl carbonate.

#### **Graphical Abstract**



**Keywords** Tin chloride · Urea · Terpenic alcohols · Carbamates

# **1** Introduction

The development of greener catalytic routes would be highly attractive mainly when feedstock are renewable and abundant as terpenic alcohols and urea [1, 2]. Monoterpenes are inexpensive raw material extracted from biomass and are extensively employed on the production of more added value chemicals and new drugs intermediates [3–5]. The urea is a low cost and widely affordable reactant, potentially applicable on production of plentiful

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commercial compounds [6]. Arguably, a highlighted instance is the dimethyl carbonate (i.e. DMC), which is a green solvent and environmentally benign reagent can be obtained through urea alcoholysis with methanol [7, 8].

In the reactions of urea alcoholises with short carbon chain alcohols, an alkyl carbamate intermediate can be thermally produced even in absence of a catalyst (ca. 413–453 K), and it is then converted to dialkyl carbonate through a reaction with a second molecule of alcohol. Several acid and alkaline catalysts, organic tin, metal oxides have been assessed in such reaction [9]. Among them, ZnO appears to be the most active, most likely due to its acid-base properties of its surface [10]. This is an alternative process to the standard method for preparing organic carbonates, which involves the treatment of alcohols with phosgene, highly toxic reactant [11]. The most common free-phosgene methods are the oxidative carbonylation, transesterification and the direct synthesis from carbon dioxide [12, 13]. Notwithstanding, the DMC synthesis via alcoholysis of the urea is a route much more attractive, due to availability of reactants and less harsh reaction conditions [14].

We have explored the combination of urea and terpenic alcohols to synthesize terpinyl carbamates, which are suitable substrates of pivotal importance for production of medicines, pesticides, polymers (i.e. polyurethanes), and protect groups in organic synthesis [15–18]. N-methyl terpinyl carbamates are biologically active compounds due to their molluscicidal effect [19].

In this work, we report an selective and straight synthesis procedure of terpinyl carbamates through urea alcoholysis with  $\beta$ -citronellol in presence of tin(II) chloride, which is water tolerant, easy to handle and less corrosive Lewis acid catalyst [20, 21]. To demonstrate the efficiency of SnCl<sub>2</sub> catalyst, we have assessed the effects of the main reaction parameters (i.e. temperature, nature and catalyst concentration, different molar ratio of urea to alcohol), in absence or presence of solvent.

## **2** Experimental Procedures

## 2.1 Chemicals

All chemicals are commercially available and utilized without prior handling. All tin salts were Sigma-Aldrich; SnSO<sub>4</sub> (>95 wt%), SnCl<sub>2</sub>.2H<sub>2</sub>O (99.9 wt%), SnF<sub>2</sub>, SnBr<sub>2</sub> and Sn(CH<sub>3</sub>COO)<sub>2</sub> (99 wt%).  $\beta$ -citronellol (95 wt%) was purchased from Sigma-Aldrich. Dimethyl sulfoxide (99 wt%) was acquired from Sigma and used without further treatment. Urea (99.5 wt%) was GE.

#### 2.2 Catalytic Runs

Catalytic runs were carried out in a three neck round bottom glass reactor (50 mL) equipped with a magnetic stirrer and sampling septum. Typically,  $\beta$ -citronellol (2.375 mmol) and urea were dissolved in DMSO (15 mL solution) at adequate molar ratio and the solution was stirred and heated to reaction temperature (ca. 403–443 K).

In the solventless reactions, urea was solved in pure  $\beta$ citronellol (10 mL) at suitable molar ratio heating the solution to reaction temperature. Then, after adding Sn(II) catalyst (ca. 10 mol%) the reactions were started. Quantitative determinations on the reaction solutions were performed through GC analyses of aliquots taken at regular time intervals (Shimadzu GC 2010 instrument, FID, fitted with Carbowax 20 M capillary column). In solvent-free reactions, the dilution of aliquots with DMSO adjusted the  $\beta$ -citronellol concentration to the calibration curve.

## 2.3 Purification and Products Identification

The main reaction products were purified trough liquid– liquid extraction procedures. The addition of ethyl acetate to net reaction precipitated oligomers. The organic phase was extracted with aqueous NaCl solution, allowing the separation of the DMSO solvent. Unreacted  $\beta$ -citronellol and  $\beta$ -citronellyl carbamate (or  $\beta$ -citronellyl carbonate) were separated by chromatography on silica column.

The mass spectra of the reaction products were obtained on a Shimadzu MS-QP 2010 ultra mass spectrometer instrument, operating at 70 eV, coupled to a Shimadzu 2010 GC. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on the Mercury-300 Varian Spectrometer at 300 and 75 MHz respectively, in *d*-methanol solution using TMS as internal reference. FT-IR/ATR spectroscopy analyses were carried out in Varian 660 FT-IR Spectrometer. The spectroscopic data of the  $\beta$ -citronellyl carbamate (Fig. 1) are shown as follow.





