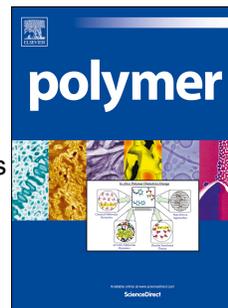


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Graphical Abstract



Upgrading castor oil: from heptanal to non-isocyanate poly(amide-hydroxyurethane)s

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Abstract

Intensive research has recently been carried out to synthesize non-isocyanate polyurethanes (NIPUs) from five-membered cyclic carbonates and amines as a sustainable route to industrial relevant polyurethanes. Herein, an activated disubstituted cyclic carbonate and methyl ester containing monomer **CE** was prepared using castor oil based heptanal and CO₂. Good results for the catalytic cycloaddition have been obtained using renewable sugar cane bagasse in combination with TBAB, and this system has been shown to be recyclable. A novel poly(amide-hydroxyurethane) (**PAHU**) was obtained by bulk ring-opening and amidation polymerization of high reactive **CE** with 1,6-diaminohexane at low temperature and in absence of catalyst. **PAHU** contains aliphatic pendant moieties allowing its self-assembling into nanoparticles in aqueous solution, showing potential application in catalysis or drug delivery among other applications.

Introduction

Polyurethanes (PUs) are one of the most important classes of polymers. Due to their versatile properties, they can be used as thermoplastics, thermosets or elastomers in a multitude of everyday life applications such as foams, coatings, sealants, adhesives or fibers.¹ Despite this wide range of applications, there

has been increased concern for the use of isocyanates, as they are toxic compounds being made from even more toxic reagents.² Another issue regarding the use of isocyanates is their sensitivity to moisture that can be problematic for their storage stability. Moreover, isocyanates and polyols are currently synthesized from petrochemical resources. Stimulated by strict regulations and the quest for sustainable development, latest advances in PU research have been driven by a growing demand for greener processes exploiting renewable resources and reducing potential hazards.

Consequently, intensive research on alternative synthesis pathways to non-isocyanate PUs (NIPUs) has been carried out.³ These studies concluded that the aminolysis of cyclic carbonates is one of the most promising alternatives. Even though six- and seven-membered cyclic carbonates are more reactive than five-membered carbonates, the focus has been placed on the last ones which are readily available from the carbonation of epoxide groups. The generation of cyclic carbonates by this route enables the fixation of the greenhouse gas carbon dioxide in a 100% atom economical reaction. CO₂ is an abundant renewable C₁-building block for the synthesis of a wide range of organic chemicals.⁴ As a matter of fact, there are yet commercial industrial processes to obtain aliphatic cyclic carbonates such as ethylene and propylene carbonates using CO₂ and a wide range of epoxides can be transformed in the corresponding cyclic carbonates by means of different catalytic systems.⁵ Moreover, it has been shown that cyclic carbonate materials can be readily obtained from renewable resources such as plant oils,⁶ fatty acids,⁷ limonene⁸ or lignocellulose.⁹ Quaternary ammonium salts, such as tetrabutylammonium bromide (TBAB), catalyses this transformation with catalysts loadings 3-5 %.⁶ Heterogeneous catalysts such as Keggin heteropolyacids Pt doped were also active but the catalyst was not recyclable.¹⁰ Two points have been identified as possibility of improvement of the catalytic activity. Firstly, it has been observed that binary catalysts improve the activity. For example, the combination SnCl₄·5H₂O/TBAB showed a synergic effect achieving a 94 % conversion in the reaction of soybean oil and CO₂ in 20h at 140°C.^{6h} In this case, toxic dimethylformamide was used as a solvent. In another example, a cooperative effect was observed using the combination of TBAB and polyoxometalates containing chromium^{6g} or TBAB and aluminium complexes in the cycloaddition of CO₂ to methyl oleate.¹¹ A second factor is the use of supercritical or condensed carbon dioxide. This has been attributed to an increase of the oil-CO₂ solubility

due to the increased pressure.⁶⁹ Nevertheless, the solubility of the catalyst in the condensed CO₂ phase was also important, since as the density of the CO₂ phase increased, the ionic catalyst became insoluble and the conversion dropped. Thus, it is necessary to find more sustainable catalytic systems which can be reused and to optimize the pressure conditions to the optimum substrate-CO₂ versus catalyst solubility.

Soybean oil and castor oil fatty acid derivatives, containing internal double bonds, have been investigated for the production of NIPUs.¹² The resulting disubstituted carbonates are less reactive than monosubstituted cyclic carbonates and elevated temperatures and long reaction times are needed to obtain high conversions. Undecylenic acid, a castor oil derivative having a terminal double bond, has also been investigated.¹³ Undecylenic acid is obtained from the thermal cracking of ricinoleic acid and in this process heptanal is also obtained. This product is widely used as a synthesis intermediate for fragrance and aroma industry. However, the use of this C7 cut of castor oil as an intermediate in polymer chemistry is practically non-existent.

The aim of this work was developing a more environmentally friendly synthetic strategy for PUs by using heptanal as biobased starting material and by avoiding isocyanates. The strategy relies on the preparation of a new five-membered disubstituted cyclocarbonate methyl ester precursor through the carbonation of a renewable heptanal derivative. The polymerization through carbonate ring opening and methyl ester amidation afforded a poly(amide hydroxyurethane) PAHU containing pendant aliphatic chains. The self-assembling of this amphiphilic structure into polymeric nanoparticles was investigated.

