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Four Different Regioisomeric Polycarbonates Derived from One Natural Product, D-Glucose

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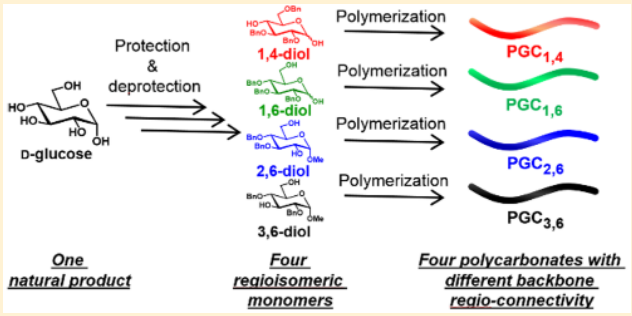
* Supporting Information

ABSTRACT: Strategies for the preparation of polycarbonates, derived from the natural product D-glucose, which have the potential to degrade back into their bioresorbable starting material and CO_2, were developed. By employing established carbohydrate protection/deprotection chemistries, two D-glucose derivatives, methyl 4,6-O-benzylidene-α-D-glucopyranoside or methyl α-D-glucopyranoside, were converted into four different regioisomeric diol monomers, i.e., 1,4-, 1,6-, 2,6-, or 3,6-diols, as confirmed by nuclear magnetic resonance (NMR) spectroscopy, infrared (IR) spectroscopy, and mass spectrometry. Each type of regioisomeric monomer was then employed in a condensation polymerization with phosgene, generated in situ from triphosgene, as a comonomer, in the presence of pyridine, to produce four types of polycarbonates with different backbone regio-connectivity, as characterized by size exclusion chromatography, NMR spectroscopy, and IR spectroscopy. Interestingly, their thermal properties, i.e., glass transition temperature (T_g) and thermal degradation behavior, were tunable by changing the topological composition of the monomeric unit. That is, polycarbonates with 2,6- and 3,6-backbone connectivity resulted in significantly higher T_g of ca. 85 and 83 °C, respectively, as compared to those with 1,4- and 1,6-backbone connectivity, showing a T_g of ca. 33 °C, as measured by differential scanning calorimetry. Furthermore, when the thermal decomposition temperature was measured by thermogravimetric analysis, the nonanomeric carbon backbone-based polycarbonates (2,6- and 3,6-) exhibited higher thermal stability and a sharper decomposition profile, with onset decomposition temperature ($T_{d,onset}$) at 363 or 336 °C, as compared with those polymers containing the anomeric carbon in the carbonate linkage (1,4- and 1,6-), having $T_{d,onset}$ at 171 and 163 °C.



INTRODUCTION

The past few decades have seen a paradigm shift in the development of polymeric materials, from nondegradable to degradable constructs, for medical and related applications,[1−3] but also for environmental and sustainability impact. Examples of biomedically relevant degradable polymeric materials vary widely from their potential utility as sutures and orthopedic devices to engineered tissues and drug delivery systems.[1,4−6] The major driving force for exploiting degradable polymeric materials for use in biomedical applications is concerns associated with their long-term biocompatibility in the human body.[7,8] For instance, artificial implants with nondegradable materials may necessitate follow-up procedures, i.e., their replacement or removal, and nondegradable drug delivery carriers may elicit translational issues regarding in vivo fate, clearance, accumulation, and possible toxicity.[3,6,9]

Creating the next generation of biomaterials, new monomeric systems need to be explored to achieve improved functionality, degradability, and biocompatibility.[5,10] While our group has reported several promising nanoscopic constructs derived from degradable precursors, e.g., polyphosphoesters,[11−17] polypeptides,[18,19] and polycarbonates,[20] as biomaterials, we have a keen interest in expanding these systems to include new natural resources, such as cyclitols,[21,22] monosaccharides,[23] terpenes,[24,25] and menthides,[26,27] as starting materials for monomer synthesis to produce polymers that are capable of degrading into bioresorbable products.[21,22,28,29]

Among different types of natural products applicable to polymeric systems, one of our foci is in saccharides that can be transformed into polycarbonates, for potential use in the field of orthopedic tissue engineering, which has been limited to simple variations on conventional systems, including aliphatic polyesters, poly(hydroxy acids), and polyanhydrides.[30−34] Previously, several elegant works reported polycarbonates composed of monosaccharides, often with the saccharide moiety as a side chain substituent,[35−37] an opened ring in the main chain of copolymers,[38−40] or an intact saccharide ring in the polymer backbone.[41−46] In addition, much interest has been devoted to modified saccharide feedstocks,[42,47,48] allowing for facile synthetic strategies as well as the generation of high-

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performing engineering polymers. With our interest in developing engineering-type polymeric materials that are synthesized from and can undergo hydrolytic degradation into natural products,[49] we have explored strategies for the transformation of carbohydrates into polycarbonates, using cellulose as a model structure with replacement of enzymatically cleavable glycosidic linkages by hydrolytically labile carbonates.

Herein, we investigated the synthesis of polycarbonates built from D-glucose, an abundant natural product that is prevalent both in nature and the human body, to afford a unique family of biosourced, potentially degradable, engineering polymers: poly(D-glucose carbonates) (PGCs). It is noteworthy that glucose is an important carbohydrate, acting as an energy source, a metabolic intermediate, and a monomeric repeat unit in many natural polymeric support structures.[50] Starting from derivatives of this appealing starting material, we employed established carbohydrate protection and deprotection chemistries to prepare four types of linear PGCs with different regioisomeric backbone connectivities and evaluated the effect of backbone connectivity on their thermal properties.

EXPERIMENTAL SECTION

Instrumentation. ^{1}H, ^{13}C, and COSY NMR spectra were recorded on a Varian Inova 500 spectrometer. Chemical shifts were referenced to the solvent resonance signals. The data obtained were processed and analyzed using MestReNova software.

IR spectra were recorded on a Shimadzu IR Prestige attenuated total reflectance Fourier transform infrared spectrophotometer (ATR-FTIR) and analyzed using IRsolution v. 1.40 software.

Size exclusion chromatography (SEC) measurements were performed on a Waters Chromatography, Inc. (Milford, MA), system equipped with an isocratic pump model 1515, a differential refractometer model 2414, and a four-column set of 5 μm Guard (50 × 7.5 mm), Styragel HR 4 5 μm DMF (300 × 7.5 mm), Styragel HR 4E 5 μm DMF (300 × 7.5 mm), and Styragel HR 2 5 μm DMF (300 × 7.5 mm) using DMF (0.05 M LiBr) as the eluent (1.00 mL/min) at 70 °C. Polymer solutions were prepared at a concentration of ca. 3−5 mg/mL, and an injection volume of 200 μL was used. Data collection and analysis were performed with Empower 2 v. 6.10.01.00 software (Waters, Inc.). The system was calibrated with polystyrene standards (Polymer Laboratories, Amherst, MA) ranging from 615 to 442 800 Da.

Glass transition temperatures (T_g) were measured by differential scanning calorimetry (DSC) on a Mettler-Toledo DSC822 (Mettler-Toledo, Inc., Columbus, OH) under N_2, with a heating rate of 10 °C/min. Measurements were analyzed using Mettler-Toledo Star^e v.10.00 software. The T_g was taken as the midpoint of the inflection tangent, upon the third heating scan. Thermogravimetric analysis (TGA) was performed under an Ar atmosphere using a Mettler Toledo model TGA/SDTA851^e apparatus with a heating rate of 10 °C/min that was coupled to a Pfeiffer ThermoStar/GSD320T3 mass spectrometer. Ions generated during TGA ranging from 0 to 300 amu were detected over a span of 30 s (10 ms/amu) during the run of the TGA with a steady flow of Ar (10 mL/min). TGA and mass spectrometry data were analyzed using Mettler-Toledo Star^e v.10.00 and Pfeiffer QUADERA software, respectively. Column chromatography was performed on a Combiflash Rf+ (Teledyne ISCO) with RediSep Rf Columns (Teledyne ISCO).

