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Biocatalytic Synthesis of Sugar-Containing Poly(acrylate)-Based Hydrogels

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ABSTRACT: A chemoenzymatic approach has been developed to prepare monosaccharide-based poly(acrylate)s. The lipase from *Pseudomonas cepacia* catalyzed the transesterification of a variety of monosaccharides with vinyl acrylate in pyridine to give the 6-acryloyl esters. The acrylate esters were polymerized in DMF with AIBN to give the poly(acrylate) products. Such a synthetic strategy has led to the synthesis of poly(methyl 6-acryloyl-β-galactoside) with M_w = 135 000 and M_n = 58 000 for a polydispersity of 2.3. The overall yield from methyl β-galactoside was 56%. The polymer was highly water soluble and soluble in polar organic solvents. Replacing the methyl aglycon with phenyl or 2-nitrophenyl moieties resulted in polymers with poor water solubilities and improved organic solvent solubilities. In the case of the phenyl aglycon the polymer was prepared in 40% isolated yield from phenyl β-galactoside. The poly(phenyl 6-acryloyl-β-galactoside) had an M_w = 52 700 and an M_n = 28 900 for a polydispersity of 1.8. Addition of ethylene glycol dimethacrylate as a cross-linker during AIBN-catalyzed polymerization in DMF resulted in water-insoluble polymers that swelled in aqueous solution. In the presence of 0.3% cross-linker, a poly(methyl 6-acryloyl-β-galactoside–hema) copolymer swelled to contain 98% water and, hence, hold nearly 50-fold its weight in water. Such materials may be useful as biocompatible hydrogels for biomedical and membrane applications.

Introduction

Incorporation of sugars into traditional polymers (e.g., poly(esters, amides, ols, acrylates, etc.)) may significantly extend the application of such materials into areas such as catalysts and reagents for organic synthesis, adsorbents with specific chirality, hydrophilicity, and water absorbency, and biodegradables.[1] Functionalization of polymers with a sugar, however, is complicated because sugars contain multiple hydroxyl groups and selective and single attachment of the sugar to the polymer is difficult.[2] A possible way to avoid multiple sugar–polymer linkages (which result in undesirable cross-linking) is to employ specific blocking reactions such as tritylation, tosylation, or sulfurization.[3] Deblocking is then required, however, and the synthetic scheme is highly complex.

Unlike chemical catalysts, enzymes are highly selective and have been used to modify sugars in both aqueous[4] and nonaqueous media.[5] Specifically in nonaqueous media, enzyme-catalyzed regioselective acylation of sugar hydroxyl groups offers an attractive alternative to poorly selective chemical catalysts. We have been successful in demonstrating enzyme-catalyzed polycondensation of sucrose with diacids to give linear polyesters.[6] The selectivity of enzymes enables sucrose to react as if it were a diol, even though it contains eight free hydroxyl groups. Most importantly, no blocking/deblocking steps were required.

We have recently extended the methodology of preparing sugar-containing polymers to chemoenzymatic synthesis.[7] Instead of enzyme-catalyzed polycondensation, in chemoenzymatic synthesis, the enzyme catalyzes the selective modification of the sugar with a polymerizable group. For example, modification of sucrose with vinyl acrylate catalyzed by an alkaline protease from a *Bacillus* sp. resulted in the facile formation of sucrose 1′-acrylate that could be polymerized to poly(sucrose 1′-acrylate) via conventional free radical methods. A similar technique has been used to incorporate optically active alcohols and amines into poly((meth)acrylates).[8] The enzymic step is stereoselective while the chemical polymerization is facile and results in high molecular weights. Thus, the advantage of chemoenzymatic approaches is the fast rates of synthesis afforded by conventional chemical catalysis coupled with the high selectivity afforded by enzymatic catalysis. In the present work, we have extended the chemoenzymatic synthesis of sugar-based acrylates to include monosaccharides and their derivatives. In this manner, a variety of modified sugar acrylates can be prepared that differ in both the glycon and aglycon moieties. Such differences