Experimental Section

Materials

The following chemicals were used as received: heptanal (Arkema, 96%), trimethyl phosphonoacetate (Aldrich, 98%), 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU, Aldrich, ≥99%), n-decane (Merck, 99%), m-chloroperbenzoic acid (MCPBA, Aldrich, 70%), 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulphide (Santonox[®]) (Aldrich), tetrabutylammonium bromide (TBAB, Aldrich, ≥99%), Ytterbium (III) trifluoromethane sulfonate hydrate (Aldrich), hexylamine (Aldrich, 99%), 1,6-diaminohexane (HDA, Aldrich, 98%). Carbon dioxide (SCF Grade,

99.999%, Air Products) was used introducing an oxygen/moisture trap in the line (Agilent). Sugar cane bagasse (SCB) was obtained from the region of Loukos (Morocco) after sugar extraction, washing with water and air dried. The inner part was then milled and dewaxed in a Soxhlet extractor with toluene ethanol (2:1, v/v) for 12 h and then dried under vacuum at 60 °C. Aluminum complex [Al(salabza)Cl]¹¹ and 2-bis(aminopyridinium) tetrachlorozincate¹⁴ were obtained following reported procedures. All solvents were purified by standard procedures.

Instrumentation

The IR analyses were performed on a FTIR- 680PLUS spectrophotometer with a resolution of 4 cm⁻¹ in the transmittance mode. NMR spectra were recorded on a Varian VNMRS400. The samples were dissolved in CDCl₃ or DMSO-d₆, and ¹H and ¹³C NMR spectra were recorded at room temperature with tetramethylsilane as an internal standard. ESI MS were run on a chromatographic system Agilent 1200 liquid chromatography coupled to 6210 Time of Flight (TOF) mass spectrometer from Agilent Technologies with an ESI interface.

Size exclusion chromatography (SEC) analysis was carried out with an Agilent 1200 series system equipped with an Agilent 1100 series refractive-index detector. DMF was used as eluents at a flow rate of 1.0 mL/min. The calibration curves for SEC analysis were obtained with polystyrene standards. Differential scanning calorimetry (DSC) measurements were carried out with a Mettler DSC822e thermal analyser with N₂ as the purge gas. Samples, 6-12 mg, were used for DSC analysis. Thermal stability studies were carried out with a Mettler TGA/SDTA851e/LF/1100 with N₂ as the purge gas at a scanning rate of 10 °C/min.

Transmission electron microscopy (TEM) was performed using a JEOL JEM-1011 TEM microscope. Before the measurement, a drop of solution was placed on a copper grid which was allowed to dry at room temperature.

Fluorescence spectra were recorded using a Shimadzu RF-5301PC fluorescence spectrometer at room temperature. The samples were excited at 335 nm, and the emission spectra were recorded from 350 to 500 nm.

Dynamic light scattering (DLS) measurements were carried out at room temperature using Zetasizer Nano ZS (Model ZEN3500) from Malvern Instruments equipped with a He-Ne laser.

Synthesis of methyl 2-nonenoate (1)

5.00 g (43.8 mol) of heptanal, 7.98 g (43.8 mmol) of trimethyl phosphonoacetate and 0.62 g (4.4 mmol, 10 mol% to heptanal) of n-decane as internal standard were added to a round-bottom flask. The flask was immersed into an ice bath with magnetic stirring and 6.57 mL (43.8 mmol) of DBU was slowly added over 15 min. The temperature was maintained at 0°C. The conversion of heptanal, determined by GC, was 97% after 3 hours. The crude of reaction was dissolved in diethyl ether and washed with 10% HCl solution, 10% K₂CO₃ solution and finally with brine. The organic phase was dried over anhydrous magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The obtained oil was distilled under reduced pressure (7 mmHg) and the fraction at 85-90°C was collected. The product was obtained as a mixture of E:Z isomers (ratio 98.5:1.5) in a 93% yield.

¹H NMR [CDCl₃, TMS, δ (ppm)] (Figure S1a): 6.96 (dt, $-\text{CH}=\underline{\text{C}}\text{H}-\text{CO}-$), 5.82 (dt, $-\underline{\text{C}}\text{H}=\text{CH}-\text{CO}-$), 3.73 (s, $-\text{O}-\underline{\text{C}}\text{H}_3$), 2.21 (m, $-\underline{\text{C}}\text{H}_2-\text{CH}=\text{CH}-$), 1.57-1.28 (m, $-\underline{\text{C}}\text{H}_2-$), 0.88 (t, $-\underline{\text{C}}\text{H}_3$).

¹³C NMR [CDCl₃, TMS, δ (ppm)] (Figure S1b): 167.41 ($-\underline{\text{C}}\text{O}-$), 150.06 ($-\underline{\text{C}}\text{H}=\text{CH}-\text{CO}-$), 120.96 ($-\text{CH}=\underline{\text{C}}\text{H}-\text{CO}-$), 51.98 ($-\text{O}-\underline{\text{C}}\text{H}_3$), 32.42 ($-\underline{\text{C}}\text{H}_2-\text{CH}=\text{CH}-$), 31.79 ($-\underline{\text{C}}\text{H}_2-$), 29.00 ($-\underline{\text{C}}\text{H}_2-$), 28.17 ($-\underline{\text{C}}\text{H}_2-$), 22.75 ($-\underline{\text{C}}\text{H}_2-$), 14.26 ($-\underline{\text{C}}\text{H}_3$).

Synthesis of 2,3-epoxynonanoic methyl ester (EE)

The epoxidation reaction was carried out by dissolving 14.8 g (60.1 mmol) of dry MCPBA (70%), 5 g (29.4 mmol) of **1** and 0.15 g (0.44 mmol) of 3-ter-butyl-4-hydroxy-5-methylphenylsulphide into 50 mL of 1,2-dichloroethane. The mixture was maintained at reflux temperature for 4 h. Then, 7.5 g (30.4 mmol) of dry MCPBA was dissolved into 25 mL of 1,2-dichloroethane and this solution was added to the reaction flask. The reaction was followed by ¹H NMR and after 2h, the crude of reaction was washed with 5% Na₂S₂O₅ solution, 5% NaHCO₃ solution, and brine. The organic phase was dried over anhydrous magnesium sulfate, and 1,2-dichloroethane was evaporated off. The obtained oil was purified

by column chromatography using hexane:ethyl acetate, 10:1, as eluent, to afford the pure compound as an oil, in a 72 % yield .

