Synthesis of five and six-membered cyclic glycerilic carbonates bearing exocyclic urethane functions

Bassam Nohra[1,2], Laure Candy[1,2], Jean-François Blanco[3], Yann Raoul[4] and Zephirin Mouloungui[1,2]

[1] University of Toulouse, INP-ENSIACET, LCA (Laboratoire de Chimie Agro-industrielle), Toulouse, France
[2] INRA, Toulouse, France
[3] University of Toulouse, INP-ENSIACET, LGC (Laboratoire de Génie Chimique), Toulouse, France
[4] Proléa, Sofiprotéol, Paris, France

Five (5CGC) and six (6CGC) membered cyclic glycerilic carbonates having exocyclic urethane functions, as potential monomers for polyurethanes and polycarbonates, were prepared by two different routes: ''two-steps'' and the ''one-pot'' synthesis. For the ''two-steps'' route, based on the consecutive aminolysis and transesterification reactions, a catalyst screening has been performed. Phosphazene showed the best catalytic activity and provided 5CGC and 6CGC in appreciable amounts whereas the other catalysts favored 5CGC formation. An increase in molar ratio of dimethyl carbonate (DMC) increased the yield and the conversion. In the ''one-pot'' synthesis, where aminolysis and transesterification were simultaneous, a competition between products formation was demonstrated. In addition to the formation of mono-hydroxyurethanes and glycerilic cyclic carbonates (5CGC and 6CGC), the fast aminolysis of 6CGC and the slower aminolysis of 5CGC was responsible for a partial di-hydroxyurethanes production. The controlled and combined effects of catalyst and DMC excess acting as solvent and reagent allowed to selectively controlling the aminolysis and the transesterification reactions. The same reaction conditions were used for the synthesis of bicyclic carbonates. These new molecules enriched with urethane functions, provided novel and more environmentally friendly synthons for the synthesis of polyurethanes without the use of phosgene or isocyanate.

Keywords: Aminolysis / Cyclic glycerylic carbonate / Glycerol carbonate / Hydroxyurethane / Transesterification

1 Introduction

The synthesis of carbonates, especially five-membered (5CC) and six-membered (6CC) cyclic carbonates, has received much attention lately due to their potential application for the synthesis of polycarbonates and polyurethanes [1–2]. In the past, phosgene, a highly toxic and corrosive reagent, was used to prepare 5CC and 6CC [3, 4]. Cyclic carbonates were also available by insertion of carbon dioxide into an epoxide. The literature reports on the catalyzed synthesis of alkylene carbonates from oxiranes or oxetanes and CO_2 [5–8]. 5CC and 6CC are mainly synthesized by transesterification. The synthesis of 5CC can be achieved by the reaction of 1,2-propanediol or ethylene glycol with dialkyl carbonates catalyzed by metal or organo-catalysts whereas the synthesis of 6CC was achieved by the reaction of 1,3-propanediol with dialkyl carbonate [9, 10]. This reaction has been described with different substituents [11, 12] or catalysts [13, 14] and the effect of the chain length on whether the formation of cyclic carbonates or polymers has been demonstrated [9, 15]. Endo and coworkers [16] have reported a method of cyclic carbonate synthesis from propane-1,3-diols and ethyl chloroformate in the presence of a stoichiometric amount of triethylamine. The application of alkylammonium hydrogen carbonate reagents to fatty acid chlorohydrins substrates has been demonstrated to give fatty cyclic carbonates, in 84–90%

Abbreviations: 5CC, five-membered cyclic carbonate; **6CC,** six-membered cyclic carbonate; **5CGC,** five-membered cyclic glycerylic carbonate; **6CGC,** six-membered cyclic glycerylic carbonate; **DMC,** dimethyl carbonate; **GC-MS,** gas chromatography-MS; **HPLC,** high performance thin layer chromatography; **HU,** hydroxyurethane; **IR,** infrared; **MS,** mass spectrometry; **NMR,** nuclear magnetic resonance

purified yields [17]. The lipase catalyzed (900% w/w of the diol) transesterification reaction between dialkyl carbonate and diol in an acetonitrile-toluene solvent system for the synthesis of trimethylene carbonate monomer has also been studied [18]. Lately, Pyo et al. showed the possibility to synthesize 6CC with functional groups by lipase-mediated reaction in a solvent-free medium [19]. Cyclic carbonates can also be obtained by the polymerization of 1,2 and 1,3-alkylene diols and then the depolymerization of the respective linear polycarbonates at high temperature and in the presence of catalysts such as Sn (II), Mn (II), Fe (II), and Mg (II) chlorides, carbonates, and oxides [16, 20]. The patent literature on the preparation of 5CC and 6CC is then fairly extensive [21–24].

Glycerol is one of the 12 ''Top value added chemicals from biomass'' [25]. The utilization of glycerol is a theme of great academic and industrial interest because of its large availability as valuable by-product in the manufacturing of biodiesel [26]. Several conversion processes are described in the literature that transforms glycerol into useful materials [26–30]. Among them are essentially the first generation chemicals like 1,2- and 1,3-alkylene diols and glycerol carbonate. As already noticed, the transesterification of 1,2- and 1,3-alkylene diols with dialkyl carbonates provides 5CC and 6CC monomers. However, these cyclocarbonates do not present additional chemical functionalities and especially exocyclic urethanes functions that could allow a direct application for the synthesis of polyhydroxyurethanes. As first generation derivative, only glycerol carbonate presents an oxygenated potential and a chemical structure permitting to forecast the obtention of such molecules. In the case of glycerol carbonate, hydrophobic functional 5CC having exocyclic urethane functions were prepared from (2-oxo-1,3-dioxolan-4-yl)methyl chloroformate and 3-chloro-1,2-propanediol. These monomers were reacted with polyamine for the synthesis of amphiphilic branched poly(ethyleneimine)s having antibacterial properties [31]. Glycerol carbonate can also be employed as a source to mixed carbonate, which reacted with diamines to obtain polyurethanes without the use of hazardous isocyanates [32, 33].

5CC and 6CC undergo number of reactions with various nucleophiles. The most explored reaction of cyclic carbonate has been that of aminolysis. Aminolysis reaction gives rise to two isomers depending on the presence of the urethane function at α or β position [34]. The reaction rate of the 6CCs at 30–70°C is known to be 29–62 times larger than those of the five-membered one with hexylamine and the activation energy for the reaction of the 6CC with primary amine was smaller than that of the five-membered one [35].

In this paper, we report the influence of medium engineering on the reaction of glycerol carbonate with dimethyl carbonate (DMC) for the preparation of new five (5CGC) and six (6CGC) membered cyclic glycerylic carbonate molecules bearing exocyclic urethane functions. Two different routes named ''two-steps'' and ''one-pot'' were studied. For the first route, 5CGC and 6CGC were obtained by two consecutive reactions: the aminolysis of glycerol carbonate followed by a transesterification reaction of the formed hydroxyurethanes (HUs) molecules. More precisely, the nucleophilic addition of several primary amines (NH_2–C_nH_{2n+1}; $n = 4$, 8, 16) on glycerol carbonate lead to HU isomers which reacted afterwards with DMC in the presence of different catalysts: phosphazene ($[(CH_3)_2N]_3P{=}NC(CH_3)_3$), sodium carbonate ($Na_2CO_3$), 2,4-pentanedionato zinc ($C_{10}H_{14}O_4Zn$) and potassium tertiary butoxide (C_4H_9OK). The catalytic activity was evaluated by the ^{13}C NMR quantitative measurement of reagents conversions and yield of 5CGC and 6CGC. The effect of the length of the alkyl chain of the reacted amine on the selectivity of 5CGC versus 6CGC was also studied. For the second route, all the reactants were mixed at the same time in the medium and the reaction was carried out using phosphazene base. Kinetic investigation was achieved by HPLC to determine the ratio of the products formed in the medium during the course of the reaction. We demonstrated the possible transformation from a 5CC having exocylic hydroxyl group (glycerol carbonate) to a mixture of 5CGC and 6CGC having exocyclic urethane functions. The great influence of the medium was also reported. Choosing to work under diluted or concentrated conditions had consequences on conversions, yields, and selectivities.

Finally, we transposed our results to the synthesis of bicyclic carbonates having two exocylic urethane functions.

2 Materials and methods

2.1 General

Glycerol carbonate (Huntsman, 99.5%), butylamine (Sigma–Aldrich, 99.5%), octylamine (Sigma–Aldrich, 99%), hexadecylamine (Fluka, ≥92%), hexamethylenediamine (Sigma–Aldrich, 98%), DMC (Sigma–Aldrich, 97%) were used as received. Acetonitrile (HPLC grade) was purchased from Merck (Germany). Phosphazene ($[(CH_3)_2N]_3P{=}NC(CH_3)_3$), (2,4-pentanedionato) zinc ($C_{10}H_{14}O_4Zn$), sodium carbonate (Na_2CO_3), and potassium tertiary butoxide (C_4H_9OK) were obtained from Sigma–Aldrich.