Materials. Aluminum chloride ($AlCl_3$), acetic anhydride (Ac_2O), acetic acid (AcOH), benzyl bromide (BnBr), borane−tetrahydrofuran complex (1.0 M in THF, BH_3·THF), methyl α-D-glucopyranoside, methyl 4,6-O-benzylidene-α-D-glucopyranoside, potassium hydroxide (KOH), sodium cyanoborohydride ($NaBH_3CN$), sodium hydride (NaH, 60% suspension in mineral oil), concentrated sulfuric acid (conc H_2SO_4), anhydrous methanol (MeOH), sodium methoxide solution (25 wt % in methanol, NaOMe in MeOH), trimethylsilyl-trifluoromethanesulfonate (TMSOTf), trimethylamine (TEA), tetrabutylammonium iodide (TBAI), magnesium sulfate ($MgSO_4$), sodium sulfate (Na_2SO_4), sodium hydroxide (NaOH), sodium bisulfate ($NaHSO_4$), sodium bicarbonate ($NaHCO_3$), phosgene (20% solution in toluene), diphosgene, and triphosgene were purchased from Sigma-Aldrich Company. Unless noted, all reagents were used as received. Dichloromethane (DCM), tetrahydrofuran (THF), N,N-dimethylformamide (DMF), and toluene were purified and dried by passage through a solvent purification system (J.C. Meyer Solvent Systems). Monomers 4, 8, 11, and 12 were dried under reduced pressure over P_2O_5 and stored under argon environment. Likewise, all polymer samples, 13, 14, 15, and 16, were dried over P_2O_5 under reduced pressure overnight prior to characterizations.

Synthesis of Glucose Monomer 4. Synthesis of Methyl 2,3-Di-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside (2). Methyl 4,6-O-benzylidene-α-D-glucopyranoside, 1 (12.4 g, 43.9 mmol), KOH (14.7 g, 262 mmol), and BnBr (45.1 g, 264 mmol) were suspended in 200 mL of toluene and heated to reflux. Water generated *in situ* was collected by a Dean−Stark apparatus. The reaction was monitored by thin layer chromatography (TLC) until complete consumption of starting material was observed, and the reaction mixture was then allowed to cool to room temperature. The mixture was washed with water and the aqueous layer was extracted with DCM. The organic layer was dried with $MgSO_4$ and concentrated under vacuum. The residue was then purified by column chromatography on silica gel, eluting with a 85:15 mixture of hexane and acetone, resulting in a white solid (18.7 g, 92.0% yield). FTIR (ATR): 3100−3000, 3950−2800, 1450, 1367, 1329, 1175, 1084, 1050, 1028, 964, 732, 692, 652 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 7.59−7.26 (b, 15H), 5.62 (s, 1H), 4.99 (d, J= 11.0 Hz, 1H), 4.93 (d, J= 2.5 Hz, 1H), 4.91(d, J= 2.0 Hz, 1H), 4.77 (d, J= 12.5 Hz, 1H), 4.68 (d, J= 4.0 Hz, 1H), 4.34 (dd, J= 5.0 Hz, J= 10.0 Hz, 1H), 4.13 (t, J= 9.5 Hz, 1H), 3.90 (td, J= 5.0 Hz, J= 9.5 Hz, 1H), 3.77 (t, J= 10.0 Hz, 1H), 3.68 (t, J= 9.5 Hz, 1H), 3.63 (dd, J= 4.0 Hz, J= 9.5 Hz, 1H), 3.47 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 138.8, 138.2, 137.5, 129.1−127.5 (m), 126.1, 101.3, 99.3, 82.2, 79.3, 78.7, 75.4, 73.8, 69.1, 62.4, 55.4. +ESI MS: calculated $[M + Li]^+$ for $C_{28}H_{30}O_6$: 469.2202; found: 469.2191.

Synthesis of Methyl 2,3,6-Tri-O-benzyl-α-D-glucopyranoside (3). Compound 2 (14.8 g, 32.0 mmol) was suspended in 500 mL of THF under N_2 atmosphere, and $NaBH_3CN$ (14.5 g, 230 mmol) was added. After stirring for 45 min at room temperature, the temperature was decreased to 0 °C, and $AlCl_3$ (38.4 g, 288 mmol) was added. Following an additional hour of stirring, the reaction mixture was filtered to remove the aluminum salts. The filtrate was extracted with 500 mL of DCM and washed with water. The aqueous phase was extracted with DCM, and the organic layers were combined, dried with Na_2SO_4, and then concentrated under vacuum. The residue was purified by column chromatography on silica gel, eluting with a 7:3 mixture of hexane and ethyl acetate, to produce a colorless oil (12.6 g, 84.8% yield). FTIR (ATR): 3600−3250, 3100−3000, 2950−2800, 1720, 1703, 1452, 1047, 910, 735, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 7.48−7.28 (b, 15H), 5.05 (d, J= 12.0 Hz, 1H), 4.81 (dd, J= 7.5 Hz, J= 11.0 Hz, 2H), 4.70 (overlapping, 2H), 4.61 (q, J= 12.0 Hz, 2H), 3.85 (t, J= 9.5 Hz, 1H), 3.80−3.70 (overlapping, 3H), 3.66 (t, J= 9.5 Hz, 1H), 3.59 (dd, J= 10.0 Hz, J= 3.5 Hz, 1H), 3.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 138.9, 138.1, 128.9−127.3 (m), 98.2, 81.5, 79.7, 75.5, 73.6, 73.2, 70.7, 70.0, 69.5, 55.3. +ESI MS: calculated $[M + Li]^+$ for $C_{28}H_{32}O_6$: 471.2359; found: 471.2365.

Synthesis of 2,3,6-Tri-O-benzyl-D-glucopyranoside (4). Compound 3 (3.944.0 g, 8.48 mmol) was dissolved in 75 mL of AcOH at room temperature. The solution was heated to 110 °C, and 40 mL of HCl (4 N) was added. The reaction was monitored by TLC and stopped after 35 min. The reaction mixture was added to 500 mL of water and neutralized by the addition of 2 M NaOH. The solution was extracted with 500 mL of DCM. The organic layer was dried with Na_2SO_4 and concentrated under vacuum. The residue was purified by chromatography on silica gel, eluting with a 7:3 mixture of hexane and ethyl acetate, and then concentrated under vacuum. The product was recrystallized in a 7:1 mixture of hexanes and ethyl acetate resulting in 1.22 g (32.1% yield) of 4, which was used without further purification.

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FTIR (ATR): 3500−3300, 3100−3000, 2950−2800, 1498, 1453, 1337, 1216, 1132, 1101, 1048, 1024, 910, 865, 755, 695 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 7.44−7.28 (b, 15H), 5.26 (d, J= 3.5 Hz, 1H), 5.04 (d, J= 11.5 Hz, 1H), 4.82 (d, J= 11.5 Hz, 1H), 4.75 (dd, J= 17.2 Hz, J= 12.5 Hz, 2H), 4.60 (dd, J= 22.0 Hz, J= 12.0 Hz, 2H), 4.06 (m, 1H), 3.88 (t, J= 9.0, 2H), 3.76−3.66 (m, 2H), 3.64−3.55 (overlapping, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 138.7, 137.9, 128.8−127.4, 91.2, 81.2, 79.7, 75.4, 73.6, 72.9, 70.9, 70.0, 69.7 ppm. +ESI MS: calculated $[M + Li]^+$ for $C_{27}H_{30}O_6$: 457.2202; found: 457.2195.