^1H NMR [CDCl_3 , TMS, δ (ppm)] (Figure S2a): 3.79 (s, $-\text{O}-\underline{\text{C}}\text{H}_3$), 3.23 (d, $-\text{O}-\underline{\text{C}}\text{H}-\text{COO}-$), 3.16 (dt, $-\text{O}-\underline{\text{C}}\text{H}-\text{CH}_2-$), 1.57-1.28 (m, $-\underline{\text{C}}\text{H}_2-$), 0.89 (t, $-\underline{\text{C}}\text{H}_3$).

^{13}C NMR [CDCl_3 , TMS, δ (ppm)] (Figure S2b): 169.93 ($-\underline{\text{C}}\text{O}-$), 58.69 ($-\text{O}-\underline{\text{C}}\text{H}-\text{CH}_2-$), 53.05 ($-\text{O}-\underline{\text{C}}\text{H}-\text{COO}-$), 52.52 ($-\text{O}-\underline{\text{C}}\text{H}_3$), 31.76 ($-\text{CH}-\underline{\text{C}}\text{H}_2-$), 31.57 ($-\underline{\text{C}}\text{H}_2-$), 29.01 ($-\underline{\text{C}}\text{H}_2-$), 25.79 ($-\underline{\text{C}}\text{H}_2-$), 22.64 ($-\underline{\text{C}}\text{H}_2-$), 14.16 ($-\underline{\text{C}}\text{H}_3$).

HRMS (ESI-TOF) m/z: $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{10}\text{H}_{18}\text{O}_3$ 186.1252; found 186.1256.

Synthesis of methyl 2,3-carbonyldioxynonanoate (CE)

The reactions were carried out in a 25 mL Parr reactor equipped with a magnetic stirrer and automatic temperature control system. The reactor was charged with epoxide (1.5 g, 8.1 mmol) and TBAB (5 or 3 mol %). When a binary catalyst system was employed, cocatalyst was also added to the reactor. The reactor was purged with vacuum and argon several times and after that heated to the specific temperature (80, 100 or 120 °C depending on the experiment) and finally was pressurized with CO_2 to reach the desired pressure (300, 600 or 1275 Psi). After the desired reaction time (1, 3 or 6 hours), the reactor was cooled to room temperature and gradually depressurized. The conversion of epoxide and the yield were determined by ^1H NMR of the crude reaction mixture using mesitylene as internal standard. The reaction mixture was dissolved in diethyl ether (10 mL) and washed with water (3 x 15 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The product was purified by column chromatography using hexane:ethyl acetate, 40:1 to 20:1, as eluent, to afford the carbonate cyclic as viscous oil, in a 46 % yield.

^1H NMR [CDCl_3 , TMS, δ (ppm)] (Figure S3a): 4.66, 3.87, 1.84, 1.55-1.25, 0.90.

^{13}C NMR [CDCl_3 , TMS, δ (ppm)] (Figure S3b): 167.78, 153.38, 79.68, 76.98, 53.30, 34.34, 31.50, 28.65, 24.12, 22.47, 14.02.

HRMS (ESI-TOF) m/z: $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{18}\text{O}_5$ 230.1150; Found 230.1154.

Polymerization of CE and 1,6-diaminohexane

2,3-carbonyldioxynonanoate (CE) (4.2g, 1.8 mmol) and 1,6-diaminohexane (2.2g, 1.8 mmol) and 1.5mL of anhydrous DMF were added to a dry 10 mL round-bottom flask. The reaction mixture was stirred at room temperature for 30

min under nitrogen purge. Then, the polymerization was continued under reduced pressure (30 mBar). After 24h, the polymer was precipitated into diethyl ether, centrifuged, filtered and dried in vacuum. The polymer was obtained as a white solid in 84 % yield.

^1H NMR [DMSO, δ (ppm)] (Figure S5a): 7.58, 6.80, 4.82, 3.87, 3.59, 3.51, 3.04, 2.91, 2.59, 1.80-1.15, 0.85.

^{13}C NMR [DMSO, δ (ppm)] (Figure S5b): 172.52, 171.35, 169.01, 156.12, 73.82, 72.34, 51.59, 38.32, 31.36, 30.55, 29.59, 29.26, 28.77, 26.22, 24.97, 22.17, 14.05.

Results and Discussion

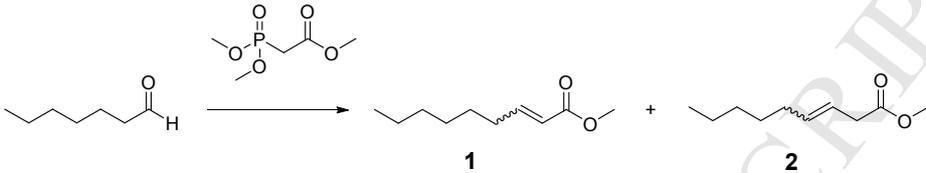
Synthesis of 2,3-epoxynonanoic methyl ester (EE)

The Horner-Wadsworth-Emmons (HWE) reaction is one of the most popular and powerful method for the generation of C-C double bonds.¹⁵ This modification of the Wittig reaction is widely used for the preparation of α,β -unsaturated esters. It has several advantages over the Wittig reaction, which are a result of the strong nucleophilic nature of the phosphonate carbanion created during the reaction. This increase in nucleophilicity allows milder reaction conditions, tolerance of a variety of functional groups and use of less electrophilic aldehydes and ketones. The HWE reaction of triethyl phosphonoacetate with a variety of aldehydes using stoichiometric amounts of DBU¹⁶ or catalyzed by DBU in presence of K_2CO_3 ¹⁷ was described to give α,β -unsaturated esters with high yield and E-selectivity.