#### 2.4 Spectroscopic Data

<sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>OD): δ (integration, multiplicity, coupling constant, attribution); δ 0.92 (d, 3H, J = 6.5 Hz, H-10); 1.09–1.46 (m, 5H, H-2/H-3/H-4); 1.60 (s, 3H, H-8); 1.67 (s, 3H, H-9); 1.95–2.05 (m, 2H, H-5); 4.04–4.12 (m, 2H, H-1); 4.56 (s, -NH<sub>2</sub>); 5.10 (t, 1H, J = 7,2 Hz, H-6).

<sup>13</sup>C NMR (75 MHz, CD<sub>3</sub>OD): δ (integration, multiplicity, coupling constant, attribution); δ 17,74 (C-8); 19.83 (C-10); 25.92 (C-5); 26.45 (C-9); 30.55 (C-3); 37.09 (C-4); 38.22 (C-2); 64.13 (C-1); 125.72 (C-6); 132.12 (C-7); 160.30 (OCONH<sub>2</sub>).

(FT-IR/ATR) v(cm<sup>-1</sup>): 3460; 3350; 3200 (v N–H); 2960; 2910; 2860 (v C-H); 1710 (v C=O carbamate); 1330 (v assim. N-CO–O); 1070 (v C-O); 1600 ( $\delta$  N–H); 1410 ( $\delta$ CH<sub>3</sub>); 1450 ( $\delta$  CH<sub>2</sub>); 840 ( $\gamma$  sim N–CO–O); 780 ( $\gamma$  N–H).

GC-MS (m/z/relative intensity): 138/40; 123/68; 109/31; 95/86; 81/100; 67/71; 55/46 and 41/63.

#### **3** Results and Discussion

# 3.1 General Aspects

In most of urea alcoholysis processes, the alkyl carbonates are the main goal. Herein, the focus was to synthesize terpinyl carbamates through urea alcoholysis, generating compounds potentially active as agrochemicals and drugs intermediate (Scheme 1).

El-Zemity et al. have synthesized terpinyl carbamates through reaction of isocyanate and terpenic alcohols in the presence of a catalytic amount of triethylamine [22]. However, despite 70 % yielding, it was necessary 1 week to complete the reaction at room temperature. Lewis acids such as organotin(IV) compounds have shown active in reactions of urea alcoholysis to synthesize alkyl carbonates, being an option to the enzymatic or alkaline catalysts [23]. Nonetheless, organotin(IV) catalysts require expensive and laborious synthesis conditions.

# 3.2 Effects of Sn(II) Catalyst Nature on Urea Alcoholysis with β-Citronellol

Conversely, commercially available tin salts are low cost catalysts and have been active in plentiful organic reactions [24–26]. Nevertheless, as far we know the activity of Sn(II) catalysts on terpenic carbamates synthesis was not yet report.

Thus, initially we have assessed the catalytic activity of different tin salts on urea alcoholysis with  $\beta$ -citronellol. Kinetic curves and main results are summarized in Fig. 2 and Table 1, respectively.

The choice of temperature is a key-aspect on these reactions. In general, the urea alcoholysis reactions are carried out temperatures between 423 and 453 K; however, in the reactions carried out to these temperatures monoterpenes may have been converted to oligomers [9, 27]. Thus, to screening of tin catalyst, the reactions were performed at relatively moderate temperature (ca. 413 K).

A comparison between the consumed substrate GC peak area and those of the products formed during the reaction allowed determining the oligomers amount. Although blankreactions have reached a conversion comparable to those of the catalyzed-reactions, in the absence of catalyst the carbamate selectivity was drastically minor. In according with Table 1, the oligomerization was much more pronounced in the reactions carried out in absence of tin catalyst.

Remarkably, the presence of Sn(II) cations in the solution decreases the oligomerization and improves the carbamate selectivity. We suppose that Sn(II) coordination to urea carbonyl group makes more favorable its attack by the hydroxyl group of alcohol. Thus, it was possible that tin catalysts containing ligands with high electron withdrawing character could be more active [28]. Nevertheless, among catalysts tested, only the SnCl<sub>2</sub> was totally soluble. Therefore, to compare the effect of different anions on activity of the tin(II) catalysts was difficult due to the different solubility.

The  $SnCl_2$  was the most selective catalyst and it was selected to evaluating the effect of others reaction variables. It is important **to** highlight that in all the experiments it was important showing the conversion and selectivity achieved in the blank-reactions, which can be affected by the variation of parameters such as reactants stoichiometry and temperature reaction.

# 3.3 Effect of Catalyst Concentration in the SnCl<sub>2</sub>-Catalyzed Urea Alcoholysis with β-citronellol

The solubility of tin chloride catalyst in the reaction medium was dependent of the concentration and limited the assessing range of 0-20 mol% (Table 2).