2.2 Analytical methods

^1H and ^{13}C NMR spectra were achieved on a Bruker Avance® 300 MHz instrument using tetramethylsilane as an internal standard and equipped with QNP probe (^1H, ^{19}F, ^{31}P, ^{13}C). A preliminary study of ^1H (zg30), J-mod, and dept135 signals, completed with 2D studies (COSY, HSQC) lead to the attribution of the NMR signals. The selectivity of α versus β and 5CGC versus 6CGC isomers, but also the residual reagents (glycerol

carbonate and amine), were determinated at 293.2 K, with zgig ^{13}C pulse program. In the latest experiments, the delay time D1 is greater than or equal to 30 s in order to permit the full relaxation of all nuclei concerned in the assay.

Fourier transform infrared (IR) spectra were achieved by transmission on a PerkinElmer Spectrum 65 spectrometer.

Low resolution MS analyses were performed on a triple quadruple instrument TSQ 700 (Thermofisher). Mass calibration was conveniently carried out using the precursor ion NH_4^+ ($m/z = 18$). High resolution MS was performed using the chemical ionization method.

HPLC analyses were performed on a Dionex RSLC chain using Chromasil® Performance (C18-A, 250 mm × 4.6 mm, 5 μm) column and a precolumn (20 mm × 4.6 mm, 5 μm) (Varian, France) at 30°C with a UVD340U diode-array UV detector ($\lambda = 205$ nm) at a flow rate of 1 mL/min using acetonitrile/water as elution solvents. The injection volume was 20 μL. Chromatograms were treated by Chromeleon software.

GC-MS analyses were recorded on a Hewlett-Packard Agilent HP 6890 GC instrument with a capillary column (30 m × 0.25 mm × 0.25 μm) and a Thermo-Scientific triple quadrupole TSQ 700 mass detector. Scans were per-formed from 80 to 650 m/z at rate of 1.0 scans/s. The oven temperature program was: initial temperature 95°C, hold for 1 min, ramp at 15°C/min to 200°C, hold for 2 min, ramp at 15°C/min to 300°C, hold for 5 min. The injector transfer line temperature was set to 250°C. Measurements were performed in the split–split mode using helium as carrier gas (flow rate 1.0 mL/min).

2.3 Computational calculations

Computational calculations were performed with Scigress® using DFT-B88LYP functional to optimize the physical properties. The initial conformations and geometries were obtained by molecular mechanics calculations. The $LogP_{Ow}$ and the dipole moment (μ) were estimated by this method.

2.4 Catalytic synthesis of (2-oxo-1,3-dioxolan-4-yl) methyl alkylcarbamate (N°4) and 2-oxo-1,3-dioxan-5-yl alkylcarbamate (N°5)

2.4.1 ''Two-steps'' synthesis (a)

Glycerol carbonate N°**1** (25 g, 0.212 mol) was reacted with an equimolar quantity of primary amines (0.212 mol). The reaction was kept at 50°C under mechanical stirring for 2 h. DMC (38.2 g, 0.424 mol) and 5%wt/N°**1** of catalyst were then added to the medium that was stirred at 80°C for 7 h. 5%wt of catalyst, in the medium, correspond to 0.0111 mol C_4H_9OK, 0.018 mol Na_2CO_3, 0.00474 mol $C_{10}H_{14}O_4Zn$, and 0.00533 mol phosphazene, respectively. At the end of the reaction, methanol and the excess of DMC were eliminated by concentration under reduced pressure.

2.4.2 ''One-pot'' synthesis (b)

Twenty five gram of glycerol carbonate N°**1** (0.212 mol), 38.2 g (0.424 mol) of DMC; the amine (0.212 mol) and the catalyst (5%wt/N°**1**; 0.00533 mol phosphazene) were placed in a mechanical stirred reactor (500 rpm). The reaction mixture was heated at 80°C for 7 h under atmospheric pressure. To monitor the reaction, samples were taken every 30 min and analyzed using HPLC chromatography. At the end of the reaction, methanol and the excess of DMC were eliminated by concentration under reduced pressure.

2.5 Characterization of (2-oxo-1,3-dioxolan-4-yl) methyl alkylcarbamate (N°4) and 2-oxo-1,3-dioxan-5-yl alkylcarbamate (N°5)

2.5.1 (2-Oxo-1,3-dioxolan-4-yl) methyl butylcarbamate (N°4A) and 2-oxo-1,3-dioxan-5-yl butylcarbamate (N°5A)

^{1}H NMR (300 MHz, CD_3OD): δ_H(ppm) = 0.93 (t, 6H, C**H$_3$**), 1.34 (m, 4H,–C**H$_2$**–CH_3), 1.47 (m, 4H, –C**H$_2$**–CH_2), 3.12 (t, 4H, –C**H$_2$**–NH), 4.32 and 4.21 (dd, 2H,–C**H$_2$**O–(C = O)–NH–), 4.35 and 4.57 (t, 2H, –C**H$_2$**O–(C = O)–O–CH–), 4.97 (m, 1H, –C**H**O–(C= O)–O–), 4.13 (t, 4H, –C**H$_2$**O–(C=O)–O–C**H$_2$**–), 3.98 (m,1H,–C**H**O–(C=O)–NH–). **^{13}C NMR** (75 MHz, CD_3OD): δ_C(ppm) = 157.23 (N°**4A** –O–(**C**=O)–O–), 157.41 (N°**5A** –O–(**C**=O)–O–), C=O), 158.24 (N°**4A** –(**C**=O)–NH–), 158.84 (N°**5A** –(**C**=O)–NH–), 14.25 (**C**H_3), 21.03 (**C**H_2–CH_3), 33.10 (**C**H_2–CH_2), 41.62 (**C**H_2–NH), 64.69 (N°**4A** **C**H_2O–(C=O)–NH–), 67.59 (N°**4A** **C**H_2O–(C=O)–O–CH–), 76.62 (N°**4A** **C**HO–(C= O)–O–), 69.82 (N°**5A** **C**H_2O–(C=O)–O–**C**H_2–), 68.82 (N°**5A** **C**HO–(C=O)–NH–). **IR** (KBr): 3342 cm^{-1} (υ-NH), 1706 cm^{-1} (υ-OC(=O)NH–), 1793 and 1814 cm^{-1} (–O(C=O)–O–). Theorical mass $C_9H_{16}NO_5$: 217 (M). **LRMS (CI)**: 218 ($M + H^+$), 235 ($M + NH_4^+$). **HRMS (CI)**: 218.1026 ($M + H^+$).

2.5.2 (2-Oxo-1,3-dioxolan-4-yl) methyl octylcarbamate (N°4B) and 2-oxo-1,3-dioxan-5-yl octylcarbamate (N°5B)

^{1}H NMR (300 MHz, CD_3OD): δ_H(ppm) = 0.90 (t, 6H, CH_3), 1.31 (m, 20H, –C**H$_2$**–CH_2–C**H$_2$**–C**H$_2$**–C**H$_2$**–C**H$_2$**), 1.47 (m, 4H, –C**H$_2$**–CH_2–CH_3), 3.07 (t, 4H, –C**H$_2$**–NH), 4.32 and 4.21 (dd, 1H,–C**H$_2$**O–(C=O)–NH–), 4.57 and 4.35 (t, 1H, –C**H$_2$**O–(C=O)–O–CH–), 4.97 (m, 1H, –C**H**O–(C= O)–O–), 4.13 (t, 4H, –C**H$_2$**O–(C=O)–O–C**H$_2$**–), 3.98 (m,1H,–C**H**O–(C=O)–NH–). **^{13}C NMR** (75 MHz, CD_3OD): δ_C(ppm) = 157.23 (N°**4B** –O–(**C**=O)–O–), 157.41 (N°**5B** –O–(**C**=O)–O–), 158.24 (N°**4B** –(**C**= O)–NH–), 158.84 (N°**5B** –(**C**=O)–NH–), 14.59 (**C**H_3), 23.87 (**C**H_2–CH_3), 31.05 (**C**H_2–CH_2), 30.54

($\mathbf{C}H_2$–CH_2–CH_2), 30.56 ($\mathbf{C}H_2$–CH_2–CH_2–CH_2), 27.98 ($\mathbf{C}H_2$–CH_2–CH_2–CH_2–CH_2), 33.15 ($\mathbf{C}H_2$–CH_2–CH_2–CH_2–CH_2–CH_2), 42.03 ($\mathbf{C}H_2$–NH), 64.69 (N°**4B** $\mathbf{C}H_2O$–(C=O)–NH–), 67.59 (N°**4B** $\mathbf{C}H_2O$–(C=O)–O–CH–), 76.62 (N°**4B** **C**HO–(C=O)–O–), 69.82 (N°**5B** $\mathbf{C}H_2O$–(C=O)–O–$\mathbf{C}H_2$–), 68.82 (N°**5B** **C**HO–(C=O)–NH–). **IR** (KBr): 3342 cm^{-1} (υ-NH), 1706 cm^{-1} (υ-OC(=O)NH–), 1793 and 1814 cm^{-1} (–O(C=O)–O–). Theorical mass $C_{13}H_{24}NO_5$: 273 (M). **LRMS (CI)**: 274 ($M + H^+$), 292 ($M + NH_4^+$). **HRMS (CI)**: 274.1662 ($M + H^+$).

