JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
Cite This: J. Am. Chem. Soc. XXXX, XXX, XXX−XXX
pubs.acs.org/JACS

Controlled Living Cascade Polymerization To Make Fully Degradable Sugar-Based Polymers from D-Glucose and D-Galactose

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Supporting Information

ABSTRACT: Monomers derived from glucose and galactose, which contain an endocyclic alkene (in the sugar ring) and a terminal alkyne, underwent a cascade polymerization to prepare new polymers with the ring-opened sugar incorporated into the polymer backbone. Polymerizations were well-controlled, as demonstrated by a linear increase in molecular weight with monomer-to-initiator ratio and generally narrow molecular weight dispersity values. The living nature of the polymerization was supported by the preparation of a block copolymer from two different sugar-based monomers. The resulting polymers were also fully degradable. They underwent fast and complete depolymerization to small molecules under acidic conditions.

Limited quantities of fossil fuels and increased awareness of the environmental impact of petroleum-based plastics have fueled the search for new sustainable polymers.[1,2] Materials from biomass-derived polymers have the potential to be more environmentally friendly, and may have interesting properties such as biocompatibility or degradability.[3−6] The most common forms of biomass from which polymers can be derived include vegetable oils,[7] terpenes,[8] amino-acids,[9] lignin,[10] and carbohydrates (saccharides) such as cellulose[11] and starch (polysaccharides).[12] Sugars (mono- or disaccharides), in particular, are an attractive option for polymer building blocks given that they are widely available, environmentally benign, generally nontoxic, structurally diverse, and relatively easy to functionalize.[13,14]

Polymers in which sugars are attached as pendent groups to the backbone, often called glycopolymers, are well established in the literature.[15,16] Sugar-based polymers (SBPs),[17−20] in which the sugar is incorporated into the backbone of the polymer, have been much less developed and are typically prepared by step-growth condensation reactions,[13] or ring-opening polymerization.[14] The latter polymers are attractive as they have the potential to yield polymers with degradable backbones. Of particular interest to our group was the use of olefin metathesis polymerizations to prepare degradable SBPs. Acyclic diene metathesis (ADMET) polymerization,[21,22] ring-opening metathesis polymerization (ROMP),[23−26] and cyclopolymerization[27,28] are powerful polymerization techniques that have been used to prepare a wide range of functional polymers. While these techniques have been used to prepare various partially or fully backbone-degradable polymers,[29−37] they have rarely been used to prepare degradable SBPs.

Enholm and Mondal functionalized D-ribose derivatives with terminal alkenes and used ADMET polymerization to prepare polymers with the sugar intact.[38] Meier, Gross, and co-workers demonstrated the entropy-driven ROMP of a macrocyclic monomer containing a disaccharide unit.[39] They achieved polymers with high number-average molecular weight (M_n > 75 kDa) with Grubbs second or third generation catalysts (G2 or G3, respectively), but with broad molecular weight dispersity ($Đ_M$ values of 1.6−1.7). Of note, there are several reports on ADMET polymerization or ROMP of biomass-derived monomers, that do not contain sugars, but are still derived from carbohydrate feedstocks, such as glucose,[40,41] mannitol,[38] pentose,[42−44] and cellulose.[45] Unfortunately, the majority of these monomers did not enable controlled polymerizations.

We sought to develop new monomers from widely available glucose (GL) and its C-4 epimer galactose (GA) (Figure 1A). In particular, we envisioned modifying sugars such that they contained an endocyclic alkene which could serve as a handle for ring-opening metathesis. However, 6-membered cycloalkenes have very low ring strain and typically do not undergo ROMP.[46,47] Fortunately, we recently demonstrated that cascade metathesis polymerizations can open 6-membered rings when functionalized with terminal alkynes.[48−50] Herein, we report the controlled living cascade polymerization of monomers derived from sugars which yield fully degradable polymers.