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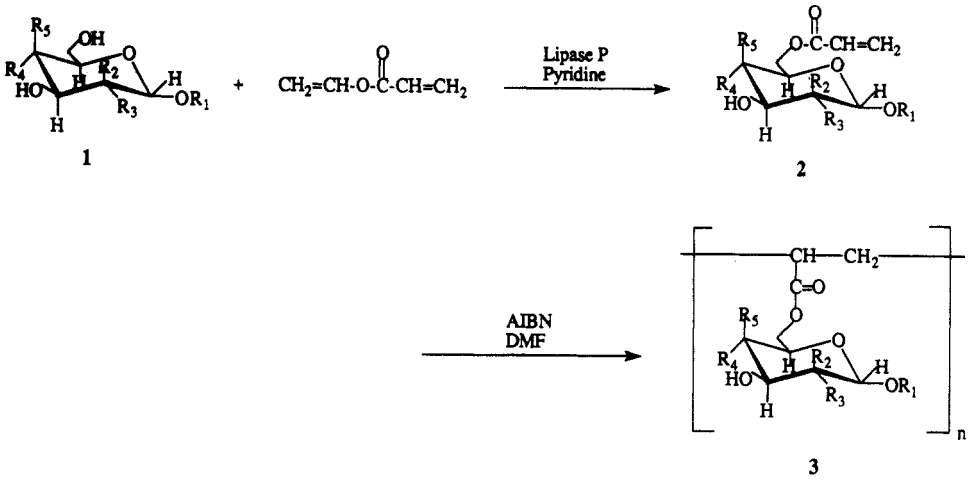
Scheme I



1 2 3

Compound	R_1	R_2	R_3	R_4	R_5
1a	β-CH_3	H	OH	H	OH
1b	β-C_6H_5	H	OH	H	OH
1c	β-(2-NO_2)-C_6H_5	H	OH	H	OH
1d	β-CH_3	H	OH	OH	H
1e	α-CH_3	H	OH	H	OH
1f	α-CH_3	H	OH	OH	H
1g	β-C_6H_5	H	OH	OH	H
1h	α-C_6H_5	H	OH	OH	H
1i	α-CH_3	OH	H	OH	H

have been exploited in the preparation of sugar-containing hydrogels with different water-swelling characteristics.

Results and Discussion

The synthesis of linear sugar-containing poly(acrylate)s requires the selective acryloylation of a single hydroxyl moiety on the sugar. Enzymes, and in particular lipases, are well-suited to catalyze the selective acylation of monosaccharides.[5] Coupled with free radical initiation, this chemoenzymatic strategy can be used to prepare sugar-containing polyacrylates.

Chemoenzymatic Synthesis of Poly(methyl 6-acryloyl-β-galactoside). Our initial synthesis involved the preparation of methyl 6-acryloyl-β-galactoside (**2a**) via enzyme-catalyzed transesterification of methyl β-D-galactoside (**1a**) with vinyl acrylate in anhydrous pyridine (Scheme I).[9] Several lipases were screened for their abilities to catalyze this reaction and the lipase from *Pseudomonas cepacia* (lipase P) was found to give the highest conversion of 1 to acrylate ester products.[10] Preparative acryloylation of **1a** resulted in the synthesis of **2a** with a conversion of 92% in 40 h with an additional (<5% by TLC) amount of a presumed diacrylate ester which was not further characterized. The reaction was terminated by filtering off the enzyme, and the pyridine was evaporated to give a tan oil. The oil was subjected to silica gel chromatography, and 2.92 g of **2a** was obtained (75% isolated yield) as a white powder. The structure of **2a** was verified by ^1H and ^{13}C NMR, and elemental analysis.

Polymerization of 2.0 g of **2a** was performed in DMF containing 0.1% AIBN. Following 24 h of incubation, the reaction was terminated by precipitating the polymer with ethyl acetate and washing with acetone, resulting in 1.48 g of **3a** (74% isolated yield, and 56% overall isolated yield from **1a**) (Scheme I). GPC analysis of **3a** indicated an M_w = 135 000 and M_n = 58 000 (M_w/M_n = 2.3). The polymer was soluble in water and highly polar organic solvents including pyridine, DMF, and DMSO, and was highly hygroscopic. When 10 mg of powder was exposed to air for 30 min, it absorbed 8 mg of water from the atmosphere. Comparison of the ^{13}C NMR spectra of **2a** and **3a** shows that the acrylate double bond in the former is absent in the latter.