We evaluated the reactivity of heptanal and trimethyl phosphonoacetate in bulk using 1 eq of DBU at room temperature (Table 1). The aldehyde consumption was measured by GC using an internal standard. A conversion of 98% was reached after 3h. The reaction was also monitored by ^1H NMR spectroscopy through the appearance of signals at 6.96 and 5.82 ppm corresponding to the carbon double bond protons and signal at 3.73 ppm corresponding to the methyl protons of the methyl 2-nonenoate (**1**). Isomers E and Z could be identified thus allowing their quantification. Moreover, unexpected signals at 5.54 and 3.02 ppm

could be observed, that can be ascribed to methyl 3-nonenoate (**2**) as the isomerization product. Isomerization of 2-pentenoates to 3-pentenoates has been described to occur in presence of catalytic amounts of cyclic tertiary amines such as DBU at temperatures higher than 50°C.¹⁸ The extension of isomerization was 18% as obtained by ¹H NMR.

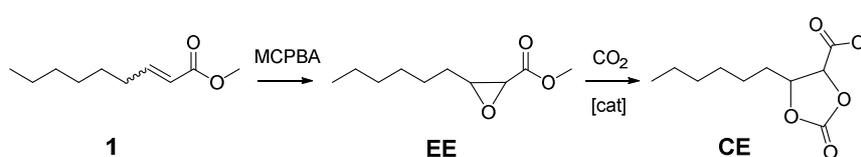
Table 1. HWE reaction in bulk and using equimolar amounts of aldehyde and phosphonate



Entry	T (°C)	DBU (eq)	Conv (%) ^[a]	E1:Z1 ^[b]	1:2 ^[c]	Yield (%)
1	25	1.00	98	98.8:1.2	82:18	81
2	0	1.00	98	98.5:1.5	97:3	98
3	0	0.75	97	98.5:1.5	98:2	94
4	0	0.50	94	98.5:1.5	99:1	90

[a] Heptanal conversion from GC. [b] **E1:Z1** isomers ratio from ¹H NMR [c] **1:2** isomers ratio from ¹H NMR

To avoid the isomerization process, the reaction was carried out at 0°C, reaching similar aldehyde conversion and **E1:Z1** ratio, and higher **1:2** ratio and yield. Attempts to diminish the DBU amount were carried out. A slight conversion decrease with no significant variations in α,β -unsaturated ester selectivity were observed. However, a yield decrease was observed, thus 1 eq. was used for **1** synthesis. After purification by distillation under reduced pressure, **1** was epoxidized using *m*-chloroperbenzoic acid to obtain methyl 2,3-epoxynonanoate (**EE**) in a 72% yield (Scheme 1). Both compounds were characterized by ¹H and ¹³C NMR spectroscopy (Figures S1 and S2)



Scheme 1. Epoxidation of methyl 2,3-nonen-1-yl ester and cycloaddition of CO₂ to methyl 2,3-epoxynonanoate

Cycloaddition of CO₂ to methyl 2,3-epoxynonanoate

The cycloaddition of CO₂ to **EE** producing the corresponding cyclic carbonate, methyl 2,3-carbonylidioxynonanoate **CE** (Scheme 1) was first attempted using tetrabutylammonium bromide (TBAB), which is a common low cost and easy to handle catalyst for this reaction.¹⁹

The reaction of the substrate **EE** with CO₂ at 600 psi and 80°C using 5 mol % of catalyst provided an oily mixture. The ¹H NMR spectra of the crude reaction (Figure 1) showed a multiplet signal at 4.66 ppm, attributed to the cyclic carbonate (44% yield) (entry 1, Table 2). Signals observed at 4.01-4.41 ppm were attributed to the presence of the diol from the hydrolysis of the substrate. Other signals at 3.54 and 2.84 ppm seems to indicate the presence of 1,2 and 1,3-dicarbonylic compounds as a result of the diol elimination.

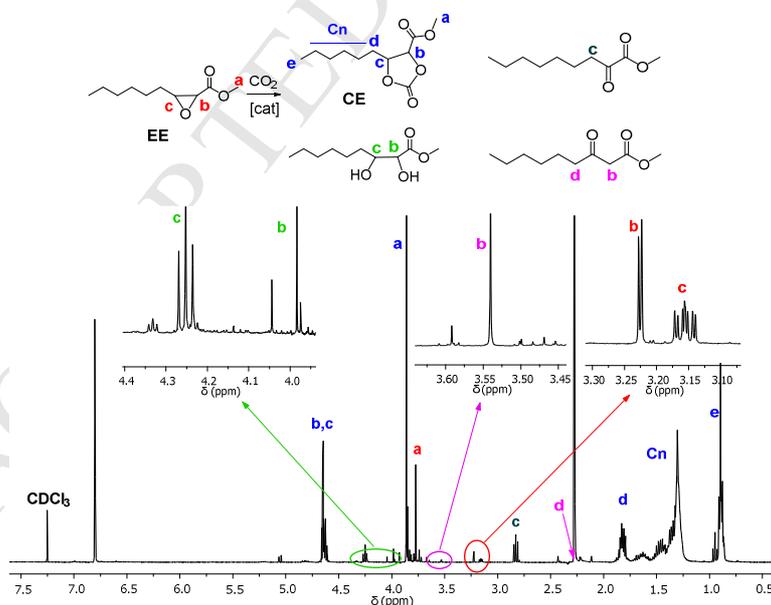


Figure 1. ¹H NMR spectra (CDCl₃) of the crude reaction of **EE** and CO₂ (entry 1, table 2)