In all catalytic runs where the  $SnCl_2$  salt was completely soluble, an increase on catalyst concentration until to







Fig. 2 Kinetic curves of tin(II)-catalyzed urea alcoholysis reactions with  $\beta$ -citronellol. *Reaction conditions* molar ratio of urea to  $\beta$ -citronellol (1:20); temperature (413 K); catalyst (15 mol%) DMSO (15 mL)

15 mol% resulted in an increase on the reaction rate (Fig. 3). However, when it was used with highest load (ca. 20 mol% concentration), the  $SnCl_2$  was partially soluble; consequently, only a poor conversion and selectivity could be obtained (see Fig. 5; Table 2).

Kinetic curves obtained by variation  $SnCl_2$  load showed that initial rate of reaction were proportional to increasing on catalyst concentration in solution (Fig. 3).

An only exception was verified when 20 mol% catalyst was used; nevertheless, at this concentration the  $SnCl_2$  became almost insoluble within first 10 min of reaction. So, similarly to the others insoluble tin(II) catalysts (see Table 1; Sect. 3.2), the activity of  $SnCl_2$  was noticeably lower when it was not totally solved in reaction solution.

We have find that the both  $\beta$ -citronellyl carbamate selectivity and reaction conversions were equally improved by the increasing on catalyst concentration (Table 3). It was suggestive that the presence of tin(II) cations in solution promoted the citronellol carbamoylation reaction and inhibited its conversion to oligomers (Fig. 4). Thus, from this point forward all the catalytic tests were carried out using catalyst at 15 mol% concentration.

# **3.4** Effect of Temperature in the SnCl<sub>2</sub>-Catalyzed Urea Alcoholysis with β-Citronellol

Since the carbamate formation can occur even in absence of catalyst, we have assessed this effect also in the catalyzed or non-catalyzed reactions (Table 3). The kinetic curves obtained carrying reactions with catalyst are displayed in the Fig. 4.

In general, an increase of the temperature resulted in an increase on reaction conversion and selectivity of  $\beta$ -citronellyl carbamate, regardless the presence or not of catalyst (Table 3). Conversely, although also favored by

Run	Catalyst	Conversion <sup>a</sup> (%)	Selectivity <sup>a</sup> (%)			
			β-citronellyl carbamate	oligomersb		
1	_	41	20	80		
2	$SnF_2$	47	69	31		
3	$SnCl_2$	57	85	15		
4	SnBr <sub>2</sub>	49	58	42		
5	$SnSO_4$	48	71	29		

*Reaction conditions* β-citronellol (2.375 mmol); urea (47.5 mmol); temperature (413 K); catalyst (15 mol%) DMSO (15 mL)

<sup>a</sup> Determined by GC

' Calculated from mass balance of reaction

Table 2	Effect of SnCl <sub>2</sub>
concentra	ation in the urea
alcoholys	sis reaction with
β-citrone	llol

**Table 1** Effect of tin catalyst on urea alcoholysis with

β-citronellol

SnCl <sub>2</sub> (mol%)	Conversion (%)	Product selectivity (%)			
		β-citronellyl carbamate	Oligomers		
0	39	20	80		
5	54	58	42		
10	55	57	43		
15	57	85	15		
20.0	30	46	54		
	SnCl <sub>2</sub> (mol%) 0 5 10 15 20.0	SnCl <sub>2</sub> (mol%)       Conversion (%)         0       39         5       54         10       55         15       57         20.0       30	$\begin{array}{c} {\rm SnCl}_2 \ ({\rm mol}\%) & {\rm Conversion} \ (\%) & \\ \hline \\ 0 & \\ 39 & \\ \\ 5 & \\ 54 & \\ 58 & \\ 10 & \\ 55 & \\ 57 & \\ 15 & \\ 57 & \\ 85 & \\ 20.0 & \\ 30 & \\ \hline \\ \end{array} \begin{array}{c} {\rm Product \ selectivity} \ (\%) & \\ \hline & \\ \hline & \\ \hline & \\ \hline \\ \hline \\ \hline \\ \hline \\ \hline$		

Reaction conditions β-citronellol: urea ratio molar (1:20); temperature (413 K); time (2 h); DMSO (15 mL)



Fig. 3 Effect of SnCl<sub>2</sub> catalyst concentration on the kinetic curves of urea alcoholysis reactions with β-citronellol. Reaction conditions βcitronellol: urea molar proportion (1:20); temperature (413 K); time (2 h); DMSO (15 mL)

temperature increases, the oligomer formation was always higher in the reaction in absence of a catalyst SnCl<sub>2</sub>.

The changes triggered by the increasing of temperature were more noticeable on SnCl<sub>2</sub>-catalyzed reaction rates than one in absence of catalyst (Fig. 4). Mainly at temperatures higher than 423 K, the highest conversion was achieved within first 45 min of the reaction.

# 3.5 Effect of Reactants Molar Ratio in the SnCl<sub>2</sub>-Catalyzed Urea Alcoholysis Reaction with β-Citronellol

The effect of reactants stoichiometry on conversion and reaction selectivity was evaluated in the proportion of 1:5 to 1: 30 of  $\beta$ -citronelol: to urea in the presence or absence of catalyst (Fig. 5).

