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Synthesis of Glycopolymers of Controlled Molecular Weight by Ring-Opening Metathesis Polymerization Using Well-Defined Functional Group Tolerant Ruthenium Carbene Catalysts[†]

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ABSTRACT: A series of sugar-substituted norbornenes were synthesized in order to determine whether monodisperse glycopolymers might be prepared by ring-opening metathesis polymerization (ROMP) using the ruthenium carbene initiators $(R_3P)_2Cl_2Ru{=}CHCH{=}CPh_2$ (R = phenyl (Ph), **1**; R = cyclohexyl (Cy), **2**). The polymerization of 2-((±)-*exo*-5-norbornene-2-carboxamido)-2-deoxy-D-glucopyranose (**3**) and the protected sugar derivatives based on this monomer, 2-((±)-*exo*-5-norbornene-2-carboxamido)-2-deoxy-1,3,4,6-tetra-*O*-acetyl-D-glucopyranose (**4**), 2-((±)-*exo*-5-norbornene-2-carboxamido)-2-deoxy-1,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**5**), 2-((±)-*exo*-5-norbornene-2-carboxamido)-2-deoxy-1,3,4,6-tetra-*O*-triethylsilyl-D-glucopyranose (**6**), and 2-((±)-*exo*-5-norbornene-2-carboxamido)-2-deoxy-6-*O*-trityl-D-glucopyranose (**7**), were investigated. The Cy_3PRu catalyst, **2**, initiated the polymerization of monomers **3**−**7**; only the acetate monomer, **4**, could be polymerized by the less active Ph_3PRu catalyst **1**. Benzene is a more effective polymerization solvent than methylene chloride for the ether-protected sugar derivatives **5**−**7**, whereas methylene chloride is a better solvent for the acetate monomer, **4**, which is prone to gelation. The reaction rates are highly dependent upon the sugar protecting group and range from <5 min for the acetate protected sugar, **4**, to 2−3 days for the triethylsilyl ether derivative, **6**. Narrow-dispersity materials were obtained using **2** when reactions were run at elevated temperature (50 °C). For example, the polydispersity indices of poly[**5**] and poly[**6**] prepared in benzene solution at 50 °C were 1.17 and 1.10, respectively. More polydisperse products resulted from reactions at 25 °C. Deprotonation of poly[**4**], poly[**5**], and poly[**6**] was also investigated. The silyl ether polymer, poly[**6**], was readily deprotected using tetrabutylammonium fluoride (TBAF) in THF. Incomplete reaction and complex products were observed in preliminary attempts to remove the acetate and benzyl ether groups. Due to poor solubility, the unprotected sugar monomer, **3**, could not be polymerized by **2** in homogeneous solution. However, water-insoluble **3** was quantitatively polymerized in an aqueous emulsion system containing dodecyltrimethylammonium bromide (DTAB) and a small amount of CH_2Cl_2 to dissolve the catalyst, **2**.

Introduction

Carbohydrates on the surfaces of cells play important roles in mediating a wide range of recognition events.[1−3] For example, certain infections are initiated by the binding of viral or bacterial proteins (i.e., lectins) to sugar residues such as sialic acids on the cell surface. Selectins, adhesion proteins expressed in damaged cells, bind to white blood cells via the carbohydrate sialyl Lewis x.[2,3] This is an important event in the inflammatory response. It has also been observed that certain sugars such as Lewis x accumulate on the surfaces of rapidly growing tumor and embryonic cells.[2,4] These "tumor antigens" have been proposed to be involved in the altered morphology and adhesion of cancer cells and perhaps may play a role in the invasive properties of these systems.[2,5,6]

An important feature of these sugar−protein interactions is their polyvalency.[7] Proteins bind to several cell surface carbohydrate moieties at once to elicit a biological response. This observation has prompted the synthesis of polymeric materials bearing pendant carbohydrates to serve, in essence, as cell surface mimics.[8] In this capacity, glycopolymers have found a variety of biotechnological applications. Some of the earliest sugar polymers reported were used for lectin or antibody binding assays,[9−12] as chromatographic supports for the isolation of proteins with specificity for different sugar residues,[11] or as matrices for cell culture.[13,14] In addition, a polymer with pendant glucose residues was conjugated with various enzymes, imbuing the enzymes with enhanced stability.[15] The polyvalency of carbohydrate recognition also represents a challenge to the traditional monovalent approach to drug design. New polymeric drugs might better disrupt carbohydrate−protein interactions between cells and viruses. For example, they could serve as antiinflammatory agents, or perhaps they might enhance or trigger desirable biological responses such as for use in cancer immunotherapy. Developments in this area include reports of polymers with appended sialic acid residues serving as in vitro inhibitors of the agglutinization of chicken erythrocytes by the influenza virus.[8,16] This inhibition was considerably stronger than that typically seen with monomeric carbohydrate analogues.[8,17,18]

To date, most of the glycopolymers reported have been prepared by radical polymerization of olefin or acrylamide monomers that are attached to sugar residues via flexible extenders.[4,8] Sugars have been derivatized via O−, S−, or C−glycosidic linkages or through amine groups at different positions on the saccharide ring. The effects of these modes of attachment, of flexible linker length,[11,19,20] and of copolymer composition[21] on biological activity have been investigated. The advantage of these radical reactions is that they may be run in aqueous solution on unprotected sugar monomers. One disadvantage is that it is not possible to control the molecular weight of the resulting polymer product; neither the molecular weight distribution (PDI) nor the average molecular weight of the material (M_w or M_n) may be regulated. Typically, very high molecular weight polydisperse products are obtained. More re-

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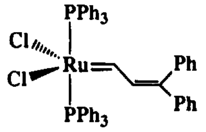
cently the olefin metathesis reaction has been employed in the synthesis of a new class of sugar-substituted polymers, which exhibit very promising activity in biological assays.[18,22] However, since metathesis polymerizations initiated by $RuCl_3$ are not living, they suffer from the same lack of molecular weight specificity as is observed in radical reactions. With nonliving mechanisms, it is only possible to bias molecular weight in a rough way by dialysis of the sugar polymer product using tubing with a specific size cutoff[8,16] or by chain transfer.[23] Specific oligomers are accessible by tedious iterative syntheses or by fractionation of product mixtures.[20,23,24]

It has already been demonstrated that high molecular weight, polydisperse glycopolymers are useful for certain applications. However, a more detailed understanding of the mechanism of sugar recognition and its disruption by polyvalent inhibitors might be gained if glycopolymers could be prepared by living mechanisms and, thus, the length of the polymer chain could be varied at will.[25,26] With living polymerization there is also the possibility of preparing block copolymers. High-performance materials in which one block possesses pendant sugar moieties for recognition with other features incorporated into the second block for enhanced solubility, biocompatibility, drug delivery, or other purposes are envisioned.[27-31]

Recently it was reported by our group that ruthenium carbene catalysts, **1** and **2**, promote the living polymerization of strained monomers such as norbornene and cyclobutene with exceptional tolerance of functionality in both substrates and solvent mixtures.[32-36] Given these features, we sought to further test the scope of these systems to include highly functionalized biomolecules, in this case carbohydrates, and to determine whether glycopolymers could be generated with molecular weight control (eq 1). As a model system, norbornene was coupled to glucose derivatives via an amide linkage (Figure 1). The syntheses of these new monomers and features of their polymerization chemistry are discussed below.