Optimization of the catalytic reaction conditions was then undertaken. At 600 psi, increasing the temperature to 100°C and 120°C, an increase of conversion up to near completion was observed (entries 1-3, Table 2). In fact, at 120°C the epoxide was not detected but the selectivity to the cyclic carbonated decreased due to secondary reactions. To determinate if the presence of the catalyst promoted the opening of the epoxide an experiment was run with less amount of catalyst (3 mol%) and during a longer period of time (6 h) but similar selectivity was obtained (entry 4, Table 2). Regarding the influence of the CO₂ pressure, conversion and selectivity were inferior when the pressure decreased to 300 psi, but increasing the pressure to 1275 psi, the conversion and selectivity did not improve either (entries 5 and 6, Table 2). Finally, the reduction of time to 1 h did not decrease the formation of by-products (entry 7, Table 2).

Table 2. Results of the cycloaddition of CO₂ to **EE** using TBAB as catalyst. ^[a]

Entry	Catalyst (mol%) ^[b]	T (°C)	P (psi)	t (h)	Conv (%) ^[c]	Yield (%) ^[d]
1	5	80	600	3	62	44
2	5	100	600	3	92	59
3	5	120	600	3	>99	51
4	3	100	600	6	86	60
5	5	100	1275	3	92	58
6	5	100	300	3	80	47
7	5	100	600	1	72	43

[a] Reaction conditions: catalysts: tetrabutylammonium bromide (TBAB) substrate: 1.5 g. [b] mol % in relation to the substrate. [c] Conversion determined by NMR using mesitylene as internal standard. [d] Yield determined by NMR using mesitylene as internal standard.

In the literature it has been proved that binary catalytic systems formed by one component able to activate the epoxide (a hydrogen bonding donor or Lewis acid) and a nucleophile for the ring open step increased the conversion of the epoxides into cyclic carbonates.^{5c,20} The effect of adding a co-catalyst was analysed at the reaction conditions 80°C, 600 psi and 5 mol%. Among the possible co-catalysts reported in the literature, we selected a bio renewable product such as sugarcane bagasse SCB (**3**),²¹ 2-bis(aminopyridinium) tetrachlorozincate (**4**),¹⁴ ytterbium triflate (**5**) and an aluminum complex [Al(salabza)Cl]¹¹ (**6**) (salabza: N,N'-bis(salicylene)-2-aminobenzylamine). The –OH

groups of the components of SCB (cellulose, hemicelluloses and lignin) have been reported to act as hydrogen-bonding donors to accelerate the ring-opening of the epoxide.²¹ The addition of SCB (2.5% w/w at 80°C, 600 psi and at 5 mol% TBAB) produced an increase in conversion and selectivity (entry 1, Table 3). When the reaction was run at the optimized temperature (100 °C, entry 2, Table 3) a 94 % of conversion was obtained (54 % yield) in 1 h reaction time using catalytic systems SCB/TBAB. Addition of **4** to TBAB produced also high conversion and good selectivity (entry 3, Table 3). Co-catalysts such as **5** and **6** produced a decrease of selectivity (entries 4 and 5, Table 3).

Table 3. Results of the cycloaddition of CO₂ to **EE** using **3-6**/TBAB as catalysts.^[a]

Entry	Catalyst	T (°C)	P (psi)	t (h)	Conv (%) ^[b]	Yield (%) ^[c]
1	3 /TBAB	80	600	3	79	60
2	3 /TBAB	100	600	1	94	54
3	4 /TBAB	100	600	1	93	48
4	5 /TBAB	100	600	1	91	30
5	6 /TBAB	100	600	1	72	26

[a] Reaction conditions: catalysts: **3** SCB 2.5 % w/w; **4** [pyNH₂]₂[ZnCl₄] 1 mol %; **5** Yb(OTf)₃ 1 mol %; **6** [Al(salabza)Cl] 1 mol %; TBAB 5 mol %; substrate: 1.5 g. [b] Conversion determined by NMR using mesitylene as internal standard. [c] Yield determined by NMR using mesitylene as internal standard.

The advantage of using the insoluble SCB was that it could be separated by filtration after the catalytic reaction and reused. Indeed, after the catalytic reaction the SCB was separated, washed with ether and dried. After adding fresh TBAB, it could be reused 5 more times without significant loss of activity and selectivity (Figure 2). **CE** was purified by column chromatography and characterized by NMR spectroscopy (Figure S3).

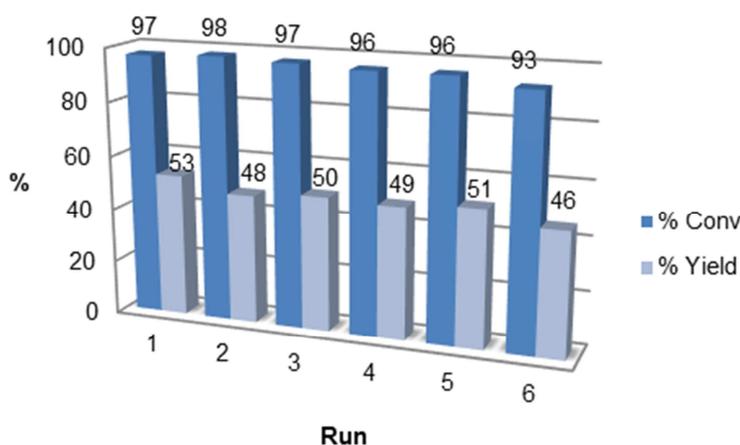


Figure 2. Recycling experiments of catalytic system **3**/TBAB in the cycloaddition of CO₂ to **EE**. Reaction conditions: **3**: 2.5 % w/w, TBAB: 5 mol %, substrate: 5 g, 80°C, 600 psi, 3h.