We have found that either initial rate of reaction (i.e. not shown herein) as well as final conversion were not affected by variation on reactant proportion (ca. maximum of

Table 3 the SnCl



Fig. 4 Temperature effects on urea alcoholysis with β-citronellol in the presence of the SnCl<sub>2</sub> catalyst. *Reaction conditions* β-citronellol: urea molar ratio (1:20); DMSO (15 mL); reaction time (2 h). SnCl<sub>2</sub> (10 mol%)

conversion equal to 45 and 55 %, in the absence or presence of SnCl<sub>2</sub>, respectively, 1:20 citronellol urea molar ratio). Nonetheless, different of conversion, the reaction selectivity was strongly impacted. The reaction's selectivity was remarkably improved by the combination of usage a high molar ratio of urea to  $\beta$ -citronellol in presence of SnCl<sub>2</sub> catalyst.

The selectivity of reactions were remarkably improved by the combination of the use of a high molar ratio of urea to  $\beta$ -citronellol in presence of tin(II) chloride catalyst. Whilst in the catalyst absence the substrate oligomerization compromised the selectivity of carbamate, in the catalytic reactions the  $\beta$ -citronellol was majority converted to  $\beta$ citronellyl carbamate, achieving the highest (ca. 85 %) when an excess of twenty times of urea to  $\beta$ -citronellol was employed (Fig. 5).

Although acceptable selectivity obtained in the reactions (i.e. compared to the literature), the conversion of processes did not exceed 60 % [19]. The uses of urea excess

Table 3 Temperature effects in the SnCl <sub>2</sub> -catalyzed β-	Run	T (K)	Conversion <sup>a</sup> (%)		Products selectivity <sup>a</sup> (%)			
citronellol carbamoylation					β-citronellyl carbamate		Oligomers <sup>b</sup>	
through urea alcoholysis			Blank	SnCl <sub>2</sub>	Blank	SnCl <sub>2</sub>	Blank	SnCl <sub>2</sub>
	1	403	32	37	16	67	84	33
	2	413	41	54	22	85	78	15
	3	423	43	57	40	85	60	15
	4	433	44	58	75	97	25	3
	5	443	60	60	74	90	26	10

Reaction conditions β-citronellol (2.375 mmol); urea (47.5 mmol); SnCl<sub>2</sub> (15 mol%); DMSO (15 mL); 2 h <sup>a</sup> Determined by GC

<sup>b</sup> Calculated from mass balance of reaction



Fig. 5 Effect of reactants stoichiometry on the urea alcoholysis with  $\beta$ -citronellol in absence (a) or presence of SnCl<sub>2</sub> (b). a Without catalyst reactions. b SnCl<sub>2</sub>-catalyzed reactions. Reaction conditions:

may be a suitable strategy to improve conversion. Urea is an inexpensive reactant and its use in excess had a beneficial effect on the reaction selectivity.

Indeed, the consumption excessive of urea could be a negative aspect. Nonetheless, the urea is essential on reaction to provide CNO<sup>-</sup> species, which will be more easily attacked by the  $\beta$ -citronellol when coordinate to the Sn(II) catalyst (see Sect. 3.9). Therefore, an excess of urea is desirable for the improvement of conversion and reaction selectivity. Moreover, the thermal decomposition becomes important because provide the CNO<sup>-</sup> species.

Nevertheless, we could not explore further this option because when used in equal amount or greater than twenty times in relation to  $\beta$ -citronellol its solubility in the reaction medium was not complete.

# 3.6 Reactions of Urea Alcoholysis with β-Citronellol Carried Out Under Air Flux

Alternatively to increase the urea amount, since that the urea alcoholysis is a reversible reaction, we tried to shift equilibrium toward the products removing the ammonium generated throughout the process.

We find out that by removing the volatile products from the reaction through the air flux shifted the reaction equilibrium toward the higher formation of  $\beta$ -citronellyl carbamate (Fig. 6a). This effect was noticeable only on the catalyzed reactions (Fig. 6b). It is possible that ammonia formed during the reaction act blocking the tin(II) catalyst, that resulted in an decrease **of** its activity. Nonetheless, in absence of catalyst, only a poor selectivity for  $\beta$ -citronellyl carbamate was achieved under air flux. Thus the formation of oligomers was preferentially favored.



 $\beta\text{-citronellol}$  (2.375 mmol); SnCl2 (10 mol%); DMSO (15 mL); T (413 K); 2 h. Determined by GC. Calculate from mass balance of reaction

Remarkably, after 120 min of reaction heated to 413 K temperature and using reactants at 1:20 molar ratio we have achieved highest  $\beta$ -citronellyl carbamate selectivity (ca. 93 %) and high conversion (ca. 88 %) as show the Fig. 6a. This result is highly superior to that reached in the reactions without flux of air, where although a high  $\beta$ -citronellyl carbamate selectivity (ca. 85 %), the maximum conversion was ca. 54 % (Table 1).