Synthesis of Glucose Monomer 8. Synthesis of Methyl 2,3,4,6-Tetra-O-benzyl-α-D-glucopyranoside (6). NaH (60% suspension in mineral oil, 41.3 g, 1.72 mol) was washed with hexane under N_2. Hexane was removed *in vacuo*, and NaH was suspended in DMF (600 mL). Methyl α-D-glucopyranoside (21.0 g, 0.108 mmol) was added over 45 min to the stirring reaction mixture at 0 °C and was left for 4 h. TBAI (3.85 g, 10.4 mmol) was added, followed by the dropwise addition of BnBr (83.2 g, 486 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 20 h. To quench the reaction, H_2O (100 mL) was added dropwise over 20 min. The mixture was extracted with DCM and washed with brine. The organic layers were collected, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel, eluting with 7:3 mixture of hexane and ethyl acetate, to yield the benzylated product (47.9 g, 80.0% yield). FTIR (ATR): 3550−3300, 3100−3000, 2975−2800, 1740, 1452, 1360, 1155, 1088, 1070, 1044, 1028, 912, 735, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 7.46−7.20 (b, 20H), 5.10−4.52 (b, 9H), 4.08 (t, J = 9.0 Hz, 1H), 3.86−3.78 (overlapping, 2H), 3.75−3.69 (overlapping, 2H), 3.65 (dd, J = 9.5, J = 3.5 Hz, 1H), 3.46 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 138.9, 138.3, 138.2, 138.0, 128.8−127.4 (m), 98.3, 82.2, 79.9, 77.8, 76.0−73.2 (m), 70.2, 68.6, 55.2 ppm. +ESI MS: calculated $[M + Li]^+$ for $C_{35}H_{38}O_6$: 561.2828; found: 561.2835.

Synthesis of Acetyl 2,3,4-Tri-O-benzyl-6-acetyl-D-glucopyranoside (7). Compound 6 (5.47 g, 9.85 mmol) was dissolved in a solution of AcOH/ Ac_2O (1:1, 50 mL). The solution was cooled to 0 °C while stirring. Concentrated H_2SO_4 (1 mL) was added dropwise. After stirring for 1 h, 50 mL of sataturated $NaHCO_3$ and 50 mL of cold distilled H_2O were added sequentially. The aqueous solution was extracted with DCM. The collected organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated. The resulting residue was purified by column chromatography on silica gel, eluting with a gradient of hexane and ethyl acetate to yield the product 7 as an oil (3.31 g, 62.9% yield). FTIR (ATR): 3100−3000, 2975−2825, 1742, 1497, 1454, 1369, 1227, 1150, 1066, 1010, 933, 735, 695 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 7.43−7.27 (b, 15H), 6.38 (d, J= 3.5 Hz, 1H), 5.05 (d, J= 11.0 Hz, 1H), 4.95 (d, J= 11.0 Hz, 1H), 4.89 (d, J= 11.0 Hz, 1H), 4.76 (d, J= 11.5 Hz, 1H), 4.69 (d, J= 11.5 Hz, 1H), 4.64 (d, J= 11.0 Hz, 1H), 4.36−4.28 (m, 2H), 4.04 (t, J= 9.0 Hz, 1H), 4.02−3.98 (m, 1H), 3.73 (dd, J= 9.5 Hz, J= 3.5 Hz, 1H), 3.63 (dd, J= 9.5 Hz, J= 1.0 Hz, 1H), 2.20 (s, 1H), 2.07 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 170.7, 169.4, 138.5, 137.6, 137.5, 127.5−128.9 (m), 89.7, 81.7, 78.9, 76.6, 75.8, 75.3, 73.3, 71.1, 62.7, 21.1, 20.9. +ESI MS: calculated $[M + Li]^+$ for $C_{31}H_{34}O_8$: 541.2414; found: 541.2427.

Synthesis of 2,3,4-Tri-O-Benzyl-D-glucopyranoside (8). Compound 7 (1.99 g, 3.73 mmol) was weighed in a flame-dried 50 mL Schlenk flask under N_2 atmosphere. Anhydrous THF (24 mL) and anhydrous MeOH (8 mL) were added sequentially, and the solution was stirred at 0 °C. After addition of NaOMe solution (25% in MeOH) dropwise, the reaction mixture was allowed to stir for 40 min. The reaction was neutralized by adding $NaHSO_4$ (1 M) and saturated $NaHCO_3$. After adding ethyl acetate (100 mL), the reaction mixture was washed with distilled H_2O (75 mL) and brine (75 mL), dried with $MgSO_4$, filtered, and concentrated. The resulting residue was purified by column chromatography on silica gel, eluting with a gradient of hexane and ethyl acetate, to yield the product 8 (1.58 g, 93.8% yield), which was observed by ^1H NMR spectroscopy as a 1:1 mixture of the α and β isomers in $CDCl_3$. FTIR (ATR): 3600−3100, 3028, 2990−2800, 1452, 1362, 1232, 1213, 1145, 1085, 1062, 1028, 989, 731, 694 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 7.43−7.30 (b, 30H), 5.26 (d, J= 3.5 Hz, 1H), 5.06−4.66 (broad overlapping, 13H), 4.11 (t, J= 9.0 Hz, 1H), 4.06 (m, 1H), 3.94−3.84 (m, 2H), 3.76−3.65 (overlapping, 3H), 3.62−3.43 (overlapping, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 138.7, 138.5, 138.4, 138.0, 137.9, 128.8−127.2 (m), 97.3, 91.0, 84.5, 83.3, 81.6, 80.1, 77.9, 76.0−74.6 (m), 73.1, 71.1, 62.0. +ESI MS: calculated $[M + Li]^+$ for $C_{27}H_{30}O_6$: 457.2202; found: 457.2217.

Synthesis of D-Glucose-Derived Monomers 11 and 12. Synthesis of Methyl 3-O-Benzyl-4,6-O-benzylidene-α-D-glucopyranoside (9) and Methyl 2-O-Benzyl-4,6-O-benzylidene-α-D-glucopyranoside (10). Methyl 4,6-O-benzylidene-α-D-glucopyranoside (1) (10.2 g, 36.1 mmol), BnBr (10.5 g, 61.4 mmol), and tetrabutylammonium hydrogen sulfate (2.53 g, 7.44 mmol) were dissolved in 600 mL of DCM. To this solution, 50 mL of 5% NaOH (aq) was added, and the mixture was heated to reflux for 26 h. The mixture was separated, and the aqueous layer was extracted with 50 mL of DCM. The organic layers were combined, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by column chromatography eluting with a gradient of hexane and ethyl acetate to afford methyl 3-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside 9 (7.61 g, 56.6%) and methyl 2-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside 10 (5.42 g, 40.3%) as white solids.

Methyl 3-O-Benzyl-4,6-O-benzylidene-α-D-glucopyranoside (9). FTIR (ATR): 3500−3100, 3100−3000, 2980−2800, 1450, 1366, 1211, 1172, 1136, 1070, 1056, 1028, 991, 968, 935, 922, 898, 735, 695, 650 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 7.57−7.26 (b, 10H), 5.61 (s, 1H), 5.01 (d, J= 11.5 Hz, 1H), 4.84 (d, J= 12.5 Hz, 2H), 4.34 (dd, J= 10.5 Hz, 4.0 Hz, 1H), 3.93−3.83 (overlapping, 2H), 3.83−3.73 (overlapping, 2H), 3.68 (t, J= 9.5 Hz, 1H), 3.48 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 138.6, 137.4, 129.2−125.8 (m), 101.3, 100.0, 82.0, 78.9, 74.9, 72.5, 69.0, 62.6, 55.4. +ESI MS: calculated $[M + H]^+$ for $C_{21}H_{24}O_6$: 373.1651; found: 373.1652.

Methyl 2-O-Benzyl-4,6-O-benzylidene-α-D-glucopyranoside (10). FTIR (ATR): 3600−3200, 3100−3000, 2950−2800, 1720, 1454, 1379, 1359, 1273, 1197, 1147, 1076, 1026, 962, 921, 748, 698, 678, 660, 617 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 7.56−7.32 (b, 10H), 5.54 (s, 1H), 4.81 (d, J= 12.0 Hz, 1H), 4.72 (d, J= 12.5 Hz, 1H), 4.64 (d, J= 3.5 Hz, 1H), 4.29 (dd, J= 10.0 Hz, J= 5.0 Hz, 1H), 4.18 (t, J= 9.5 Hz, 1H), 3.84 (td, J= 10.0 Hz, J= 5.0 Hz, 1H), 3.72 (t, J = 10.5 Hz, 1H), 3.55−3.47 (overlapping, 2H), 3.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 138.0, 137.2, 129.5−126.0 (m), 102.0, 98.7, 81.3, 79.6, 73.4, 70.3, 69.0, 62.1, 55.4. +ESI MS: calculated $[M + H]^+$ for $C_{21}H_{24}O_6$: 373.1651; found: 373.1655.