Table I
Initial Rates of Lipase P-Catalyzed Acryloylation of Monosaccharide Glycosides in Pyridine[a]

compd	initial rate[b] (μmol/((mg of powder) h))	conversn[c] (%)	compd	initial rate[b] (μmol/((mg of powder) h))	conversn[c] (%)
1a	1.70	86	1f	0.13	73
1b	0.40	91	1g	0.18	70
1c	0.45	93	1h	0.036	62
1d	0.13	45	1i	0.009	39
1e	0.82	74			

[a] Conditions: 0.4 M monosaccharide glycoside; 0.6 M vinyl acrylate; 2 mL of pyridine containing 0.25 g/mL lipase P. The reactions were shaken at 250 rpm at 30 °C. [b] Measured via HPLC for the disappearance of monosacchraide glycoside. [c] After 30 h, except for 1c which was after 20 h.

Monosaccharide Specificity of *P. cepacia* Lipase. A variety of other monosaccharides were acryloylated by lipase P catalysis (Scheme I). Table I details the initial rates of acryloylation of these sugars in pyridine. The activity of lipase P was highly dependent on the substrate structure. The enzyme clearly prefers galactosides over glucosides. For example, methyl galactoside is 6- and 13-fold more reactive than methyl glucoside for the α and β

anomers, respectively. This difference may be due to the proximity of the C-4 hydroxyl moiety on acylation at the C-6 hydroxyl group. The poor reactivity of methyl α-D-mannoside (**1i**) (over 14-fold less reactive than **1f**), however, is intriguing as mannose is the C-2 epimer of glucose (axial C-2 hydroxyl in mannose) which is remote from the C-6 position of acylation. To ascertain whether the axial hydroxyl at C-2 of mannose sterically did indeed hinder the binding and/or reactivity of the sugar into the lipase's active site, we acryloylated 2-deoxy-β-D-glucose (same as 2-deoxymannose) under equivalent conditions for **1a** and compared the rate of acylation to that for free β-D-glucose. The rates of acylation were identical for these compounds (0.1 μmol/((mg of powder) h); ca. 75% of that for methyl β-glucoside (**1d**)), indicating that the axial hydroxyl of mannose derivatives interferes with acylation, perhaps because of steric hindrance of the C-2 hydroxyl group. The binding of sugars in the active site of the lipase is expected to be dominated by hydrogen-bonding interactions between the sugar hydroxyls and polar amino acid moieties of the enzyme. Perhaps the axial C-2 hydroxyl group of mannose results in an unfavorable hydrogen-bonding interaction with the lipase's active site. This, in turn, would lower the reactivity of the sugar with the enzyme. In addition to potential hydrogen-bonding interactions, steric considerations must exist for sugar binding and reactivity. For example, given that the natural reaction of lipases is to hydrolyze triacylglycerol esters, the alcoholic binding pocket of the enzyme must be optimal for a three-carbon glycerol moiety. The bulkier sugar substrate would not be expected to bind as efficiently as the smaller glycerol. Hence, a larger sugar substrate, such as a bulkier aglycon moiety at position C-1, would be expected to reduce catalytic activity. In fact, this is observed as the bulkier phenyl group, which in general (compare **1b** to **1a** and **1h** to **1f**) lowers the enzyme's activity anywhere from 4- to 7-fold.

Synthesis of Other Poly(sugar acrylate)s. The acryloylation of the 6-position leaves open the possibility to control the polymeric properties by varying the aglycon moiety on the 1-position. This was further investigated by using phenyl β-D-galactoside as the starting material for chemoenzymatic poly(acrylate) synthesis. In a manner similar to that of **2a**, 1.80 g of **2b** (53% overall isolated yield from **1b**) was synthesized. Polymerization was performed with AIBN in DMF, and the resulting polymer was precipitated with acetone and dried. The polymer **3b** was a white solid with M_w = 52 700 and M_n = 28 900 (M_w/M_n = 1.8) and was isolated in 40% yield from the starting material (**1b**). The polymer was water-insoluble but soluble in pyridine, DMF, and DMSO, and was not hygroscopic, in stark contrast to **3a**. Hence, the additional hydrophobicity of the aglycon moiety significantly reduced the hydrophilicity of the polymer. Likewise, poly(2-nitrophenyl 6-acryloyl-β-galactoside) (**3c**) was synthesized using AIBN in DMF; however, the product was produced in low molecular weight (M_w < 10 000). The lower molecular weight for **3c** as compared to **3a** and **3b** was possibly due to the free radical scavenging ability of the nitro group.