2.5.3 (2-Oxo-1,3-dioxolan-4-yl) methyl hexadecylcarbamate (N°4C) and 2-oxo-1,3-dioxan-5-yl hexadecylcarbamate (N°5C)

^{1}H NMR (300 MHz, $CDCl_3$): δ_H(ppm) = 0.84 (t, 6H, CH_3), 1.21 (m, 24H, –$\mathbf{C}H_2$–CH_2–$C\mathbf{H}_2$–$\mathbf{C}H_2$–$C\mathbf{H}_2$–$\mathbf{C}H_2$–$C\mathbf{H}_2$–$\mathbf{C}H_2$–$C\mathbf{H}_2$–$\mathbf{C}H_2$–$C\mathbf{H}_2$–$\mathbf{C}H_2$–$C\mathbf{H}_2$–$\mathbf{C}H_2$), 1.44 (m, 4H, –$\mathbf{C}H_2$–CH_2–CH_3), 3.11 (t, 4H, –$\mathbf{C}H_2$–NH), 4.11 (m,2H,–$\mathbf{C}H_2O$–(C=O)–NH–), 4.27 (m,2H, –$\mathbf{C}H_2O$–(C=O)–O–CH–), 4.88 (m,1H, –C**H**O–(C=O)–O–), 4.53 (t,4H, –$\mathbf{C}H_2O$–(C=O)–O–$\mathbf{C}H_2$–), 3.89 (m,1H,–C**H**O–(C=O)–NH–). **^{13}C NMR** (75 MHz, MeOD): δ_C(ppm) = 154.90 (N°**4C** –O–(**C**=O)–O–), 155.40 (N°**5C** –O–(**C**=O)–O–), 158.70 (N°**4C** –(**C**=O)–NH–), 158.87 (N°**5C** –(**C**=O)–NH–), 14.27 ($\mathbf{C}H_3$), 22.84 ($\mathbf{C}H_2$–CH_3), 29.98 ($\mathbf{C}H_2$–CH_2), 29.44 ($\mathbf{C}H_2$–CH_2–CH_2), 29.51 ($\mathbf{C}H_2$–CH_2–CH_2–CH_2), 29.70–29.85 ($\mathbf{C}H_2$–$\mathbf{C}H_2$–$\mathbf{C}H_2$–$\mathbf{C}H_2$–$\mathbf{C}H_2$–$\mathbf{C}H_2$–$\mathbf{C}H_2$–$\mathbf{C}H_2$), 26.87 ($\mathbf{C}H_2$–CH_2–CH_2–NH–), 32.08 (–$\mathbf{C}H_2$–CH_2–NH–), 41.18 ($\mathbf{C}H_2$–NH), 63.48 (N°**4C** $\mathbf{C}H_2O$–(C=O)–NH–), 61.58 (N°**4C** $\mathbf{C}H_2O$–(C=O)–O–CH–), 74.60 (N°**4C** **C**HO–(C=O)–O–), 66.11 (N°**5C** $\mathbf{C}H_2O$–(C=O)–O–$\mathbf{C}H_2$–), 70.72 (N°**5C** **C**HO–(C=O)–NH–). **IR** (KBr): 3342 cm^{-1} (υ-NH), 1706 cm^{-1} (υ-OC(=O)NH–), 1793 and 1814 cm^{-1} (–O(C=O)–O–). Theorical mass $C_{21}H_{40}NO_5$: 385 (M). **LRMS (CI)**: 386 ($M + H^+$), 403 ($M + NH_4^+$). **HRMS (CI)**: 386.2906 ($M + H^+$).

2.6 Synthesis of 3-hydroxypropyl-1,2-di(butylcarbamate) (N°6A) and 2-hydroxypropyl-1,3-di(butylcarbamate) (N°7A)

N-butylamine (15.49 g, 0.212 mol) was added at 80°C to an equimolar quantity of 5CGC and 6CGC (0.212 mol). The reaction was kept at 80°C under mechanical stirring for 1 hour. Residual butylamine was removed by washing the product solution with 1% aqueous HCl. **^{1}H NMR** (300 MHz, CD_3OD): δ_H(ppm) = 0.93 (t, 6H, CH_3), 1.34 (m, 4H,–$\mathbf{C}H_2$), 1.47 (m, 4H, –$\mathbf{C}H_2$–CH_2), 3.09 (t, 4H, –$\mathbf{C}H_2$–NH), 4.06 (N°**6A** m, 2H,–$\mathbf{C}H_2O$–(C=O)–NH–), 4.17 (N°**7A** m, 2H, –$\mathbf{C}H_2O$–(C=O)–NH–), 3.95 (N°**7A** m, 1H, –C**H**OH), 3.65 (N°**6A** m, 2H, –$\mathbf{C}H_2$OH), 4.80 (N°**6A** m,1H,–C**H**O–(C = O)–NH–). **^{13}C NMR** (75 MHz, CD_3OD): δ_C(ppm) = 158.94 ((**C**=O)–NH–), 158.55 ((**C**=O)–NH–), 14.25 ($\mathbf{C}H_3$), 21.03 ($\mathbf{C}H_2$–CH_3), 33.10 ($\mathbf{C}H_2$–CH_2), 41.62 ($\mathbf{C}H_2$–NH), 64.52 ($\mathbf{C}H_2O$–(C=O)–NH–), 66.60 ($\mathbf{C}H_2O$–(C=O)–NH–), 62.01 ($\mathbf{C}H_2$OH), 69.26 (**C**HOH), 64.52 (**C**HO–(C=O)–NH–). **IR** (KBr): 3342 cm^{-1} (υ-NH), 1706 cm^{-1} (υ-OC(=O)NH–). Theorical mass $C_9H_{16}NO_5$: 290 (M). **LRMS (CI)**: 291 ($M + H^+$), 308 ($M + NH_4^+$). **HRMS (CI)**: 291.1028 ($M + H^+$).

3 Results and discussion

The synthesis of 5CGC (N°**4**) and 6CGC (N°**5**) was studied by two different routes (Fig. 1) that consisted in the combination of an aminolysis and a transesterification reaction. For the first route, the two reactions were consecutive (a) whereas they were simultaneous in the second route (b). The first one is a two steps reaction (**a**). The aminolysis reaction ($\mathbf{a_1}$) of glycerol carbonate N°**1** with different amines at 50°C for 2 h affords α HU (N°**2**) and β HU (N°**3**) isomers [34] that react in a second step ($\mathbf{a_2}$) with DMC in the presence of a catalyst at 80°C for 7 h to form the corresponding 5CGC (N°**4**) from α HU (N°**2**) and 6CGC (N°**5**) from β HU (N°**3**). In the two steps process, the medium can be considered as concentrated and free from catalyst during the aminolysis whereas DMC and the methanol generated as a by-product acted as reactants but also as solvents for the catalyzed transesterification reaction. For the one pot synthesis (7 h, 80°C), as all the reagents are mixed at the same time with the catalyst, the transesterification can occur as soon as the aminolysis provides HU isomers. The effects of catalyst and dilution of the medium benefit to both aminolysis and transesterification.

3.1 Characterization of N°4, N°5, N°6, and N°7

^{13}C NMR was the analytical tool to achieve a complete study of the media. It allowed quantitatively measuring the conversion of α and β HU (N°**2** and N°**3**) and the yield of 5CGC and 6CGC (N°**4** and N°**5**). It then also provided α/β HU and 5CGC/6CGC selectivities. Moreover, the quantitative evaluation of residual reactants and of eventual by-products was also possible. The measurement of the integral of the specific carbon i.e.,: 76.62 ppm (N°4A CHO–(C=O)–O–); 68.82 ppm (N°5A CHO–(C=O)–NH–), 64.52 (N°6A CHO–(C=O)–NH–), 69.26 (N°7A CHOH) with ^{13}C NMR zgig acquisition permits to compute quantitative parameters. By this integral calculation, one can obtain the molar composition of the reaction medium for the molecules N°1 to N°8. We reach by this calculation the yield of 5CGC (N° 4) and 6CGC (N°5) in the reaction medium. The selectivity of 5CGC and 6CGC were defined by the equation:

$$\text{Ratio of 5CGC} = \frac{\text{Int5CGC}}{\text{Int5CGC} + \text{Int6CGC}}$$

where Int_x = integral of specific carbon of x. The same calculation was performed for α/β HU selectivity.

