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Synthesis of Novel Maleicamido Saccharides and Their Copolymerization with Vinylamides

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ABSTRACT

A new synthesis for anionic unsaturated saccharide monomers from maleic anhydride with amino carbohydrates is described. Various primary and secondary amines with mono and disaccharide moieties were used. The reactions were performed in water at 0°C in the presence of a mineral base, and high yields were achieved. These monomers were found not to be homopolymerizable, but free radical copolymerizations with several N-vinylamides were successfully carried out in water to form a new class of anionic poly(maleicamido saccharide)s (PMAS). As comonomers, N-vinylacetamide (VAA), N-methylvinylacetamide (MVAA) and N-vinylformamide (VFA) were used. In this way linear polyelectrolytes with high average molecular weight could be obtained. The copolymers were characterized by NMR-spectroscopy, IR-spectroscopy, elementary analysis, light scattering, and viscosimetry.

Key Words: Maleicamido saccharides; Glycopolymers; Poly(vinylsaccharide)s; Water soluble polymers.

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INTRODUCTION

Poly(maleicamido saccharide)s contain a carbon backbone chain and carbohydrate side groups comparable to the so called poly(vinylsaccharide)s[1–4] and belong to the rapidly expanding group of water soluble glycopolymers with high potential for various applications. Most commonly, such saccharide polymers are prepared by free radical polymerization or copolymerization of carbohydrate derivatives linked to a polymerizable group by coupling agents like unsaturated anhydrides, carboxylic acid halides, or isocyanates.[1–4] These polymers might be useful for biological purposes as drug carriers, immunodiagnostic reagents, targeting devices or enzyme stabilizators,[5–9] as well as technical viscosifiers,[10] dispergent and complexing agents or biodegradable materials to name a few.[11] Usually, poly(vinylsaccharide)s are neutral polymers, but also some ionic, mostly anionic derivatives are known from earlier reports.[3,12] In the present paper, we report on a new convenient method to prepare anionic unsaturated saccharide derivatives with many advantages compared to former procedures.[12] For the polymerizable functional group, maleic anhydride was found as an optimal coupling agent which is available as a cheap bulk chemical. Maleic anhydride can be transformed in a simple one-step reaction with various amino derivatives of mono- or disaccharides to maleicamido carbohydrates. The N-acylation of the amino sugar is carried out in aqueous solution at 0°C in the presence of sodium carbonate or hydroxide. These anionic saccharide monomers are easily copolymerizable with e.g. vinylamides to form water soluble poly(maleicamido saccharide)s (PMAS), most likely with alternating constitution. The best known vinylamide is N-vinylpyrrolidon, but also other acyclic vinylamides like N-vinylacetamide (VAA) or N-vinylformamide (VFA) became more important in recent years.[13,14] Their polymers and copolymers have potential, e.g. as peptide hormone conjugates with anti-cancer activity,[15] drug delivery systems,[16] and other applications typical for water soluble polymers.[17] Panarin et al. for example, copolymerized nonionic methacrylamido saccharides with vinylamides for drug delivery purposes.[18,19]

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EXPERIMENTAL

Measurements

The NMR-data were recorded in D_2O at 100.6 MHz (^{13}C) and 400 MHz (^{1}H) using an AM-400 spectrometer from Bruker. FT-IR spectra were taken on a Bio-Rad FTS-25 using a KBr pellet. All light scattering measurements were conducted with a Dawn DSP from Wyatt at 632.8 nm in batch mode. For the determination of the weight-average molecular weight (M_w) and the root mean square radius of gyration (R_G), the method by Zimm was used (Software: Wyatt Astra 4.7). The refractive index increments were determined with a differential refractometer Brice-Phoenix BP-2000V from Virtis. Viscosimetry experiments were carried out in a capillary viscosimeter of the Ubbelohde type from Schott. The intrinsic viscosities were calculated using the Huggins procedure. All measurements in solution were carried out at 25°C in 0.1 M Na_2SO_4 to eliminate polyelectrolyte effects. For

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elemental analysis, a heat conductivity detector from Carlo Erba Instrumentazione was used.

Materials

All solvents, saccharides, and maleic anhydride were obtained from Fluka. The vinylamides for the copolymerization are commercially available by Aldrich. Dialysis was carried out in dialysis membranes obtained from Medicell (MWCO = 12–14000 Da and MWCO = 8000 Da).