From commercially available acetylated GL and GA, we prepared monomers **1**−**6** in three to four steps depending on the desired α/β stereochemistry of the anomeric carbon (see Figure S1 in the Supporting Information, SI). We initially explored the polymerization of **1** (*N*-tosyl) in tetrahydrofuran (THF) using G3 as catalyst, which was the optimal solvent/catalyst combination in our previous studies.[48] With a monomer-to-initiator ratio (M/I) of 50, we observed 56% monomer conversion and a polymer with an M_n of 15.7 kDa ($Đ_M$ of 1.39; see Table 1, entry 1). Attempts to significantly increase conversion and lower the dispersity were unsuccessful (see Table S1). By ^{1}H nuclear magnetic resonance (NMR) experiment revealed nearly equivalent and relatively fast conversion of both α- and β-isomers in the first minute of reaction (see Figure S2), but conversion quickly tapered off (see Figure S3), suggesting degradation of the catalyst. We envisioned that increasing the steric bulk of the sulfonamide group might enhance the polymerization by speeding the

Received: May 31, 2019

DOI: 10.1021/jacs.9b05822
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

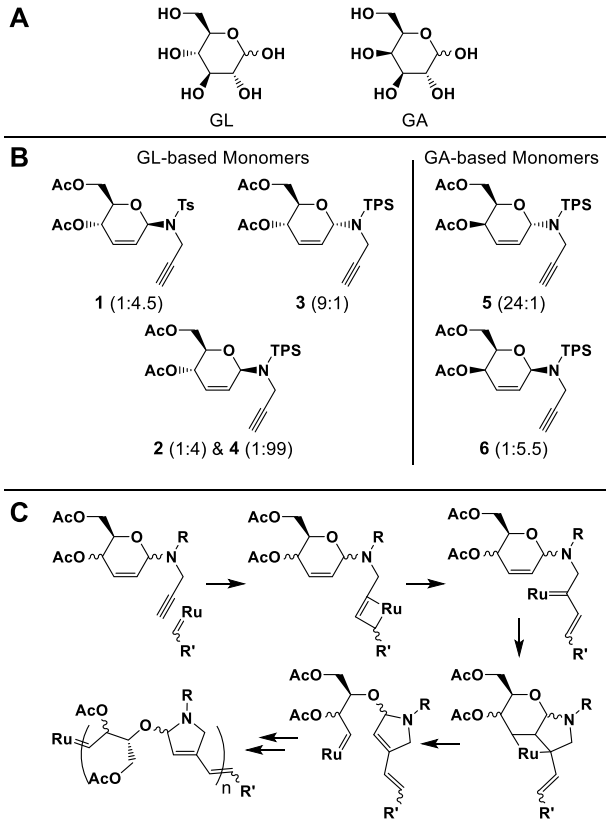


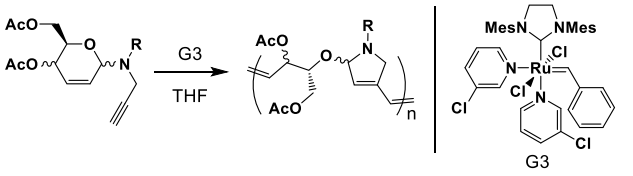
Figure 1. (A) Chemical structures of glucose (GL) and galactose (GA). (B) Chemical structures and α:β ratios for GL- and GA-based monomers used in this study. (C) Proposed polymerization mechanism.[48] Ts = tosyl. TPS = 2,4,6-triisopropylbenzenesulfonyl.

reaction further via the Thorpe−Ingold effect,[50] or helping stabilize the propagating carbene via steric shielding.[51] Thus, we pursued the polymerization of monomers with bulkier *N*-2,4,6-triisopropylbenzenesulfonyl (TPS) substituents.

As expected, for the GL-based monomer **2** (α:β of 1:4) with the bulky TPS substituent, we observed much higher conversion (>75%). With our standard conditions (0.1 M concentration at 15 °C, see Table S1), we obtained high molecular weight polymer (26.7 kDa) with narrower dispersity (1.13) for a M/I of 50 (Table 1, entry 2). As we changed the M/I ratio (as high as 100, entries 3−5), we observed a linear increase in M_n (up to 54.8 kDa), while maintaining the $Đ_M$ between 1.04 and 1.44 (Figure 2A). Polymerization of monomers with higher stereopurity, **3** (α:β of 9:1, entry 6) and **4** (α:β of 1:99, entry 7), gave comparable results to **2** at a M/I of 50 (consistent with our observation of nearly equivalent reactivity of the α- and β-isomers by ^{1}H NMR spectroscopy, see Figure S4). The GL-*N*-TPS monomers reached ca. 4% conversion in 1 min (see Figure S2), and conversion continued over several hours. This is in contrast to the GL-*N*-Ts monomer (**1**) which had faster initial conversion (ca. 11% in 1 min) and nearly stopped within 1 h. These results suggested that the *N*-TPS group was serving as a steric shield to protect the propagating carbene from decomposition, which is further supported by ^{1}H NMR experiments that show much faster carbene decomposition during the polymerization of **1** than **2** (see Figure S5).