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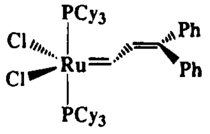

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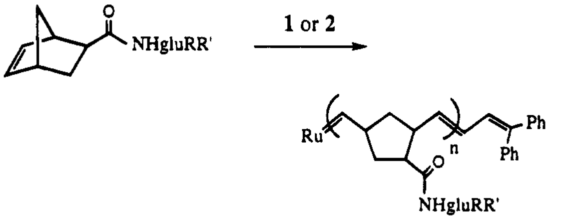

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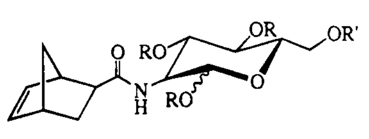
Results and Discussion

Monomer Synthesis. Since the catalysts **1** and **2** are not sensitive to alcohol functionality,[32-34] initial efforts were directed to the synthesis and reactivity of the unprotected sugar derivative, **3**. The glucose-substituted norbornene monomer, NBEglu(H)$_4$ (**3**), was prepared most effectively by the condensation of (±)-*exo*-5-norbornene-2-carbonyl chloride with glucosamine in methanol-containing Et_3N at reduced temperature. Upon removal of the Et_3NHCl byproduct by sequential treatment with basic followed by acidic ionic exchange resins, pure **3** was obtained as a white crystalline solid in 51% yield. This approach minimizes the production of norbornene methyl ester side product which is obtained in greater amounts when different bases or higher reaction temperatures are employed. Although ion-exchange treatment or silica gel column chromatography (EtOAc/MeOH) both gave pure product, considerably better yields were obtained with the former method. The unprotected sugar monomer **3** is soluble in polar aprotic solvents such as DMF and DMSO, is very sparingly soluble in methanol and methanol-containing solvent mixtures, but is essentially insoluble in less polar organic solvents such as CH_2Cl_2, THF, or benzene.



RR' = H; NBEglu(H)$_4$ **3**

RR' = -COCH$_3$; NBEglu(Ac)$_4$ **4**

RR' = -CH$_2$Ph; NBEglu(Bn)$_4$ **5**

RR' = -SiEt$_3$; NBEglu(SiEt$_3$)$_4$ **6**

R = H; R' = -CPh$_3$; NBEglu(Tr) **7**

Figure 1. Glucose-substituted norbornene derivatives.

The poor solubility of the unprotected sugar monomer, **3**, combined with our interest in further probing the reactivity and functional group tolerance of the Ru catalysts prompted us to synthesize a series of protected sugar monomers, **4–7**. In addition, a strategy in which the sugar moieties are deprotected after polymerization could be useful for certain applications. All of the sugar monomers, with the exception of **4**, were prepared by subsequent functionalization of the parent compound, **3**. The acetate derivative, **4**, was made by condensation of per-O-acetylated glucosamine with norbornene acid chloride. All of the protected sugar monomers, **5–7**, are soluble in common organic solvents such as methylene chloride, ethyl acetate, THF, and benzene; however, it was observed that the trityl monomer, **7**, precipitates from chloroform or benzene solution over time at temperatures <25 °C.

The monomers **3–7** were obtained as mixtures of four diastereomers which arise from the *R* and *S* chirality of the amide-bearing carbon center on norbornene and the α and β anomers of the sugar. All four diastereomers are clearly evident in the ^1H NMR spectrum of NBEglu(H)$_4$ (**3**) in DMSO-d_6 solution, wherein four unique signals attributable to the anomeric protons, $H_{\alpha 1}$, $H_{\alpha 2}$, $H_{\beta 1}$, and $H_{\beta 1}$, are observed at 6.37, 6.42, 6.46, and 6.48 ppm, respectively, in a ratio of 2.3:2.3:1:1 (Figure 2). In most cases the signals arising from the bridgehead protons at ~2.8 ppm are also good indicators of the relative ratios of α and β diastereomers. For example, for NBEglu(H)$_4$ these appear at 2.74 (β isomers) and 2.81 ppm (α isomers). Estimates of the isomer ratios for each derivative are indicated, when possible, in the Experimental Section.

Polymer Synthesis. *Homopolymers*. The reactivity of all the monomers was probed with the two Ru catalysts, **1** and **2** (eq 1; Tables 1–5). The unprotected sugar monomer, **3**, did not undergo efficient ring-

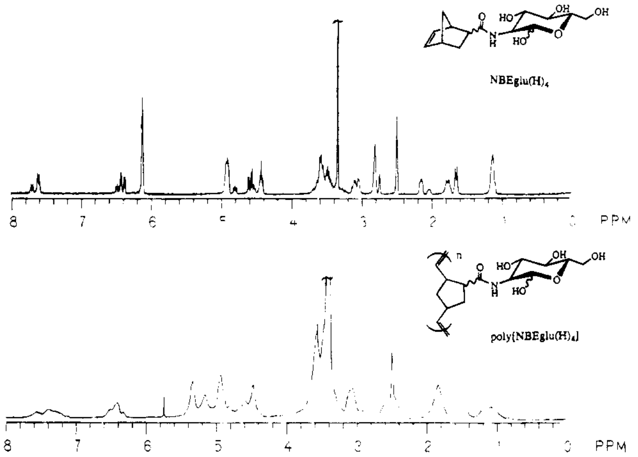


Figure 2. ^{1}H NMR spectra of NBEglu(H_4) and poly[NBEglu-(H)$_4$] in DMSO-d_6 solution.

Table 1. Polymerization of NBEglu(H)$_4$

catalyst (R)	solvent system	temp, °C	[M]/[E]/[I]^a	time, days	yield, %
Ph	2:1 MeOH/CH_2Cl_2	40	160/0/1	1	0
Ph	4:1 H_2O/CH_2Cl_2	50	50/0/1	4	0
Cy	3:2 MeOH/CH_2Cl_2	50	55/0/1	2	trace
Cy	6:1 H_2O/CH_2Cl_2	50	35/3/1	1	99

[a] M = monomer; I = catalyst initiator; E = emulsifier = dodecyltrimethylammonium bromide.