Preparation of Monomers

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N-Maleicamido-1-deoxy-lactitol Sodium Salt (**4**)

30.0 g (87.6 mmol) D-lactosamine (**1**), synthesized by reductive amination as described in Ref.[2] are dissolved with 5.1 g (48.2 mmol) Na_2CO_3 in 300 mL dest. water. The solution is cooled to 0°C. Then 9.0 g (92.0 mmol) maleic anhydride are added slowly in order to hold the reaction at pH = 8–9. After the anhydride is reacted (pH = 7), the solution is poured into the 8th–10th amount of acetone. The sticky precipitate is sucked off and dissolved in water. The white strong hygroskopic salt can be isolated by freeze drying. Yield: 36.7 g (90.5 mol-%). ^{1}H-NMR (D_2O) 3.3–3.9 (m, 13H, 1-H, 2-H, 3-H, 4-H, 5-H, 6-H, 2″-H, 3″-H, 4″-H, 5″-H, 6″-H), 4.44 (d, 1H, J = 7.8 Hz, 1″-H), 5.90 (d, 1H, J = 12.3 Hz, 3′-H), 6.28 (d, 1H, J = 12.3 Hz, 2′-H); ^{13}C-NMR (D_2O) 44.47 (C-1), 63.35 (C-6), 64.63 (C-6″), 71.13, 72.73, 72.84, 73.64, 73.86, 75.13, 77.56 (C-2, C-3, C-5, C-2″, C-3″, C-4″, C-5″), 81.96 (C-4), 105.64 (C-1″), 126.80 (C-3′), 138.81 (C-2′), 170.80 (C-1′), 177.24 (C-4′).

N-Maleicamido-2-deoxy-glucose Sodium Salt (**5**)

100.0 g (464 mmol) D-glucosamine (**2**) are dissolved in 200 mL dest. water and the solution is cooled to 0°C. Then, 46.0 g (496 mmol) maleic anhydride are added slowly in portions to the mixture. During this procedure, 37.5 g NaOH (938 mmol) in 50 mL water are added dropwise to the solution to hold the reaction at pH = 6–7. After the anhydride is reacted (pH = 7), the solvent is evaporated under reduced pressure to give a light yellow crude product. This product is dissolved in methanol and the salt NaCl is then filtered off. The filtrate is poured into the 8th–10th amount of acetone. The white solid is filtered and dried under vacuo. Yield: 102.6 g (74 mol%). The solid is a mixture of anomers. ^{1}H-NMR (D_2O) 3.40–3.90 (m, 6H, α + β-anomer 2-H, 3-H, 4-H, 5-H, 6-H), 4.72 (d overlaid with HDO-signal, 1H, β-anomer 1-H), 5.17 (d, 1H, J = 3.5 Hz, α-anomer 1-H), 5.93 (2 × d, 1H, J = 12.3 Hz, α + β-anomer 3′-H), 6.32 (2 × d, 1H, J = 12.3 Hz, α + β-anomer 2′-H), α:β = 55:45 mol-%; ^{13}C-NMR (α-anomer) (D_2O) 56.56 (C-2), 63.17 (C-6), 72.55, 73.55, 74.17 (C-3, C-4, C-5), 93.47 (C-1), 126.45 (C-2′), 139.37 (C-3′), 170.57 (C-1′), 177.28 (C-4′); ^{13}C-NMR β-anomer (D_2O): δ = 56.27 (C-2), 63.30 (C-6), 72.28,

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76.60, 78.52 (C-3, C-4, C-5), 97.40 (C-1), 126.50 (C-2′), 139.37 (C-3′), 170.87 (C-1′), 177.44 (C-4′).

N-Maleicamido-1-deoxy-glucitol Sodium Salt (**6a**)

100.0 g (552 mmol) D-glucamine (**3a**) are dissolved in 200 mL dest. water and the solution is cooled to 0°C. Then 55.0 g (561 mmol) maleic anhydride are added slowly in portions to the mixture. During this procedure, 22.1 g NaOH (553 mmol) in 50 mL water are added dropwise to the solution to hold the reaction at pH = 7–8. After the anhydride is reacted (pH = 7), the solvent is evaporated under reduced pressure to its half volume and poured into the 8th–10th amount of acetone. The white solid is filtered and dried under *vacuo*. Yield: 174.3 g (100 mol%). ^{1}H-NMR (D_2O) 3.27 (dd, 1H, J = 7.9 Hz, J = 14.1 Hz, 1-H), 3.45 (dd, 1H, J = 4.2 Hz, J = 14.1 Hz, 1-H), 3.61, 3.74, 3.87 (m, 6H, 2-H, 3-H, 4-H, 5-H, 6-H), 5.93 (d, 1H, J = 12.3 Hz, 3′-H), 6.30 (d,1H, J = 12.3 Hz, 2′-H); ^{13}C-NMR (D_2O) 44.41 (C-1), 65.34 (C-6), 72.82, 73.59, 73.65, 73.88, (C-2, C-3, C-4, C-5), 126.89 (C-2′), 138.78 (C-3′), 170.89 (C-1′), 177.31 (C-4′).