We next explored the polymerization of GA-based monomers. In contrast to the GL-based monomer reactivity, we found that the α-isomer had a significantly faster

Table 1. Polymerization Results for Sugar-Based Monomers (M)[a]



entry	M	M/I	time (h)	conv.[b] (%)	yield (%)	theor. M_n[c] (kDa)	M_n[d] (kDa)	$Đ_M$[d]
1[e]	**1**	50	5	56	44	11.8	15.7	1.39
2	**2**	50	7	94	76	25.1	26.7	1.13
3	**2**	25	3	95	52	12.7	8.9	1.04
4	**2**	75	12	87	72	38.0	47.2	1.32
5	**2**	100	15	77	69	41.1	54.8	1.44
6	**3**	50	7	90	77	24.0	32.1	1.21
7	**4**	50	7	89	75	23.7	25.3	1.18
8	**5**	25	1	>99	79	13.2	13.5	1.04
9	**5**	50	5.5	>99	93	26.4	29.4	1.08
10	**5**	75	5.5	>99	83	39.6	37.6	1.21
11	**5**	100	7	>99	86	52.8	53.3	1.22
12	**5**	125	9	>99	83	66.0	64.2	1.28
13[f]	**5**	150	12	97	83	77.7	66.0	1.36
14[f]	**5**	200	14	97	86	103.5	92.6	1.26
15[f]	**5**	300	16	97	86	155.3	135.3	1.44
16	**6**	50	7	86	78	22.9	27.5	1.23

[a]All polymerization conducted with a monomer concentration of 0.1 M and at a temperature of 15 °C, unless otherwise noted. [b]Conversion: determined by crude ^{1}H NMR. [c]Theoretical M_n: determined by multiplying the monomer molecular weight by M/I and conversion. [d]Determined by size exclusion chromatography (SEC) using a multiangle light scattering (MALS) detector. [e]Monomer concentration of 0.03 M. [f]Polymerization at room temperature (RT, ca. 23 °C).

conversion rate than the β-isomer (ca. 11 vs <1% conversion in 1 min, respectively, see Figures S2 and S6). Therefore, we focused on the polymerization of the α-rich monomer **5** (Table 1, entries 8−15). To achieve higher conversion and molecular weight for large M/I values (150−300), we slightly modified conditions by increasing the temperature to RT (entries 13−15, see the SI for more details). Overall, we observed a relatively linear increase in M_n up to 135 kDa (M/I of 300), while maintaining the $Đ_M$ between 1.05 and 1.44 (Figure 2B). Polymerization of the β-rich monomer **6** (α:β of 1:5.5, entry 16), with a M/I of 50, gave a comparable M_n to **5**, but with increased dispersity (comparable to that of **3** and **4**). Monomer **5** is the only monomer in which the alkyne is on the opposite face of the sugar ring, respective to both the OAc and CH_2OAc substituents (see Figure S7). Thus, the alkyne may be less sterically hindered for catalyst approach, which may explain the enhanced reactivity of **5** (see the SI for more details).

To demonstrate the living nature of this polymerization, a block copolymer was prepared. Monomer **2** was added to an active **P5** (first) block (Figure 2C). Sampling after polymerization of the first and second blocks revealed a clear shift in the SEC peak to the higher molecular weight region, without any residual **P5** block or tailing, and maintaining a $Đ_M$ of 1.05. This supports the living nature of the chain end.

In addition to influencing their reactivity, the stereochemistry of monomers also influenced the resulting stereochemistry of the polymers, and led to differences in polymer properties. For instance, **P5** and **P6** had higher *E*-alkene