Table 2. Polymerization of NBEglu(Ac)$_4$^{a}

catalyst (R)	[M]/[I]	time	yield, %	$\overline{M}_n \times 10^{-4\,b}$	$\overline{M}_w \times 10^{-4\,b}$	PDI^b
Ph	110/1^c	20 h	gel			
Ph	35/1	20 h	50	1.87	2.63	1.40
Cy	50/1^d	1 day	gel			
Cy	40/1	1 h	71	1.34	3.02	2.25
Cy	30/1	5 min	68	1.31	2.70	2.09
Cy	50/1 or 20/1^e	15 min	gel			

[a] Reaction conditions: CH_2Cl_2; 50 °C; [M] = 0.14–0.18 M. [b] By GPC; polystyrene calibration. [c] [M] = 0.5 M. [d] 25 °C; [M] = 0.45 M. [e] C_6H_6.

opening metathesis polymerization in the presence of either catalyst 1 or 2 in any of the solvent systems tested (Table 1, entries 1 and 2). The very low reactivity of this monomer may be attributed to its poor solubility in all of the solvents compatible with the metathesis catalysts. In addition, the poly[NBEglu(H)$_4$] product is also insoluble in these solvent systems and precipitates from the reaction mixture. This difficulty was overcome by using a different polymerization technique, which will be discussed in the ensuing sections.

Of all of the monomers, only the acetate-protected sugar monomer, **4**, was efficiently polymerized by the less active triphenylphosphine catalyst, **1** (Table 2). The benzyl ether monomer **5** reacted to give only a very small amount of polymer product (Table 3). The acetate polymers were very prone to gelation. The gels swelled upon addition of organic solvents such as CH_2Cl_2, but they did not dissolve in any of a number of common polar and nonpolar solvents that were tested. For both catalysts, soluble poly[NBEglu(AC)$_4$] was obtained for lower monomer to catalyst feed ratios (<40:1) and when the reactions were conducted in CH_2Cl_2 at elevated temperature. These results suggest a possible explanation for acetate polymer gelation. Since the acetate monomer, **4**, is very reactive, propagation may be much faster than initiation at room temperature. In this case, poorly soluble high molecular weight materials could result.

The less reactive benzyl ether **5**, silyl ether **6**, and trityl ether **7** monomers only undergo ring-opening metathesis polymerization with the more reactive initiator, **2** (Tables 3–5). Unlike the acetate monomer, **4**, which is more prone to gelation in benzene, the polymerization of these ether monomers is more efficient and controlled in this solvent. Benzene may also have a favorable effect on the relative rates of initiation and propagation since slightly narrower molecular weight distributions are observed for polymers synthesized in this solvent. The trityl ether monomer (**7**) and polymer both precipitate from CH_2Cl_2 over time, and the reaction proceeds only to a small extent. In benzene the reaction runs smoothly to give poly[NBEglu(Tr)] in reasonable yield (Table 5). After precipitation of the trityl polymer in methanol, it is no longer soluble in CH_2Cl_2 or benzene, unless DMF or DMSO is added. The polymerization of the benzyl ether monomer occurs in either CH_2Cl_2 or benzene to give products with narrow molecular weight distributions (Table 3); however, better yields were obtained for reaction in benzene solution. The triethylsilyl ether derivative may only be polymerized with the active catalyst **2** at elevated temperature (Table 4). Typically, when monomer or polymer solubility is not a factor, olefin metathesis catalyzed by the ruthenium carbene catalysts is faster in CH_2Cl_2 as compared with benzene. With the silyl ether monomer, **6**, however, the opposite is true. Number-average molecular weights greater than ~12 000 (~15-mer) may not be achieved in CH_2Cl_2. The reaction proceeds slowly for 3 days, after which time there is no increase in either the molecular weight or the polydispersity index. This suggests that the propagating species is deactivated. It has been observed previously that the ruthenium carbene propagating species is not stable after prolonged heating in chlorinated solvents.[32,33] In contrast, reactions employing benzene go to completion in 2 days with no evidence of unreacted monomer in the methanol fraction. Silyl ether polymers were obtained with PDIs = 1.10–1.16.

In most cases, heating is not required for the polymerization to occur when the more active Ru initiator, **2**, is used. However, it was discovered with these monomers, as well as with simpler functionalized norbornene derivatives, that monodisperse materials are obtained with the active catalyst **2** if the reactions are run at elevated temperature (~50 °C). This might be due to differential effects of temperature on the rates of initiation and propagation. If inter- and intramolecular chain-transfer reactions are a factor at all, these processes occur primarily once all or most of the monomer is consumed since PDIs can increase for longer reaction times. For example, with the acetate monomer **4**, very large PDIs (>5) were observed for reaction times longer than a few hours (Table 2). These values become smaller and approach PDI = 2 as the reaction time is decreased. Even for very short reaction times (5 min), the polymer products of this reactive monomer still exhibit somewhat broad molecular weight distributions.[37]

These results further demonstrate the functional group tolerance of the ruthenium carbene initiators **1** and **2**. Monomers with silyl, trityl, and benzyl ethers, esters, and even potentially chelating alcohol groups are readily polymerized. In most cases, the norbornene monomers substituted with bulky, and more polar,

Table 3. Polymerization of NBEglu(Bn)$_4$[a]

catalyst (R)	solvent	temp, °C	[M]/[I]	time, h	yield, %	$\overline{M}_n \times 10^{-4}$ [b]	$\overline{M}_w \times 10^{-4}$ [b]	PDI[b]
Ph	CH_2Cl_2	45	45/1	24	trace	0.56	0.95	1.68
Cy	CH_2Cl_2	45	35/1	5	53	2.75	3.36	1.22
Cy	C_6H_6	50	20/1	10	91	1.69	1.99	1.17

[a] [M] = 0.13 M; [I] = 3.2–4.6 mM. [b] By GPC; polystyrene calibration.

Table 4. Polymerization of NBEglu(SiEt$_3$)$_4$

catalyst (R)	[M]/[I][a]	time, days	yield, %	$\overline{M}_n \times 10^{-4}$ [b]	$\overline{M}_w \times 10^{-4}$ [b]	PDI[b]
Ph	35/1[c]	1	0			
Cy	40/1[c]	0.7	32	0.69	0.79	1.14
Cy	45/1[d]	2	55	0.91	1.11	1.12
Cy	40/1[d]	3	45	1.16	1.35	1.16
Cy	35/1[d,e]	2	78	4.01	4.41	1.10

[a] Reaction conditions: R = Cy; CH_2Cl_2; 50 °C. [b] By GPC; polystyrene calibration. [c] [M] = 45 mM. [d] [M] = 90–120 mM. [e] C_6H_6.

Table 5. Polymerization of NBEglu(Tr)

catalyst (R)	solvent system	temp, °C	[M]/[I][a]	time	yield, %
Ph	6/1 CH_2Cl_2/MeOH	50	30/1	3 days	0
Cy	CH_2Cl_2	25	50/1	15 h	trace[b]
		50		3 h	
Cy	C_6H_6	50	25/1[c]	4 h	60[b]

[a] M = monomer; I = catalyst initiator. [b] Monomer and polymer precipitate from the reaction solution. [c] [M] = 0.11 M. Polymer is only soluble in the presence of DMF or DMSO.

sugar substituents react more slowly than simple *exo*-norbornene derivatives as might be expected. Among the various sugar derivatives, however, the dramatic differences in reactivity are striking and are unprecedented in similarly substituted simple norbornenes.[37] Selected data for the different monomers **3**–**7** that were polymerized under similar reaction conditions are collected in Table 6 for comparison. When available, data for reactions in benzene and CH_2Cl_2 are both included. Ring-opening metathesis polymerization of the acetate monomer is complete in 5 min or less, whereas the silyl ether monomer requires several days under similar reaction conditions. The ether monomers, benzyl and silyl, which might be expected to exhibit similar reactivity also require vastly different reaction times. The unprotected sugar monomer with free hydroxyl groups is essentially unreactive under these reaction conditions, even in mixed solvent systems selected for enhanced monomer solubility. Further studies are required before these dramatic differences in reactivity may be understood.

Copolymers. Both block and random copolymers were prepared using norbornene and the acetate sugar derivative, **4**, to demonstrate their accessibility and to see what effect copolymerization would have on the properties of the resultant materials. In the block copolymer, the norbornene was polymerized first followed by addition of the sugar monomer (Scheme 1; L = ancillary ligands on the Ru initiator). Digitalized gel permeation chromatographs for the poly(NBE) block and the poly(NBE)–poly[NBEglu(Ac)$_4$] block copolymer are shown in Figure 3. Gelation is suppressed in both the random and block copolymers, and soluble higher molecular weight materials are obtained under these reaction conditions (Table 7).

Polymer Deprotection Reactions. Preliminary experiments were conducted to assess the ease with which protecting groups might be removed from the sugar residues of the soluble poly[NBEgluRR′] products. Best results were obtained for poly[NBEglu(SiEt$_3$)$_4$] which was quantitatively deprotected using tetrabutylammonium fluoride in THF as evidenced by the complete absence of the silyl ethyl signals in the ^{1}H NMR of the poly[NBEglu(H)$_4$] product. The ease of deprotection and the very narrow molecular weight distributions of the silyl ether sugar polymer make this protecting group optimal if a protection/deprotection strategy is required for a particular glycopolymer synthesis. Efficient hydrolysis of the ester groups in poly[NBEglu(Ac)$_4$] using NaOMe in MeOH/THF was hindered by the poor solubility of the partially deprotected polymer in this solvent mixture. Poly[NBEglu(Bn)$_4$] was subjected to catalytic hydrogenation in an attempt to remove the benzyl groups and to simultaneously hydrogenate the polymer backbone;[38] however, complex partly deprotected product mixtures were obtained.

Polymerization of the Unprotected Sugar Monomer, 3, in an Aqueous Emulsion System. During the deprotection of poly[NBEglu(SiEt$_3$)$_4$], it was observed that the product, poly[NBEglu(H)$_4$], remained soluble in THF in the presence of the ammonium halide reagent. Ordinarily, poly[NBEglu(H)$_4$] is only soluble in polar aprotic solvents such as DMF or DMSO. This suggested the possibility that another polymerization technique might be more suitable for reactions with the unprotected sugar monomer, namely, polymerization in the presence of ammonium halide salts as emulsifiers in an aqueous system. With certain simple norbornene derivatives, polymerization in organic/aqueous mixed-solvent systems containing emulsifiers has been shown to give rise to polymers with PDI ≤ 1.1 in high yield.[39] Reaction of NBEglu(H)$_4$, **3**, in H_2O containing dodecyltrimethylammonium bromide with the ruthenium carbene initiator, **2**, dissolved in a small amount of CH_2Cl_2 resulted in polymer product in essentially quantitative yield (Table 1, entry 4).

Conclusion

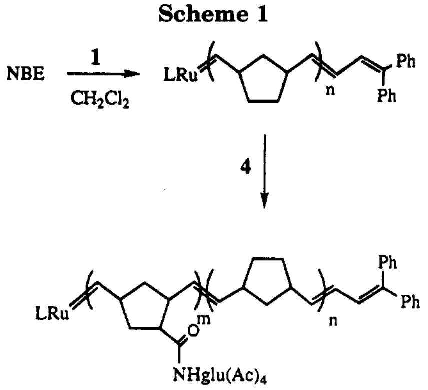
The polymerization of a series of norbornene–glucose derivatives has been investigated. Only the reactive acetate-protected sugar monomer, **4**, could be polymerized by the less active triphenylphosphine-substituted ruthenium carbene catalyst, **1**. All of the remaining derivatives (**3** and **5**–**7**) were effectively polymerized by the more active Cy$_3$PRu initiator, **2**. Broad molecular weight distributions were seen for polymerization reactions run at room temperature using **2** as an initiator, whereas narrow PDIs were obtained when polymerization reactions were run at elevated temperature (50 °C). Thus, it has been demonstrated that glycopolymers may be generated with molecular weight control using ruthenium carbene initiators for ring-opening metathesis polymerization, and block copolymers of these derivatives may also be prepared. Among the various monomers there was observed a dramatic difference in reaction rates ranging from <5 min for the acetate monomer, **4**, to 2–3 days for the slowly reacting silyl ether substrate, **6**. Since the silyl ether-protected monomers give rise to polymers of low polydispersity from which the protecting groups are readily removed,

Table 6. Sugar Substituent Effects on Reaction Rates[a]

RR′	solvent	[M]/[I][a]	time	yield, %	$\overline{M}_n \times 10^{-}$ [b]	$\overline{M}_w \times 10^{-4}$ [b]	PDI[b]
Ac	CH_2Cl_2	30/1	5 min	68	1.31	2.70	2.09
Tr	C_6H_6	30/1	4 h	60[c]			
Bn	CH_2Cl_2	35/1	5 h	53	2.75	3.36	1.22
Bn	C_6H_6	20/1	10 h	91	1.69	1.99	1.17
$SiEt_3$	C_6H_6	35/1	2 days	78	4.02	4.41	1.10
$SiEt_3$	CH_2Cl_2	40/1	3 days	45	1.16	1.31	1.16
H	3:2 $MeOH/CH_2Cl_2$	20/1	1 day	trace[d]			

[a] Reaction conditions: R = Cy; 50 °C; [M] = 0.10−0.14 M. [b] By GPC; polystyrene calibration. [c] Product only soluble in DMF- or DMSO-containing solvent systems. [d] Monomer and product are poorly soluble.

Scheme 1



this groups is ideal if a monomer protection−polymerization−polymer deprotection sequence is required for the generation of a particular polymeric material. However, even for the poorly soluble sugar derivative, **3**, protection is obviated if emulsion polymerization is employed. Further characterization of poly[NBEglu(H)$_4$] and the extension of the emulsion technique to other unprotected sugar monomers in which biologically relevant carbohydrates are linked to polymerizable groups via flexible extenders are currently underway.

Experimental Section

General Considerations. Argon was purified by passage through columns containing BASF R3-11 catalyst (Chemalog) and 4-Å molecular sieves (Linde). NMR spectra were recorded on a GE QE-300 spectrometer (300.10 MHz ^{1}H; 75.49 MHz ^{13}C). Gel permeation chromatographs were obtained with methylene chloride as the eluent (flow rate: 1.0 mL/min) using an HPLC system equipped with an Altex Model 110A pump, a Rheodyne Model 7125 injector, a 100-μL injection loop, an American Polymer Standards 10-μm mixed-bed column, and a Knauer differential refractometer. Molecular weights, M_w and M_n, and polydispersities are calculated from the chromatographs relative to monodisperse polystyrene standards. High-resolution mass spectra was performed by the Southern California Mass Spec Facility (University of California, Riverside, Riverside CA).

Materials. Prior to use in polymerization reactions, methylene chloride was distilled from CaH_2 and was degassed by repeated freeze−pump−thaw cycles and benzene was passed through solvent purification columns.[40] Distilled deionized water and methanol used for polymerizations were degassed by stirring under high vacuum just before use. The ruthenium carbene catalysts **1** and **2** were prepared as previously described.[32,33] DMF was dried over 4-Å molecular sieves. Pyridine and triethylamine were distilled from CaH_2 under argon. Cyclopentadiene was cracked just prior to use by heating a ~1:1 mixture of dicyclopentadiene and mineral oil containing a CaH_2 chip using a Vigreux column. Ion-exchange resins were pretreated by soaking in methanol for >1 h, followed by collection and additional methanol washes (~3× or until colorless). All other solvents and chemicals were reagent grade and were used without further purification unless otherwise indicated.

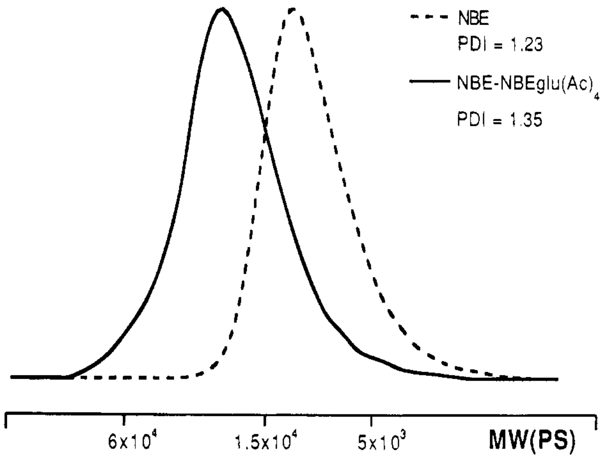


Figure 3. Digitalized gel permeation chromatographs of polynorbornene (NBE) (corresponding to the first block) and a block copolymer of norbornene and **4** (NBE−NBEglu(Ac)$_4$). The molecular weights and polydispersity indices (PDIs) were determined relative to polystyrene (PS) standards.

Table 7. Copolymers of Norbornene and NBEglu(Ac)$_4$ with 1 as the Initiator

type	$[M_1]/[M_2]/[I]$[a]	$\overline{M}_n \times 10^{-4}$ [d]	$\overline{M}_w \times 10^{-4}$ [d]	PDI[d]	*n*:*m*	
					calcd[e]	obsd[f]
random	50/50/1[a]	2.91	4.53	1.55	1.7	2.0
homopolymer	67/0/1[b]	1.11	1.36	1.23		
block	67/67/1[c]	2.05	2.77	1.35	2.3	2.1

[a] M_1 = norbornene; M_2 = NBEglu(Ac)$_4$, **4**; I = **1**. Reaction conditions: CH_2Cl_2, 25 °C, 1 day and then 50 °C, 1 day. [b] Reaction conditions: CH_2Cl_2, 25 °C, 1 day. [c] First block: as in *b*. Second block: 25 °C, 1.5 days and then 50 °C, 6 h. [d] By GPC; polystyrene calibration. [e] Determined based on the feed ratio and yield. [f] Determined by ^{1}H NMR.

Monomer Synthesis. 2-((±)-*exo*-5-Norbornene-2-carboxamido)-2-deoxy-D-glucopyranose, 3. (±)-*exo*-5-Norbornene-2-carbonyl chloride was prepared by the method of Roberts et al.[41] from the Diels−Alder adduct of cyclopentadiene and methyl acrylate. Epimerization of this methyl ester followed by hydrolysis gave (±)-5-norbornene-2-carboxylic acid as an endo/exo mixture, from which the exo isomer was separated by an iodolactonization procedure.[42−44] After purification of the exo acid by column chromatography on silica (1:4 EtOAc/petroleum ether with 1% AcOH), it was converted to the acid chloride by reported methods[45] with oxalyl chloride and a catalytic amount of DMF in CH_2Cl_2. The pure product was obtained as a water white oil after distillation under reduced pressure. Glucosamine·HCl (5 g, 0.023 mol) was stirred with Amberlite IRA-400 (OH^-) resin in MeOH (200 mL) for 2 h at 0 °C. The white solid disappeared over time upon neutralization. The resin was filtered off and washed with additional MeOH. To the combined MeOH fractions at 0 °C was added with stirring Et_3N (7.4 mL, 0.053 mol), followed by dropwise addition of a CH_2Cl_2 solution (10 mL) of (±)-*exo*-5-norbornene-2-carbonyl chloride (4.36 g, 0.028 mol). The reaction was allowed to warm to room temperature. Upon standing for ~15 h, a white powder, **3**, precipitated from solution. The solid was collected, washed with MeOH, and then dried *in vacuo* (2.02 g). A second crop of **3** was obtained by sequential treatment of the MeOH filtrate with Amberlite

IRA-400 (OH^-) followed by Dowex 50WX2-400 (H^+) ion-exchange resins. After filtration to remove the resin and partial concentration of the MeOH solution, a second crop of **3** precipitated as a white crystalline solid. This solid was collected, washed with a small amount of cold MeOH, and then dried *in vacuo* (1.50 g). Combined yield: 51%. ^1H NMR (DMSO-d_6):[44] δ 1.12 (m, H_7, 2 H), 1.65 (br d, $J = 7.24$ Hz, H_3 (*endo*), 1 H), 1.73−1.81 (m, H_3 (*exo*), 1 H), 2.04 (m, H_2 (*endo*), minor (β) diastereomers) and 2.15 (m, H_2, major (α) diastereomers) (1 H (combined)), 2.74 (br s, H_1 and H_4, β diastereomers) and 2.81 (br s, H_1 and H_4, α diastereomers) (2 H (combined)), 3.09 (m, 1H), 3.23−3.70 (m, −C*H*OH−, −C*H*NH−, 5 H), 4.42 (t, $J = 5.64$ Hz, 1 H), 4.53−4.61 (m, 1 H), 4.79 (m, β isomers) and 4.91 (m, α isomers) (2 H (combined)), 6.11 (br s, H_5 and H_6, 2 H), 6.37 (d, $J = 4.5$ Hz, $H_{\alpha 1}$), 6.42 (d, $J = 4.6$ Hz, $H_{\alpha 2}$), 6.46 (dd, $J = \sim 8.2$ and 1 Hz, $H_{\beta 1}$), 6.48 (dd, $J = \sim 7.6$ and 1.0 Hz, $H_{\beta 2}$) (1 H (combined)), 7.60 (d, $J = 7.7$ Hz, CON*H*, α diastereomers) and 7.69 (d, $J = 8.0$ Hz, CON*H*, β diastereomers) (1 H (combined)). Isomer ratio: $\alpha 1$:$\alpha 2$:$\beta 1$:$\beta 2$ = ~35:35:15:15. Peaks are also present at 2.74 (minor β isomer) and 2.81 (major α isomer). ^{13}C NMR (DMSO-d_6): δ 29.69, 29.88, 41.03, 41.08, 42.73, 43.31, 43.43, 45.57, 45.71, 46.89, 47.08, 47.17, 47.19, 54.41, 54.46, 57.17, 61.14, 61.20, 70.45, 70.90, 70.93, 71.19, 72.07, 72.11, 74.35, 74.37, 76.83, 90.56, 95.65, 136.34 (*C*=C), 136.37 (*C*=C), 136.41 (*C*=C), 136.51 (*C*=C), 137.62 (2 *C*=C?), 137.78 (2 *C*=C?), 174.82 (−*C*ONH−), 174.87 (−*C*ONH−), 174.99 (−*C*ONH−), 175.11 (−*C*ONH−). HRMS. Calcd for $C_{14}H_{21}NO_6$ $(M - H)^+$: *m/z* 300.1454. Found: *m/z* 300.1447.

2-((±)-*exo*-5-Norbornene-2-carboxamido)-2-deoxy-1,3,4,6-tetra-*O*-acetyl-D-glucopyranose, 4. 2-Amino-2-deoxy-D-glucopyranose·HCl was reacted with anisaldehyde by the method of Bergmann et al.[46] The resulting imine product was peracetylated with acetic anhydride in pyridine by standard conditions. The peracetylated imino sugar was hydrolyzed to the free amine during acidic work, was purified by recrystallization from hot EtOH, and was dried by azeotropic removal of water with toluene prior to use. The amino sugar derivative (1.17 g, 3.67 mmol) was suspended in dry CH_2Cl_2 (20 mL) containing pyridine (0.65 mL, 8.10 mmol). After cooling to 0 °C (±)-*exo*-5-norbornene-2-carbonyl chloride was added dropwise to the suspension and was stirred for 2 h. The reaction was allowed to warm to room temperature and then was poured into a dilute HCl solution and extracted into EtOAc several times. Combined organic extracts were washed with H_2O, were shaken with brine, and then were dried over Na_2SO_4. After filtration and concentration *in vacuo*, the crude product was purified by silica gel column chromatography (EtOAc). Pure **4** was obtained as a thick pale yellow oil: 1.20 g. Yield: 81%. ^1H NMR ($CDCl_3$): δ 1.58−1.90 (m, 6 H), 1.97−2.38 (m, 12 H), 2.50−3.21 (m, 3 H), 3.92 (m, 2 H), 4.36 (m, 1 H), 5.10 (m, 1 H), 5.94 (m, 1 H), 6.17 (m, 2 H), 6.54 (m, 1 H). ^{13}C NMR ($CDCl_3$): δ 20.40, 20.45, 20.61, 20.73, 21.03, 25.15, 26.93, 26.95, 31.78, 32.22, 32.29, 32.53, 41.68, 41.74, 41.80, 43.12, 43.77, 43.93, 46.33, 46.59, 46.81, 46.95, 47.16, 59.87, 59.91, 60.90, 61.48, 68.71, 68.80, 68.88, 70.06, 70.30, 70.39, 70.58, 72.32, 90.71, 90.81, 135.66, 135.84, 136.08, 137.99, 138.36, 138.39, 138.77, 138.92, 167.96, 168.06, 168.12, 169.48, 169.65, 169.75, 169.80, 170.55, 173.47, 173.54, 174.32, 174.48, 180.41, 180.46, 180.70, 180.75. HRMS. Calcd for $C_{22}H_{28}NO_{10}$ $(M - H)^+$: *m/z* 466.1713. Found: *m/z* 466.1700.

2-((±)-*exo*-5-Norbornene-2-carboxamido)-2-deoxy-1,3,4,6-tetra-*O*-benzyl-D-glucopyranose, 5. NBEglu(H)$_4$ (**3**) was converted to the tetra-*O*-benzyl ether derivative, **5**, by the method of Harrison et al.[47] for the perbenzylation of 2-(acetamido)-2-deoxy-D-glucopyranose. The crude product was crystallized from MeOH to give pure **5** as a white crystalline solid: 0.656 g. Unoptimized yield: 28%. ^1H NMR ($CDCl_3$): δ 1.27 (m, 2 H), 1.64 (m, 1 H), 1.84 (m, 2 H), 2.82 (br s, 1 H), 2.87 (br s, 1 H), 3.5−3.8 (m, 6 H), 4.17 (m, 1 H), 4.5−5.0 (m, PhCH_2−, 8 H), 5.65 (d, $J = 8.24$ Hz, $H_{\beta 1}$), 5.69 (d, $J = 7.86$ Hz, $H_{\beta 2}$) (1 H (combined)), 6.04 (m, −C*H*=CH−, 1 H), 6.12 (m, −C*H*=CH−, 1 H), 7.31 (m, −Ph*H*−, 20 H). Isomer ratio: ^1H NMR indicates that predominantly β anomers are present in roughly the same amount as suggested by the equal intensity signals at 2.82 and 2.87 ppm. ^{13}C NMR ($CDCl_3$): δ 30.40, 41.54, 44.84, 46.28, 46.96, 47.03, 56.65, 56.83, 69.13, 70.80, 73.47, 74.38, 74.85, 78.47, 80.35, 99.13, 99.23, 127.59, 127.75, 127.96, 128.03, 128.37, 135.85, 135.90, 138.14, 138.24, 175.70, 175.77. HRMS. Calcd for $C_{42}H_{46}NO_6$ $(M - H)^+$: *m/z* 660.3325. Found: *m/z* 660.3341.

2-((±)-*exo*-5-Norbornene-2-carboxamido)-2-deoxy-1,3,4,6-tetra-*O*-triethylsilyl-D-glucopyranose, 6. NBEglu(H)$_4$ **3** (0.31 g, 1.04 mmol) was suspended in dry distilled CH_2Cl_2 (15 mL) containing Et_3N (1.74 mL, 12.5 mmol). The mixture was cooled to 0 °C and then Et_3SiOTf was added dropwise with stirring. After 15 min, all solid starting material had dissolved, and after 1 h, the reaction was allowed to warm to room temperature. The reaction mixture was washed with cold pH 7 buffer. The buffer solution was extracted with additional CH_2Cl_2, and combined organic layers were washed with H_2O (2×) and with saturated salt brine (1×) and then were dried over Na_2SO_4. Filtration and concentration of the solution *in vacuo* yielded crude silyl ether product, which was purified by silica gel column chromatography (CH_2Cl_2). Pure silyl ether product **6** was obtained as a pale yellow oil in essentially quantitative yield. ^1H NMR ($CDCl_3$): δ 0.62 (m, −SiCH_2−, 24 H), 0.96 (m, −SiCH$_2$CH_3, 36 H), 1.10−1.40 (m, 2 H), 1.77−2.05 (m, 3 H), 2.92 (m, 2 H), 3.60−4.07 and 4.34 (m, 6 H), 4.93 (m, H_β) and 5.18 (d, $J = 2.49$ Hz, H_α) (1 H (combined)), 6.02−6.15 and 6.75 (m, 3 H). Isomer ratio: α:$\beta \approx 3$:1 as determined by integration of the anomeric H signals. The bridgehead peak at ~2.92 ppm is split into three separate signals, 1 large:2 small = 3:1. ^{13}C NMR ($CDCl_3$): δ 4.08, 4.46, 4.65, 4.73, 4.88, 5.03, 5.19, 5.27, 5.41, 6.28, 6.71, 6.86, 6.92, 30.05, 30.18, 30.27, 30.99, 41.55, 41.63, 44.98, 45.10, 45.46, 46.11, 46.33, 46.36, 46.44, 46.56, 46.70, 47.12, 47.40, 47.83, 52.77, 53.00, 53.34, 61.32, 61.45, 63.73, 68.72, 68.11, 69.76, 69.79, 71.20, 71.38, 72.98, 73.06, 76.58, 77.00, 77.21, 77.42, 77.87, 78.41, 78.45, 78.55, 79.05, 89.42, 89.72, 93.54, 129.09, 129.22, 135.82, 136.05, 136.13, 136.22, 138.10, 138.14, 138.30, 174.92, 175.25. HRMS. Calcd for $C_{38}H_{77}NO_6Si_4$ $(M - H)^+$: *m/z* 756.4906. Found: *m/z* 756.4886.

2-((±)-*exo*-5-Norbornene-2-carboxamido)-2-deoxy-6-*O*-trityl-D-glucopyranose, 7. NBEglu(H)$_4$ (**3**; 0.448 g, 1.50 mmol) and Ph_3CCl (0.417 g, 1.50 mmol) were dissolved in dry distilled pyridine (20 mL) and were stirred at room temperature for 3 days. The reaction was concentrated *in vacuo*. The resulting residue was suspended in EtOAc, was washed with H_2O (3×) and brine (1×), and then was dried over Na_2SO_4. Filtration and concentration yielded crude product which was further purified by silica gel column chromatography (70:30 EtOAc/petroleum ether). Concentration of appropriate column fractions yielded the trityl ether product, **7**, as a foamy solid: 0.628 g. Yield: 77%. ^1H NMR ($CDCl_3$): δ 1.34 (m, H_7, 2 H), 1.71 (br d, $J = 7.94$ Hz, H_3 (*endo*), 1 H), 1.95 (m, H_3 (*exo*), 1 H), 2.06 (m, H_2 (*endo*), 1 H), 2.95 and 2.99 (br s, H_1 and H_4, major and minor isomers, 2 H combined), 3.41 (m, 2 H), 3.65 (m, 2 H), 3.79 (t, $J = 10.21$ Hz, 1 H), 3.97−4.12 (m, 3 H), 4.57 (m, H_α minor isomers) and 5.28 (m, H_β major isomers) (1 H (combined)), 6.12 (br d, $J = 4.98$ Hz) and 6.30 (m, minor isomer) (3 H (combined)), 7.32 (m, trityl, 9 H), 7.50 (m, trityl, 6 H). Isomer ratio: α:β = ~3:1; α_1:α_2 = ~3:1 as observed by ^1H NMR. ^1H NMR (MeOH-d_4): δ 4.53 (m), 4.56 (m), 5.07 (d, $J = 3.5$ Hz), 5.10 (d, $J = 3.5$ Hz). Bridgehead signals are present at 2.95 (α) and 2.99 ppm (β) (3:1) in $CDCl_3$. The large signal splits in MeOH. ^{13}C NMR ($CDCl_3$): δ 30.54, 30.66, 41.60, 44.56, 44.68, 46.33, 47.30, 54.04, 63.73, 70.17, 72.80, 73.16, 73.51, 73.60, 73.87, 73.93, 86.95, 91.87, 97.64, 127.12, 127.22, 127.33, 127.89, 128.03, 128.55, 128.68, 135.81, 135.97, 138.19, 138.36, 143.24, 143.66, 177.88. HRMS. Calcd for $C_{33}H_{36}NO_6$ $(M - H)^+$: *m/z* 542.2543. Found: *m/z* 542.2545.

Polymer Synthesis. A typical polymerization reaction was conducted as follows. Any deviations from this general procedure are indicated below for the specific case. The monomer was weighed into a 4-dram vial equipped with a Teflon-lined cap, was degassed and transferred to an inert atmosphere glovebox, and was dissolved in dry, degassed solvent (CH_2Cl_2 or C_6H_6). The catalyst was weighed into a separate vial and was dissolved in solvent. The green, **1**, or orange, **2**, catalyst solution was added to the vial containing the monomer solution. The vial was capped, was removed from the box, and then was wrapped with electrical tape prior to heating in an oil bath or standing at room temperature. For block copolymerizations, the vial was returned to the box for addition of the second monomer. Upon completion, the reactions were stabilized by addition of a few crystals of BHT and were terminated by addition of ethyl vinyl ether followed either by heating for 30 min at ~50 °C or by stirring at room temperature for >2 h. The polymers were purified by precipitation from MeOH (2×), were collected by centrifugation, and were dried *in vacuo* prior to characterization.

Reactions conducted in solvent mixtures were set up as above but in a Kontes flask with a Teflon valve or in a round-bottom flask equipped with a rubber septum. The catalyst and monomers were dissolved in the nonpolar solvent in the glovebox. Immediately after removal from the box, the second polar solvent (degassed H_2O or MeOH) was added under Ar via syringe.

Poly[NBEglu(Ac)$_4$]. After precipitation and drying, poly[NBEglu(Ac)$_4$] was obtained as a brittle, opaque tan-colored material. ^{1}H NMR (CDCl$_3$):[48] δ 1.24 (m, 2 H), 2.08 (m, 14 H), 2.21 (s, 1 H), 2.36 (s, 1 H), 2.92 (m, 2 H), 3.69 (s, 1 H), 4.04, 4.08 (m, 1 H), 4.35 (m, 1 H), 5.09 (m, 1 H), 5.29 (m, $-CH{=}CH-$, 2 H), 5.92 (m, anomeric Hs, 1 H), 6.51 (m, $-CONH-$, 1 H).

Poly[NBEglu(Bn)$_4$]. The benzyl ether polymer was precipitated from MeOH (1×). An attempt was made to precipitate the polymer a second time from MeOH; however, it remained suspended. Hence, the second precipitation was conducted in pentane. After drying, poly[NBEglu(Bn)$_4$] was obtained as a white powdery solid. ^{1}H NMR (CDCl$_3$):[48] δ 0.6, 0.92, 1.95, 2.42, 2.93, 3.42, 3.62, 3.72, 4.12, 4.53, 4.70, 4.84, 5.13, 7.25.

Poly[NBEglu(Tr)]. During reaction of the trityl monomer in CH_2Cl_2 or benzene at 50 °C, a precipitate formed. In addition, after precipitation in MeOH the resulting polymer was only soluble in polar aprotic solvents such as DMF and DMSO. Thus, the polymer was dissolved in DMF and precipitated a second time from MeOH, to yield, after drying, an amber-colored glassy solid. ^{1}H NMR (DMSO-d_6):[48] δ 1.11 (1 H), 1.47 (1 H), 1.83 (1 H), 1.94 (1 H), 2.35 (1 H), 2.55 (1 H), 3.17, 3.27, 3.38, 3.52, 3.60 (6 H), 3.82 (2 H), 4.40 (br, 2 H), 5.02, 5.12, 6.27, 6.47, 7.18 (trityl H, 9 H), 7.37 (trityl H, 6 H).

Poly[NBEglu(SiEt$_3$)$_4$]. The silyl ether polymer was obtained as an off-white glassy solid. ^{1}H NMR (CDCl$_3$):[48] δ 0.61 (q, J = 7.8 Hz, 24 H), 0.95 (t, J = 7.7 Hz, 36 H), 1.15 (m, 1 H), 1.90, 2.12, 2.25, (m, 3 H), 2.64 (m, 2 H), 3.01 (m, 1 H), 3.75 (m, 6 H), 4.30, 4.81, 4.92 (m, 1 H), 5.33 (m, 2 H), 5.88, 6.60 (m, 1 H).

Polymerization of NBEglu(H)$_4$, 3, in an Aqueous Emulsion System.[39] Poly[NBEglu(H)$_4$]. The unprotected sugar monomer, **3** (69.4 mg, 0.23 mmol), and the emulsifier, dodecyltrimethylammonium bromide (204 mg, 0.66 mmol), were weighed into a 10-mL round-bottom flask in the glovebox. The PCy$_3$ catalyst, **2** (6.1 mg, 0.0066 mmol), was weighed and dissolved in dry degassed CH_2Cl_2 (165 μL) in a vial in the glovebox. The catalyst solution was drawn into a gas-tight syringe which was sealed with a rubber septum. The reaction flask and the syringe containing the catalyst solution were removed from the box. Degassed H_2O (1 mL) was added to the flask. After stirring for ~5 min at room temperature, the catalyst solution was added and the reaction was heated in an oil bath at 50 °C for 1 day with vigorous stirring. Initially the reaction mixture was cloudy white, containing "beads" of orange catalyst solution and undissolved monomer. After several hours no insoluble monomer remained and the reaction solution was more clear and orange in color. After 1 day, a small amount of precipitate was present in the reaction flask. Ethyl vinyl ether (~50 μL) was added, and the reaction mixture was stirred overnight at room temperature, during which time additional precipitate formed in the flask. The reaction was poured into a centrifuge tube containing MeOH (~10 mL), and the heterogeneous mixture was stirred for several hours. The polymer was collected by centrifugation, and the pale orange filtrate was decanted. The polymer was resuspended and stirred with fresh MeOH (~10 mL) (2×) to leach out catalyst, surfactant, and any unreacted monomer. After collection and drying *in vacuo* the polymer was obtained in essentially quantitative yield. ^{1}H NMR (DMSO-d_6):[48] δ 1.04 (1 H), 1.15 (1 H), 1.18 (2 H), 2.44, 2.51 (2 H), 2.89, 3.00 (2 H), 3.34, 3.52 (5 H), 4.40, 4.51, 4.77, 4.88 (4 H), 5.11, 5.29 ($-HC{=}CH-$, 2 H), 6.26, 6.35, 6.44 (1 H, anomeric H), 7.34, 7.51 ($-CONH-$, 1 H).

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