Methyl 3,4-Di-O-benzyl-α-D-glucopyranoside (11). To a solution of 9 (0.824 g, 2.21 mmol) in 22 mL of anhydrous DCM, in a flame-dried round-bottom Schlenk flask with 3 Å molecular sieves, was added BH_3·THF complex (1.0 M in THF, 11.0 mL, 11.0 mmol) and TMSOTf (0.100 mL, 0.550 mmol) under a N_2 atmosphere. After 90 min, the reaction was quenched by addition of 10 mL of methanol and 1.5 mL of TEA. The solution was filtered, concentrated, evaporated with 50 mL of methanol three times, and then purified by column chromatography on silica gel, eluting with a gradient of hexane and ethyl acetate, to yield 11 as a white solid as a white solid (0.691 g, 83.5% yield). FTIR (ATR): 3525−3225, 3100−3000, 2950−2775, 1500, 1452, 1358, 1329, 1206, 1142, 1093, 1059, 1026, 901, 760, 731, 692 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 7.45−7.28 (m, 10H), 4.97 (d, J= 11.0 Hz, 1H), 4.92 (q, J= 5.5 Hz, 2H), 4.77 (d, J= 4.0 Hz, 1H), 4.71 (d, J = 11.0 Hz, 1H), 3.87−3.80 (overlapping, 2H), 3.77 (dd, J= 12.0 Hz, J= 4.0 Hz, 1H), 3.74−3.68 (overlapping, 2H), 3.59 (t, J= 9.5 Hz, 1H), 3.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 138.6, 138.1, 128.9−127.3 (m), 99.4, 83.0, 77.3, 75.4, 75.0, 73.0, 71.1, 61.7, 55.2. + ESI MS: calculated $[M + Li]^+$ for $C_{21}H_{26}O_6$: 381.1889; found: 381.1898.

Methyl 2,4-Di-O-benzyl-α-D-glucopyranoside (12). To a solution of 10 (2.05 g, 5.50 mmol) in 60 mL of DCM, in a flame-dried round-bottom Schlenk flask with 3 Å molecular sieves was added BH_3·THF complex (1.0 M in THF, 28.0 mL, 28.0 mmol) and TMSOTf (0.25 mL, 1.38 mmol) under a N_2 atmosphere. After 90 min the reaction

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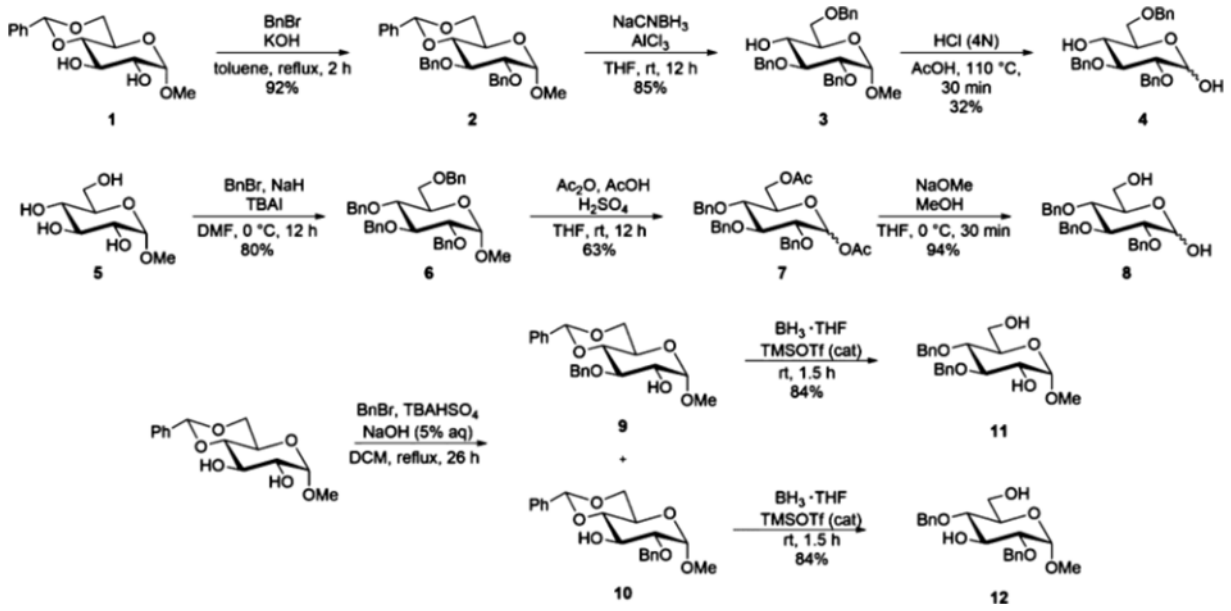
Scheme 1. Synthesis of D-Glucose-Based Diol Monomers 4, 8, 11, and 12



was quenched by addition of 30 mL of methanol and 3 mL of TEA. The solution was filtered, concentrated, evaporated with 75 mL of methanol three times, and then purified by column chromatography on silica gel, eluting with a gradient of hexane and ethyl acetate, to yield 12 as a white solid (1.73 g, 84.1% yield). FTIR (ATR): 3400−3150, 3100−3000, 2975−2775, 1454, 1367, 1192, 1101, 1065, 1028, 993, 901, 841, 732, 694, 636 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 7.42−7.28 (b, 10H), 4.95 (d, J = 11.0 Hz, 1H), 4.73 (d, J = 11.0 Hz, 2H), 4.67 (d, J = 13.0 Hz, 1H), 4.62 (d, J = 4.0 Hz, 1H), 4.15 (t, J = 9.0 Hz, 1H), 3.80 (dd, J = 12.0 Hz, J = 2.5 Hz, 1H), 3.73 (dd, J = 11.5 Hz, J = 4.5 Hz, 1H), 3.66 (td, J = 10.0 Hz, J = 3.0 Hz, 1H), 3.50 (t, J = 9.5, 1H), 3.38 (dd, J = 9.5 Hz, J = 3.5 Hz, 1H), 3.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 138.3, 137.9, 127.4−128.8 (m), 97.5, 79.7, 77.2, 74.5, 73.3, 73.0, 70.4, 61.7, 55.1. +ESI MS: calculated [M + Li]+ for $C_{21}H_{26}O_6$: 381.1889; found: 381.1881.

General Procedure of Polycondensation Using D-Glucose-Derived Monomers, 4, 8, 11, or 12, and Triphosgene. Triphosgene was added to a cold solution (0 °C) of the appropriate diol in anhydrous pyridine at a concentration of 400 mg/mL under a N_2 atmosphere. The reaction was allowed to stir for 5 min and then warmed to RT and allowed to react for 48 h. The reaction was then quenched with a saturated solution of Na_2CO_3 (ca. 2 mL) until no further evolution of carbon dioxide was observed. The residue was diluted with dichloromethane; the organic layer was washed with 10% aqueous HCl and then dried over $MgSO_4$, filtered, and concentrated under reduced pressure.

Poly(D-glucose)$_{1,4}$ Carbonate, 13. SEC: M_w = 5500 g/mol, M_n = 5000 g/mol, Đ = 1.13. FTIR (ATR): 3100−3000, 3000−2750, 1759, 1454, 1364, 1246, 1099, 989, 894, 735, 695 cm^{-1}. ^1H and ^{13}C NMR spectra are included in the Supporting Information, Figures S31 and S32. DSC: $T_{g,midpoint}$ = 33 °C. TGA in Ar: 267 °C, 15% mass loss; 345 °C, 74% mass loss; 26% mass remaining above 345 °C.

Poly(D-glucose)$_{1,6}$ Carbonate, 14. SEC: M_w = 4800 g/mol, M_n = 4400 g/mol, Đ = 1.09. FTIR (ATR): 3100−3000, 3000−2800, 1755, 1454, 1356, 1248, 1070, 1026, 1001, 735, 696 cm^{-1}. ^1H and ^{13}C NMR spectra are attached in the Supporting Information, Figures S33 and S34. DSC: $T_{g,midpoint}$ = 33 °C. TGA in Ar: 294 °C, 22% mass loss; 367 °C, 74% mass loss; 26% mass remaining above 367 °C.