DOI: 10.1021/jacs.9b05822
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

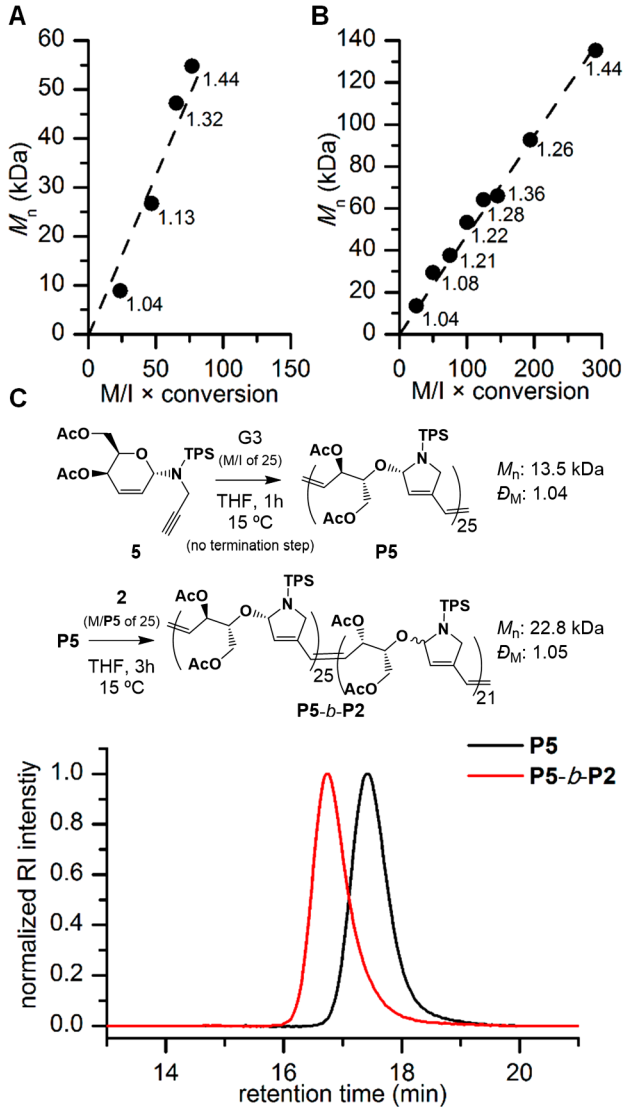


Figure 2. Demonstrating controlled cascade metathesis polymerization of sugar-based monomers. (A) Linear plots of M_n versus M/I × conversion for **2** and (B) **5**. Labels represent the corresponding $Đ_M$. (C) Demonstrating the living nature of cascade polymerizations via the production of a **P5**-*b*-**P2** block copolymer. Molecular weight characterization from SEC with MALS.

content than **P2**−**P4** (*E*:*Z* for **P1**, **P2**, **P3**, **P4**, **P5**, and **P6** are 54:46, 49:51, 61:39, 50:50, 69:31, and 73:27, respectively; see the SI for details). This is in contrast to our previous reports, in which we only observed *E*:*Z* values of 6:4.[48,49] The glass transition temperature was also slightly elevated for **P5** and **P6** (51.5 and 54.7 °C, respectively) compared to **P2**−**P4** (43.0, 47.1, and 46.0 °C, respectively). Finally, the optical activity varied with the stereochemistry (see Table S2), with α- and β-rich polymers rotating light in opposite directions.

A key aspect of these SBPs is that the hemiaminal ether in the monomers is incorporated into the polymer backbone. Hemiaminal ethers,[52] and related derivatives,[34,36] are known to be acid sensitive; thus, we conducted several experiments to test the degradability of these polymers. We sequentially added small amounts of HCl to **P2** in THF, and monitored the degradation by SEC (Figure 3A; see the SI for details). With increasing acid content, the SEC peak shifted to the lower molecular weight region and increased in breadth. Only at the later stages of degradation did we see the accumulation of a single low molecular weight species, which was consistent with a random backbone cleavage process.