Poly(amide-hydroxyurethane) synthesis

The aminolysis of cyclic carbonates has been widely investigated. Not only the size but also the nature of the substituents attached to the cyclic carbonate influence the reactivity, as well as the structure of the amines and other parameters like the catalyst or the solvent. 5-membered cyclic carbonates are the least reactive cyclic carbonates. 6- and 7-membered cyclic carbonates are more reactive, but aminolysis of these compounds still requires the use of high temperatures.²² N-substituted 8-membered cyclic carbonates appeared to be much more reactive than the smaller cyclic carbonates.²³ Even being the less reactive, the 5-membered cyclic carbonates are still the most used ones and the influence of the substituent on the reactivity has been studied and attributed to electronic effects. Electron-withdrawing substituents increase the electrophilicity of carbonyl and activate nucleophilic attack of the amine.¹³ Moreover, the steric hindrance of the substituents and the effect of hydrogen bonds have also been considered.²² The remarkable reactivity of α -alkylidene substituted 5-membered cyclic carbonates has been recently described.²⁴

We investigated the aminolysis of the five membered carbonate **CE**. Primary aliphatic amines are the most reactive for the aminolysis of cyclic carbonates, thus n-hexylamine was used as a model compound. The reaction was carried out with a molar ratio **CE**/amine 1:1 at 70°C in bulk and monitored by ¹H NMR spectroscopy. The appearance of urethane methylene signals at 3.13 ppm (**f**₁ and **f**₂) and methyne signals at 4.00-5.20 ppm (**b**₁, **b**₂, **c**₁ and **c**₂) confirmed the hydroxyurethane formation (Figure 3b, Figure S4). Moreover, intense signals at 3.26 ppm (**e**₁ and **e**₂) can be seen that can be attributed to amide formation, as well as at 3.49 ppm, due to the presence of methanol obtained as a by-product. The reaction of the primary amine with the ester function has been previously described as a side reaction at high temperatures and could be avoided by working at 25°C.^{12,13} Other side reactions²⁵ that can take place during the aminolysis of cyclic carbonates such as the formation of ureas, oxazolidinones and dehydration products seems not to take place.

To further elucidate the relative reactivity of the carbonate and the ester functions in front of primary amines, we carried out the reaction using a **CE**/amine molar ratio 1:0.5 at 25°C in bulk. Hydroxyurethane and amide signals can be observed, thus indicating that both carbonate aminolysis and amide formation are taking place. After 40 min of reaction, a conversion of 20% for carbonate and 24% for ester moieties can be obtained by ¹H NMR spectroscopy (Figure 3c). This seems to indicate that the reactivity of both moieties does not differ significantly. When the reaction is carried out at 25°C using a molar ratio **CE**/amine 1:2, a mixture of amide-hydroxyurethanes **AHU1** and **AHU2** (81:19) is obtained after 30 min (Figure 3d).

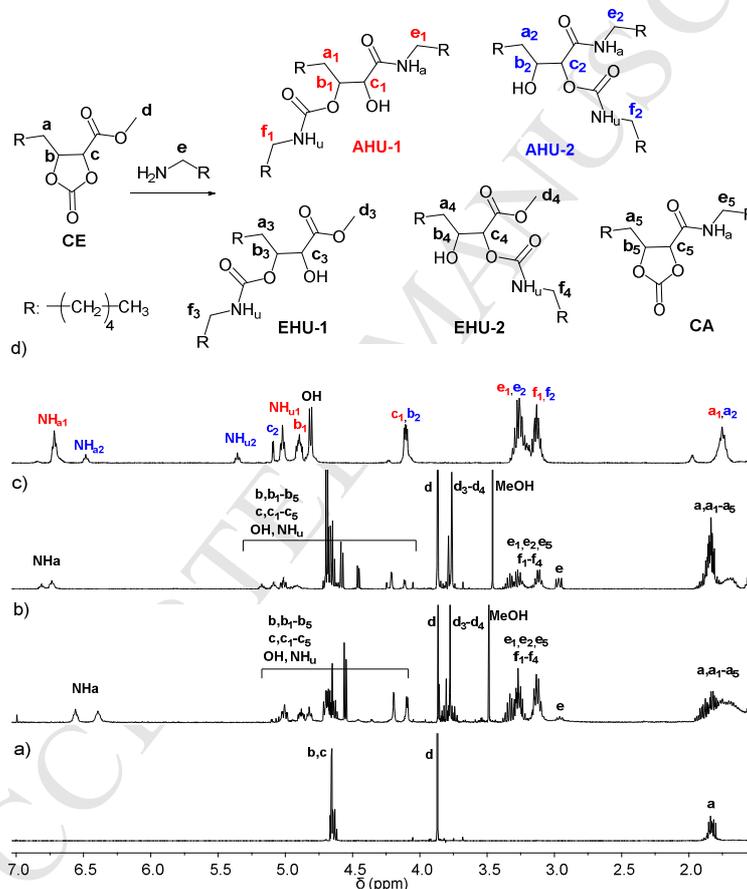
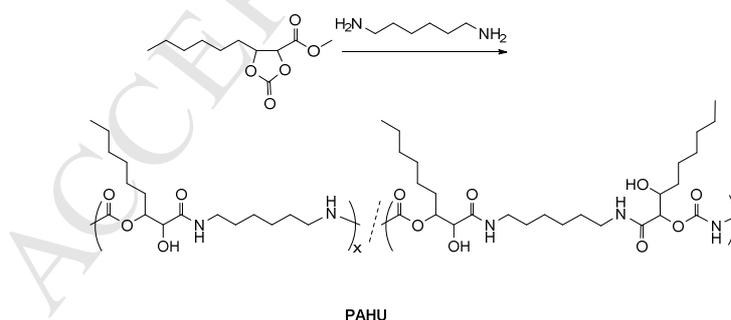