N-Maleicamido-N-methyl-1-deoxy-glucitol Sodium Salt (**6b**)

50.0 g (256 mmol) D-methylglucamine (**3b**) are dissolved in 100 mL dest. water and the solution is cooled to 0°C. Then 25.3 g (258 mmol) maleic anhydride are added slowly in portions to the mixture. During this procedure 10.3 g NaOH (258 mmol) in 40 mL water are added dropwise to the solution to hold the reaction at pH = 7–8. After the anhydride is reacted (pH = 7) the solvent is evaporated under reduced pressure to its half volume and poured into the 8th–10th amount of acetone. The white solid is filtered and dried under vacuum. Yield: 80.0 g (99 mol%). ^{1}H-NMR (D_2O) double signals caused by 2 rotamers (~50:50%) of amide group (dynamical equilibrium) 2.95, 3.05 (2 × s, 3H, 7-H), 3.38–3.78, 3.90, 4.06 (m, 8H, 1-H, 2-H, 3-H, 4-H, 5-H, 6-H), 6.08 (2 × d overlaid, 1H, J = 12.0 Hz, 3′-H), 6.32 (2 × d, 1H, J = 12.0 Hz, 2′-H); ^{13}C-NMR (D_2O) 35.73, 39.92 (C-7), 52.68, 55.91 (C-1), 65.25, 65.29 (C-6), 72.59, 72.72, 72.81, 73.63, 73.66, 74.13, 74.22 (C-2, C-3, C-4, C-5), 132.23, 132.32 (C-2′), 134.35, 134.58 (C-3′), 173.90, 173.95 (C-1′), 175.84 (C-4′).

Copolymerization

Polymerization is conducted in glass reaction vessels. For a typical procedure, the maleicamido sugar and the equivalent amount of the comonomer are dissolved in degassed dest. water. Afterwards, the solution is purged with nitrogen for several hours. The polymerization is started by thermally decomposition of 2,2′-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride at 50°C, and the reaction mixture is stirred for several hours. The reaction is stopped by injection of air. To remove remaining monomer and oligomer the solution is dialyzed against water for several days. The white polymer is isolated by freeze drying. For additional data, see Table 1.

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Table 1. Conditions of copolymerization of maleicamido carbohydrates with several N-vinylamides.

No.	Monomer	Comonomer	V_{H2O} [mL]	Initiator [mol%]	T [°C]	Time [h]	M_1	Yield [wt.-%]
Pl	6.0 g **6a**	2.1 g MVAA	150	1.0	50	43	0.5	22.2
P2	6.0 g **6a**	3.5 g VAA	150	1.0	50	43	0.5	63.6
P3	6.0 g **6b**	2.0 g MVAA	150	1.0	50	45	0.5	19.5
P4	6.0 g **6b**	1.7 g VAA	150	1.0	50	45	0.5	31.7
P5	6.0 g **5**	2.0 g MVAA	150	1.0	50	43	0.5	68.0
P6	6.0 g **5**	4.0 g MVAA	100	1.0	50	2	0.33	43.7
P7	6.0 g **5**	1.7 g VAA	150	1.0	50	43	0.5	75.9
P8	6.0 g **5**	3.4 g VAA	100	1.0	50	1	0.33	42.0
P9	5.0 g **4**	1.1 g MVAA	10	0.5	50	74	0.5	64.3
P10	5.0 g **4**	0.9 g VAA	10	0.5	50	19	0.5	65.2
P11	5.0 g **4**	0.8 g VFA	10	0.5	50	27	0.5	70.7

M_1: Mole ratio of maleicamido carbohydrate in the feed.

^{13}C-NMR Characterization of the Copolymers

Poly(N-Maleicamido-1-deoxy-glucitol-*co*-MVAA) (**P1**)

(D_2O) 23–25 ($H_3CCON(CH_3)$-), 29.5–36 ($H_3CCON(CH_3)$-), 43.5–48 (-CH_2-CH(NR)-, C-1), 53–58 (-CH_2-CH(NR)-, C-2′, C-3′), 65 (C-6), 72–76 (C-2, C-3, C-4, C-5), 176–179 ($H_3CCON(CH_3)$-, C-1′), 179–184.5 (C-4′).

Poly(N-Maleicamido-1-deoxy-glucitol-*co*-VAA) (**P2**)

(D_2O) 24–25.5 (H_3CCONH-), 33.5–44 (-CH_2-CH(NR)-, C-1), 44–60 (-CH_2-CH(NR)-, C-2′, C-3′), 65–66 (C-6), 71–76 (C-2, C-3, C-4, C-5), 175–177.5 (H_3CCONH-), 177.5–180 (C-1′), 180–184 (C-4′).

Poly(N-Maleicamido-N-methyl-1-deoxy-glucitol-*co*-MVAA) (**P3**)

(D_2O) 23–25 ($H_3CCON(CH_3)$-), 30.5–34.5 ($H_3CCON(CH_3)$-), 35–36 (C-7), 37–53 (-CH_2-CH(NR)-, -CH_2-CH(NR)-), C-2′, C-3′), 53–54 (C-1), 65–66 (C-6), 70–75 (C-2, C-3, C-4, C-5), 175–179 ($H_3CCON(CH_3)$-), 179–186.5 (C-1′,C-4′).

Poly(N-Maleicamido-N-methyl-1-deoxy-glucitol-*co*-VAA) (**P4**)

(D_2O) 24–25.30 (H_3CCONH-), 35–36 (C-7), 36–51 (-CH_2-CH(NR)-, -CH_2-CH(NR)-, C-2′, C-3′), 53–55.5 (C-1), 65–66 (C-6), 70–75 (C-2, C-3, C-4, C-5), 174–178 (H_3CCONH-), 180–183 (C-1′), 183–186 (C-4′).