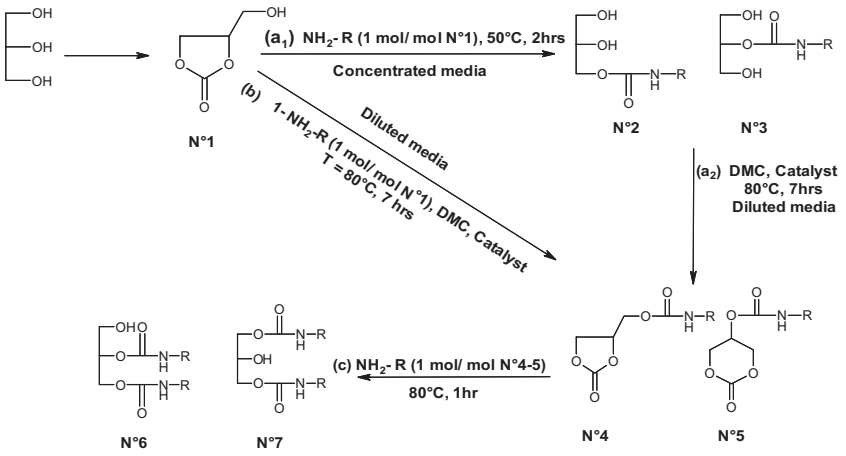


Figure 1. "Two-steps" ($\mathbf{a_1}$ and $\mathbf{a_2}$) and "one-pot" (**b**) routes for the synthesis of (2-oxo-1,3-dioxolan-4-yl)methyl alkylcarbamate (N°**4**) and 2-oxo-1,3-dioxan-5-yl alkylcarbamate (N°**5**) N°**4A** and N°**5A**: R=C_4H_9; N°**4B** and N°**5B**: R=C_8H_{17}; N°**4C** and N°**5C**: R=$C_{16}H_{33}$ and their aminolysis, 3-hydroxypropyl-1,2-di(alkylcarbamate) (N°**6**) and 2-hydroxypropyl-1,3-di(alkylcarbamate) (N°**7**) N°**6A** and N°**7A**: R=C_4H_9 by the route (**c**).

This method was completed by reversed HPLC whose analytical conditions were optimized to separate of α and β HU (N° **2** and N°**3**) from 5CGC and 6CGC (N°**4** and N°**5**). The composition in water/acetonitrile of the eluent varied depending on the length of the alkyl chain. Due to the unavailability of standard compounds, the qualitative HPLC analyses were only performed for the kinetics study in the one-pot process. Assuming identical response factors for all HU and CGC, the composition of the raw media may be calculated by area percentages, also leading to a quick evaluation of the α/β HU and 5CGC/6CGC selectivities.

To develop the NMR method, the structural elucidation of 5CGC and 6CGC was needed as the ^{13}C NMR study of HU has already been performed [34]. At the end of the two-steps synthesis, raw media were concentrated under reduced pressure to remove residual DMC and methanol. Pure 5CGC and 6CGC (N°**4** and N°**5**) were obtained by liquid/liquid extraction using chloroform/water (70/30). 5CGC and 6CGC having exocyclic urethane functions are hydrophobic systems and are found in the organic-$CHCl_3$ phase. The composition of the media was determined by low resolution MS and ^{13}C NMR before and after purification. As an indicator, IR spectroscopy showed the presence of two bands at 1785 and 1800 cm^{-1} corresponding to the cyclic carbonyl functions of 5CGC and 6CGC (N°**4** and N°**5**), respectively. The chemical shifts were elucidated by **^{1}H** and **^{13}C NMR**. In the **^{13}C NMR** spectrum (Fig. 2) the carbonyl carbon atom signals **9** and **14** at $\delta = 157.23$ and 157.41 ppm proved the presence of the two cyclocarbonates in the medium. The carbonyl carbon atom signals of the urethane **5** and **10** at $\delta = 158.24$ and 158.84 ppm corresponded to the exocyclic urethane carbonyl function.

The structural elucidation was completed by the study of the NMR spectrum of the products resulting from the aminolysis reaction on cyclic glycerylic carbonates. The characteristic carbon carbonyl signals (**9** and **14**) of the 5CGC and 6CGC disappeared after reaction with butylamine (Fig. 3). The signals at $\delta = 69.26$ ppm (carbon 8, Fig. 3) and $\delta = 62.01$ ppm (carbon 5, Fig. 3) are characteristic for isomer N°7 and N°**6**, respectively.

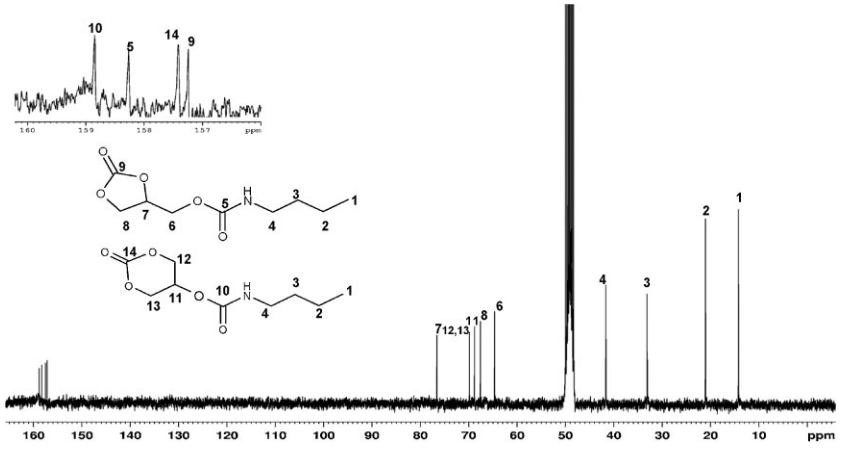


Figure 2. ^{13}C NMR spectrum of (2-oxo-1,3-dioxolan-4-yl)methyl butylcarbamate (N°4A) and 2-oxo-1,3-dioxan-5-yl butylcarbamate (N°5A) in CD_3OD.

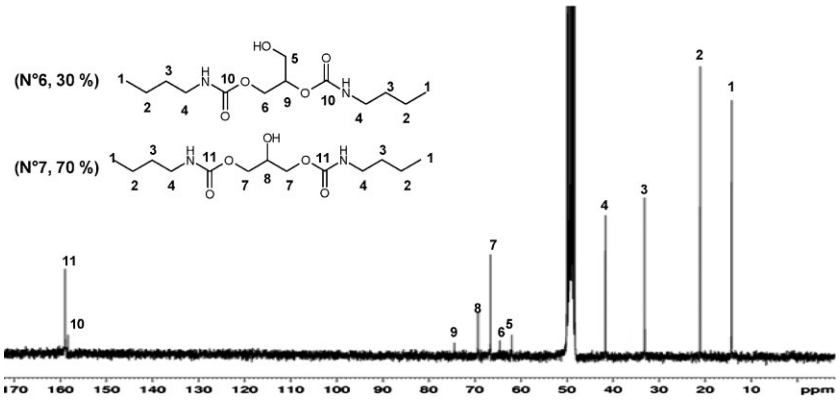


Figure 3. ^{13}C NMR spectrum of 3-hydroxypropyl-1,2-di(butylcarbamate) (N°**6**A) and 2-hydroxypropyl-1,3-di(butylcarbamate) (N°**7**A) in CD_3OD.

3.2 "Two-steps" synthesis of 5CGC (N°4) and 6CGC (N°5)

3.2.1 Aminolysis of glycerol carbonate

The first step is the total aminolysis reaction of glycerol carbonate with primary amines without the use of catalyst and solvent. In a previous publication [34], it was shown that the selectivity of the reaction favored the formation of α isomer (N°2) and that the lengths of the alkyl chain of the amine affects the regioselectivity of the ring-opening. A short alkyl chain favored α isomer's formation whereas, when the length of the alkyl chain increases, the selectivity α/β reaches the 50/50 equilibrium. This result was confirmed as the α/β ratios for the step $\mathbf{a_1}$ were 75/25, 65/35, and 49/51 for C_4H_9, C_8H_{17}, and $C_{16}H_{33}$, respectively. In addition to α and β HU, the aminolysis reaction product is made of 10% glycerol whatever the amine used. The presence of glycerol is due to the catalytic role of the amine used as reagent and came from the partial carbonate glycerol's decomposition in basic conditions [34]. This catalytic effect also promotes the aminolysis in concentrated conditions.

3.2.2 Transesterification of α HU (N°2) and β HU (N°3)

The second step is the transesterification of α and β HU (N°**2** and N°**3**) using DMC as a carbonate source. The reaction was performed for 7 h at 80°C without shifting the equilibrium by methanol continuous removal. We studied the effects of the catalyst and of the molar ratio of HU to DMC for HU having a C_4H_9 alkyl chain (N°2A and N°3A) but also the effect the alkyl chain's length of the HU. The parameters were the yield in 5CGC and 6CGC and the 5CGC/6CGC selectivity and they were both quantitatively evaluated by ^{13}C NMR.