Figure 3. ¹H NMR spectra (CDCl₃) of a) **CE** and of the reaction of **CE** and hexylamine in bulk b) molar ratio 1:1 at 70°C, c) molar ratio 1:0.5 at 25°C, d) molar ratio 1:2 at 25°C

As has been previously reported,²² the electron-withdrawing effect of the ester moiety increases the electrophilicity of the carbonyl and activates the nucleophilic attack of the amine and the opening of the carbonate ring. According to the proposed reaction mechanism, the nucleophilic attack of the

amine to the carbonyl takes place, followed by the carbonate ring opening and the formation of secondary hydroxyurethanes. The rupture of the carbon-oxygen bond α to the ester group position seems to be more favoured than the one in the β position, according to a higher electron-withdrawing effect of the ester group, thus leading to a higher amount of **AHU1**. Moreover, the amide formation seems to be activated by the presence of the carbonate moiety, being the carbonyl ester more reactive than the 5-membered cyclic carbonate derived from methyl 9-decenoate, when the amidation takes place at 70-180°C using TBD as catalyst.²⁶

Taking into account the model reaction results, we carried out the one pot polymerization using 1,6-diaminohexane (Scheme 2, Table 4). The mixture of reactants was kept at the initial temperature for 30 min and vacuum was applied in the next step to remove the methanol byproduct and reach high conversion. **PAHU** formation was followed by ¹H NMR spectroscopy by the appearance of new methyne signals at 4.82 ppm (**b**₁, **c**₂), 3.87 (**c**₁, **b**₂) and methylene signals at 2.91 ppm (**f**₁, **f**₂) attributed to the hydroxyurethane moiety and methylene signals at 3.04 ppm (**e**₁, **e**₂) linked to the amide group (Figure 4a, Figure S5a). Signals labelled as * can be attributed to end groups. ¹³C NMR spectra showed the disappearance of carbonate and ester signals and the appearance of hydroxyurethane signals at 156.12 and 155.94 (**h**₁, **h**₂), 73.82 and 72.34 (**b**₁, **b**₂, **c**₁, **c**₂) ppm and amide signals at 172.57, 171.35 ppm (**g**₁, **g**₂) (Figure 4b, Figure S5b).



Scheme 2. Synthesis of poly(amide-hydroxyurethane)

The **PAHU** formation was also confirmed by IR spectroscopy by the appearance of bands at 1692cm⁻¹ and 1637cm⁻¹ attributed to the carbonyl of the urethane and amide moieties respectively, a broad band between 3590cm⁻¹ and 3150cm⁻¹

due to NH and OH groups and the disappearance of bands at 1810 and 1748 cm^{-1} due to carbonate and ester groups (Figure S6)

When the reaction was carried out in bulk at 25°C for 3h and the obtained solid showed a molar mass of 5800 g mol^{-1} from the SEC analysis in DMF (Table 4). Higher reaction time and temperature and solvent conditions were examined after this preliminary experiment. When DMF or higher reaction temperatures were used, higher molar masses were obtained. However, increasing reaction time seems not to have a significant effect on polymer molar masses (Figure S7).

Table 4. PAHU synthesis

Entry	T (°C)	Solvent	t (h) ^[a]	Mn (g mol^{-1}) ^[b]	\bar{D}
1	25	-	3	5800	1.7
2	25	DMF	6	7200	1.6
			24	8200	1.6
			48	7800 9700 ^[c]	1.7 1.4 ^[c]
3	60	-	3	8200 9700 ^[c]	1.5 1.4 ^[c]
				4	60

[a] Vacuum was applied after 30 min at atmospheric pressure [b] Molar mass by SEC in DMF prior to precipitation [c] Molar mass by SEC in DMF after precipitation

In spite of the high reactivity of **CE**, low molar masses were obtained. The synthesis of polyhydroxyurethanes from bis(cyclic carbonate)s and polyamines usually leads to low molar mass polymers. The presence of numerous side reactions that disturbs the stoichiometric carbonate/amine ratio and creates non reactive chain ends has been demonstrated when the reaction takes place at 80°C.²⁵ Moreover, the formation of high amounts of hydrogen bonds between urethane, hydroxyl and amine groups at room temperature can also limit the diffusion of the reactants thus limiting molar masses.²² This effect can explain the results in our case, in bulk as well in presence of an aprotic solvent.

The polymer was found to be soluble in DMF and DMSO and insoluble in water, acetone, THF and CHCl_3 . It was purified by precipitating in diethyl ether from the

crude of reaction in DMF and isolated as a white solid with high yield (76%). The poly(amide-hydroxyurethane) was characterized using spectroscopic methods and thermal analysis, showing a Tg at 47°C and a 5% of weight loss at 219°C (Figure S8).