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Poly(N-Maleicamido-2-deoxy-glucose-*co*-MVAA) (**P5**)

(D_2O) 22.5–25 (H_3*C*CON(CH_3)-), 30.5–36.5 (H_3CCON(*C*H_3)-), 45–48 (-*C*H_2-CH(NR)-,C-2′), 53–61.5 (-CH_2-*C*H(NR)-, C-2, C-2′, C-3′), 62–65 (C-6), 71.5–80 (C-3, C-4, C-5), 92.5–94.4 (C-1α), 96–98 (C-1β), 174.5–178.5 (H_3C*C*ON(CH_3)-, C-1′), 178.5–181.5 (C-4′).

Poly(N-Maleicamido-2-deoxy-glucose-*co*-VAA) (**P7**)

(D_2O) 23–26 (H_3*C*CONR-), 33–42 (-*C*H_2-CH(NR)-), 43–51 (-CH_2-*C*H(NR)-), 55–60 (C-2, C-2′, C-3′), 63–65 (C-6), 71.5–79.5 (C-3, C-4, C-5), 92–95 (C-1α), 96.5–98.5 (C-1β), 173.5–177.5 (H_3C*C*ONR-), 177.5–179 (C-1′), 179.5–182 (C-4′).

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Poly(N-Maleicamido-1-deoxy-lactitol-*co*-MVAA) (**P9**)

(D_2O) 22.5–27 (H_3*C*CON(CH_3)-), 30–37 (H_3CCON(*C*H_3)-), 42.5–48 (-*C*H_2-CH(NR)-, C-1, C-2′), 52–60 (-CH_2-*C*H(NR)-, C-2′, C-3′), 63–64 (C-6), 64.5–65 (C-6″), 71–78 (C-2, C-3, C-5, C-2″, C-3″, C-4″, C-5″), 81–85 (C-4), 105–107 (C-1″), 177–180 (C-1′, C-4′, H_3C*C*ON(CH_3)-).

Poly(N-Maleicamido-1-deoxy-lactitol-*co*-VAA) (**P10**)

(D_2O) 24–26 (H_3*C*CONH-), 33–40 (-*C*H_2-CH(NR)-), 43–50 (-CH_2-*C*H(NR)-, C-1), 63–64 (C-6), 63.5–65 (C-6″), 71–78 (C-2, C-3, C-5, C-2″, C-3″, C-4″, C-5″), 81–83 (C-4), 104–106 (C-1″), 174–176 (H_3C*C*ONH-), 177–179 (C-1′), 179–182 (C-4′).

Poly(N-Maleicamido-1-deoxy-lactitol-*co*-VFA) (**P11**)

(D_2O) 35–43 (-*C*H_2-CH(NR)-), 44–48 (-CH_2-*C*H(NR)-, C-1), 53–59 (C-2′, C-3′), 63–64 (C-6), 64–65 (C-6″), 71–78 (C-2, C-3, C-5, C-2″, C-3″, C-4″, C-5″), 81–83.5 (C-4), 105–106 (C-1″), 165–167.5 (H*C*ONH-), 175–185 (C-1′, C-4′).

IR Data of the Copolymers

Poly(N-Maleicamido-1-deoxy-glucitol-*co*-MVAA) (**P1**)

3403 (vs, OH), 2936 (CH_2), 1614 (s, C═O, amide, carboxylate), 1407 cm^{-1} (m, C═O, carboxylate).

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Poly(N-Maleicamido-1-deoxy-glucitol-*co*-VAA) (**P2**)

3380 (vs, OH), 2934 (CH_2), 1652 (s, C═O, amide), 1575 (s, N—H, amide, C═O, carboxylate), 1403 cm^{-1} (m, C═O, carboxylate).

Poly(N-Maleicamido-N-methyl-1-deoxy-glucitol-*co*-MVAA) (**P3**)

3404 (vs, OH), 2935 (CH_2), 1620 (s, C═O, amide, carboxylate), 1410 cm^{-1} (m, C═O, carboxylate).

Poly(N-Maleicamido-N-methyl-1-deoxy-glucitol-*co*-VAA) (**P4**)

3395 (vs, OH), 2934 (CH_2), 1642 (s, C═O, amide), 1567 (s, N—H, amide, C═O, carboxylate), 1400 cm^{-1} (m, C═O, carboxylate).

Poly(N-Maleicamido-2-deoxy-glucose-*co*-MVAA) (**P5**)

3418 (vs, OH), 2935 (CH_2), 1607 (s, C═O, amide, carboxylate), 1407 cm^{-1} (m, C═O, carboxylate).

Poly(N-Maleicamido-2-deoxy-glucose-*co*-VAA) (**P7**)

3407 (vs, OH), 2928 (CH_2), 1652 (s, C═O, amide), 1575 (s, N—H, amide, C═O, carboxylate), 1379 cm^{-1} (m, C═O, carboxylate).