Preparation of Galactose-Based Hydrogels. Hydrogels are often prepared by polymerizing a water-soluble (meth)acrylic acid-containing compound in the presence of a small amount of cross-linker. Sugars are highly hydrophilic and water-soluble and have the potential to comprise the functional parts of hydrogel matrices. Our synthetic strategy involved the polymerization of 1.0 g of **2a** in DMF with 0.5% (w/w) AIBN plus different amounts of ethylene glycol dimethacrylate as cross-linker. The polymerization reactions were carried out for 12 h, after which the residual DMF was removed by washing with copious amounts of water. The gel-like materials were vacuum dried to give, on average, 0.88 g of a white solid. The solids were placed in water and allowed to equilibrate for 12 h. Figure 1 depicts the equilibrium percentage of water contained in the hydrogels as a function of the cross-linker content (%, w/w). The percentage of water contained in the hydrogel based on **2a** is independent of the cross-linker content between 0.5% and 6% (w/w) and is ca. 90%. Thus, the hydrogel holds 9 times its weight in water. Conversely, a similar set of experiments with **2c** showed markedly poorer hydrogel characteristics (<30%, w/w) (Figure 1), suggesting that the more hydrophobic aglycon moiety repelled water when directly compared to the methyl moiety. The hydrogel based on **2a** is expected to contain methyl galactoside units packed close together as the acrylic acid moieties that separate each sugar side chain are only three carbons in length. We reasoned that this might cause sugar–sugar interactions that could reduce the hydrophilicity of the gel. To avoid this tight packing of the sugar moieties, copolymerization of **2a** with 2-hydroxyethyl methacrylate (hema) was carried out in equimolar concentrations in the presence of ethylene glycol dimethacrylate as cross-linker, and further improvement was observed in the amount of water contained in the hydrogel matrices (Figure 2). In the presence of 0.5% (w/w) cross-linker, the percentage of water contained in the hydrogel reached 95% and reached 98% with 0.3% cross-linker. Hence, the hydrogel based on 50% **2a** and 50% hema holds up to 50-fold its weight in water. Attempts to reduce the cross-linker content below 0.3% failed to produce a gel material. The lower the cross-linker concentration, the higher the water content of the resulting hydrogel. This is consistent with the less rigid nature of lightly cross-linked polymers. As a comparison, hema was polymerized in the absence of **2a** with 0.3% (w/w) cross-linker. The poly(hema)-based hydrogel was capable of holding ca. 5-fold its weight in water. Thus, the presence of hydrophilic sugar moieties in the hydrogel

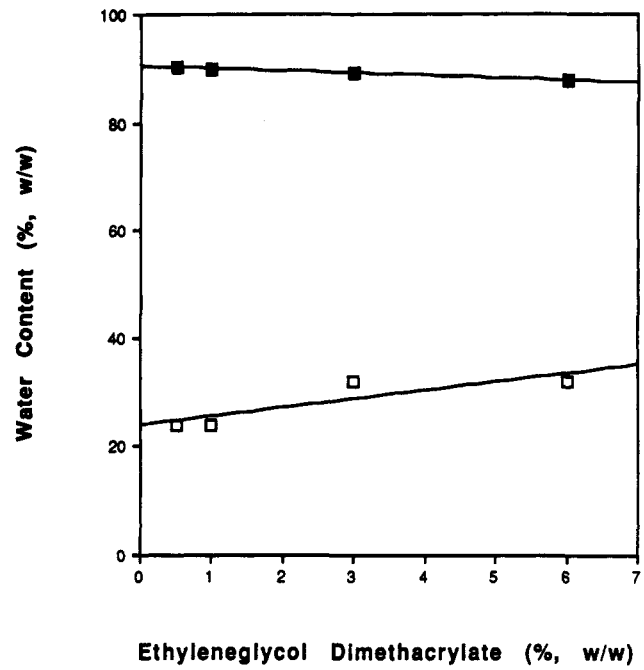


Figure 1. Water-swelling characteristics of poly(6-acryloylgalactoside) derivatives as a function of cross-linker concentration. Aglycons are methyl (■) and phenyl (□). See text for experimental details.