3.2.3 Effect of the catalyst

The formation of 5CGC and 6CGC from α and β HU without using any catalyst was negligible (run r**1**, Table 1). The conversion of α HU (N°**2**) was poor and reached 10% whereas no β HU (N°**3**) was converted even if an excess of DMC was used. Different catalysts were evaluated for the transesterification of α (N°2A) and β (N°3A) with DMC to yield 5CGC and 6CGC (Table 1, Fig. 4). Using Na_2CO_3 as

Table 1. Catalytic transesterification synthesis of 5CGC and 6CGC by route a_2

Run	DMC/HU	Catalyst	Conv. α[a)]	Conv. β[a)]	5CGC/6CGC[b)]	Yield 5CGC + 6CGC[c)]
1	2	–	10	0	100/0	5
2	2	Na_2CO_3	35	0	100/0	23
3	3	Na_2CO_3	52	27	85/15	39
4	2	$C_{10}H_{14}O_4Zn$	71	0	100/0	40
5	3	$C_{10}H_{14}O_4Zn$	76	17	90/10	49
6	2	C_4H_9OK	74	9	93/7	42
7	3	C_4H_9OK	78	30	81/19	50
8	2	$[(CH_3)_2N]_3P{=}NC(CH_3)_3$	86	75	63/37	72
9	3	$[(CH_3)_2N]_3P{=}NC(CH_3)_3$	92	78	68/32	76

[a)] Conversions (%) of α/β *N*-butylHU (75/25 at $t = 0$, route a_1) calculated by zgig ^{13}C NMR after 7 h at 80°C.
[b)] Selectivity of 5CGC/6CGC calculated by zgig ^{13}C NMR.
[c)] Yield (%) of 5CGC and 6CGC calculated by zgig ^{13}C NMR.

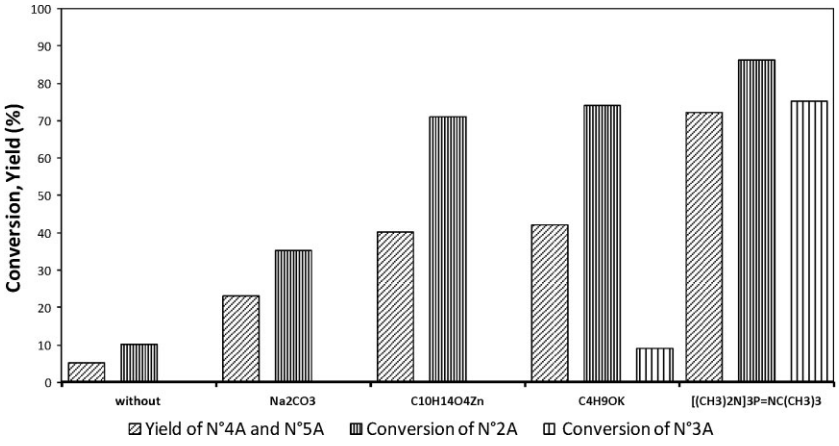


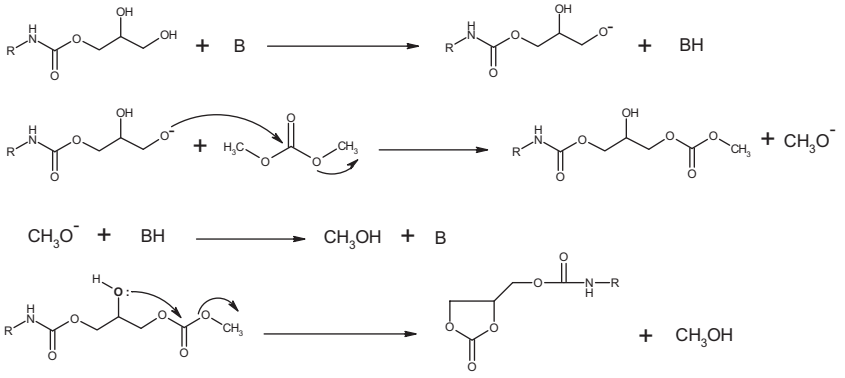
Figure 4. Influence of the catalyst on the transesterification of **α** and **β** *N*-butylHU (N°2A and N°3A) with DMC (DMC/HU = 2, 7 h, 80°C); conversions (%) of **α**/**β** *N*-butylHU and yield (%) of 5CGC (N°4A) and 6CGC (N°5A) calculated by Zgig ^{13}C NMR.

catalyst (run **2**); the conversion rate of α HU reached 35% whereas still no conversion of β HU was detected. This explained 100% selectivity in 5CGC (N°4). The 3 other catalysts tested demonstrated a good activity toward the transesterification reaction. For (2,4-pentanedionato)zinc and potassium tertiary butoxide, the conversion rates of α HU reached 71 and 74%, respectively. However, for these catalysts, the conversion of β HU was very weak and the presence of the 5CGC was predominant. This effect is due to the highest ring strain of the 6CGC instead of 5CGC leading to the highest selectivity of the 5CGC [35]. With phosphazene, the highest conversion of α and β HU was observed and reached 86 and 75%, respectively. We can classify the catalytic activity in the descending order of: $[(CH_3)_2N]_3P{=}NC(CH_3)_3 > C_4H_9OK > C_{10}H_{14}O_4Zn >> Na_2CO_3$.

The basic phosphazene catalyst promotes the transesterification reaction and also affects the regioselectivity of the ring closure. In contrary to the other catalysts, phosphazene facilitates the transesterification of β isomer. It can be stated that for the synthesis of cyclic carbonates, a higher basicity of the catalysts leads to higher conversion of α and β HU. Moreover, intramolecular interactions by H-bonding are highlighted showing the highest basicity of the imino nitrogen atom. The presence of H-bonding in the catalyst permits a better reactivity of the catalyst and a better conversion. This could explain the surprising effect of the phosphazene base instead of the other catalysts.

This suggests that the basic catalyst shifts the transesterification equilibrium and that the reaction mechanism proceeds through an alkoxide anion (Scheme 1.). The first step is a reaction between the weak acid proton of one of the two primary hydroxyl groups of α and β HU isomers and the basic catalyst to yield the corresponding anion plus the conjugated acid (BH) of the base. Taking into account the low acidity of the hydroxyl group, a strong base is required in this step. In the second step, the oxide anion attacks the carbonyl carbon of a DMC molecule leading to formation of the methyl hydroxyl urethane carbonate intermediate plus a methoxide anion which reacts with the base conjugated acid (BH) formed in the first step, yielding methanol and regenerating the base (step 3). Finally, in the fourth step the methyl hydroxyl urethane carbonate undergoes a cyclization reaction through a nucleophilic attack of the oxygen from the secondary hydroxyl group to the carbonyl carbon yielding 5CGC (N°4) and 6CGC (N°5) plus methanol.

In the base catalyzed transesterification between HU and DMC, it is easily conceivable that the first step for the generation of an active species is the acid–base interaction



Scheme 1. Mechanism of the transesterification reaction of **α** HU isomer (N°2) with DMC in the presence of a basic catalyst.

between a hydroxyl group and the basic catalyst. In this context, the generation of the active species from sodium carbonate and potassium tertiary butoxide seemed to be much more difficult than that from phosphazene.

Moreover, the activity of a catalyst is greatly affected by the dissolution time and the degree of dissolution: the more soluble the catalyst, the higher the catalytic activity, suggesting that the transesterification proceeds mostly in a homogeneous way [36]. Therefore, the significantly lower activity of Na_2CO_3 can be ascribed in part to its lower solubility in the reaction mixture. Liquid phosphazene has the highest solubility in the system and acts as a homogeneous catalyst.

Na_2CO_3, $C_{10}H_{14}O_4Zn$, and C_4H_9OK catalysts are selective of the α HU isomer (N°2) transesterification into 5CGC whereas $[(CH_3)_2N]_3P{=}NC(CH_3)_3$ catalyst proved its efficiency for the transesterification of both α and β HU isomers to give 5CGC and 6CGC. With this catalyst, after 1 h reaction, HPLC analyses showed that the conversion of α HU has started while no conversion of β isomer has occurred. Hereupon, the use of phosphazene affects the conversion of the HU and the regioselectivity of the ring closure. Indeed, the reactivity of α HU is higher than that of β HU. The highest catalytic activity of phosphazene base permit to oppose the weaker reactivity of the isomer N°3 (β HU) having hydroxyl groups at 1, 3 positions that are less spatially accessible than hydroxyl groups at 1, 2 positions (isomer N°2, α HU). The highest conversion of β isomer (N°**3**) gives the highest selectivity in 6CGC and the highest yield of the cyclic carbonates.