Poly(N-Maleicamido-1-deoxy-lactitol-*co*-MVAA) **(P9**)

3406 (vs, OH), 2933 (CH_2), 1607 (s, C═O, amide, carboxylate), 1406 cm^{-1} (m, C═O, carboxylate).

Poly(N-Maleicamido-1-deoxy-lactitol-*co*-VAA) (**P10**)

3390 (vs, OH), 2927 (CH_2), 1651 (s, C═O, amide), 1576 (s, N—H, amide, C═O, carboxylate), 1403 cm^{-1} (m, C═O, carboxylate).

Poly(N-Maleicamido-1-deoxy-lactitol-*co*-VFA) **(P11**)

3378 (vs, OH), 2930 (CH_2), 1669 (s, C═O, amide), 1580 (s, N—H, amide, C═O, carboxylate), 1396 cm^{-1} (m, C═O, carboxylate).

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RESULTS AND DISCUSSION

Monomer Synthesis

The syntheses of the maleicamido carbohydrates were carried out in water using different amino sugars and maleic anhydride (Sch. 1) with sodium carbonate or sodium hydroxide as base for the complete conversion of the amine. The sugars used for this report varied from monosaccharides like glucosamine (**2**) to disaccharides like 1-deoxy-D-lactitol (**1**). Also N-alkyl amino sugars like the open chain N-methyl-D-glucamine (**3b**) could be used successfully. One can suppose that this method is useful for all water soluble primary and secondary amino sugars. The advantage of using water as solvent is the poor solubility of maleic anhydride at 0°C in order to keep the maleic anhydride concentration at a low level to react with the more nucleophilic amine. This prevents a reaction with the hydroxylgroups in the carbohydrate moiety on one side and with water on the other side. Hydrophobic interactions between the amino sugar and the unsolved anhydride under heterogeneous conditions might be another reason for the selective conversion of the amino group. All the syntheses described here led to high yields and a quantitative reaction can be proposed. The structures could be verified by ^{1}H- and ^{13}C-NMR (e.g. Fig. 1).

Synthesis and Properties of the Polymers

The maleicamido carbohydrates did not homopolymerize as it is known from other maleic derivatives.[20] We found that vinylamides like N-methylvinylacetamide (MVAA), N-vinylacetamide (VAA) and vinylformamide (VFA) could be used as efficient polymerization partners probably because of their electron donating character. Other water soluble monomers like acrylamide or acrylic acid proved to be poor comonomers. Copolymerizations were carried out in aqueous solution with feeds differing from equimolar to a small excess of the comonomer ($M_1 = 0.5$; $M_1 = 0.33$) as it can be taken from Table 1. The reactions were initiated by thermally decomposition of the initiator 2,2′-azo-bis[2-(2-imidazolin-2-yl)propane]dihydrochloride (0.5 mol%; 1.0 mol%) at 50°C and led to linear polymers with high average molecular weight as measured by light scattering with average degrees of polymerization (P_w) between 50 and 1690 (Table 2). FT-IR spectra of the copolymers showed characteristic absorption bands at 1614–1669 cm^{-1} due to C═O stretching of amide, at 1567–1580 cm^{-1} (combination of N—H bending with C═O stretching of amide and carboxylate) and at 1396–1410 cm^{-1} due to C═O stretching of carboxylate. The ^{13}C-NMR spectra of Poly(N-maleicamido-1-deoxy-lactitol-*co*-VAA) for example, are presented in Fig. 2. These NMR spectra show the atoms of both saccharide and vinylamide units. All carbon atoms of the polymer backbone resulted as broad signals with chemical shifts at $\delta = 33–60$ ppm. The shifts of the sugar components were found in the area from 62 to 85 ppm except of the down-field shifted anomeric centres (92–106 ppm). Carboxyl groups appeared at $\delta = 173–187$ ppm. NMR data of each polymer can be taken from the Experimental section.

The compositions of the polymers were calculated from elemental analysis. Due to the fact that the maleicamido carbohydrates do not homopolymerize, one has to assume that sugar carrying units are not connected directly and in between the vinylamide units