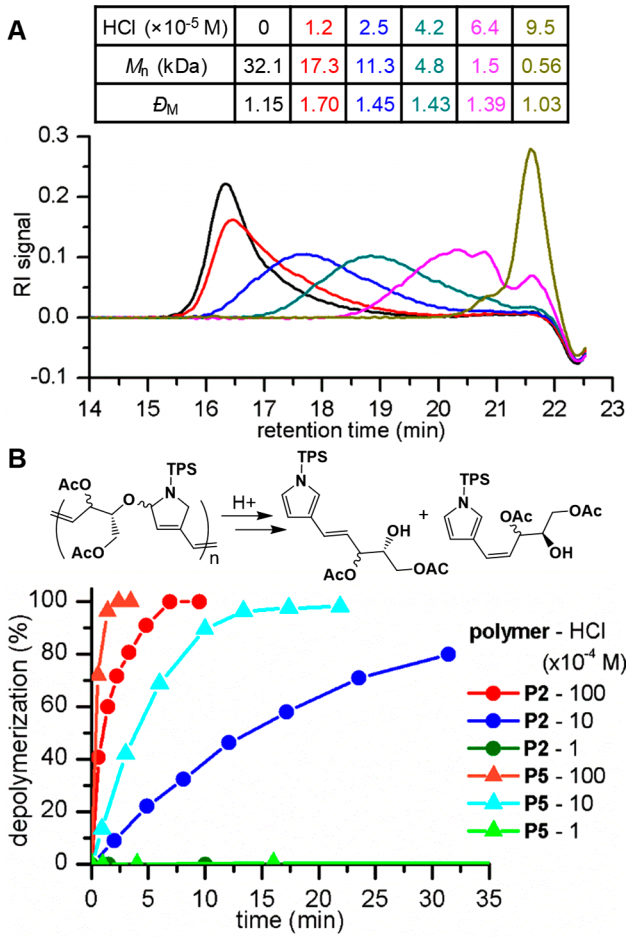


Figure 3. Demonstrating complete depolymerization of SBPs. (A) Acidic degradation of **P2** (initially at 1 mg/mL) in THF as monitored by SEC with MALS. (B) Acidic degradation of **P2** and **P5** at various HCl concentrations in 10% D_2O in acetone-d_6 (polymer at ca. 23 mg/mL).

Next, to follow the continuous degradation of polymers, **P2** or **P5** was dissolved in acetone-d_6 and acidic D_2O was added (10% by volume) to give solutions with varying HCl concentrations (ranging 1×10^{-2} to 1×10^{-4} M). By ^{1}H NMR, we observed faster depolymerization of **P5** than **P2** with increasing acid content (see the SI for details) and complete degradation to small molecules in as short as 2.5 min (Figure 3B; see Figure S8 for plots out to ca. 24 h). We identified that polymers degraded into pyrrole-based products with *E*- or *Z*-alkene stereochemistry (see Figure S9 for a proposed mechanism). Pyrroles are known to have a wide range of biological activity (*N*-arylsulfonyl pyrroles show antiviral activity);[53,54] thus, the degradation products may have added utility. Regardless, these studies demonstrate the highly degradable nature of GL- and GA-based polymers.

In conclusion, we have demonstrated, for the first time, the cascade metathesis polymerization of sugar-based monomers in which the sugar ring is opened and incorporated into the polymer backbone. Polymerizations were well-controlled and high molecular weights were obtained (M_n up to 135 kDa) with generally narrow dispersity (1.04−1.44). Kinetics experiments supported that the bulky TPS substituent (which

DOI: 10.1021/jacs.9b05822
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

suppressed decomposition of the propagating carbene) and monomer stereochemistry (which influenced propagation rates and led to differences in polymer properties) played important roles in the polymerization. The living nature of the polymerization was supported by the preparation of a block copolymer from two different sugar-based monomers. Degradation experiments also supported the fully degradable nature of the polymers. Our future plans include optimizing the sustainability of the monomer synthesis, exploring postpolymerization functionalization (e.g., making polymers water-soluble), further studying the influence of monomer/polymer stereochemistry, and tuning the degradability of polymers.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.9b05822.

Supplemental figures, experimental details, and characterization of monomers, polymers, and degradation products (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This paper is dedicated to Prof. Kwang-Sup Lee on the occasion of his 65th birthday and life-long achievements in research and education at Hannam University. We are thankful for financial support from the NRF, Korea through the following grants: Creative Research Initiative Grant, Creative Material Discovery Program, and Young Investigator Grant (Grant 2018R1C1B6003054).

■ REFERENCES

(1) Zhu, Y.; Romain, C.; Williams, C. K. Sustainable polymers from renewable resources. *Nature* **2016**, *540*, 354−362.

(2) Llevot, A.; Dannecker, P.-K.; von Czapiewski, M.; Over, L. C.; Söyler, Z.; Meier, M. A. R. Renewability is not Enough: Recent Advances in the Sustainable Synthesis of Biomass-Derived Monomers and Polymers. *Chem. - Eur. J.* **2016**, *22*, 11510−11521.

(3) Gandini, A.; Lacerda, T. M.; Carvalho, A. J. F.; Trovatti, E. Progress of Polymers from Renewable Resources: Furans, Vegetable Oils, and Polysaccharides. *Chem. Rev.* **2016**, *116*, 1637−1669.