Three conditions are necessary for an optimal activity of the catalyst used in the transesterification reaction between HU and DMC: (i) close contact between basic catalytic sites and HU isomers, (ii) catalyst base strength must be high enough to abstract a proton from the primary hydroxyl group of the HU, and (iii) the dissolution time and the degree of dissolution of the catalyst, the transesterification reaction proceeds mostly in a homogeneous way.

3.2.4 Effect of molar ratio DMC/HU

The transesterification has been achieved with an excess of DMC reactant to shift the equilibrium. Ratios of 2 or 3 moles DMC/mole HU were tested with the four different catalysts. The molar ratio DMC/HU affects the conversion of HU isomers to CGC and the selectivity 5CGC/6CGC. The GC-MS analysis of the post-reaction mixture indicated the presence of the 5CGC and 6CGC (N°**4** and N°**5**) as well as α and β HU isomers (N°**2** and N°**3**).

For a ratio DMC/HU of 2 (runs r2, r4, r6, r8), the reaction product still contained significant amount of HU molecules. Using a higher excess of DMC (runs r3, r5, r7, r9), the conversion of α and β HU increased and the yield of 5CGC/6CGC was improved. More precisely, with a threefold excess of DMC, the conversion of β HU significantly increased whereas the conversion of α HU was only slightly higher (Table 1, runs r3, r5, r7, and r9). Using phosphazene with a threefold excess of DMC, 5CGC, and 6CGC were formed in significant amount with yields higher than 70%.

The probable reason is that the solubility of the system increased with the increase of DMC concentration [36]. It is likely that the increased concentration of DMC in the reaction solution improved the interaction of the catalyst with HU isomers and so the better accessibility to β isomer. Therefore, no additional solvent was needed as the excess of DMC works as both reactant and solvent. As reactant, DMC in excess shifts the equilibrium to the products. As a solvent, DMC contributes to the development of a favorable medium for homogeneous reactions such as the cyclocarbonation catalyzed by soluble phosphazene. Moreover, it is an inexpensive, environmentally benign chemical having interesting solvating properties, low toxicity, and high biodegradability. It can be easily removed as an azeotropic mixture with methanol at the end of the reaction.

3.2.5 Effect of the length of the HU alkyl chain

The effect of the alkyl chain length of the HU on this reaction was studied using phosphazene as catalyst, with a DMC/HU ratio of 2. The series include molecules substituted with alkyl chains of different length (with C_4H_9, C_8H_{17}, $C_{16}H_{33}$). At 7 h, the conversion of α HU versus the length of the alkyl chain was in order of C_4H_9 (86%)>C_8H_{17} (79%)>$C_{16}H_{33}$ (71%). The longer the alkyl chain of the HU increases, the more the conversion and the yield decreases. This result suggests that the transesterification of HU closely correlates to their octanol/water partition coefficient, also abbreviated as LogP_{Ow} parameter, which increases with the length of the alkyl chain. LogP_{Ow} C_4H_9 HU (0.231) < LogP_{Ow} C_8H_{17} HU (1.816) < < LogP_{Ow} $C_{16}H_{33}$ HU (4.986). Indeed, the differing hydrophobicity of the HU is a probable reason for this clear difference. $C_{16}H_{33}$ HU seems to introduce a balance effect of a hydrophobic/hydrophilic system. The system is not homogeneous anymore. Its heterogeneity compromises the solubility of the reactant (DMC) and of the catalyst (phosphazene). This limits the transesterification of hydroxyl groups.

3.2.6 Other reaction products

Glycerol is the secondary product from the reaction of glycerol carbonate N°**1** with amine [34]. The presence of glycerol carbonate (N°**1**) in the reaction medium was due to the transesterification of glycerol with DMC in the presence of basic catalysts such as phosphazene [36, 37].

3.3 "One-pot" synthesis of 5CGC and 6CGC

For an industrial purpose, achieving simultaneously both reactions (aminolysis and transesterification) may represent

Table 2. Catalytic transesterification synthesis of 5CGC (N°4) and 6CGC (N°5) by route a_2: effect of the alkyl chain's length

Run	Alkyl chain	Initial ratio α/β[a)]	Conv. α[b)] (N°2)	Conv. β[b)] (N°3)	Yield (%) 5CGC + 6CGC[c)] (N°4 + N°5)
8	C_4H_9	75/25	86	75	72
10	C_8H_{17}	65/35	79	68	64
11	$C_{16}H_{33}$	49/51	71	62	57

[a)] Initial selectivity of α/β HU obtained by route a_1 calculated by zgig ^{13}C NMR.
[b)] Conversions (%) of α and β HU calculated by zgig ^{13}C NMR (7 h, 80°C, DMC/HU = 2, $[(CH_3)_2N]_3P{=}NC(CH_3)_3$).
[c)] Yield (%) of 5CGC and 6CGC calculated by zgig ^{13}C NMR.

an improvement of the productivity of the process by decreasing the total reaction time and reactant's handling. Nevertheless, the effects of this strategy on conversions, yields, and selectivities of the products had to be studied before to conclude on its interest.

This route describes an in-situ reaction, coupling of the total aminolysis and the catalytic transesterification reaction. All the reagents were mixed in the medium at the same time and the reaction was held at 80°C for 7 h under reflux. We studied the ''one-pot'' synthesis of 5CGC and 6CGC using phosphazene base and DMC/GC ratio of 3. The reaction was carried out under equilibrium conditions without methanol removing.

3.3.1 Ratio of products formation versus time

The composition of the reaction medium versus time has been evaluated. We firstly focus only on HU isomers and CGC products. Figure 5 show the ratios of N°**2A**, N°**3A**, N°**4A**, and N°**5A** versus time determined by HPLC analysis. The results reported herein account for the two consecutive reactions: (i) aminolysis of glycerol carbonate with *N*-butylamine and (ii) the transesterification of α and β HU with DMC. At 15 min reaction, the aminolysis of glycerol carbonate (N°**1**) formed 84% of α isomer (N°**2A**) and only 5% of β isomer (N°**3A**). The transesterification of α isomer (N°**2A**) was also shown to form 5CGC (N°**4A**) in an amount of 10% approximately from the whole ratio of the products. At 30 min, more β isomer (N°**3A**) was formed (~30%) and the quantity of 5CGC (N°**4A**) remains stable. At 1 h reaction, the formed quantity of β isomer (N°**3A**) remains stable and the consumption of α isomers went on to form 5CGC (N°**4A**). At 2 h reaction, 6CGC (N°5A) was obtained and the consumption of β isomer (N°**3A**) went on. The medium is then composed of equivalent quantities of CGC and HU. At 7 h, the principal compounds are CGC: 59% of N°**4A** and 25% of N°**5A**. This first approach of the reaction medium composition demonstrated that the two reactions are consecutive with a difference in the reactivity of HU isomers.

3.3.2 Other reaction products

In the ''one-pot'' route (**b**), other reactions must be considered such as the formation of *N*-dibutylurea (N°**8A**) that results from the reaction of butylamine with DMC at 80°C in the presence of phosphazene. The presence of glycerol in the aminolysis reaction and the presence of side reactions in the transesterification reaction of the ''one-pot'' route could be both explained by the catalytic activity of the amine [34].

Table 3 shows the final composition of the media using phosphazene with a DMC/GC ratio of 2 and 3. Increasing the DMC/GC ratio increases the percentage of N°**4A** and N°**5A** in the medium. At a molar ratio of 2, a competition between the consumption of β isomer (N°**3A**) to form 6CGC (N°**5A**)

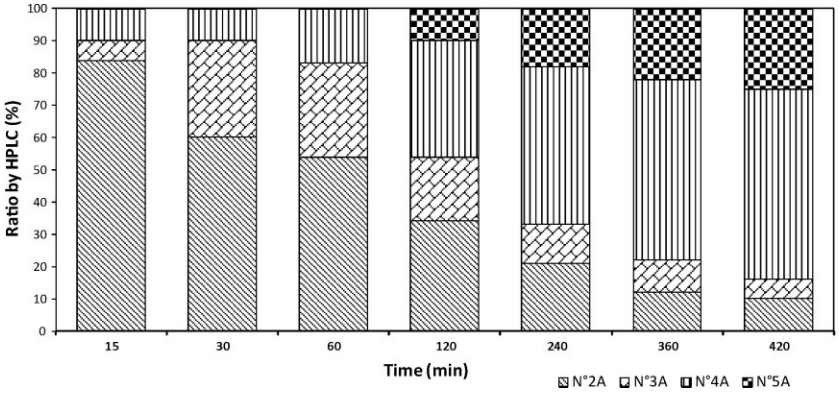


Figure 5. Kinetic study of the one pot synthesis of 5CGC and 6CGC (phosphazene, 80°C, DMC/HU = 3). Ratios of N°**2A**, N°**3A**, N°**4A**, and N°**5A** determined by HPLC analysis.