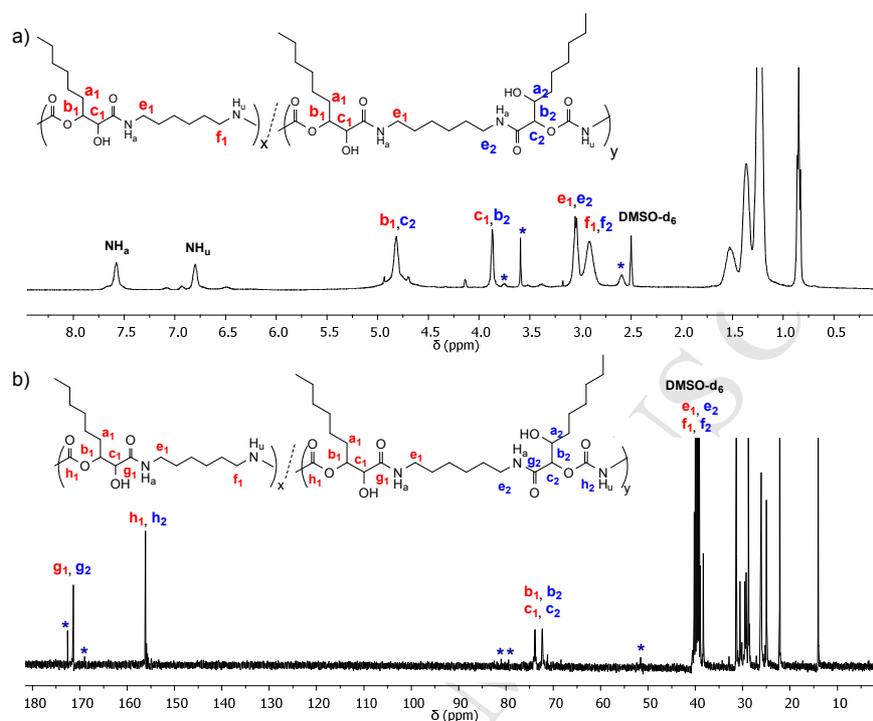


Figure 4. a) ^1H NMR and b) ^{13}C NMR spectra of PAHU (DMSO- d_6)

The obtained polymer contains an aliphatic amide-hydroxyurethane amphiphilic backbone and aliphatic hydrophobic pendant chains. Thus, it can self-assemble into nanoparticles in aqueous solution and be used in catalysis or drug delivery among other applications. It has been described that the presence of pendant aliphatic chains plays an important role in creating nanocavities when solvent diffusion method is used to obtain polymer nanoparticles.²⁷ We investigated the ability of the poly(amide-hydroxyurethane) to form nanoparticles with hydrophobic cavities using a water-based solvent diffusion method. The polymer was dissolved in DMF and added dropwise to stirring water and dynamic light scattering experiments confirmed the formation of stable and monodisperse nanoparticles with an average diameter of 106 nm (PI=0.1) (Figure 5a) that could be observed by TEM (Figure 5b). To determine the critical micelle concentration (CMC), pyrene was encapsulated as a fluorescent probe. The intensity variation of fluorescence emission peaks at 384 and 374 nm confirmed the effective encapsulation of the hydrophobic probe and the self-assembling bringing the hydrophobic moieties into the cavities (Figure 5c). A CMC value of 0.75 mg/L was

obtained (Figure 5d). This low value ensures high stability of the nanoparticles and less disruption with dilution, which can be very important in medical applications that involve intravenous injection.

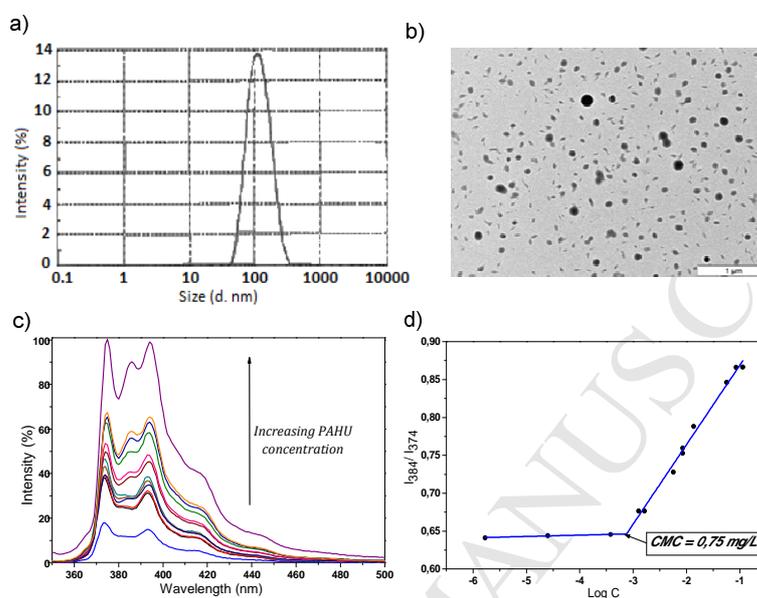


Figure 5. a) DLS size distribution by intensity of **PAHU** (0.8 mg/mL). b) TEM image of nanoparticles of **PAHU** (0.8 mg/mL). c) Fluorescence spectra of an aqueous solution of pyrene (6.0×10^{-7} M) and different concentrations of **PAHU** (1.7×10^{-6} to 0.12 mg/mL). d) Fluorescence intensity ratio I_{384}/I_{374} as a function of **PAHU** concentration.

Conclusions

In conclusion, heptanal, the by-product of thermal cracking of ricinoleic acid, has been functionalized by a HWE reaction and the obtained **1** has been epoxidized to obtain **EE** in good yield. To obtain **CE**, the catalytic cycloaddition of CO_2 to the epoxide has been investigated and good results have been obtained using renewable SCB in combination with TBAB catalytic system, which has been shown to be recyclable.

The reactivity of **CE** in front of amines has been investigated and the results show that not only the ester activated five-membered cyclic carbonate displayed a high reactivity, but also the ester moiety turn out to be very reactive. This allowed to carry out the bulk polymerization of **CE** and 1,6-diaminohexane at low temperature and in absence of catalyst, leading to NIPUs of molar mass similar

to the ones previously described. The obtained polymer forms stable and monodisperse nanoparticles in water, showing potential application in catalysis or drug delivery among other applications.

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