Poly(D-glucose)$_{2,6}$ Carbonate, 15. SEC: M_w = 32 100 g/mol, M_n = 19 200 g/mol, Đ = 1.67. FTIR (ATR): 3100−3000, 3000−2800, 1747, 1454, 1361, 1338, 1246, 1126, 1047, 1001, 785, 735, 696 cm^{-1}. ^1H and ^{13}C NMR spectra are attached in the Supporting Information, Figures S35 and S36. DSC: $T_{g,midpoint}$ = 85 °C. TGA in Ar: 397 °C, 82% mass loss; 18% mass remaining above 397 °C.

Poly(D-glucose)$_{3,6}$ Carbonate, 16. SEC: M_w = 21 000 g/mol, M_n = 15 000 g/mol, Đ = 1.40. FTIR (ATR): 3100−2800, 1753, 1454, 1369, 1238, 1070, 1041, 1028, 999, 905, 781, 736, 696, 605 cm^{-1}. ^1H and ^{13}C NMR spectra are attached in the Supporting Information, Figures S37 and S38. DSC: $T_{g,midpoint}$ = 83 °C. TGA in Ar: 379 °C, 82% mass loss; 18% mass remaining above 379 °C.

RESULTS AND DISCUSSION

Based upon our overall goal of producing engineering types of polymers that are modeled from cellulose, derived from glucose, yet capable of undergoing hydrolytic degradation without the requirement of cellulase enzymes, we initially designed a 1,4-diol monomer of glucose and then expanded the scope to other regioisomeric glucose diol analogues. It was hypothesized that a series of glucose-derived diols could be copolymerized with a carbonylation agent to afford a series of regioisomeric polycarbonates. The series of poly(D-glucose carbonate)s were designed to mimic certain aspects of cellulose and glycogen. The 1 → 4-β-D-glycosidic linkages of cellulose facilitate chain packing to create crystallinity and provide for

Table 1. Conditions and Results of the Experimental Design for the Copolymerizations of Monomer 4 and Carbonylation Agents (Phosgene, Diphosgene, or Triphosgene)

expt	concn (g/L)[a]	carbonylation agent	equiv of carbonylation agent[b]	duration (h)	M_p[c] (Da)
1	200	phosgene	1	48	9000
2		diphosgene	2	72	5500
3		triphosgene	3	24	5600
4	400	phosgene	3	72	8800
5		diphosgene	1	24	5600
6		triphosgene	2	48	8700
7	600	phosgene	2	24	5600
8		diphosgene	3	48	5600
9		triphosgene	1	72	6600

[a]Concentration of 4 in pyridine. [b]Number of equivalents of carbonylation agents vs 4. [c]Peak average molecular weight determined by SEC-DMF for crude polymers vs polystyrene standards.

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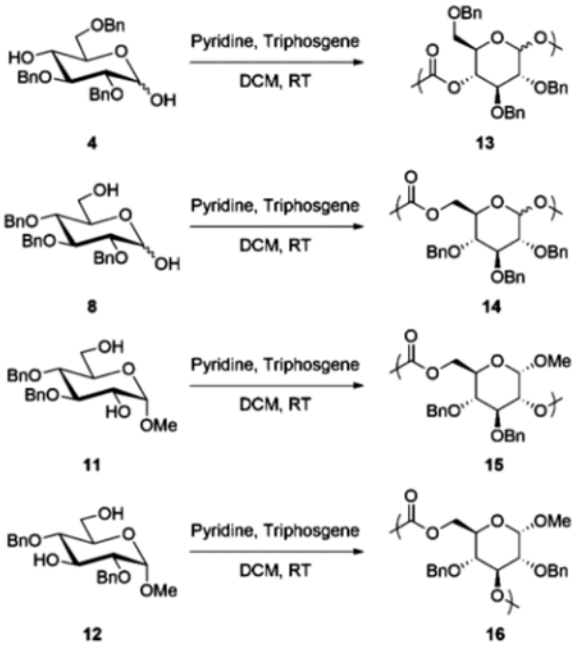
Table 2. Effect of Each Factor Evaluated by Placket−Burman Experiment ($\hat{y}$ = Average of Each Factor)

conditions	$\hat{y}$	effect
concn (g/L)		
200	6690	−80
400	7710	930
600	5920	−850
duration (h)		
24	5580	−1200
48	7800	1020
72	6950	170
equiv of carbonylation agent		
1	7050	280
2	6600	−170
3	6670	−100
carbonylation agent		
phosgene	7780	1010
diphosgene	5550	−1230
triphosgene	6990	220

Scheme 2. Polymerization of Four Regioisomeric Diols, 4, 8, 11, and 12, with Phosgene, Generated in Situ from Triphosegene, as a Comonomer and Pyridine as a Base



appropriate mechanical properties.[51] The crystallinity also contributes to the relative hydrolytic stability and its need of enzymatic catalysis for degradation.[52] Unlike glucose, glycogen, connected by linear α-1,4- and 1,6-repeat units as well as branching 1,4,6-repeat units, does not share the same hydrolytic stability and mechanical strength. In contrast to the relative stability of the 1,4-glycosidic linkages of cellulose, 1,4-carbonate connectivity of the glucose repeat units was expected to reduce hydrolytic and thermal stability due to the carbonate linkage being through a hemiacetal functionality of the anomeric site.[53,54] With proper understanding of structure−property relationships with regards to various regiochemistries of possible glucose monomers, a polymer system with the ability to fulfill a myriad of applications can be developed. Therefore, a series of monomers and corresponding polymers having 1,4-, 1,6-, 2,6-, and 3,6-regiochemistries were investigated.

Synthesis of Four Regioisomeric Diols from D-Glucose. Starting from commercially available protected glucose compounds, methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (1) or methyl α-D-glucopyranoside (5), four different regioisomeric monomers 4, 8, 11, and 12, having 1,4-, 1,6-, 2,6-, and 3,6-diols, respectively, were prepared through three synthetic routes (Scheme 1). The structure of each compound was thoroughly characterized by ^{1}H, ^{13}C, and COSY NMR spectroscopies, IR spectroscopy, and high-resolution mass spectrometry (HR-MS). All relevant NMR and IR spectra are included in the Supporting Information (Figures S1−S52).

Synthesis of 1,4-Diol Monomer, 2,3,6-Tri-*O*-benzyl-D-glucopyranoside, 4. In the first step, protection of two hydroxyl groups at the C2 and C3 positions of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (1) with benzyl groups afforded the completely protected glucose derivative, methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (2). Selective benzylidene ring-opening, using $NaBH_3CN$ and $AlCl_3$, was then performed to give a free hydroxyl group at C4 as the major product in ca. 85% yield. Ring-opening of the benzylidene was confirmed by the complete disappearance of the ^{1}H NMR resonance at 5.62 ppm and the ^{13}C NMR resonance peak at 101.3 ppm, corresponding to the acetal methine in the starting material. Finally, demethylation at C1 of methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (3) under acidic conditions resulted in the desired monomer 4 in ca. 32% yield, after column chromatography and recrystallization in a solution of hexane and ethyl acetate. Interestingly, single ^{1}H and ^{13}C NMR resonance peaks at 5.26 and 91.2 ppm, respectively, for the anomeric carbon, C1, appeared in the NMR spectra, despite the potential formation of two isomers, α and β, generated during acidic treatment.