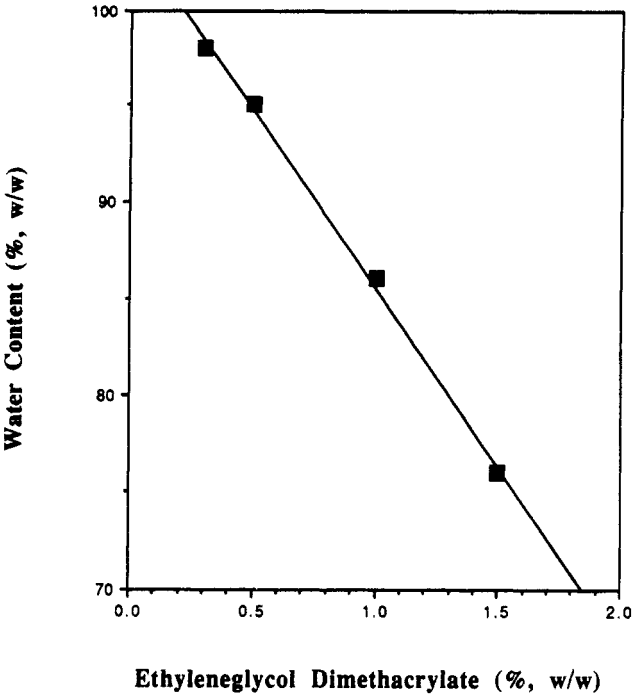


Figure 2. Water-swelling characteristics of poly(methyl 6-acryloyl-β-galactoside–hema) copolymer as a function of the cross-linker concentration. See text for experimental details.

improves the water-swelling characteristics of a hema-based cross-linked polymer.

In conclusion, several monosaccharide-containing poly(acrylate)s have been prepared via a chemoenzymatic approach. 6-*O*-Acryloyl esters of galactosides and glucosides can be synthesized in high yields using a bacterial lipase in anhydrous pyridine. Subsequent free radical polymerization using a conventional chemical initiator results in the preparation of high molecular weight poly(sugar acrylate)s. The ability to initiate the synthesis with different aglycons may be of general use to control the physicochemical properties of the polymers. These materials may have application as hydrogels, for use in biomaterials, or as functional components of membranes for separations. In the case of a copolymer of poly(methyl 6-acryloyl-β-galactoside–hema), the hydrogel material could hold up to 50-fold its weight in water.

Experimental Section

General Procedures. Lipases P (from *P. cepacia*), AY (from *Candida rugosa*), and G (*Penicillium* sp.) were obtained from Amano Enzyme Co. (Philadelphia, PA). Porcine pancreatic lipase was obtained from Sigma (St. Louis, MO), and lipolase was a gift from Novo Nordisk (Bagsvaerd, Denmark). All sugars were obtained from Sigma, and the vinyl acrylate was purchased from Tokyo Kasei (Portland, OR). Azobisisobutyronitrile (AIBN), poly(ethylene glycol) molecular weight standards (200–20000), dextrans (10000–170000), and polystyrenes (1000–100000) were obtained from Polysciences (Warington, PA). All other compounds and solvents were of the highest purity commercially available. Pyridine was dried prior to use with Linde molecular sieves (4 Å) for 24 h. Optical rotations were measured at 589 nm (sodium line) at 25 °C in a Jasco DIP-360 optical polarimeter. ^{1}H and ^{13}C NMR were recorded on a Brüker AMX 600-MHz instrument with TMS as the internal reference and DMSO-d_6 as the solvent in all cases.

Enzymic reactions were followed by HPLC for the conversions of the sugar glycoside starting materials. A carbohydrate analysis column (Waters Associates, Milford, MA) was used with an elution system consisting of 83% acetonitrile and 17% water. Detection was performed by refractive index measurements (model 410, Waters). Gel permeation chromatography (GPC) of **3a** was performed using an Ultrahydrogel linear column (Waters) with an eluant of 0.1 M $NaNO_3$ and a flow rate of 1 mL/min. Molecular weight calibration was performed with poly(ethylene glycol) and dextran standards. GPC of **3b** and **3c** were performed with an Ultrastyragel of 10^4-Å pore size (Waters) with DMF as eluant (1 mL/min) and polystyrenes as molecular weight standards.