# 3.7 Solvent-Free SnCl<sub>2</sub>-Catalyzed Urea Alcoholysis Reaction

To agree with principles of green chemistry, it is desirable to carry the reactions respecting the environmentally benign conditions. On this regard, always when possible, the usage of solvent should be avoided, or alternatively, the use of biodegradable and less pollutant solvent, such as alcohols or not halogenated solvents. However, the urea alcoholysis requires high temperatures (ca. 413–443 K), which implies that solvents must have high boiling point, or alternatively, it should be used under high pressures.

Therefore, the DMSO was solvent selected herein; it has a high boiling point, avoids that reactions are carried out under high pressures, an arguably unfavorable condition for reactions where products gas such as NH<sub>3</sub> are formed. As  $\beta$ -citronellol is a liquid with high boiling point (ca. 498 K), a nice approach would be to carry reactions without solvent. Figure 7 summarizes the main results.

It is important noting that to carry the reactions without solvent brought some experimental difficulties. The low solubility of urea in the pure  $\beta$ -citronelol was an aspect that hampered the assessing of the solventless reactions, mainly when an excess of urea was used. Indeed, at proportions



**Fig. 6** Effect of air flux on the conversion (**a**) and selectivity (**b**) of urea alcoholysis reactions with  $\beta$ -citronellol in the absence or presence of SnCl<sub>2</sub> catalyst. **a**  $\beta$ -citronellol conversion. **b**  $\beta$ -citronellyl

higher than 1:1 (i.e.  $\beta$ -citronellol to urea), the urea was insoluble in the  $\beta$ -citronellol. To circumvent this obstacle, we tried adding small amounts of DMSO to increase urea solubility. Nevertheless, the system became biphasic. Therefore, the solvent-free reactions were carried out using 1:1 proportion of urea to  $\beta$ -citronellol. Moreover, also due to the solubility problems, the reactions were carried out with 5 mol% of catalyst (Fig. 8).

Although low molar ratio, the urea undergoes fast decomposition in the beginning of the reaction, when pure



Fig. 7 Comparing reactions of  $\beta$ -citronellol with urea in absence or presence of solvent. *Reaction conditions in DMSO*  $\beta$ -citronelol to urea molar ratio (1:20); DMSO (15 mL); temperature (413 K); time (2 h). SnCl<sub>2</sub> (15 mol%). *Reaction conditions in DMSO*  $\beta$ -citronelol to urea molar ratio (1:20); DMSO (15 mL); temperature (413 K); time (2 h). SnCl<sub>2</sub> (15 mol%). *Reaction conditions without DMSO*  $\beta$ citronellol to urea molar ratio (1:1); temperature (413 K); time (2 h). SnCl<sub>2</sub> (5 mol%)



carbamate selectivity.  $\beta$ -citronellol (2.375 mmol); urea (47.5 mmol); DMSO (15 mL); temperature (413 K); time (2 h). SnCl<sub>2</sub> (15 mol%)

 $\beta$ -citronellol was the liquid phase employed. The immediate formation of white vapor inside the reactor comprised its decomposition. Probability, the rapid consume of the urea resulted in the low selectivity of carbamate obtained in the solvent-free reactions (Fig. 7). Thus, notwithstanding the high  $\beta$ -citronellol conversion, the target product (i.e. carbamate) was minority (ca. 15 %) and oligomers were the major product (ca. 85 %). Therefore, we can conclude that in this case it is not favorable to carry reactions without solvent.

# 3.8 Synthesis of the Carbonate β-Citronellyl Through SnCl<sub>2</sub>-Catalyzed Carbamate βcitronellyl Alcoholysis Reaction with β-Citronellol

The catalytic activity of  $\text{SnCl}_2$  was investigate in the reactions of synthesis of terpenic carbonates, which are products with potential biologic activity [19]. We employed a slight excess of  $\beta$ -citronellol to shift equilibrium toward of desired product ( $\beta$ -citronellyl carbonate) (Scheme 2).

The carbamate  $\beta$ -citronellyl conversion to  $\beta$ -citronellyl carbonate achieved 83 % after 10 h of reaction. We should highlight that literature described that long period of time (ca. 1 week) were required to complete this reaction at room temperature [22].

The oligomers amount was calculated by comparing the area consumed of  $\beta$ -citronellol GC peak and the area consumed of  $\beta$ -citronellyl carbamate GC peak (i.e. after adequate correction by the response factor). Noteworthy that after 4 h the reaction achieved the highest selectivity for  $\beta$ -citronellyl carbonate (ca. 80 %).



#### 3.9 Mechanistic Insights

To assess the reaction mechanism, we firstly recorded FT-IR spectra of the pure reactants (i.e.  $\beta$ -citronellol, urea), SnCl<sub>2</sub> catalyst and also of the reaction mixture (Fig. 9a). FT-IR spectroscopy measurements were a strategy successfully employed by Zhank et al. to elucidate the adsorption mechanism of the reactants on dimethyl carbonate synthesis from urea methanolysis [29].

Additionally, we measured these spectra in absence of  $\beta$ -citronellol (Fig. 9b). The DMSO displays strong absorption bands in the wavenumber region between 350 and 550 cm<sup>-1</sup> and was not be used as solvent.

Herein, the main goal it was to detect a possible formation of the intermediates obtained from  $SnCl_2$  catalyst and  $\beta$ -citronellol or urea (Fig. 9). The absorption band of stretching of the Sn–Cl bond is present in the spectra of pure SnCl<sub>2</sub> or mixtures of urea/SnCl<sub>2</sub> Nonetheless, it was not possible to detect the Sn–O bond absorption bands on the reaction mixture (i.e.  $\beta$ -citronellol/urea/SnCl<sub>2</sub>, Fig. 9a).

Indeed, FT-IR spectrum of  $\beta$ -citronellol has strong absorption bands on the region of 350–550 cm<sup>-1</sup>, where typically are the absorption bands assigned to the vibration of Sn–O or Sn–N bonds [30, 31]. Therefore, we tried measure the spectra of mixture SnCl<sub>2</sub>/urea in absence of  $\beta$ -citronellol. The FT-IR spectrum of reaction mixture in liquid phase (i.e. melted urea and SnCl<sub>2</sub>) provides the

typical absorption bands of Sn–O and Sn–N bonds (ca. 513 and  $385 \text{ cm}^{-1}$ , respectively, Fig. 9c).

As can be seen in Fig. 9c, we have detected the absorption bands related to vibration of Sn–N or Sn–O bonds (i.e. urea/SnCl<sub>2</sub>), nevertheless, it was not possible to identify the absorption bands relative to the intermediate where both reactants (i.e. urea and  $\beta$ -citronellol) would be coordinate to the tin(II) catalyst.

Although some of the FT-IR spectra did not be conclusive, we find out an auspicious resulted after catalytic runs; we verified via GC–MS analysis that OCNH (i.e. isocyanic acid) were present in the reaction aliquots.

The formation of isocyanic acid can be explained by the thermal decomposition of urea as depicted by Scheme 3, which may have occurred throughout reaction of  $SnCl_2$ -catalyzed urea alcoholysis with  $\beta$ -citronellol.

The literature data and experimental results led us to propose a reaction mechanism for the SnCl<sub>2</sub>-catalyzed urea alcoholysis where isocyanic acid plays a vital role [32]. As depicted in Scheme 3, the thermal decomposition of urea produces ammonia and isocyanic acid molecules. The reaction of isocyanic acid with an alcohol molecule and SnCl<sub>2</sub> may give an tin(II) intermediate, where both alcohol and isocyanic acid are weakly coordinated to the tin chloride [33].

To verify this hypothesis, we carried out FT-IR measurements after heating of samples OCNK/SnCl<sub>2</sub> under



Scheme 2 SnCl<sub>2</sub>-catalyzed carbamate  $\beta$ -citronellyl alcoholysis reaction with  $\beta$ -citronellol





(c)

FT-IR spectra of b

Fig. 9 FT-IR spectra of the  $\beta$ -citronellol, urea and reaction mixture ( $\beta$ -citronellol/ urea/ SnCl<sub>2</sub> (9a); urea, SnCl<sub>2</sub> and its mixture (9b); region of low wavenumber of the spectrum of b (9c). Reaction conditions: (9a)  $\beta$ -citronellol (5.8 mmol); (9a and 9b): urea



Scheme 3 Thermal decomposition of urea into isocyanic acid and ammonium

reaction conditions. Additionally, were recorded spectra of these pure compounds, which are also presented in the Fig. 10.

The FT-IR spectroscopy measurements showed an absorption band at  $385 \text{ cm}^{-1}$ , assigned to the stretching of the Sn–N bond. It is suggestive that isocyanate anion, responsible by the absorption band at wavenumber  $1325 \text{ cm}^{-1}$ , may be coordinate to the tin(II) via nitrogen atom [31]. Another significant result was the absence of the



(5.8 mmol); SnCl2 (5 mol%), temperature (413 K); time of reaction

(30 min); (9c) region of low wavenumber obtained from expansion

**Fig. 10** FT-IR spectra obtained from SnCl<sub>2</sub>, pure KCNO and mixture of them. *Conditions* The mixture was heated to 413 K by 30 min; KCNO/ SnCl<sub>2</sub>, (1:1 molar ratio, *ca.* 0.29 mmol) 0.29 mmol)

Scheme 4 Possible reaction mechanisms proposed for the synthesis of  $\beta$ -citronellyl carbamate from SnCl<sub>2</sub>catalyzed urea alcoholysis with  $\beta$ -citronellol



absorption bands of Sn–Cl bonds; these bands are commonly found at  $305 \text{ cm}^{-1}$  [34, 35]. These observations may means that these anionic ligands were replaced by the isocyanate anion.