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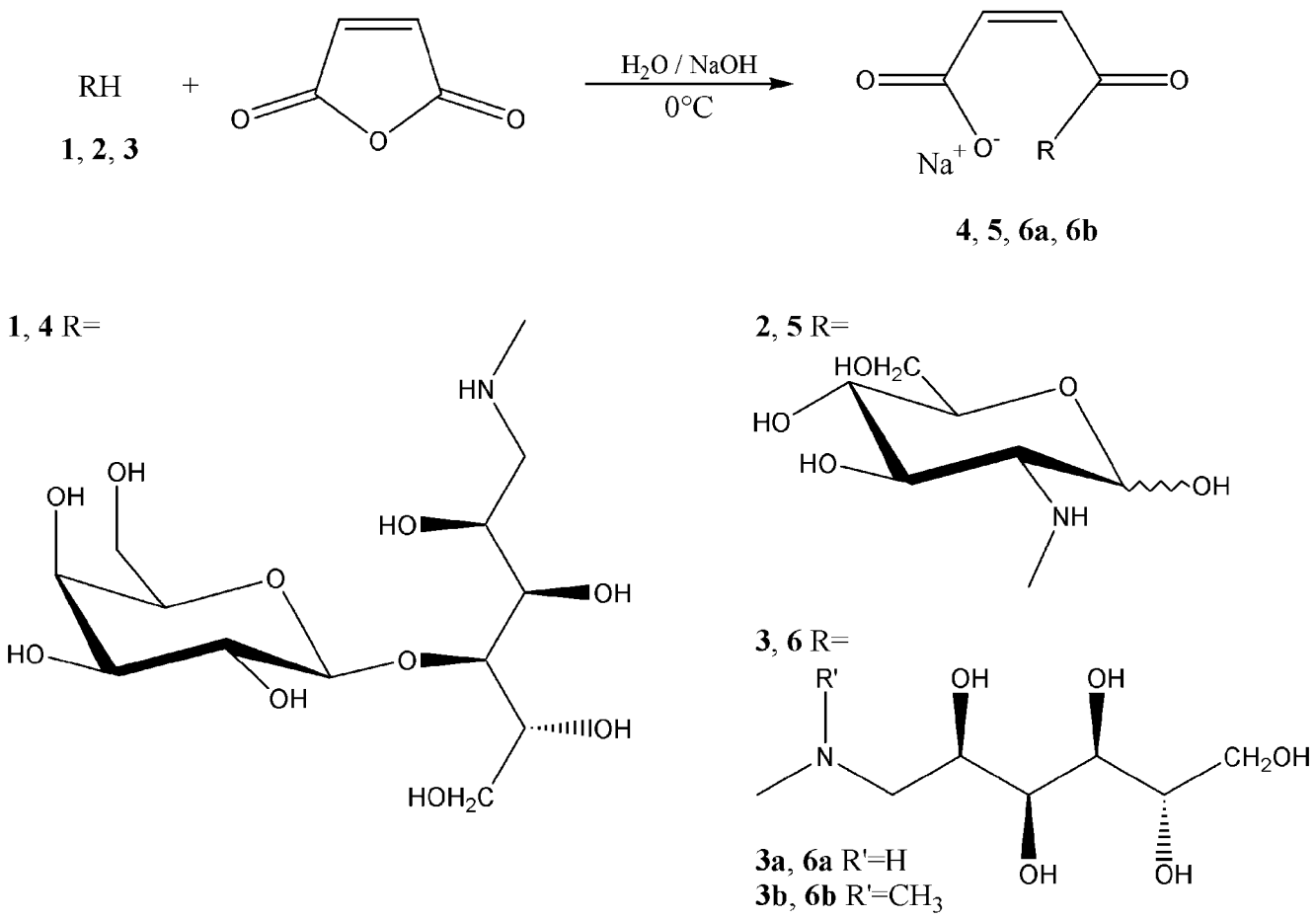

Scheme 1. Synthesis of maleicamido carbohydrates.

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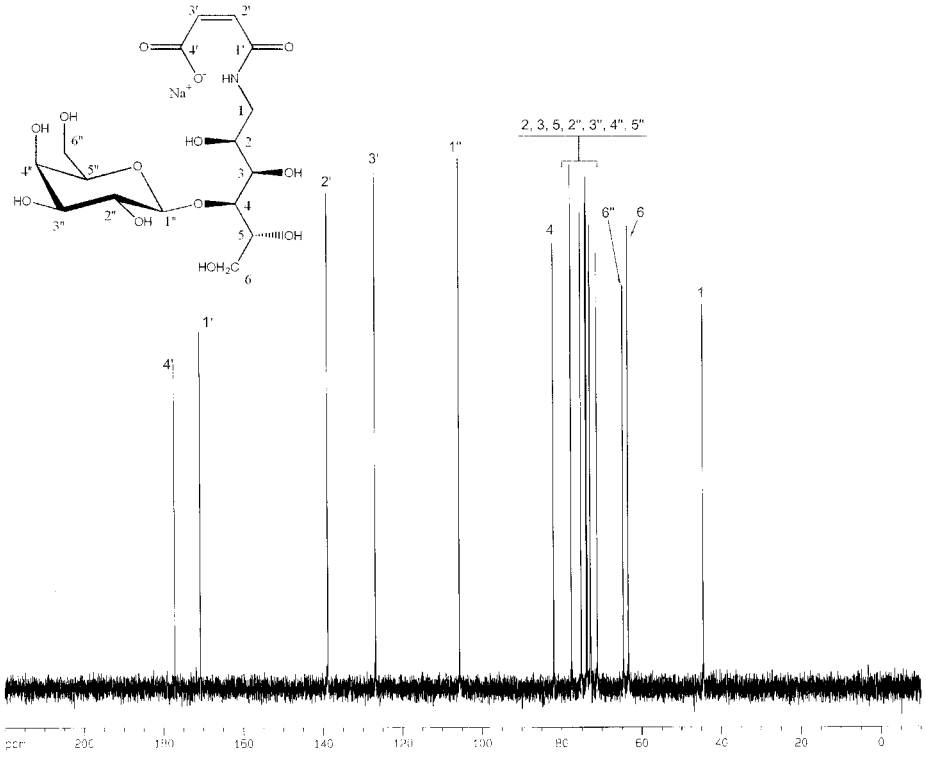