Enzymatic Synthesis of Methyl 6-Acryloyl-β-galactoside (2a). A solution of 3.0 g (0.4 M) of **1a** in 40 mL of anhydrous pyridine was prepared, and 3.3 mL (0.6 M) of vinyl acrylate was added. The reaction was initiated by the addition of 0.25 g/mL lipase P and the mixture stirred at 200 rpm at 25 °C. After 40 h, 92% of the substrate had reacted. The reaction was stopped by filtering off the enzyme, and the filtrate was dried under rotary vacuum to give a tan oil. The oil was subjected to silica gel chromatography (4 × 60 cm) with ethyl acetate–MeOH–H_2O (720:5:4). The fractions corresponding to **2a** were pooled and dried to give 2.92 g (75% yield) of a white powder: $[\alpha]^{25}_D$ −10.1° (*c* 1, DMF); ^{1}H NMR (DMSO-d_6) δ 3.53 (dd, *J* = 9.91, 7.90 Hz, H-2), 3.56 (3 H, s, CH_3O–), 3.67 (1 H, dd, *J* = 9.91, 3.52 Hz, H-3), 3.97 (1 H, m, H-5), 3.99 (1 H, d, *J* = 3.52 Hz, H-4), 4.34 (1 H, d, *J* = 7.90 Hz, H-1), 4.38 (1 H, dd, *J* = 11.7, 4.8 Hz, H-6), 4.40 (1 H, dd, *J* = 11.7, 7.7 Hz, H-6), 6.03 (1 H, dd, *J* = 10.58, 0.92 Hz, H-3′), 6.24 (1 H, dd, *J* = 10.58, 17.37 Hz, H-2′), 6.47 (1 H, dd, *J* = 17.37, 0.92 Hz, H-3′); ^{13}C NMR δ 59.97 (CH_3O), 66.49 (C-6), 71.41 (C-4), 73.34 (C-2), 75.23 (C-5), 75.39 (C-3), 106.6 (C-1), 129.9 (C-2′), 136.2 (C-3′), 170.9 (C=O). Anal. Calcd for $C_{10}H_{16}O_7$: C, 48.39; H, 6.69; O, 45.16. Found: C, 48.38; H, 6.45; O, 45.29.

Enzymatic Synthesis of Phenyl 6-Aryloyl-β-galactoside (2b). A solution of 4.08 g (0.4 M) of **1b** in 40 mL of anhydrous pyridine was prepared, and 3.3 mL (0.6 M) of vinyl acrylate was added. The reaction was initiated by the addition of 0.25 g/mL lipase P and the mixture stirred at 200 rpm at 25 °C. After 40 h, 98% of the substrate had reacted. The reaction was stopped by filtering off the enzyme, and the filtrate was dried under rotary vacuum to give a tan oil. The oil was subjected to silica gel chromatography (4 × 60 cm) with ethyl acetate–MeOH–H_2O (720:2:1). The fractions corresponding to **2b** were pooled and dried to give 2.95 g (59% yield) of a white powder: $[\alpha]^{25}_D$ −24.3° (*c* 1, DMF); ^{1}H NMR (DMSO-d_6) δ 3.52 (1 H, dd, *J* = 9.45, 3.34 Hz, H-3), 3.64 (1 H, dd, *J* = 9.45, 7.77 Hz, H-2), 3.78 (1 H, br d, *J* = 3.34 Hz, H-4), 3.96 (1 H, ddd, *J* = 8.37, 3.94, 0.86 Hz, H-5), 4.25 (1 H, dd, *J* = 11.43, 3.94 Hz, H-6), 4.38 (1 H, dd, *J* = 11.43, 8.37 Hz, H-6), 4.88 (1 H, d, *J* = 7.77 Hz, H-1), 6.03 (1 H, dd, *J* = 10.41, 1.48 Hz, H-3′), 6.23 (1 H, dd, *J* = 17.37, 10.41 Hz, H-2′), 6.39 (1 H, dd, *J* = 17.37, 1.48 Hz, H-3′), 7.04 (3 H, m, H-3″, H-4″, H-5″), 7.31 (1 H, ddd, *J* = 7.35, 2.35, 2.07 Hz, H-2″ or H-6″), 7.32 (1 H, ddd, *J* = 7.31, 2.32, 2.04 Hz, H-2″ or H-6″); ^{13}C NMR δ 65.44 (C-6), 69.83 (C-4), 71.61 (C-2), 73.97 (C-5), 74.55 (C-3), 102.2 (C-1), 117.7 (C-3″, C-5″), 123.2 (C-4″), 129.7 (C-2′), 130.8 (C-2″, C-6″), 133.1 (C-3′), 158.9 (C-1″), 166.7 (C=O). Anal. Calcd for $C_{15}H_{18}O_7$: C, 58.06; H, 5.81; O, 36.13. Found: C, 57.87; H, 6.01; O, 35.90.