Therefore, inspired by Fujita et al. and based on experimental data obtained by us, we have built a mechanistic proposal, depicted in the Scheme 4 [36]. Fujita et al. have assessed the catalytic activity of Zn(II) compounds on the urea glycerolysis, in order to produce glycerol carbonate. As in the present work, they also have detected intermediate species via FT-IR spectroscopy, which were assigned to intermediates that support its mechanistic proposal [36]. The coordination of isocyanic acid to the metal center (i.e. Zn, Al) in urea alcoholysis reactions was also proposed by other groups such as Wei et al. [37].

After be heated to the reaction temperature, urea was thermally decomposed into isocyanic acid and ammonium (Scheme 3). Because FT-IR spectroscopy measurements suggested that chloride ions are absent, it is reasonable that they were released as  $NH_4Cl$  besides ammonium generated by the thermal decomposition of urea.

Thus,  $\text{SnCl}_2$  may react with isocyanic acid generating complex 1, which has two ammonia molecules weakly coordinated to the tin(II). The exchanges of the ammonia molecule by the  $\beta$ -citronellol may result in the complex 2, where the alcohol will be coordinated to the Sn(II) via oxygen atom (Scheme 4). We suppose that hydroxyl group of  $\beta$ -citronellol may has an intermolecular interaction with the neighboring isocyanate group, producing a carbamate intermediate complex 3. The coordination of alcohol through the oxygen atom to the metal center was also previously described in Zn(II)-catalyzed urea glycerolysis reactions, where the glycerolate species were detected [36].

It is important to note that we did not assure that alcooltin(II) intermediate was truly formed, because no evidence could be detected. Indeed, SnCl<sub>2</sub> is hydrate salt that displays absorption bands at 513 cm<sup>-1</sup> wavenumber. These bands were attributed to the Sn–O bonds due to water present in the tin(II) salt, and were found even in the FT-IR spectra of pure SnCl<sub>2</sub> [38, 39]. Therefore, the bands resulting of the  $\beta$ -citronellol coordination to the Sn(II), probably may have been overlapped by the bands originated from Sn–O (i.e. oxygen atom of water).

The formation of the Sn(II)-alcohol intermediate is favored by remove of ammonium from reaction medium. We experimentally confirm that reaction conversions were improved when ammonium was removed by using of air flux.

After the formation of the complex 2 containing a carbamate ligand coordinated to the Sn(II), it may be then converted to  $\beta$ -citronellyl carbamate, releasing ammonia. Then, after isocyanic acid be coordinates once more to the tin(II), the active specie can be then regenerated and restart the catalytic cycle.

It is important to note that the Lewis acidity of tin(II) displays an important role on formation of intermediate with containing isocyanate ligand and  $\beta$ -citronellol. The electron acceptor character of the empty orbitals belonging to the Sn(II) (i.e. "p" orbitals) is determining to allow that this intermediate can be formed because it should be able to accommodate electrons of the hydroxyl oxygen atom and nitrogen atom belonging to the isocyanate group.

# 4 Conclusions

A straightforward and selective process to synthesize terpenic carbamate was achieved through the use of SnCl<sub>2</sub> catalyst in urea alcoholysis reactions with  $\beta$ -citronellol SnCl<sub>2</sub> is an inexpensive, commercially available and water tolerant Lewis acid was the most active and selective among the tin(II) catalyst assessed,. Remarkably, the presence of SnCl<sub>2</sub> in DMSO solution was a key-aspect to conversion of  $\beta$ -citronellol to carbamate; in absence of catalyst, the  $\beta$ -citronellol was preferentially converted to oligomers. Conversely, in presence of SnCl<sub>2</sub>, the carbamate selectivity was arguably favoured (ca. 85 % selectivity, ca. 54 % conversion). In similar reaction conditions,  $\beta$ citronellyl carbonate was selectively obtained (ca. 80 %). The removing of ammonium generated during the carbamoylation reactions using air flux notably increased process selectivity. Under those conditions, SnCl<sub>2</sub> catalyst efficiently promoted the  $\beta$ -citronellol conversion to  $\beta$ citronellyl carbamate achieving high conversion (ca. 88 %) and selectivity (ca. 93 %) after 2 h of reaction at 413 K. The low solubility of urea in pure  $\beta$ -citronellol hampered the solventless reactions. Investigating the effect of reaction parameters, we find out that  $\beta$ -citronellyl carbamate selectivity was highly dependent on the molar ratio of urea to  $\beta$ -citronellol. However, in proportions higher than 20:1 the urea it is not completely soluble in reaction medium. The reaction mechanism was assessed via FT-IR spectroscopy analyses, carrying reactions under different conditions. The presence of isocianate (CNOH) at reaction end was verified by GC-MS analysis. FT-IR spectroscopy measurements showed that the active species could be a complex of a Sn(II) atom coordinated with N=C=O. The tin-catalyzed urea alcoholysis is phosgene-free reaction, more selective and faster than processes for synthesis of terpenic carbamates reported in the literature.