(4) Iwata, T. Biodegradable and Bio-Based Polymers: Future Prospects of Eco-Friendly Plastics. *Angew. Chem., Int. Ed.* **2015**, *54*, 3210−3215.

(5) Garrison, T. F.; Murawski, A.; Quirino, R. L. Bio-Based Polymers with Potential for Biodegradability. *Polymers* **2016**, *8*, 262−283.

(6) Haider, T. P.; Völker, C.; Kramm, J.; Landfester, K.; Wurm, F. R. Plastics of the Future? The Impact of Biodegradable Polymers on the Environment and on Society. *Angew. Chem., Int. Ed.* **2019**, *58*, 50−62.

(7) Zhang, C.; Garrison, T. F.; Madbouly, S. A.; Kessler, M. R. Recent advances in vegetable oil-based polymers and their composites. *Prog. Polym. Sci.* **2017**, *71*, 91−143.

(8) Thomsett, M. R.; Storr, T. E.; Monaghan, O. R.; Stockman, R. A.; Howdle, S. M. Progress in the synthesis of sustainable polymers from terpenes and terpenoids. *Green Mater.* **2016**, *4*, 115−134.

(9) Bauri, K.; Nandi, M.; De, P. Amino acid-derived stimuli-responsive polymers and their applications. *Polym. Chem.* **2018**, *9*, 1257−1287.

(10) Grossman, A.; Vermerris, W. Lignin-based polymers and nanomaterials. *Curr. Opin. Biotechnol.* **2019**, *56*, 112−120.

(11) Rose, M.; Palkovits, R. Cellulose-Based Sustainable Polymers: State of the Art and Future Trends. *Macromol. Rapid Commun.* **2011**, *32*, 1299−1311.

(12) Niranjana Prabhu, T.; Prashantha, K. A review on present status and future challenges of starch based polymer films and their composites in food packaging applications. *Polym. Compos.* **2018**, *39*, 2499−2522.

(13) Galbis, J. A.; García-Martín, M. d. G.; de Paz, M. V.; Galbis, E. Synthetic Polymers from Sugar-Based Monomers. *Chem. Rev.* **2016**, *116*, 1600−1636.

(14) Gregory, G. L.; López-Vidal, E. M.; Buchard, A. Polymers from sugars: cyclic monomer synthesis, ring-opening polymerisation, material properties and applications. *Chem. Commun.* **2017**, *53*, 2198−2217.

(15) Varma, A. J.; Kennedy, J. F.; Galgali, P. Synthetic polymers functionalized by carbohydrates: a review. *Carbohydr. Polym.* **2004**, *56*, 429−445.

(16) Ladmiral, V.; Melia, E.; Haddleton, D. M. Synthetic glycopolymers: an overview. *Eur. Polym. J.* **2004**, *40*, 431−449.

(17) Song, Y.; Ji, X.; Dong, M.; Li, R.; Lin, Y.-N.; Wang, H.; Wooley, K. L. Advancing the Development of Highly-Functionalizable Glucose-Based Polycarbonates by Tuning of the Glass Transition Temperature. *J. Am. Chem. Soc.* **2018**, *140*, 16053−16057.

(18) Xiao, R.; Zeng, J.; Grinstaff, M. W. Biologically Active Branched Polysaccharide Mimetics: Synthesis via Ring-Opening Polymerization of a Maltose-Based β-Lactam. *ACS Macro Lett.* **2018**, *7*, 772−777.

(19) Su, L.; Khan, S.; Fan, J.; Lin, Y.-N.; Wang, H.; Gustafson, T. P.; Zhang, F.; Wooley, K. L. Functional sugar-based polymers and nanostructures comprised of degradable poly(d-glucose carbonate)s. *Polym. Chem.* **2017**, *8*, 1699−1707.

(20) Felder, S. E.; Redding, M. J.; Noel, A.; Grayson, S. M.; Wooley, K. L. Organocatalyzed ROP of a Glucopyranoside Derived Five-Membered Cyclic Carbonate. *Macromolecules* **2018**, *51*, 1787−1797.

(21) Mutlu, H.; de Espinosa, L. M.; Meier, M. A. R. Acyclic diene metathesis: a versatile tool for the construction of defined polymer architectures. *Chem. Soc. Rev.* **2011**, *40*, 1404−1445.

(22) Atallah, P.; Wagener, K. B.; Schulz, M. D. ADMET: The Future Revealed. *Macromolecules* **2013**, *46*, 4735−4741.