Figure 1. ^{13}C-NMR spectra of N-maleicamido-1-deoxy-lactitol.

will be located. Therefore, at a maximum value of 50 mol% of the sugar carrying units in the copolymers, an alternating constitution can be assumed. Further investigations of these copolymerization systems, which lead to determination of copolymerization parameters are in progress and will be discussed in following publications. The results of this first report show that with increasing amounts of the vinylamide comonomers in the feed, a growing excess of them could be found in the resulting polymers (see m_1 data in Table 2). Comparison of the copolymer composition drives to the fact that N-methylated vinylacetamide (MVAA) seemed to be inserted in a more favorable way than the non-N-methylated VAA. Probably the stronger electron donating character of the MVAA is responsible for this effect. The opposite trend was observed comparing the degrees of polymerization. Using VAA as comonomer led to longer chains than the reaction with MVAA possibly because of steric hindrance.

All polymers were readily water soluble. Intrinsic viscosities of the copolymers (Table 2) increased with the degree of polymerization. It is remarkable that this increase seemed to be independent from variation of neither the different sugar moiety, nor the choice of the comonomer as it can be seen by graphical comparison of intrinsic viscosity with P_w (Fig. 3). The reason for this behavior could be the strong ionic repulsive

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Table 2. Characteristic data of the polymers.

No.	Polymer	$[\eta]$ [mL/g]	M_w [g/mol]	P_w	R_G [nm]	R_η [nm]	m_1
P1	**6a**-co-MVAA	14.9	$1.99*10^4$	100	—	3.6	0.49
P2	**6a**-co-VAA	123.7	$3.20*10^5$	1800	39.9	18.4	0.41
P3	**6b**-co-MVAA	6.3	$1.04*10^4$	53	—	2.2	0.44
P4	**6b**-co-VAA	14.2	$1.54*10^4$	90	—	3.3	0.38
P5	**5**-co-MVAA	59.9	$1.23*10^5$	670	21.9	10.5	0.42
P6	**5**-co-MVAA	113.2	$9.72*10^5$	6000	73.6	25.9	0.32
P7	**5**-coVAA	96.9	$2.33*10^5$	1300	31.5	15.3	0.41
P8	**5**-co-VAA	147.8	$2.97*10^5$	1970	44.4	19.1	0.31
P9	**4**-co-MVAA	147.6	$2.43*10^6$	8600	117.5	38.5	0.50
P10	**4**-co-VAA	208.6	$4.30*10^6$	16900	159.3	52.2	0.45
P11	**4**-co-VFA	120.1	$5.88*10^5$	2500	43.9	22.4	0.42

$[\eta]$: Intrinsic viscosity.
M_w: Weight-average molecular weight.
P_w: Weight-average degree of polymerization.
R_G: Root mean square radius of gyration.
R_η: Hydrodynamic radius.
m_1: Mole ratio of carbohydrate units in the copolymer.

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interactions along the main chain and the relative similar charge density of the polymers. As shown in earlier work,[3] even under the addition of some low molecular weight electrolytes ionic repulsive effects can be observed clearly, where the position of the ionic group close to the backbone chain and shielding effects by adjacent carbohydrate groups have to be considered. In Fig. 4, the root mean square radius R_G, which was obtained from light scattering, and the hydrodynamic radius R_η (Einstein-radius), calculated from the intrinsic viscosity by Eq. 1, for the polymers with $P_w > 1000$ are compared.

$$R_\eta = \sqrt[3]{\frac{3M_w[\eta]}{10\pi N_A}} \tag{1}$$

For each polymer, the value for R_G is significantly higher than for R_H which gives an idea of the coil structure in solution. Such difference means a strong extension of the coil probably caused by ionic interactions of the carboxylic groups along the main chain. This can be expressed with the shape-factor or asymmetry-factor p (Eq. 2).

$$p = \frac{R_G}{R_H} \tag{2}$$

Usually the values of p vary from 0.8 for ideal homogeneous sphere up to >2 for extended coils and ellipsoids.[21] For the copolymers in Fig. 4, the calculated values varied from 2.0–3.1.