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#### References

- 1. Gallezot P (2007) Catal Today 121:76
- 2. Carari DM, Da Silva MJ (2012) Catal Lett 142:251
- 3. Chapuis C, Jacoby D (2001) Appl Catal A 221:93
- Lenardao EJ, Botteselle GV, Azambuja F, Perin G, Jacob RG (2007) Tetrahedron 63:6671
- 5. Ortar G, Moriello AS, Morera E, Nallia M, Di Marzo V, De Petrocellis L (2014) Bioorg Med Chem Lett 24:5507
- Wua X, Kanga M, Yina Y, Wang F, Zhao N, Xiao F, Wei W, Suna Y (2014) Appl Catal A 473:13
- 7. Zhang C, Lu B, Wang X, Zhao J, Cai Q (2012) Catal Sci Technol 2:309
- Cornely J, Ham LMS, Meade DE, Dragojlovic V (2003) Green Chem 5:34
- Wang D, Yang B, Zhai X, Zhou L (2007) Fuel Process Technol 88:807
- Wang P, Liu X, Zhue F, Yang B, Alshammari AS, Deng Y (2015) RSC Adv 5:19534
- Saleh RY, Michaelson RC, Suciu EN, Kuhlmann B (1996) US Patent No. 5561094
- Bhanage BM, Fujita S, He Y, Ikushima Y, Shirai M, Torii K, Arai M (2002) Catal Lett 83:137
- Leino E, Mäki-Arvela P, Eta V, Murzin DY, Salmi T, Mikkola JP (2010) Appl Catal A 383:1
- Wang M, Wang H, Zhao N, Wei W, Sun Y (2007) Ind Eng Chem Res 46:2683
- 15. Woods G (1994) The ICI polyurethanes book. Wiley, New York
- 16. Rice PJ, Coats JR (1994) Pestic Sci 41:195
- Rios ER, Rocha NF, Carvalho AM, Vasconcelos LF, Dias ML, De Sousa DP, de Sousa FC, Fonteles MM (2013) Chem Biol Interact 203:573
- 18. Wuts PGM, Greene TW (2007) Greene's Protective Groups in organic synthesis. Wiley, Hoboken

- 19. El-Zemity SR (2006) J Appl Sci Res 2:86
- 20. Da Silva MJ, Da Silva ML, Figueiredo AP, Cardoso AL, Natalino R (2011) J Am Oil Chem Soc 88:1431
- Menezes FL, Guimaraes MDO, Da Silva MJ (2013) Ind Eng Chem Res 52:16709
- 22. Radwan MA, El-Zemity SR, Mohamed SA, Sherby SM (2008) Ecotoxicol Environ Safe 71:889
- Suciu EN, Kuhlmann B, Knudsen GA, Michaelson RC (1998) J Organomet Chem 556:41
- 24. Cardoso AL, Neves SCG, Da Silva MJ (2009) Energ Fuel 23:1718
- 25. Da Silva MJ, Goncalves CE, Laier LO (2011) Catal Lett 141:1111
- 26. Yamaguchi S, Motokura K, Sakamoto Y, Miyaji A, Baba T (2014) Chem Commun 50:4600
- 27. Golets M, Ajaikumar S, Blomberg D, Grundberg H, Wärnå J, Salmi T, Mikkola J-P (2012) Appl Catal A 43:435
- 28. Ferreira AB, Cardoso AL, Da Silva MJ (2013) Catal Lett 143:1240

- 29. Wang D, Zhang X, Ma J, Yu H, Shen J, Wei W (2016) Catal Sci Technol 6:1530
- Nath M, Pokharia S, Song X, Eng G, Gielen M, Kemmer M, Biesemans M, Willem R, de Vos D (2003) Appl Organometal Chem 17:305
- 31. Aggarwal RC, Singh PP (1964) J Inorg Nucl Chem 26:2185
- 32. Fujita S-I, Yamanishi Y, Arai M (2013) J Catal 297:137
- Zhao W, Peng W, Wang D, Zhao N, Li J, Xiao F, Wei W, Sun Y (2009) Catal Commun 10:655
- 34. Taimsalu P, Wood JL (1984) Spectrochim Acta 20:1043
- 35. Leles LA, Zabula AV, Bukalov SS, Koroteev OS, Maslennikova OS, Egorov MP, Nefedov OM (2005) Russ Chem Bull 54:1117
- 36. Fujita SI, Yamanishi Y, Arai M (2013) J Catal 297:137
- Wu X, Kanga M, Yina Y, Wanga F, Zhaoa N, Xiao F, Weic W, Suna Y (2014) Appl Catal A 473:13
- Niknam K, Zolfigol MA, Saberi D, Molaee H (2009) J Chin Chem Soc 56:1257
- 39. Abu-Samn RH (1983) J Chem Soc Pak 5:23