(23) Bielawski, C. W.; Grubbs, R. H. Living ring-opening metathesis polymerization. *Prog. Polym. Sci.* **2007**, *32*, 1−29.

(24) Schrock, R. R. Living ring-opening metathesis polymerization catalyzed by well-characterized transition-metal alkylidene complexes. *Acc. Chem. Res.* **1990**, *23*, 158−165.

(25) Nuyken, O.; Pask, S. D. Ring-Opening Polymerization—An Introductory Review. *Polymers* **2013**, *5*, 361−403.

(26) Choinopoulos, I. Grubbs' and Schrock's Catalysts, Ring Opening Metathesis Polymerization and Molecular Brushes—Synthesis, Characterization, Properties and Applications. *Polymers* **2019**, *11*, 298−328.

(27) Buchmeiser, M. R. Recent Advances in the Regio- and Stereospecific Cyclopolymerization of α,ω-Diynes by Tailored Ruthenium Alkylidenes and Molybdenum Imido Alkylidene N-Heterocyclic Carbene Complexes. *Polym. Rev.* **2017**, *57*, 15−30.

(28) Peterson, G. I.; Yang, S.; Choi, T.-L. Synthesis of Functional Polyacetylenes via Cyclopolymerization of Diyne Monomers with Grubbs-type Catalysts. *Acc. Chem. Res.* **2019**, *52*, 994−1005.

(29) Parkhurst, R. R.; Balog, S.; Weder, C.; Simon, Y. C. Synthesis of poly(sulfonate ester)s by ADMET polymerization. *RSC Adv.* **2014**, *4*, 53967−53974.

(30) Lv, A.; Cui, Y.; Du, F.-S.; Li, Z.-C. Thermally Degradable Polyesters with Tunable Degradation Temperatures via Postpolyme-