Synthesis of 1,6-Diol Monomer, 2,3,4-Tri-*O*-benzyl-D-glucopyranoside, 8. Initially, attempts to prepare methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside, 6, were made by following a similar synthetic strategy to 4, that is, protection of the two hydroxyl groups at C2 and C3, selective ring-opening of the benzylidene, followed by demethylation of the hydroxyl group at C1. However, isolation of the desired product during the final demethylation step with methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside was challenging, and thus, an alternate strategy was chosen. First, benzylation of methyl-α-D-glucopyranoside (5) was conducted in the presence of NaH, BnBr, and a catalytic amount of TBAI in DMF to give methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (6) in ca. 80% yield. Simultaneous removal of the methyl and benzyl protecting groups at C1 and C6, respectively, was performed in a one-pot manner by acid-catalyzed acetolysis, as described by Gervay-Hague et al.,[55] resulting in 1,6-diacetate compound 7 in ca. 63% yield. Conversion from methyl and benzyl substituents at C1 and C6, respectively, to acetyl groups at both positions was confirmed by disappearance of the ^{1}H NMR signal of the methyl group resonating at 3.46 ppm and the ^{13}C NMR resonance at 55.2 ppm, coincident with the appearance of acetyl ^{1}H NMR resonances at 3.76−3.65 (3Hs) and 3.62−3.43 (3Hs) and ^{13}C NMR resonances at 170.7, 169.4, 21.1, and 20.9 ppm. Compound 7 was then converted to the 1,6-diol monomer, 2,3,4-tri-*O*-benzyl-D-glucopyranoside (8) in near-quantitative yield, ca. 94%, upon deprotection using NaOMe in MeOH. The collected product 8 was observed as a mixture (1:1) of α and β isomers, as demonstrated by the occurrence of

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Table 3. Results of Polymerization Using Four Regioisomeric Monomers 4, 8, 11, and 12 To Afford 13, 14, 15, and 16, Respectively

monomer	solvent	duration (h)	equiv of triphosgene	equiv of pyridine	[M]	M_n[a] (Da)	M_w[a] (Da)	Đ
4	DCM	1	0.40	2.5	0.56	5000	5500	1.13
	DCM	5	0.46	4.2	0.57	6200	6700	1.08
	DCM	24	0.40	4.7	0.26	7800	8500	1.09
8	DCM	1	0.40	3.8	0.12	5700	6600	1.16
	DCM	24	0.33	2.0	1.0	5900	7000	1.20
	DCM	24	0.33	4.0	0.50	7100	8200	1.16
	DCM	24	0.33	4.0	1.0	4400	4800	1.09
	1,4-dioxane	24	0.33	4.0	1.0	5085	5250	1.03
11	DCM	1	0.33	4.0	0.50	12400	15100	1.22
	DCM	12	0.33	4.0	0.50	15500	19400	1.25
	DCM	24	0.33	2.0	0.50	38000	52000	1.37
	DCM	24	0.33	4.0	0.50	19200	32100	1.67
	DCM	24	0.50	2.0	0.50	17000	18000	1.06
	DCM	24	0.50	4.0	0.50	42000	57000	1.36
	DCM	48	0.33	4.0	0.50	25000	30100	1.20
12	bulk	24	0.50	4.0	-	28400	38000	1.34
	DCM	24	0.33	4.0	0.50	15000	21000	1.40
	DCM	72	0.33	4.0	0.50	21200	25300	1.19

[a]Molecular weight determined by SEC-DMF for crude polymers vs polystyrene standards.

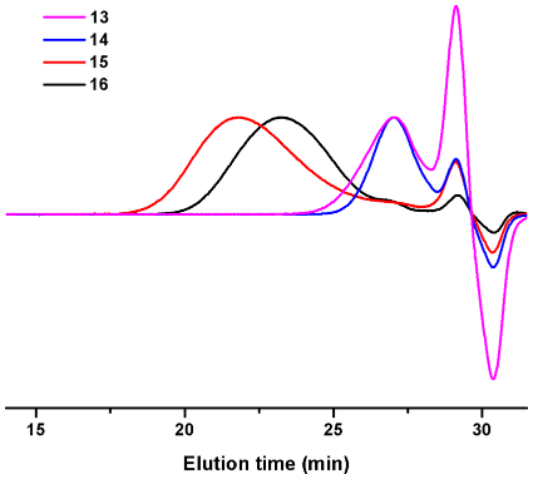

Figure 1. SEC traces of representative polymers of 13, 14, 15, and 16.

Table 4. Summary of Thermal Properties of PGCs 13, 14, 15, and 16, Measured by DSC and TGA

polymer	T_g (°C)	$T_{d1,onset}$ (°C)	$T_{d2,onset}$ (°C)
13	33	171	267
14	33	163	294
15	85	363	
16	83	336	

^{13}C NMR resonance peaks at 97.3 and 91.0 ppm from the C1 anomeric carbon. Finally, HR-MS measurement demonstrated the presence of compound 8 as an isomeric form of compound 4, having the identical molecular weight of 457 m/z (457.2217, with Li in a positive mode).

Synthesis of Methyl 3,4-Di-O-benzyl-α-D-glucopyranoside, 11, and Methyl 2,4-Di-O-benzyl-α-D-glucopyranoside, 12. The other two diol monomers 11 and 12 were derived from 1 as a single, common starting material. Specifically, benzylation of the two hydroxyl groups at C2 and C3 using the bulky phase transfer agent TBAH led to two separable isomers, 9 and 10, in near 1:1 ratio. Then, their conversion to monomers 11 and 12, respectively, was performed by selective benzylidene ring-opening with TMSOTf and BH_3 THF complex in high yields ca. 84%. The benzylidene ring-opening was confirmed by the complete disappearance of ^{1}H NMR singlet resonances at 5.61 and 5.54 ppm and ^{13}C NMR resonances at 101.3 and 102.0 ppm corresponding to the acetals of compounds 9 and 10, respectively. Furthermore, HR-MS analysis confirmed the formation of two isomeric compounds 11 and 12, resulting in an identical molecular weight of 381 m/z (381.1898 and 381.1881, respectively, with Li in a positive mode).

Preparation of D-Glucose-Derived Polymers with Different Backbone Regiochemistries. Screening of Polymerization Conditions Using Diol Monomer 4. Screening for appropriate polycondensation conditions was performed using 4, which could generate a polycarbonate analogue of cellulose, having 1,4-backbone connectivity. Initial efforts were focused on employing alternative carbonylation reagents to phosgene, such as diphenyl, di-p-nitrophenyl, dimethyl, and diethyl carbonates. However, it was observed that these conditions were either too harsh, causing degradation of the starting material, or not conducive to forming large molecular weight polymers, as monitored by NMR spectroscopy or SEC.

The reaction duration, monomer concentration, and the quantity of phosgene analogues, i.e., phosgene, diphosgene, or triphosgene, were tested by a Plackett−Burman experimental design (matrix 4^3, where 4 is the number of factors and 3 is the number of levels tested for each factor) based on nine experimental conditions (Table 1, experiments 1−9) conducted on scales of 150 mg of monomer in the volume of solvent needed to give the three desired monomer concentrations (combined pyridine and toluene (in the case of phosgene reagent)).[21,56] This study of the effects of individual factors indicated that PGCs with the highest molecular weights could be produced under polymerization conditions that included a monomer concentration of 400 g/L, phosgene and triphosgene as carbonylation agents at a stoichiometry of one molar equivalence (Table 2). However, phosgene was precluded from further study because of its instability and safety concerns