Table 3. Composition (%) of the final media, yield and selectivity in CGC determined by zgig ^{13}C NMR (amine = NH_2–C_4H_9, phosphazene, 80°C)

Run	Route	Initial ratio DMC/CG	Composition (%) N°4A	N°5A	N°2A	N°3A	N°1	N°6	N°7	N°8	Yield (%) N°4A + N°5A	Selectivity N°4A/N°5A
8	a	2	45	33	7	9	4	0	0	0	72	63/37
9	a	3	59	20	5	11	5	0	0	0	76	68/32
10	b	2	31	21	15	9	7	11	2	4	51	59/41
11	b	3	44	24	10	8	7	0	0	5	64	64/35

and its aminolysis to form 1,2-hydroxyldiurethane (N°**6A**) was observed. As already known, the reactivity of 6CC is higher than that of 5CC due to the larger ring-strain in six-membered carbonate rings [35]. That explains the higher amount of N°**6A** instead of N°**7A** in the medium. An excess of DMC promotes the transesterification reaction and limits the aminolysis of the 6CGC.

3.4 Comparison of ''two-steps'' versus ''one-pot'' routes

The ''two-steps'' synthesis affords the highest yields whatever the molar ratio DMC/HU in the medium. However, the yield of 5CGC (N°**4A**) and 6CGC (N°**5A**) decreases with the ''one-pot'' synthesis due to the presence of secondary products (N°**6A**, N°**7A**, and N°**8A**), consuming these molecules.

In the ''one-pot'' route, the selectivity 5CGC/6CGC was displaced toward 6CGC formation thanks to the easier dissolution of β HU isomer in the system GC (N°**1**)/DMC/liquid catalyst in the medium. Working with the ''two-steps'' route which is 2 h longer than the ''one-pot'' process, allowed reaching higher yields of CGC but the final media were poorer in 6CGC.

Economically, an improvement of the productivity of the process by decreasing the total reaction time and reactant's handling is a very important parameter.

By engineering the medium, it is possible to select experimental conditions according to the objective: high yields in CGC or a well-targeted selectivity.

3.5 Reactivity comparison of 5CGC and 6CGC

An aminolysis reaction, at 80°C for 1 h, of 5CGC (N°4A) and 6CGC (N°5A) with a 1.0 equiv. of butylamine was studied. As aforementioned, the reactivity of 6CC is higher than that of 5CC [35]. The aminolysis reaction of 5CGC and 6CGC shows a faster ring-opening for the 6CGC as, after 20 min, a total consumption of this molecule was observed. The results were in agreement with those obtained by Keul and coworkers [38]. Due to the asymmetry of the substituted 5CGC, two regioisomers N°**6A** and N°**7A** are expected (Fig. 1) whereas only regioisomer N°**6A** is obtained from 6CGC.

3.6 Effect of the urethane function on the cyclic carbonate

We deliberately focused our work toward hydrophobic exocyclic urethane functions since these are widely used to turn the hydrophilic properties of the glycerol carbonate afforded by the presence of intramolecular hydrogen bonds between the hydroxyl and carbonyl groups. As aforementioned, a $CHCl_3$/water liquid/liquid extraction leads to the separation of glycerol carbonate in the aqueous phase from 5CGC and 6CGC in the organic phase. This could be explained by the $\mathrm{Log}P_{\mathrm{OW}}$ value (Table 4) of glycerol carbonate and 5CGC having exocylic urethane function, determined by computational calculation. $\mathrm{Log}P_{\mathrm{Ow}}$ increases by adding urethane functions, $\mathrm{Log}P_{\mathrm{OW}}$ GC (−0.061) < $\mathrm{Log}P_{\mathrm{OW}}$ HU (0.231) < $\mathrm{Log}P_{\mathrm{OW}}$ CGC (1.251). Aminolysis of glycerol carbonate affords an increase of the $\mathrm{Log}P_{\mathrm{OW}}$ from −0.061 to 0.231 even in the presence of hydroxyl groups, and so on the transesterification of HUs affording 5CGC and 6CGC increases the $\mathrm{Log}P_{\mathrm{OW}}$ to 1.251. Indeed, the differing hydrophobicity is a probable reason for this clear increase of $\mathrm{Log}P_{\mathrm{OW}}$. Moreover, the dipole moment (μ) increases by passing from GC (μ = 4.411 Debye) to 5CGC (μ = 5.607 Debye).

3.7 Extension on the synthesis of Bis5CGC, Bis6CGC, and Bis56CGC

The synthesis of bicyclic carbonates was carried out using the ''one-pot'' route (**b**) at 90°C for 8 h without methanol removal. A DMC/GC ratio of 4 was necessary for a total conversion of hydroxyl groups. The final medium was a homogeneous liquid. The control of the medium engineering achieved by the implementation of the solubilizing properties

Table 4. Log P_{OW} and dipole moment (μ) of N°1 and N°2A, N°3A and N°4A, N°5A

Properties	GC (N°1)	α HU and β HU (N°2A)	(N°3A)	5CGC and 6CGC (N°4A)	(N°5A)
$\mathrm{Log}P_{\mathrm{OW}}$	−0.061	0.231		1.251	
μ (Debye)	4.411	4.502	3.949	5.607	6.474

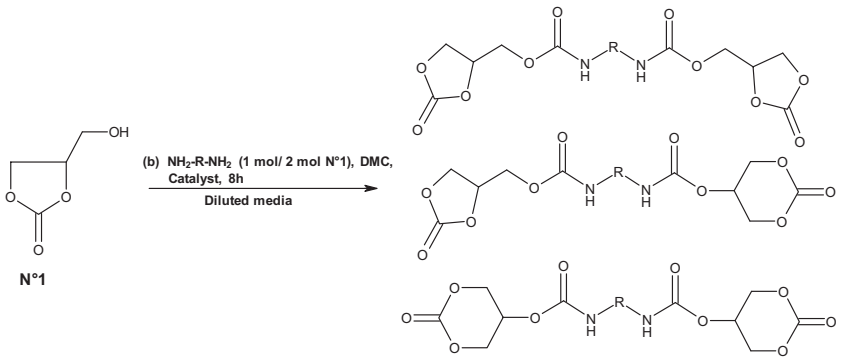


Figure 6. "One-pot" (**b**) scheme for the synthesis of Bis5CGC, Bis6CGC and Bis56CGC with R=C_6H_{12}.

of DMC and methanol, combined to the use of a strong basic liquid catalyst also provided optimal conditions for the synthesis of biscyclocarbonates.

The selectivity 5CGC/6CGC was calculated to be 70/30. Statistically, three different bicyclic carbonates forms could be obtained: bis5CGC, Bis6CGC, and Bis56CGC corresponding to respective conversions of αα, ββ, and αβ HU isomers (intermediate reaction) (Fig. 6). The selectivity of the bis5CGC/bis6CGC was not affected by the use of diamine [10, 32]. The same 5CGC/6CGC ratio was obtained for primary mono or diamine having short alkyl chain length.

4 Conclusions

New 5CGC and 6CGC were successfully synthesized by "two-steps" and "one-pot" routes and characterized. The results obtained provide the following conclusions:

The two-steps route consisted in two consecutive reactions.

(i) The total aminolysis of glycerol carbonate in a concentrated medium without the use of a catalyst was carried out at 50°C for 2 h. It afforded 2 HU isomers in a ratio α/β varying versus the length of the alkyl chain.

(ii) The isomers were transesterified in a second step using different catalysts at 80°C for 7 h. Good yields and conversions were obtained using phosphazene. Na_2CO_3, $C_{10}H_{14}O_4Zn$, and C_4H_9OK afforded mostly 5CGC whereas phosphazene proved its efficiency for the transesterification of both α and β HU isomers to provide 5CGC and 6CGC, respectively. The activity of a catalyst is greatly affected by the dissolution time and the degree of dissolution. As phosphazene was the more soluble catalyst, it presented the higher catalytic activity and promoted the homogeneous transesterification process.

(iii) Higher yields and conversions were obtained for DMC/HU ratios higher than 2. DMC playing both a role of reagent and solvent increased the system compatibility.

(iv) The reaction was also affected by increasing the length of the alkyl chain. The best conversion of HU isomers was given with the shorter alkyl chains of the HU.

For the "one-pot" synthesis that is an in situ reaction coupling of the aminolysis and transesterification reactions, a competition of the products was shown during the course of the reaction. Moreover, this route favored the formation of side reactions like the aminolysis of 6CGC and the formation of dialkyl urea.

The "two-steps" synthesis affords the highest yield of 5CGC/6CGC and the "one-pot" synthesis gives a better conversion of β isomer and a better selectivity of the 6CGC. By medium engineering, it is possible to select experimental conditions according to the objectives: high yields in CGC or a well-targeted selectivity.

Cyclic carbonates having exocyclic urethane functions are hydrophobic systems widely used to switch the hydrophilic properties, $\mathrm{Log}P_{\mathrm{OW}}$ and the dipole moment of glycerol carbonate.

Finally, results used for the synthesis of monofunctional cyclic carbonates were transposed to the synthesis of bifunctional cyclic carbonates. In the future, Bis5CGC, Bis6CGC, and Bis56CGC will be used for the synthesis of polycarbonates and poly(HUs) having also urethane functions.

The authors have declared no conflict of interest.

References

[1] Guan, J., Song, Y., Lin, Y., Yin, X. et al., Progress in study of non-isocyanate polyurethane. *Ind. Eng. Chem. Res.* 2011, *50*, 6517–6527.

[2] Howard, G. T., Biodegradation of polyurethane: A review. *Int. Biodeterior. Biodegrad.* 2002, *49*, 245–252.

[3] Rokicki, G., Lazinski, R., Epoxy resins modified by carbon dioxide. *Angew. Makromol.* 1987, *148*, 53–66.

[4] Burk, R. M., Roof, M. B., A safe and efficient method for conversion of 1,2- and 1,3- diols to cyclic carbonates utilizing triphosgene. *Tetrahedron Lett.* 1993, *34*, 395–398.

[5] Nomura, R., Ninagawa, A., Matsuda, H., Synthesis of cyclic carbonates from carbon dioxide and epoxides in the presence of organoantimony compounds as novel catalysts. *J. Org. Chem.* 1980, *45*, 3735–3738.

[6] Calo, V., Nacci, A., Monopoli, A., Fanizzi, A., Cyclic carbonate formation from carbon dioxide and oxiranes in tetrabutylammonium halides as solvents and catalysts. *Org. Lett.* 2002, *4*, 2561–2563.

[7] Kuran, W., Active sites, nature and mechanism of carbon dioxide-propylene oxide copolymerization and cyclization reactions employing organozinc-oxygen catalysts. *Appl. Organomet. Chem.* 1991, *5*, 191–194.

[8] Darensbourg, D. J., Ganguly, P., Choi, W., Metal salen derivatives as catalysts for the alternating copolymerization of oxetanes and carbon dioxide to afford polycarbonates. *Inorg. Chem.* 2006, *45*, 3831–3833.

[9] Carothers, W. H., Van Natta, F. J., Studies on polymerization and ring formation. III. Glycol esters of carbonic acid. *J. Am. Chem. Soc.* 1930, *52*, 314–318.

[10] Tomita, H., Sanda, F., Endo, T., Structural analysis of polyhydroxyurethane obtained by polyaddition of bifunctional five-membered cyclic carbonates and diamine based on model reaction. *J. Polym. Sci., Part A: Polym. Chem.* 2001, *39*, 851–859.

[11] Sarel, S., Pohoryles, L. A., The stereochemistry and mechanism of reversible polymerization of 2,2-disubstituted 1,3-propanediol carbonates. *J. Am. Chem. Soc.* 1958, *80*, 4596–4599.

[12] Sarel, S., Pohoryles, L. A., Ben Shoshan, R., Organic carbonates. IV. 1a, b, c factors affecting formation of homologous cyclic carbonates. *J. Org. Chem.* 1959, *24*, 1873–1880.

[13] Albertson, A.-C., Sjoeling, M., Homopolymerization of 1,8-dioxan-2-one to high molecular weight poly(trimethylene carbonate). *J. Macromol. Sci. Pure Appl. Chem.* 1992, *29*, 43–54.

[14] Hu, B., Zhuo, R. X., Fan, C. L., Synthesis of copolymer of 1,3-dioxan-2-one and 2-hydro-2-oxo-1,3,2-dioxaphosphorinane. *Polym. Adv. Technol.* 1998, *9*, 145–149.

[15] Rokicki, G., Aliphatic cyclic carbonates and spiroorthocarbonates as monomers. *Prog. Polym. Sci.* 2000, *25*, 259–342.

[16] Matsuo, J., Aoki, K., Sanda, F., Endo, T., Substituent effect on the anionic equilibrium polymerization of six-membered cyclic carbonates. *Macromolecules* 1998, *31*, 4432–4438.

[17] Kenar, J. A., Tevis, I. D., Convenient preparation of fatty acid ester carbonates. *Eur. J. Lipd Sci. Technol.* 2005, *107*, 135–137.

[18] Tasaki, H., Toshima, K., Matsumara, S., Enzymatic synthesis and polymerization of cyclic trimethylene carbonate monomer with/without methyl substituent. *Macromol. Biosci.* 2003, *3*, 436–441.

[19] Pyo, S.-H., Persson, P., Lundmark, S., Hatti-Kaul, R., Solvent-free lipase-mediated synthesis of six-membered cyclic carbonates from trimethylolpropane and dialkyl carbonates. *Green Chem.* 2011, *13*, 976–982.

[20] Spanagel, E. W., Carothers, W. H., Macrocyclic esters. *J. Am. Chem. Soc.* 1935, *57*, 929–934.

[21] Krimm, H., Buysh, H. J., Cyclic carbonic acids and derivatives, US Patent 4, 501, 905, 1983.

[22] Kiso, Y. M., Preparation of cyclic carbonate, Mitsui Petrochemical industries Ind., US Patent 0 300, 794, 1988.

[23] Clements, J. H., 6-membered cyclic carbonates, US Patent 03 089, 424, 2003.

[24] Buysh, H.-J., Process for the preparation of cyclic carbonates having 6-membered, US Patent 5 861, 107, 1997.

[25] Werpy, T., Peterson, G., *Top Value Added Chemicals from Biomass*, Vol. *1*, U.S. Department of Energy, Oak Ridge, TN, USA 2004, 67 pages.

[26] Zhou, C.-H., Beltramini, J. N., Fan, Y.-X., Lu, G. Q., Chemoselective catalytic conversion of glycerol as a biorenewable source to valuable commodity chemicals. *Chem. Soc. Rev.* 2008, *37*, 527–549.

[27] Roice, M., Subhashchandran, K. P., Gean, A. V., Franklin, J., Rajasekharan Pillai, V. N., Synthesis and characterization of glycerol dimethacrylate cross-linked polymethyl methacrylate: A resin for solid phase peptide synthesis. *Polymer* 2003, *44*, 911–922.

[28] Wittlich, P., Themann, A., Vorlop, K. D., Conversion of glycerol to 1,3-propanediol by a newly isolated thermophilic strain. *Biotechnol. Lett.* 2001, *23*, 463–466.

[29] Clacens, J. M., Pouilloux, Y., Barrault, J., Selective etherification of glycerol to polyglycerols over impregnated basic MCM-41 type mesoporous catalysts. *Appl. Catal., A: Gen.* 2000, *227*, 181–190.

[30] Vieville, C., Yoo, J. W., Pelet, S., Mouloungui, Z., Synthesis of glycerol carbonate by direct carbonatation in supercritical CO_2 in the presence of zeolites and ion exchange resins. *Catal. Lett.* 1998, *56*, 245–247.

[31] Pasquier, N., Keul, H., Heine, E., Moeller, M. et al., Amphiphilic branched polymers as antimicrobial agents. *Macromol. Biosci.* 2008, *8*, 903–915.

[32] Ubaghs, L., Fricke, N., Keul, H., Hocker, H., Polyurethanes with pendant hydroxyl groups: Synthesis and characterization. *H. Macromol. Rapid Commun.* 2004, *25*, 517–521.

[33] Bernard, J. M., Process for the preparation of polyhydroxyurethanes. FR Patent, 2, 911, 878, 2008.

[34] Nohra, B., Candy, L., Blanco, J. F., Raoul, Y., Mouloungui, Z., Aminolysis reaction of glycerol carbonate in organic and hydroorganic medium. *J Am Oil Chem Soc* 2012, *89*, 1125–1133.

[35] Tomita, H., Sanda, F., Endo, T., Reactivity comparison of five- and six-membered cyclic carbonates with amine. *J. Polym. Sci., Part A: Polym. Chem.* 2001, *39*, 162–168.

[36] Simanjuntak, F. S., Kim, T. K., Lee, T., Ahn, B. S. et al., CaO-catalyzed synthesis of glycerol carbonate from glycerol and dimethyl carbonate: Isolation and characterization of an active Ca species. *Appl. Catal., A: Gen.* 2011, *401*, 220–225.

[37] Ochoa-Gomez, J. R., Gomez-Jimenez-Aberasturi, O., Maestro-Madurga, B., Pesquera-Rodriguez, A. et al., Synthesis of glycerol carbonate from glycerol and dimethyl carbonate by transesterification: Catalyst screening and reaction optimization. *Appl. Catal., A: Gen.* 2009, *366*, 315–324.

[38] He, Y., Keul, H., Moller, M., Synthesis, characterization, and application of a bifunctional coupler containing a five- and six-membered ring carbonate. *React. Funct. Polym.* 2011, *71*, 175–186.