DOI: 10.1021/jacs.9b05822
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

rization Modification and Intramolecular Cyclization. *Macromolecules* **2016**, *49*, 8449−8458.
(31) Fraser, C.; Hillmyer, M. A.; Gutierrez, E.; Grubbs, R. H. Degradable Cyclooctadiene/Acetal Copolymers: Versatile Precursors to 1,4-Hydroxytelechelic Polybutadiene and Hydroxytelechelic Polyethylene. *Macromolecules* **1995**, *28*, 7256−7261.
(32) Steinbach, T.; Alexandrino, E. M.; Wurm, F. R. Unsaturated poly(phosphoester)s via ring-opening metathesis polymerization. *Polym. Chem.* **2013**, *4*, 3800−3806.
(33) Chang, C.-C.; Emrick, T. Functional Polyolefins Containing Disulfide and Phosphoester Groups: Synthesis and Orthogonal Degradation. *Macromolecules* **2014**, *47*, 1344−1350.
(34) Fishman, J. M.; Kiessling, L. L. Synthesis of Functionalizable and Degradable Polymers by Ring-Opening Metathesis Polymerization. *Angew. Chem., Int. Ed.* **2013**, *52*, 5061−5064.
(35) Fishman, J. M.; Zwick, D. B.; Kruger, A. G.; Kiessling, L. L. Chemoselective, Postpolymerization Modification of Bioactive, Degradable Polymers. *Biomacromolecules* **2019**, *20*, 1018−1027.
(36) Mallick, A.; Xu, Y.; Lin, Y.; He, J.; Chan-Park, M. B.; Liu, X.-W. Oxadiazabicyclooctenone as a versatile monomer for the construction of pH sensitive functional polymers via ROMP. *Polym. Chem.* **2018**, *9*, 372−377.
(37) Gutekunst, W. R.; Hawker, C. J. A General Approach to Sequence-Controlled Polymers Using Macrocyclic Ring Opening Metathesis Polymerization. *J. Am. Chem. Soc.* **2015**, *137*, 8038−8041.
(38) Enholm, E. J.; Mondal, K. Acyclic Diene Metathesis Reactions of Carbohydrates. *Synlett* **2009**, 2539−2541.
(39) Peng, Y.; Decatur, J.; Meier, M. A. R.; Gross, R. A. Ring-Opening Metathesis Polymerization of a Naturally Derived Macrocyclic Glycolipid. *Macromolecules* **2013**, *46*, 3293−3300.
(40) Lillie, L. M.; Tolman, W. B.; Reineke, T. M. Structure/property relationships in copolymers comprising renewable isosorbide, glucarodilactone, and 2,5-bis(hydroxymethyl)furan subunits. *Polym. Chem.* **2017**, *8*, 3746−3754.
(41) Shearouse, W. C.; Lillie, L. M.; Reineke, T. M.; Tolman, W. B. Sustainable Polyesters Derived from Glucose and Castor Oil: Building Block Structure Impacts Properties. *ACS Macro Lett.* **2015**, *4*, 284−288.
(42) Bai, Y.; De bruyn, M.; Clark, J. H.; Dodson, J. R.; Farmer, T. J.; Honoré, M.; Ingram, I. D. V.; Naguib, M.; Whitwood, A. C.; North, M. Ring opening metathesis polymerisation of a new bio-derived monomer from itaconic anhydride and furfuryl alcohol. *Green Chem.* **2016**, *18*, 3945−3948.
(43) Bai, Y.; Clark, J. H.; Farmer, T. J.; Ingram, I. D. V.; North, M. Wholly biomass derivable sustainable polymers by ring-opening metathesis polymerisation of monomers obtained from furfuryl alcohol and itaconic anhydride. *Polym. Chem.* **2017**, *8*, 3074−3081.
(44) Blanpain, A.; Clark, J. H.; Farmer, T. J.; Guo, Y.; Ingram, I. D. V.; Kendrick, J. E.; Lawrenson, S. B.; North, M.; Rodgers, G.; Whitwood, A. C. Rapid ring-opening metathesis polymerization of monomers obtained from biomass derived furfuryl amines and maleic anhydride. *ChemSusChem* **2019**, *12*, 2393−2401.
(45) Debsharma, T.; Behrendt, F. N.; Laschewsky, A.; Schlaad, H. Ring-Opening Metathesis Polymerization of Biomass-Derived Levoglucosenol. *Angew. Chem., Int. Ed.* **2019**, *58*, 6718−6721.
(46) Hejl, A.; Scherman, O. A.; Grubbs, R. H. Ring-Opening Metathesis Polymerization of Functionalized Low-Strain Monomers with Ruthenium-Based Catalysts. *Macromolecules* **2005**, *38*, 7214−7218.
(47) Patton, P. A.; Lillya, C. P.; McCarthy, T. J. Olefin metathesis of cyclohexene. *Macromolecules* **1986**, *19*, 1266−1268.
(48) Park, H.; Choi, T.-L. Fast Tandem Ring-Opening/Ring-Closing Metathesis Polymerization from a Monomer Containing Cyclohexene and Terminal Alkyne. *J. Am. Chem. Soc.* **2012**, *134*, 7270−7273.
(49) Park, H.; Lee, H.-K.; Choi, T.-L. Tandem Ring-Opening/Ring-Closing Metathesis Polymerization: Relationship between Monomer Structure and Reactivity. *J. Am. Chem. Soc.* **2013**, *135*, 10769−10775.
(50) Park, H.; Kang, E.-H.; Müller, L.; Choi, T.-L. Versatile Tandem Ring-Opening/Ring-Closing Metathesis Polymerization: Strategies for Successful Polymerization of Challenging Monomers and Their Mechanistic Studies. *J. Am. Chem. Soc.* **2016**, *138*, 2244−2251.
(51) Kang, E.-H.; Yu, S. Y.; Lee, I. S.; Park, S. E.; Choi, T.-L. Strategies to Enhance Cyclopolymerization using Third-Generation Grubbs Catalyst. *J. Am. Chem. Soc.* **2014**, *136*, 10508−10514.
(52) Seidi, F.; Druet, V.; Huynh, N.; Phakkeeree, T.; Crespy, D. Hemiaminal ether linkages provide a selective release of payloads from polymer conjugates. *Chem. Commun.* **2018**, *54*, 13730−13733.
(53) Kaur, R.; Rani, V.; Abbot, V.; Kapoor, Y.; Konar, D.; Kumar, K. Recent synthetic and medicinal perspectives of pyrroles: An overview. *J. Pharm. Chem. Chem. Sci.* **2017**, *1*, 17−32.
(54) Artico, M.; Santo, R. D.; Costi, R.; Massa, S.; Scintu, F.; Loi, A. G.; De Montis, A.; La Colla, P. 1-Arylsulfonyl-3-(α-hydroxybenzyl)-1H-pyrroles, a novel class of anti-HIV-1 reverse transcriptase inhibitors. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1931−1936.

DOI: 10.1021/jacs.9b05822
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX