CO₂ as versatile carbonation agent of glycosides: Synthesis of 5- and 6-membered cyclic glycocarbonates and investigation of their ring-opening

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ABSTRACT

This study demonstrates the successful use of CO₂ as versatile carbonation agent for the synthesis of 5-membered and 6-membered bicyclic glycocarbonates from methyl α -D-mannopyranoside (MDM) and methyl α -D-galactopyranoside (MDG). On the one hand, these two sugars were cyclized into 5-membered glycocarbonates by mere reaction of CO₂ with their hydroxyls either at cis-2,3 or cis-3,4 positions and without resorting to phosgene or its derivatives. The reactivity of the obtained 5-membered cyclic glycocarbonates were further tested with hexyl- and dodecyl amine. The self-assembling behavior of the formed alkyl glycosides in water was investigated and characterized by transmission electron microscope (TEM).

On the other hand, secondary hydroxyls at 2- and 3- positions in MDM and MDG were first protected by a ketal group and by two ether, respectively before subjecting their respective 6-position hydroxyl to bromination. Their respective 6-bromo and 4-hydroxyl functions were subsequently reacted in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and CO₂. The resulting 6-membered cyclic glycocarbonates were then polymerized using 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) or DBU as organocatalyst. All the synthesized 5- and 6-membered cyclic glycocarbonates and polyglycocarbonates were thoroughly characterized by FT-IR, ¹H, ¹³C NMR and MALDI-ToF and Gel Permeation Chromatography (GPC).

1. Introduction

Carbohydrates, one of the most abundant renewable resources, have attracted increased interest as building blocks for polymer synthesis due to their biocompatibility, recognition properties and stereochemical diversity [1–4]. In addition to polysaccharides that are natural polymers whose sugar moieties are connected one to another through glycosidic linkages, there are two other types of synthetic sugar-based polymers where sugars are either conjugated as side groups to synthetic backbones or incorporated within the backbone and linked through ester, carbamate, peptide or carbonate bonds. The first are called glycopolymers and the second polyglycans.

Glycopolymers can be synthesized either by polymerization of sugar-carrying monomers or by post-polymerization modification [5–10]. In both cases, the derivatization of multifunctional saccharides generally necessitate several reactions due to the protection and deprotection steps. As for polyglycans, they are generally synthesized through polycondensation or ring-opening polymerization of

sugar-based monomers [4]. Similarly, selective protection-deprotection chemistry, harsh conditions and utilization of toxic compounds are usually required.

In an effort to synthesize polymers from sugars, we first made use of D-glucopyranoside and modified it to derive both hydrophilic and hydrophobic 6-membered cyclic glycocarbonates; the latter were then subjected to ring-opening polymerization and to sequential block copolymerization, allowing the synthesis of linear and macrocyclic hydrophilic and hydrophobic polyglycocarbonates [11]. We also developed another strategy to obtain polyglycocarbonates through polycondensation of methyl α -D-glucopyranoside with CO₂ [12]. In all cases and unlike the methodologies generally used to derive cyclic or linear carbonates, harsh conditions and toxic chemicals such as phosgene and its derivatives [13–17] were avoided, and instead, CO₂ was incorporated as C1 resource into the polyglycocarbonate formed. Recently, Buchard and coworkers also reported the synthesis of polyglycocarbonates through ROP of 6-membered cyclic glycocarbonates, obtained

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through carbonation of methyl α -D-mannopyranoside and thymidine attached D-deoxyribofuranoside by CO₂ [18,19].

Here we address a double challenge which is to resort to the same carbonation agent, CO₂, to first derive 5-membered cyclic glyco-carbonates by reacting it with either the 2- and 3- positions or the 3- and 4-positions of MDM and of MDG and to secondly obtain 6-membered cyclic glyco-carbonates by ring closure, using the 6- and 4-positions of these two sugars as shown in Schemes 1 and 3. Starting from MDM and

MDG the corresponding five-membered cyclic glyco-carbonates (MDMC₅, MDGC₅) could be easily formed by reaction of the two vicinal cis 2,3-and cis 3,4- hydroxyl groups of the unprotected glycosides with CO₂ in the presence of CH₂Br₂ (Scheme 1). On the other hand, after modifying hydroxyls at 2- and 3- positions of the two sugars, six-membered cyclic glyco-carbonates (MDMC₆, MDGC₆) could be isolated after bromination of their 6-hydroxyl group (Scheme 2) and ring-closure using CO₂ (Scheme 3). The synthesized 5- and 6-membered cyclic glyco-

Scheme 1. Synthesis of 5-membered cyclic glyco-carbonates, followed by their reactions with alkyl amines.

Scheme 2. Synthesis of 6-bromo-4-hydroxyl-mannoside and galactoside.

Scheme 3. Synthesis of polyglyco-carbonates (PMDMC and PMDGC).

carbonates were further reacted under distinct experimental conditions with different application prospects: six-membered glycocarbonates were indeed ring-opened and polymerized to obtain polyglycocarbonates (PMDMC, PMDGC) with sugar moieties incorporated on the main chain (Scheme 3); five-membered glycocarbonates were reacted with alkyl amine, opening up a new and facile route to conjugate sugars to the desired amino-containing substrates (Scheme 1).

2. Results and discussion

2.1. Synthesis of 5-membered cyclic glycocarbonates and of their alkyl conjugates

The synthesis of 5-membered cyclic carbonate ester of carbohydrates using phosgene or its derivatives was reported as early as in the late 60's [20,21]. Carbonation resulting in the formation of 5-membered cyclic carbonates could also be achieved through exchange reaction between dialkyl carbonates –separately prepared by coupling CO₂ and epoxides- with secondary alcohols of sugars [22,23]. We are reporting here a straightforward synthesis of 5-membered cyclic glycocarbonates directly from CO₂. We observed previously that trans hydroxyls in methyl α -D-glucopyranoside undergo polycondensation when reacted with CO₂ in the presence of CH₂Br₂ and DBU [12]. We thus reason that MDG and MDM which carry two vicinal cis hydroxyls would undergo cyclization and thus afford 5-membered cyclic glycocarbonates when reacted with CO₂, CH₂Br₂ and DBU. As anticipated and certainly because of the special cyclic structure of pyranosides, the carbonation yielded the expected 5-membered cyclic glycocarbonates with high efficiency. It should be stressed that these carbonation reactions were carried out without protection of any kind of the hydroxyls non-involved in the reaction which thus remained inert, and any activating additives such as ionic liquids [24]. In the case of MDM, the carbonation occurred between the cis-hydroxyls in 2- and 3- positions (60%) or in 3- and 4- positions (40%) to form MDMC₅ in high yield (90%, based on its acetylated derivative, Fig. 1A); as for MDG, the carbonation between the two cis-hydroxyls at 3- and 4- positions afforded MDGC₅ also in rather good yield (70%, based on its acetylated derivative, Fig. 1B). The corresponding products were isolated after acetylation of the remaining hydroxyls. Their cyclic structures were confirmed by IR characterization (1800 cm⁻¹) and by ¹³C NMR spectroscopy (153 ppm) (SI Figs. S1, S8 and S12). The molar mass measured by ESI-HRMS is 327.0679 exactly matching with the expected value (SI Figs. S4 and S5). Further, the structures were confirmed by the H's and C's coupling NMR experiments (COSY, HMBC and HSQC; see further details in Figs. S8–S15 in SI).

On the other hand one general need for sugar conjugation is resorting to powerful methodologies such as click chemistry to access to glycopolymers [6,7]. For instance for the azide functionalization of sugars the latter methodology requires in principle no protection of the hydroxyl groups but the mediation of imidazolium salts [25]. The preparation of 5-membered cyclic carbonates as described in this investigation thus offers an alternate and facile route of sugar conjugation as compared to previously reported ones.

Indeed cyclic carbonates being increasingly used as intermediates for the preparation of non-isocyanate polyurethane through their polycondensation with diamines this route of sugar conjugation appears a viable and simple method [26,27]. The reactivity of MDGC₅ and MDMC₅ towards hexyl amine and dodecyl amine was thus tested. In the same reaction pot where the carbonations of MDM and MDG were carried out, the amines were introduced and directly reacted with *in situ* formed cyclic carbonates to avoid a separation step of the latter. The isolated carbamate-containing glycoconjugates were obtained with yields ranging from 35 to 40% in agreement with values reported in

the literature for similar reactions [28,29]. The appearances of a new absorbance at 1685 cm⁻¹ instead 1800 cm⁻¹ in the IR spectrum (SI Fig. S2), and of a new peak at 156–157 ppm instead of 153 ppm in ¹³C NMR (SI Figs. S16–S23) indicate the formation of the carbamate. The aliphatic moieties were clearly detected in ¹H NMR spectra (SI Figs. S16–S23), the peaks at around 3.1 ppm are corresponding to the methylene group next to carbamate, confirming the reaction of amines with cyclic carbonates.

Made of hydrophobic alkyl tails linked by a carbamate function to the hydrophilic heads of glucosides MDMN-n and MDGN-n possess a very similar structure to that of alkyl polyglucosides (APG) but were prepared under much milder and simpler conditions than the latter obtained through etherification. APGs are reported to exhibit a range of advantages, in particular that of a bio-resourced surfactant, which exhibit dermatological and ocular safety, good biodegradability, wettability, foam production and cleaning ability [30]. The self-assembling of MDMN-6, 12 isomers and of MDGN-6, 12 in water and their surfactant behavior were investigated and characterized by transmission electron microscopy (TEM). As shown in Fig. 2, the size of the alkyl chain strongly influences the morphology of glucocarbamate self-assemblies, their sugar moieties exhibiting similar hydrophilicities. In the cases of MDMN-6 and MDGN-6, the hydrophobic tail represents 31% of the total mass, and for MDMN-12 and MDGN-12 45%. Self-assemblies carrying hexyl tails form micelles with 50–100 nm of diameter (Fig. 2A and B); on the other hand, their dodecyl-carrying homologues self-assemble into vesicular structures with diameter size of 200–400 nm (Fig. 2D and E). The TEM characterization in cryogenic conditions revealed the same morphologies as those prepared by staining with uranyl acetate, indicating the stability of the micelles and the vesicles formed (Fig. 2C and F). One-pot reactions involving glycosides, CO₂ and primary amine thus provide a new and simple tool for the conjugation of sugars to aliphatic amines, in particular for biological applications.

2.2. Synthesis and polymerization of 6-membered cyclic glycocarbonates

In our previously published work, we synthesized 6-membered cyclic glycocarbonates from methyl α -D-glucopyranoside after modifying its 6- and 4- positions for subsequent carbonation by CO₂ and protecting its 2- and 3- positions with ether groups from undesirable reactions [11]. To check the versatility of this carbonation strategy, methyl α -D-galactopyranoside and methyl α -D-mannopyranoside were also subjected to the same set of reactions (Scheme 2). In the case of the mannopyranoside, the configuration of the hydroxyls in positions 6- and 4- is trans similar to glucopyranoside, but in the galactopyranoside case that configuration is cis. Before carbonation, the hydroxyls in 2- and 3- positions of the two sugars had to be protected and the hydroxyl in 6- position brominated. We thus resorted to the same chemistry as the one reported for methyl α -D-glucopyranoside [11] and derivatized MDG into MDGBr. As for the synthesis of MDMBr, the two cis hydroxyls in 2- and 3- positions were first selectively protected with a ketal group to form methyl-2,3-O-cyclohexylidene α -D-mannopyranoside. Cyclohexanone was chosen as the ketal protecting group; after polymerization of MDMC₆ and a deprotection step, although incomplete, a hydrophilic polyglycocarbonate (PMDMC) could be isolated [18]. All the synthetic details and characterizations are described in Supporting material (Fig. 3, SI Figs. S24–S48).

In the final step of synthesis of MDMC₆ and MDGC₆, MDMBr and MDGBr were respectively submitted to carbonation using a pressure of 10 bar of CO₂ at room temperature in the presence of DBU as shown in Scheme 1. Due to the cis configuration of the 6- and 4- hydroxyls of the galactopyranoside, the formation of the corresponding cyclic carbonate was more favorable, affording higher yield of MDGC₆ than that for MDMC₆; in the latter case, some oligomers due to polycondensation

Fig. 1. ¹H NMR spectra of (A) MDM-based cyclic carbonate (MDMC₅-acetate) and (B) MDG-based cyclic carbonate (MDGC₅-acetate).

were formed concomitantly to the cyclization during reaction. NMR, HRMS and IR (SI Figs. S3, S6, S32 and S33 for MDMC₆ and Figs. 3A, S3, S7, S45 for MDGC₆), characterizations confirmed the purity and the expected structure of 6-membered MDMC₆ and MDGC₆ glycosarbonates.

The two monomers were then subjected to ring-opening polymerization using an organocatalyst. The ring opening polymerization of MDMC₆ was carried out in the presence of 4-methyl benzyl alcohol as initiator and TBD as base in anhydrous dichloromethane at room temperature. The monomer conversion reached values higher than 98% in 30min, which is a rate similar to that reported by Buchard et al. [18] and certainly faster than the one witnessed for the 6-membered glucoside-based cyclic glycosarbonates [11,14]. Although 6-membered cyclic carbonates derived from glucoside and mannoside both include carbonate rings with trans configurations, the groups protecting their 2- and 3- positions are different; this suggests that the cyclic ketal group in MDMC strongly enhances the cyclic strain of the correspond-

ing carbonate ring, which in turn increases the rate of polymerization of the latter monomer. When the same polymerization conditions were applied to MDGC₆ and due to the cis configuration of its carbonate ring monomer conversion reached 60% and a significant amount of macrocyclic polyglycoscarbonate was formed as indicated by the analysis of the reaction mixture by MALDI-ToF. Using a milder organocatalyst like DBU and 1-(3,5-bis(trifluoromethyl)phenyl)-3-cyclohexylthiourea (TU) [31,32], which is known for its ability to activate carbonyl groups of cyclic monomers, monomer conversion could reach 95% after 60h. The polymerization was thus slow but well controlled. As the cis configuration of the carbonate does not favor a high cyclic strain this resulted in a slower rate of polymerization of MDMG₆ and in the occurrence of back-biting side reactions, unless using a milder organocatalyst.

The obtained polyglycosarbonates were characterized and related data are listed in Table 1. IR absorbance of C=O slightly shifts to 1757 cm⁻¹ from 1750 cm⁻¹ after ring opening and formation of linear carbonates (SI Fig. S3). In the ¹³C NMR spectra, one distinct carbonyl

Fig. 2. TEM of self-assemblies (negatively stained with 2% uranyl acetate) obtained from A) MDMN-6, B) from MDGN-6, C) Cryo-TEM of MDMN-6, D) of MDMN-12, E) of MDGN-12, and F) Cryo-TEM of MDGN-12.

Fig. 3. The ¹H NMR spectra of the monomer **MDGC₆** (A) and the polyglycocarbonate **PMDGC** (B).

Table 1
ROP of 6-membered cyclic glycocarbonates monomers MDMC₆ and MDGC₆, and their characterizations.

En.	Polymer	Initiator /Cat	M	[M] ₀ / [I] ₀	Time (h)	Conv (%) ^a	Yield	M _{n(theo)} ^b (10 ³ g/mol)	M _{n(MALDI)} ^c (10 ³ g/mol)	M _{n(GPC)} ^d (10 ³ g/mol)
1	PMDMC	PMBA /TBD	MDMC ₆	15	0.5	98%	85%	4.5	4.0	3.2/1.3
2	PMDGC	PMBA/DBU/TU	MDGC ₆	18	60	95%	86%	4.3	3.9	2.8/1.4

^a Aliquots of the reaction mixture was analysed by ¹H NMR to calculate monomer conversion.

^b Calculated from the monomer to initiator ratio.

^c Calculated from MALDI-ToF.

^d Calculated from GPC calibrated with narrow polystyrene standards in THF as running solvent in 1 mL/min flow rate.

resonance is moving downfield to 154.5 ppm compared to the monomer signal at 147.4 ppm (SI Figs. S33, S35, S45 S46). Remarkably, in the ¹H NMR spectra, the signal of proton attached to C4 moved to 4.9 from 4.1 ppm (PDMGC, Fig. 3) and to 4.8 from 4.15 ppm (PMDMC, SI Figs. S32 and S34) after the release of the ring strain upon its opening. GPC analysis gave monomodal traces with narrow distributions (SI Fig. S47), and apparent molar masses calibrated with polystyrene samples were a little lower than expected ones. The actual molar masses given by MALDI-ToF analysis are in excellent agreement with the expected values (PMDMC 4531 g/mol, PMDGC 4364 g/mol). The main population exactly matches the expected linear structure including the initiator moiety and a peak to peak mass difference corresponding to the molar mass of monomers MDMC₆ (300.12 g/mol) and MDGC₆ (248.23 g/mol) (SI Fig. S48). Besides this main population there is also another small population which is observed without any terminal group and thus corresponding to cyclic polycarbonates due to the back biting of the growing polymer chain.

The removal of the cyclohexylidene ketal protecting group carried by the vicinal hydroxyls in 2- and 3- positions from PMDMC could be achieved by using trifluoroacetic acid:chloroform (1:1) without endangering carbonate linkages. In contrast to the 70% deprotection of isopropylidene ketal group reported by Burchard et al. [18], the deprotection efficiency in our case was close to 90% as indicates the relative intensity of signals of OMe and cyclohexylidene group due to the more hindered ketal protecting group (SI Fig. S36).

3. Conclusion

Starting from natural glucosides, namely methyl α-D-mannopyranosides and methyl α-D-galactopyranosides, both 5- and 6-membered corresponding cyclic glyccarbonates could be derived through two different methodologies using CO₂ as unique and versatile carbonation reagent. The 5-membered glyccarbonates were further reacted with alkyl amines providing a very simple route towards sugar conjugation without any protection step. Quite remarkable also was the synthesis of 6-membered cyclic glyccarbonates which could be derived from glucosides carrying either cis- or trans- hydroxyls at their 6- and 4- positions. Depending upon their respective ring strain, the obtained cyclic glyccarbonates could be polymerized with varying rates of polymerization. Back-biting reactions could be avoided upon selection of appropriate organocatalysts. The chemistry described in this study allows access to both hydrophilic and hydrophobic polyglyccarbonates.

4. Experimental section

4.1. Materials and method

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD), *p*-methyl benzyl alcohol (PMBA) were purchased from Sigma-Aldrich. DBU was dried with CaH₂ and stored in glove box after distillation. TBD was stirred in tetrahydrofuran with calcium hydride, filtered and solvent was removed under vacuum and kept in glove box. Dichloromethane, dimethyl formamide was dried with CaH₂ and stored on activated molecular sieves (4 Å) after distillation. CO₂ (99.995%) cylinder purchased from Abdullah Hashim Industrial & Gas Co. was further purified by flowing through the purifier of the VICI Co., USA.

FT-IR spectra were recorded on Perkin Elmer FT-IR spectrum GX instrument. ¹H and ¹³C NMR spectra were recorded on Bruker Spectrometers (400 MHz, 500 MHz, 600 MHz and 950 MHz). Gel permeation chromatography (GPC) was performed on a VISKOTEK TDA 305 Triple Detector equipped with two columns (T6000M, GENERAL MIXED ORG 300×7.8MM) using THF (1 mL/mL) as the eluent at 35 °C. MALDI-ToF

MS experiments were carried out by using *trans*-2-[3-(4-*t*-butyl-phenyl)-2-methyl-2-propenylidene] malononitrile (DCTB) as the matrix in THF with Na-TFA as ionizing agent. The loading ration of sample, matrix and ionization agent is 1:10:1.

The self-assembled morphology of amphiphilic polycarbonates in water were characterized by the transmission electron microscopy (Titan 80–300 CT from Thermo-Fischer Scientific, Inc.) negatively stained with 2% uranyl acetate. The specimens for cryo-TEM were prepared by using an automatic plunge-freezing system of model Vitrobot™ from FEI Company (Hillsboro, OR). A small amount of sample (4 μL) was placed on a holey-carbon coated hydrophilic copper grids and followed by blotting of the solution and its plunge freezing into liquid ethane cryogen was done. Then, grids were loaded into the Vitrobot™. In this way, several specimens were prepared for each sample in order to realize a high quality datasets from superior specimens. Further, this microscope was equipped with the low-dose option to keep the sample free of electron beam damage and a charge coupled devices (CCD) of model US4000 from Gatan, Inc. to record the images in digital format using Titan G³ Krios electron microscope from Thermo-Fischer Scientific, Inc. MDMN-6, MDGN-6, MDMN-12 and MDGN-12 were first dissolved in dimethyl sulfoxide, to which water was slowly added to get the final sample concentration of 10 mg/mL. Then the organic solvent was removed by continuous dialysis with millii Q water for two days.

4.2. General procedure for the synthesis of 5-membered cyclic glyccarbonates MDMC₅ and MDGC₅

α-Methyl D-mannopyranoside or α-methyl D-galactopyranoside (1g, 5.15 mmol) was taken in an autoclave, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (2 equiv, 10.30 mmol) and dibromomethane (4 equiv, 20.60 mmol) was added to the reaction mixture. 2 mL of dimethyl formamide (DMF) was added to the reaction mixture to solubilize completely the starting materials. Then the autoclave was charged with CO₂ at the pressure of (10 bar) and stirred at room temperature for 1 h. The temperature of the autoclave was raised to 70 °C and kept stirring for 20 h. After 20 h CO₂ was released from the reaction mixture and transferred into a round bottom flask and the synthesized cyclic glyccarbonates was tested by infrared spectroscopy (IR). The instance peak at 1800 cm⁻¹ was observed due to the presence of the cyclic glyccarbonates.

4.3. General procedure for the synthesis of acetylated cyclic glyccarbonates (MDMC₅-acetate and MDGC₅-acetate)

Freshly distilled anhydrous dichloromethane (20 mL) was added to the round bottom flask containing the cyclic glyccarbonates. Triethylamine (5 equiv) and acetic anhydride (2.5 equiv) was added to the reaction mixture and kept stirring for 12 h to obtain the acetylated cyclic glyccarbonates. After the complete acetylation of the cyclic glyccarbonates, reaction mixture was washed with 1 (N) hydrochloric acid, followed by distilled water and brine solution. Finally, the reaction mixture was dried on anhydrous sodium sulphate and the solvent was removed under vacuum. The desired cyclic glyccarbonates was isolated by the silica gel column chromatography purification using hexane/EtOAc (2:1) as mobile phase. The isolated compounds was further characterized by ESI-HRMS, IR spectroscopy, ¹H, ¹³C, DEPT135, COSY, HMBC and HSQC NMR spectroscopy to confirm the structures of those cyclic glyccarbonates (Scheme 1), yield 80%.

4.3.1. MDMC₅-acetate (isomer 1)

¹H NMR (400 MHz, CDCl₃): δ 5.07 (dd, *J* = 9.8, 6.8 Hz, 1H), 5.02 (s, 1H), 4.78 (t, *J* = 7.0 Hz, 1H), 4.67–4.63 (m, 1H), 4.28–4.11 (m, 2H), 3.91–3.88 (m, 1H), 3.40 (m, 3H), 2.10 (brs, 6H). ¹³C NMR

(400MHz, CDCl₃): δ 170.54, 169.08, 152.72, 96.24, 76.31, 75.52, 67.80, 65.36, 62.05, 55.43, 20.72.

4.3.2. MDMC₅-acetate (isomer 2)

¹H NMR (400MHz, CDCl₃): δ 5.17 (t, J = 3.4Hz, 1H), 4.71–4.66 (m, 3H), 4.34–4.26 (m, 2H), 4.11–4.06 (m, 1H), 3.38 (s, 3H), 2.10 (brs, 6H). ¹³C NMR (400MHz, CDCl₃): δ 170.37, 168.89, 152.88, 98.60, 74.28, 70.27, 67.65, 65.53, 62.89, 55.64, 20.56.

HRMS (M + Na⁺) (ESI⁺) calculated for C₁₂H₁₆O₉Na⁺ 327.06865 g/mol, found 327.06799 g/mol, FT-IR (Dichloromethane) 1800 cm⁻¹ (cyclic ν_{CO}) and 1750 cm⁻¹ for acetate (ν_{CO}).

4.3.3. MDGC₅-acetate

¹H NMR (400MHz, CDCl₃): δ 2.10 (s, 3H), 2.14 (s, 3H), 3.4 (s, 3H), 4.17–4.20 (m, 1H), 4.33–4.35 (m, 2H), 4.80–4.88 (m, 2H), 4.97–5.01 (m, 2H). ¹³C NMR (100MHz, CDCl₃): δ 20.7 (2C), 55.9 (1C), 62.0 (1C), 64.3 (1C), 69.4 (1C), 74.1 (1C), 74.6 (1C), 96.0 (1C), 153.1 (1C), 169.6 (1C), 170.4 (1C). HRMS (M + Na⁺) (ESI⁺) calculated for C₁₂H₁₆O₉Na⁺ 327.06865 g/mol, found 327.06799 g/mol, FT-IR (Dichloromethane) 1800 cm⁻¹ (cyclic ν_{CO}) and 1750 cm⁻¹ for acetate (ν_{CO}).

4.4. General procedure for the synthesis of MDMN-6 and MDGN-6

MDMC₅ and MDGC₅ cyclic carbonates reaction mixture (containing 1.0g of starting material; 5.15mmol) was taken in a schlenk tube and hexyl amine (2.27mmol) was added into it. Then 5mL of dichloromethane was added to the reaction mixture and stirred for 24h at 70°C. The significant amount disappearance of the cyclic carbonates was observed by IR spectra after 24h. Then the reaction mixture was diluted with dichloromethane and washed with 1 (N) HCl. Finally, the solvent was removed under reduced pressure and purified by column chromatography with DCM/MeOH (10:0.7) as eluent. The isolated product was analyzed by IR, ¹H and ¹³C NMR spectroscopy (yield 40%).

4.4.1. MDMN-6

¹H NMR (400MHz, CDCl₃): δ 4.91, 4.89, 4.73, 4.69, 4.06, 4.02, 3.95, 3.92, 3.79, 3.71, 3.69, 3.56, 3.52, 3.46, 3.35, 3.34, 3.12, 3.11, 1.48, 1.47, 1.27, 0.89, 0.87, 0.85.

¹³C NMR (101MHz, CDCl₃): δ 156.97, 156.29, 100.88, 99.35, 74.64, 72.49, 72.02, 69.96, 69.70, 67.14, 64.54, 61.29, 61.08, 58.35, 55.01, 41.22, 31.48, 29.70, 26.49, 22.55, 14.01.

FT-IR (Dichloromethane) 1685 cm⁻¹ ($\nu_{\text{carbamate}}$).

4.4.2. MDGN-6

¹H NMR (400MHz, CDCl₃): δ 5.77, 5.04, 4.94, 4.90, 4.83, 4.77, 4.28, 4.23, 4.05, 4.04, 4.01, 3.90, 3.85, 3.83, 3.80, 3.61, 3.59, 3.58, 3.47, 3.42, 3.40, 3.18, 3.15, 3.12, 3.11, 2.62, 2.49, 1.70, 1.62, 1.48, 1.28, 1.24, 0.89, 0.87.

¹³C NMR (101MHz, CDCl₃): δ 157.87, 99.66, 71.84, 69.34, 60.02, 55.47, 41.27, 31.33, 29.66, 28.26, 26.40, 26.03, 22.53, 22.45, 13.95.

4.5. General procedure for the synthesis of MDMN-12 and MDGN-12

MDMC₅ and MDGC₅ cyclic carbonates reaction mixture (containing 1.0g of starting material; 5.15mmol) was taken in a round bottom flask and dodecyl amine (2.04mmol, 381mg) was added to the round bottom flask. Then 5mL of methanol was added to the reaction mixture and stirred for 24h at 70°C. The significant disappearance of the cyclic carbonates was observed by IR spectra after 24h. Then the reaction was diluted with dichloromethane and washed with 1 (N) HCl. Finally, the

solvent was removed under reduced pressure and purified by column chromatography with DCM/MeOH (10:0.7) as eluent. The isolated product was analyzed by IR, ¹H and ¹³C NMR spectroscopy (yield 35%).

4.5.1. MDMN-12

¹H NMR (400MHz, CDCl₃): δ 4.91, 4.88, 4.73, 4.69, 4.09, 4.06, 4.03, 3.97, 3.94, 3.90, 3.78, 3.75, 3.59, 3.57, 3.42, 3.35, 3.34, 3.13, 3.11, 3.10, 1.47, 1.24, 0.89, 0.87, 0.85.

¹³C NMR (101MHz, CDCl₃): δ 156.97, 156.29, 100.88, 99.35, 74.64, 72.49, 72.02, 69.96, 69.70, 67.14, 64.54, 61.29, 61.08, 58.35, 55.01, 41.22, 31.48, 29.70, 26.49, 22.55, 14.01.

FT-IR (Dichloromethane) 1685 cm⁻¹ ($\nu_{\text{carbamate}}$).

4.5.2. MDGN-12

¹H NMR (400MHz, CDCl₃): δ 5.37, 5.06, 4.89, 4.79, 4.32, 3.92, 3.69, 3.58, 3.57, 3.55, 3.42, 3.40, 3.38, 2.95, 2.67, 1.73, 1.23, 0.88.

FT-IR (Dichloromethane) 1685 cm⁻¹ ($\nu_{\text{carbamate}}$).

4.6. Synthesis of methyl-2,3-di-O-cyclohexylidene α -D-mannopyranoside-4,6-cyclic carbonate (MDMC₆)

Methyl 6-bromo-4-hydroxyl-2,3-di-O-cyclohexylidene α -D-mannopyranoside (MDMBr, 0.5g, 1.48mmol), DBU (271mg, 1.78mmol) and 4mL of anhydrous DMF were added into a 50mL of dried autoclave with magnetic stirring bar inside a glove box. Then the sealed autoclave was taken out and charged with CO₂ to a pressure of 10bar. The reactor was kept stirring at room temperature for 5h. then, CO₂ was released, the reaction mixture was poured into HCl solution (1.0M) and extracted by dichloromethane. The crude product was purified by silica gel flash chromatography eluted with a mixture of hexane/ethyl acetate (1:0.1–1:0.3) to give MDMC₆ as a white solid (0.160g, 36% yield).

FT-IR (Dichloromethane) 1755 cm⁻¹ for six membered cyclic carbonate (ν_{CO}). ¹H NMR (950MHz, Chloroform-d) δ 5.02 (s, 1H), 4.50 (dd, J = 10.1, 6.2Hz, 1H), 4.29–4.23 (m, 2H), 4.21 (d, J = 5.7Hz, 1H), 4.14 (ddd, J = 10.2, 7.7, 1.0Hz, 1H), 3.99–3.94 (m, 1H), 3.43 (s, 3H), 1.75–1.53 (m, 8H), 1.44–1.37 (m, 2H). ¹³C NMR (239MHz, CDCl₃): δ 147.30, 111.07, 99.20, 79.28, 75.07, 73.43, 69.13, 57.61, 55.68, 37.83, 35.23, 24.84, 23.92, 23.54. HRMS (M + H⁺) (ESI⁺) calcd for C₁₄H₂₀O₇H⁺ 301.12g/mol, found 301.12g/mol.

4.7. Polymerization of MDMC₆ using TBD and *p*-methyl benzyl alcohol (PMDMC)

Inside a glove box, a solution of monomer MDMC₆ (147.5mg, 491.14 μ mol) in 1mL anhydrous dichloromethane was prepared in a schlenk tube; followed by a mixture of *p*-methyl benzyl alcohol (4mg, 32.74 μ mol) and TBD (2.28mg, 16.38 μ mol) in 100 μ L anhydrous dichloromethane was added to the monomer solution. After kept stirring for 1h, the polymerization was quenched with benzoic acid. The solvent was removed and dissolved in deuterated dichloromethane and analyzed by ¹H, ¹³C NMR spectroscopy, GPC and MALDI-ToF (after one time precipitation from diethyl ether 0.125mg, 85% Yield).

¹H NMR (500MHz, CDCl₃): δ 4.98–4.91 (m, 1H), 4.78–4.72 (m, 1H), 4.29–4.22 (m, 3H), 4.11 (s, 1H), 3.94–3.83 (m, 1H), 3.41–3.33 (m, 3H), 2.35 (s, 3H), 1.83–1.29 (m, 10H) ppm. Initiator *p*-methyl benzyl alcohol was also confirmed by the presence of 7.32–7.27 (m, 2H), 7.23–7.17 (m, 2H), 5.22–5.10 (m, 2H), 2.38 (s, 3H) ppm and $M_{n,NMR}$ = 4600.0.

¹³C NMR (100 MHz, CDCl₃) δ 155.39, 155.32, 110.81, 110.63, 97.96, 75.24, 74.90, 74.35, 66.57, 65.94, 55.23, 54.94, 37.39, 35.46, 24.93, 23.85, 23.55 ppm. Initiator para methyl benzyl alcohol was also confirmed by the presence of the corresponding peaks; 129.27, 128.61 (benzyl), 71.0 (CH₂-Benzyl) and 21.03 (Me-Benzyl) ppm. FT-IR (Dichloromethane) 1750 cm⁻¹ for carbonate (linear ν_{co}).

4.8. Deprotection of cyclohexylidene group of PMDMC

3 mL solution of 50 mg of PMDMC was taken in a 10 mL round bottom flask and 0.3 mL of trifluoroacetic acid (TFA) was added into it and kept stirring for 24 h at RT. Then the reaction was quenched with the addition of triethylamine and solvent was removed under vacuum. Finally, the polymer was washed with hexane and dried under vacuum. The residue was analyzed for ¹H and ¹³C NMR characterization.

4.9. Synthesis of methyl-2,3-di-O-methyl α-D-galactopyranoside-4,6-cyclic carbonate (MDGC₆)

Methyl 6-bromo-6-deoxy-2,3-di-O-methyl α-D-galactopyranoside (MDGBr, 1.0 g, 3.51 mmol), DBU (1.07 g, 7.01 mmol) and 8 mL of anhydrous DMF were added into a 100 mL of dried autoclave with magnetic stirring bar inside a glove box. Then the sealed autoclave was taken out and charged with CO₂ to a pressure of 10 bar. The reactor was kept stirring at room temperature for 4 h. then, CO₂ was released, the reaction mixture was poured into hexane and supernatant was discarded. Then, the residue was dissolved in tetrahydrofuran, solvent was decanted and removed under reduced pressure. The crude product was purified by silica gel flash chromatography eluted with a mixture of hexane/acetone (1:0.2–1:1) to give MDGC₆ as a white solid (0.4 g 46% yield). FT-IR (Dichloromethane) 1755 cm⁻¹ for six membered cyclic carbonate (ν_{co}). ¹H NMR (500 MHz, Chloroform-d) δ 4.89 (dd, *J* = 29.8, 2.4 Hz, 2H), 4.58–4.42 (m, 2H), 4.10 (s, 1H), 3.74–3.61 (m, 2H), 3.55 (s, 3H), 3.52 (s, 3H), 3.48 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 146.99, 98.59, 76.69, 76.53, 74.92, 70.25, 59.62, 59.34, 57.97, 56.02. HRMS (*M* + Na⁺) (ESI⁺) calcd for C₁₀H₁₆O₇Na⁺ 271.0788 g/mol, found 271.0786 g/mol.

4.10. Polymerization of MDGC₆ using DBU, TU and *p*-methyl benzyl alcohol (PMDGC)

Inside a glove box, a solution of monomer MDGC₆ (183 mg, 736.74 μmol) in 1 mL anhydrous dichloromethane was prepared in a schlenk tube; followed by a mixture of *p*-methyl benzyl alcohol (5 mg, 40.93 μmol), bis(trifluoromethyl)phenyl-3-cyclohexylthiourea (15.16 mg, 40.93 μmol) and DBU (6.23 mg, 40.93 μmol) in 100 μL anhydrous dichloromethane was added to the monomer solution. After kept stirring for 60 h, the polymerization was quenched with benzoic acid. The solvent was removed and dissolved in deuterated dichloromethane and analyzed by ¹H, ¹³C NMR spectroscopy, GPC and MALDI-TOF (after one time precipitation from diethyl ether 180 mg, 86% Yield).

¹H NMR (500 MHz, CDCl₃) δ 5.33–5.19 (m, 1H), 4.95–4.81 (m, 1H), 4.41–4.17 (m, 2H), 4.13–4.01 (m, 1H), 3.66–3.55 (m, 2H), 3.53–3.35 (m, 9H). Initiator para methyl benzyl alcohol was also confirmed by the presence of 7.32–7.27 (m, 2H), 7.23–7.17 (m, 2H), 5.22–5.10 (m, 2H), 2.38 (s, 3H) ppm.

¹³C NMR (100 MHz, CDCl₃) δ ¹³C NMR (239 MHz, CDCl₃) δ 155.06, 154.77, 154.57, 129.25, 128.58, 98.03, 97.70, 78.85, 77.91, 77.17, 71.92, 71.56, 67.37, 66.87, 66.38, 66.23, 59.49, 59.45, 58.17, 57.98, 55.57, 55.37 ppm. Initiator para methyl benzyl alcohol

was also confirmed by the presence of the corresponding peaks; 129.27, 128.61 (benzyl), 71.0 (CH₂-Benzyl) and 21.03 (Me-Benzyl) ppm. FT-IR (Dichloromethane) 1750 cm⁻¹ for carbonate (linear ν_{co}).

Conflict of interest

The authors declare no competing financial interests.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jcou.2018.02.008>.

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