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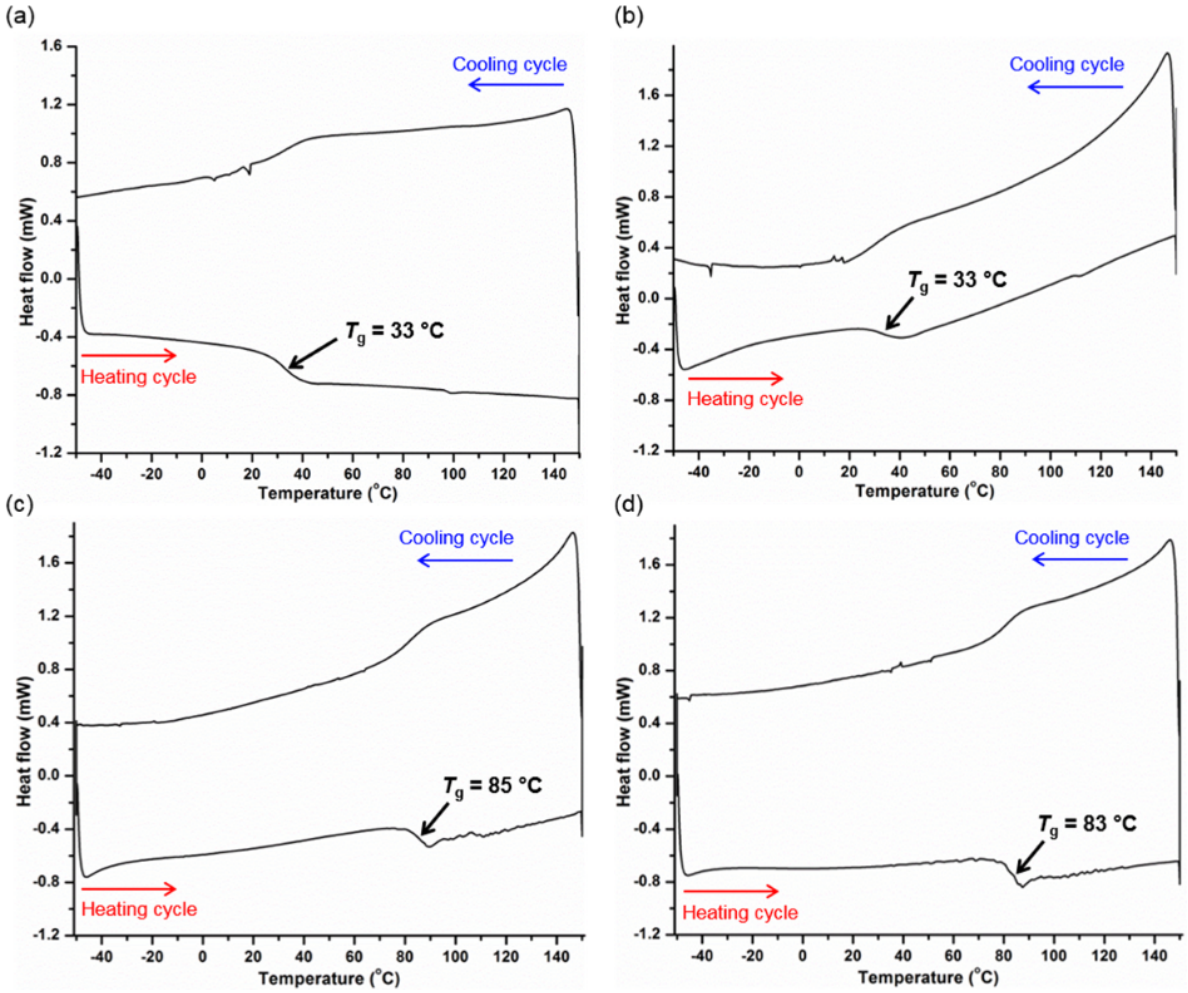

Figure 2. Differential scanning calorimetry analysis of 13 (a), 14 (b), 15 (c), and 16 (d). The T_g values determined from the heating cycles are confirmed by the cooling cycles.

associated with its use. Still, use of the more stable and more conveniently handled triphosgene led to 1,4-PGC's having comparable molecular weights.

Synthesis of Four Regioisomeric PGCs. Using the conditions from the polymerization optimization study, four regioisomeric polymers, 13, 14, 15, and 16, were synthesized from each diol monomer, 4, 8, 11, and 12, respectively (Scheme 2). Varying conditions, such as polymerization time, amount of triphosgene and pyridine, and monomer concentration, were also examined to determine their effects on molecular weight and molecular weight distributions (or dispersity, Đ) of the resulting PGCs by SEC analysis (Table 3 and Figure 1). Interestingly, copolymerization of 4 or 8, having an active hydroxyl at the anomeric position, with triphosgene resulted in 13 and 14 with limited molecular weight, below 8 kDa, whereas copolymerization of 11 and 12 led to 15 and 16 with significantly higher M_n, above 10 kDa, in all of our attempts. Most of the SEC traces were monomodal, and their distributions were heavily dependent on polymer molecular weight. In general, Đ increased with higher molecular weight polymers, which is typical of polycondensations.

Formation of the carbonate backbone linkages upon polymerization was directly observed by the introduction of a ^{13}C NMR signal at 150 ppm and was also confirmed by the appearance of a single absorbance band at ca. 1750 cm^{-1} in the IR spectra (Figures S49−S52). Furthermore, a significant reduction in intensity of broad OH stretches in the IR spectra from each diol monomer to the corresponding PGC supported the polymerization event as well as the broadening of the ^1H NMR signals.

Thermal Properties of the Prepared Regioisomeric PGCs. In the following studies, the thermal properties of the prepared polymers with four backbone regioconnectivities were examined by DSC and TGA analyses. All four polymers 13, 14, 15, and 16 exhibited amorphous behavior, and interestingly, the regiochemistry of the polymer backbone appeared to play an important role in determining the glass transition temperature, T_g, of the polymers (Table 4 and Figure 2). Both 13 and 14 contained the anomeric carbon in the carbonate backbone, and displayed lower T_g values, ca. 33 °C, than 15 and 16, ca. 85 and 83 °C, respectively. As we described previously, 13 and 14 are a mixture of stereoisomers, α and β, at the anomeric carbon, which could hinder the chain−chain packing in the final polymers. In contrast, both 15 and 16 are composed of a single isomeric backbone structure, with equatorial linkages coming from the glucose rings and may allow for better chain−chain packing and require higher energy for long-chain segmental motion as compared to 13 and 14. Although a key factor influencing the T_g could be the difference in the stereochemistries of the regioisomers, the molecular weights of 13

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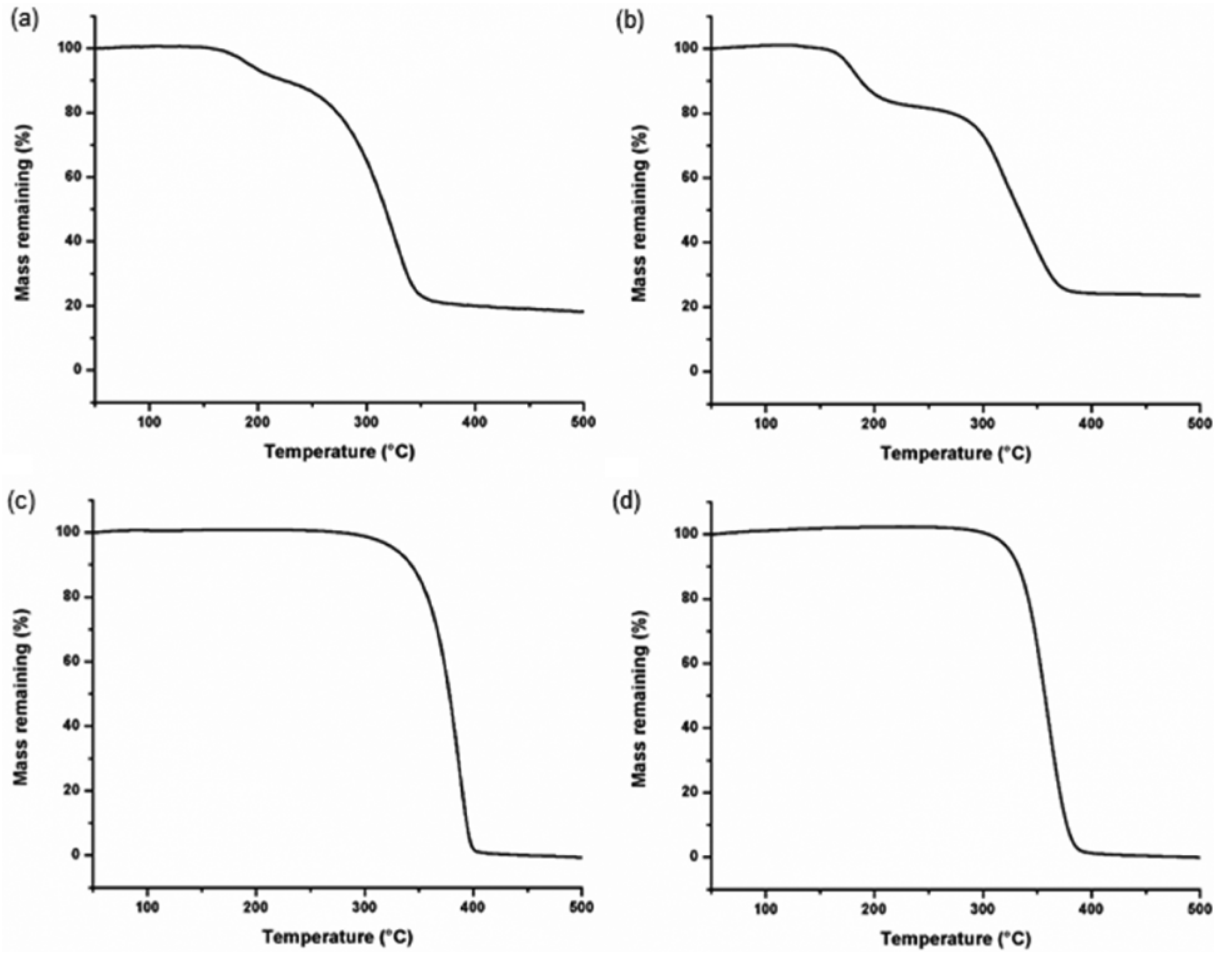
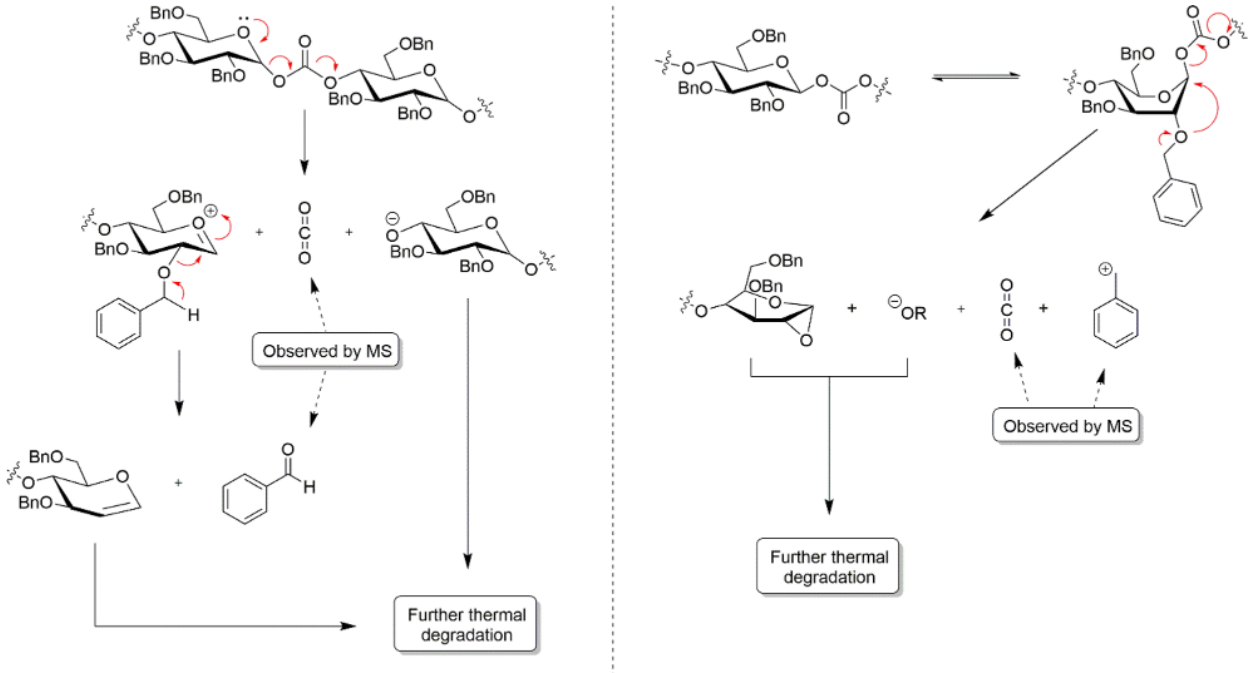


Figure 3. Thermogravimetric analysis of 13 (a), 14 (b), 15 (c), and 16 (d).

Scheme 3. Thermal Degradation Pathways for 13 Based on Tandem TGA-MS Analysis



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and 14 were significantly lower than those of 15 and 16, and polymer molecular weight is well-known to influence T_g below the $(T_g)_\infty$. In addition, the differences in methyl vs benzyl protecting groups, with 13 and 14 having three benzyl groups whereas 15 and 16 contain two benzyl and one methyl protecting groups, could increase the free volume and contribute to the decrease in T_g values for 13 and 14.

Different regiochemistries in the polymer backbone also had a significant impact on the thermal stabilities of the polymers. The two polymers 15 and 16, not incorporating the anomeric position into the polymer backbone, behaved like rigid polymers, exhibiting high thermal stability and a sharp decomposition profile, with onset decomposition temperature, $T_{d,onset}$, at 363 and 336 °C, respectively (Table 4 and Figure 3). Meanwhile, as predicted, polymers with the carbonate linkage connected through the anomeric center showed much lower thermal stabilities. For example, 13 had two different $T_{d,onset}$ values, with the first onset, $T_{d1,onset}$, appearing at 171 °C and the second, $T_{d2,onset}$, at 267 °C. Similarly, 14 had $T_{d1,onset}$ at 163 °C and $T_{d2,onset.d}$ at 294 °C. Neighboring functionality can have an effect on the thermal stability of a carbonate group. Initially, it was proposed that the endocyclic oxygen in the glucose ring was playing a role in the thermal degradation, similar to previously reported carbonate sugars,[53,54] accelerating the decomposition of the backbone. Tandem TGA-MS of polymer 13 detected peaks in increments of m/z 44, which could be attributed to the loss of $CO_2^{+\cdot}$. However, the mass loss that occurred during the first phase of degradation was too great to be attributed to the loss of only CO_2. In addition, several other peaks were also observed early in the decomposition of the polymer at increments of m/z 77, 91 and 92, as well as 105 and 106, which corresponded to phenyl, toluyl, and benzoyl radicals, respectively. Possible mechanistic pathways for the thermal degradation that led to the observed products from 13 are illustrated in Scheme 3.

CONCLUSIONS

In conclusion, we report the design, synthesis, and thermal characterization of four types of polycarbonates, constructed from D-glucose derivatives, having different backbone regiochemistries. By employing established carbohydrate protection and deprotection chemistries, two D-glucose derivatives, methyl 4,6-O-benzylidene-α-D-glucopyranoside or methyl α-D-glucopyranoside, were converted into four regioisomeric diol monomers having 1,4-, 1,6-, 2,6-, or 3,6-diols with reasonably high yields >80%, in most cases. Characterizations of each compound by NMR, IR, and mass spectrometry confirmed the reliability of our synthetic approach. After optimizing the polymerization conditions, the reactivity of each synthesized monomer was examined through a condensation polymerization with phosgene, generated *in situ* from triphosgene, as a comonomer in the presence of pyridine, resulting in the generation of four polycarbonates having different backbone regioconnectivities. The copolymerizations of monomers, where neither of the active hydroxyl groups are at the anomeric center, 2,6- or 3,6-diols, allowed for the production of PGCs with high molecular weights, >10 kDa. However, only small molecular weight PGCs, <8 kDa, were generated with monomers having an active hydroxyl group at the anomeric center, 1,4- or 1,6-diols. Interestingly, monomer regiochemistry appeared to be the crucial parameter influencing the thermal properties of the polymers. PGCs with 2,6- and 3,6-backbone connectivity resulted in significantly higher T_g materials, 85 and 83 °C, respectively, as compared to those with 1,4- and 1,6-backbone connectivities each giving polymers with a T_g of 33 °C. Finally, in the study of thermal stability, the nonanomeric backbone-based PGCs exhibited high thermal stabilities and sharp decomposition profiles, with $T_{d,onset}$, of 336 or 363 °C as compared with PGCs containing the anomeric carbon in the carbonate linkage, having $T_{d1,onset}$ of 171 and 163 °C and $T_{d2,onset}$ of 267 and 294 °C, respectively. Fundamental studies to understand the influence of the anomeric carbon as part of the polycarbonate backbone on other physical and chemical properties, including the hydrolytic stabilities, are currently under investigation. Furthermore, study of the mechanical properties of glucose-based polycarbonates is underway.

ASSOCIATED CONTENT

* Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.macromol.6b00591.

Figures S1−S52 (PDF)

Additional characterization data (TXT)

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Notes

The authors declare no competing financial interest.

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