Enzymatic Synthesis of 2-Nitrophenyl 6-Acryloyl-β-galactoside (2c). A solution of 4.82 g (0.4 M) of **1c** in 40 mL of anhydrous pyridine was prepared, and 3.3 mL (0.6 M) of vinyl acrylate was added. The reaction was initiated by the addition of 0.25 g/mL lipase P and the mixture stirred at 200 rpm at 25 °C. After 20 h, 95% of the substrate had reacted. The reaction was stopped by filtering off the enzyme, and the filtrate was dried under rotary vacuum to give a tan oil. The oil was subjected to silica gel chromatography (4 × 60 cm) with ethyl acetate–MeOH–H_2O (720:2:1). The fractions corresponding to **2c** were pooled and dried to give 4.56 g (80% yield) of a white powder: $[\alpha]^{25}_D$ −96.9° (*c* 1, DMF); ^{1}H NMR (DMSO-d_6) δ 3.47 (1 H, br d, *J* = 9.2 Hz, H-3), 3.60 (1 H, m, H-2), 3.74 (1 H, t, *J* = 3.68, H-4), 4.01 (1 H, m, H-5), 4.22 (1 H, dd, *J* = 4.02, 11.47, H-6), 4.28 (1 H, dd, *J* = 8.29, 11.47 Hz, H-6), 5.08 (1 H, d, *J* = 8.72 Hz, H-1), 5.98 (1 H, dd, *J* = 10.40, 1.46 Hz, H-3′), 6.18 (1 H, *J* = 17.29, 10.40 Hz, H-2′), 6.33 (1 H, *J* = 17.29, 1.46 Hz, H-3′), 7.18 (1 H, dt, *J* = 8.2, 0.86, H-4″), 7.37 (1 H, dd, *J* = 8.57, 0.86, H-6″), 7.60 (1 H, dt, *J* = 8.5, 1.7 Hz, H-5″), 7.85 (1 H, dd, *J* = 8.07, 1.7 Hz, H-3″); ^{13}C NMR δ 65.43 (C-6), 69.99 (C-4), 71.54 (C-2), 74.48 (C-5), 74.75 (C-3), 102.4 (C-1), 118.7 (C-6″), 123.5 (C-4″), 126.4 (C-3″), 129.9 (C-2′), 133.4 (C-3′), 135.5 (C-5″), 142.0 (C-2″), 151.1 (C-1″), 166.9 (C=O). Anal. Calcd for $C_{15}H_{17}NO_9$: C, 50.70; H, 4.79; N, 3.94; O, 40.56. Found: C, 50.66; H, 5.20; N, 3.79; O, 40.20.

Synthesis of Poly(methyl 6-acryloyl-β-galactoside) (3a). A solution of 2.0 g of **2a** in 8 mL of DMF was prepared, and 0.1% (w/w) AIBN was added. The polymerization proceeded at 65 °C under nitrogen for 16 h. The reaction was terminated by precipitating the polymer with ethyl acetate, and the white solids were washed with acetone to yield 1.48 g of **3a** (74% yield); $[\alpha]^{25}_D$ −12.8° (*c* 1, DMF); ^{1}H NMR (DMSO-d_6) δ 1.80 (2 nH, br t, H-3′), 2.44 (1 nH, br s, H-2′), 3.55 (1 nH br s, H-2), 3.60 (3 nH, s, CH_3O), 3.70 (1 nH, br s, H-3), 3.90 (1 nH, br s, H-5), 3.97 (1 nH, br s, H-4), 4.27 (2 nH, br s, H-6), 4.32 (1 nH, br s, H-1); ^{13}C NMR δ 36.58 (C-3′), 44.23 (C-2′), 59.60 (CH_3O), 67.26 (C-6), 71.49 (C-4), 73.29 (C-2), 75.19 (C-5), 75.44 (C-3), 106.5 (C-1), 167.6 (C=O). Anal. Calcd for $C_{10}H_{16}O_7$: C, 48.39; H, 6.69; O, 45.16. Found: C, 48.27; H, 6.86; O, 45.38.

Synthesis of Poly(phenyl 6-acryloyl-β-galactoside) (3b). The polymerization reaction was performed under conditions identical to those of **3a**. The polymerization yielded 1.80 g of a white powder (90% isolated yield). $[\alpha]^{25}_D$ −45.8° (*c* 1, DMF); ^{1}H NMR (DMSO-d_6) δ 1.48 (1 nH, br t, H-3′), 2.17 (1 nH, br s, H-2′), 3.40 (1 nH, br s, H-3), 3.75 (1 nH, br s, H-4), 4.00 (1 nH, br s, H-5), 4.72, 4.90 (each 1 nH, each br s, H-6), 5.20 (1 nH, br s, H-1), 6.85 (3 nH, br s, H-3″, H-4″, H-5″), 7.10 (2 nH, br s, H-2″, H-6″); ^{13}C NMR δ 64.0 (C-6), 68.3 (C-4), 69.9 (C-2), 72.0 (C-5), 72.8 (C-3), 100.5 (C-1), 116.0 (C-3″, C-5″), 121.6 (C-4″), 129.2 (C-2″, C-6″), 157.1 (C-1″), 162.2 (C=O). The carbon assignments for C-2′ and C-3′ were split into numerous signals due to mixtures of rotational configurations. Anal. Calcd for $C_{15}H_{18}O_7$: C, 58.06; H, 5.81; O, 36.13. Found: C, 57.81; H, 6.04; O, 35.94.

Synthesis of Poly(2-nitrophenyl 6-acryloyl-β-galactoside) (3c). The polymerization reaction was performed under conditions identical to those of **3a**. The polymerization yielded 1.32 g of a white powder (66% isolated yield): $[\alpha]^{25}_D$ −108.7° (*c* 1, DMF); ^{1}H NMR (DMSO-d_6) δ 1.50 (2 nH, br t, H-3′), 2.21 (1 nH, br s, H-2′), 3.51 (1 nH, br s, H-3), 3.61 (1 nH, br s, H-2), 3.75 (1 nH, br s, H-4), 4.05 (1 nH, br s, H-5), 4.78, 5.20 (each 1 nH, each br s, H-6), 5.04 (1 nH, br s, H-1), 7.05 (1 nH, br s, H-4″), 7.30 (1 nH, br s, H-6″), 7.50 (1 nH, br s, H-5″), 7.70 (1 nH, br s, H-3″); ^{13} NMR δ 63.55 (C-6), 68.10 (C-4), 69.66 (C-2), 72.59 (C-5), 72.75 (C-3), 100.5 (C-1), 116.8 (C-6″), 121.7 (C-4″), 124.5 (C-3″), 133.7 (C-5″), 139.8 (C-2″), 149.2 (C-1″), 165.1 (C=O). The carbon assignments for C-2′ and C-3′ were split into numerous signals due to mixtures of rotational configurations. Anal. Calcd for $C_{15}H_{17}NO_9$: C, 50.70; H, 4.79; N, 3.94; O, 40.56. Found: C, 50.25; H, 4.89; N, 4.28; O, 40.68.

Synthesis of Hydrogels. The polymerizations of **2a** and **2b** were carried out in an identical fashion: 1.0 g of the monosaccharide acrylate was dissolved in 4.0 mL of DMF containing different concentrations of ethylene glycol dimethacrylate (ranging from 0.5% to 6%, w/w), and 0.5% (w/w) AIBN was added. The reaction was performed at 60 °C for 12 h during which time a gel formed. The residual DMF contained no traces of monosaccharide acrylate (as determined by TLC). Vacuum drying of the gels for 24 h (40 °C) resulted in white solids with an average mass of 0.88 g. Water-swelling was measured by placing the solids in 25 mL of water for 12 h followed by removal of the bulk liquid by filtration until a surface-dry gel was obtained and the material weighed. Poly(methyl 6-acryloyl-β-galactoside–hema) copolymers were prepared in a similar manner, with the ethylene glycol dimethacrylate concentration reduced to 0.3% (w/w).

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