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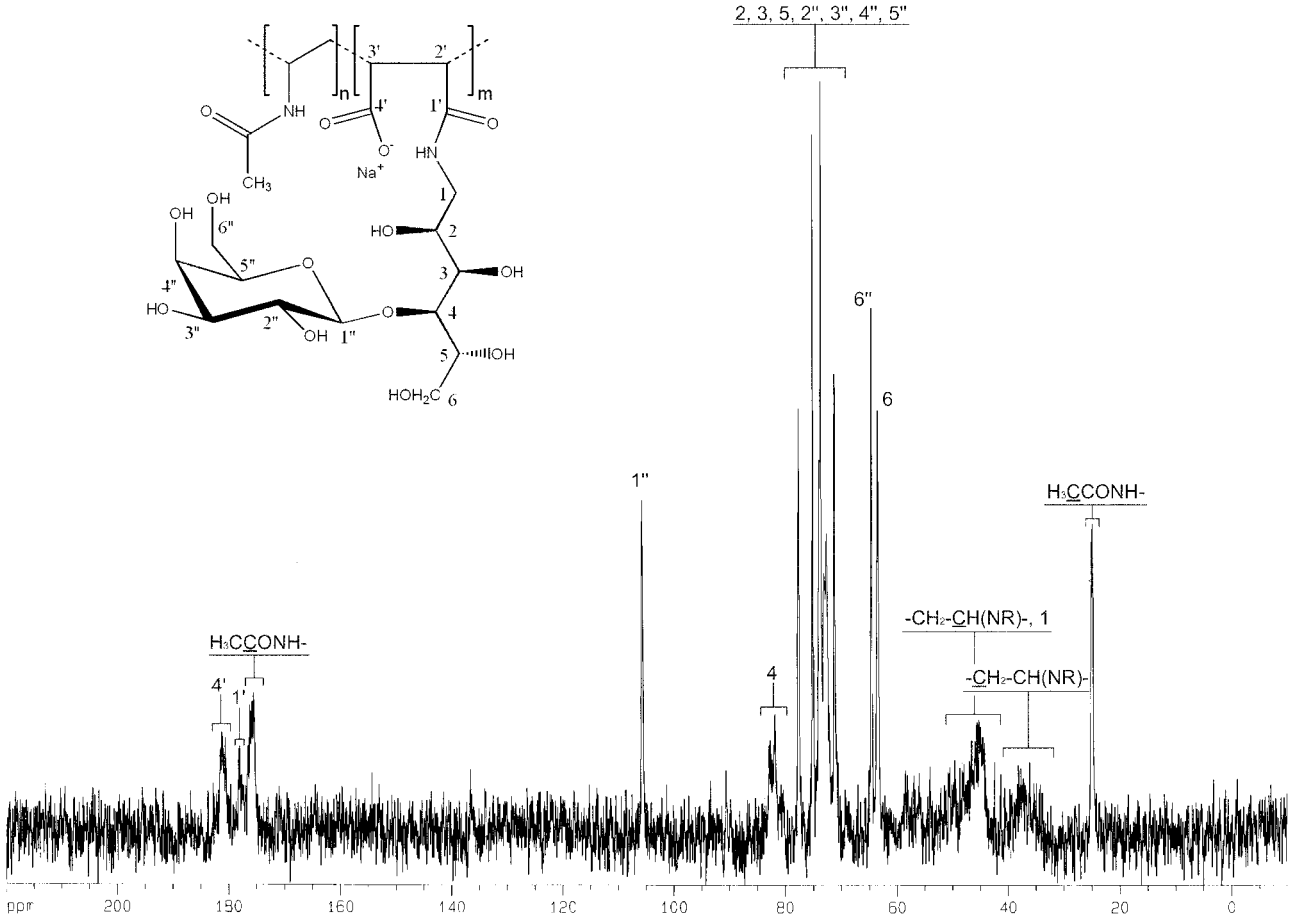

Figure 2. ^{13}C-NMR spectra of Poly(N-maleicamido-1-deoxy-lactitol-*co*-VAA).

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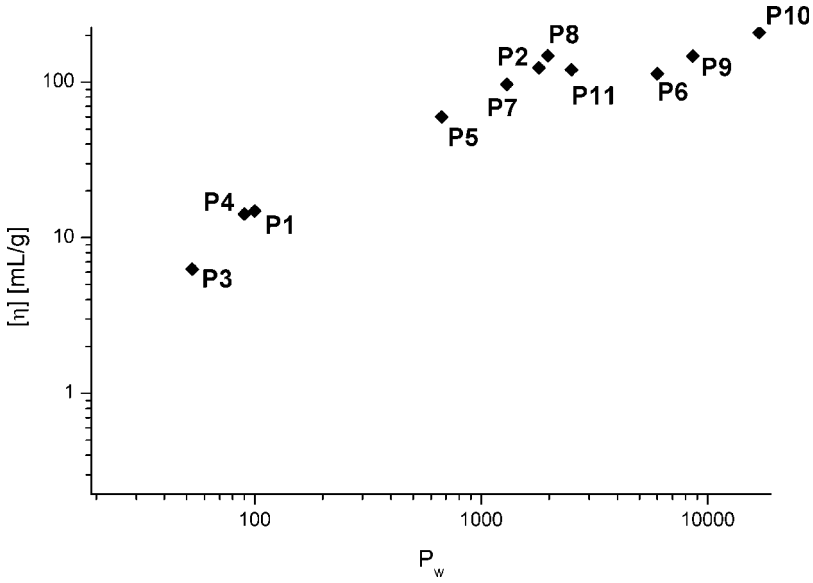

Figure 3. Intrintsic viscosity vs. degree of polymerization.

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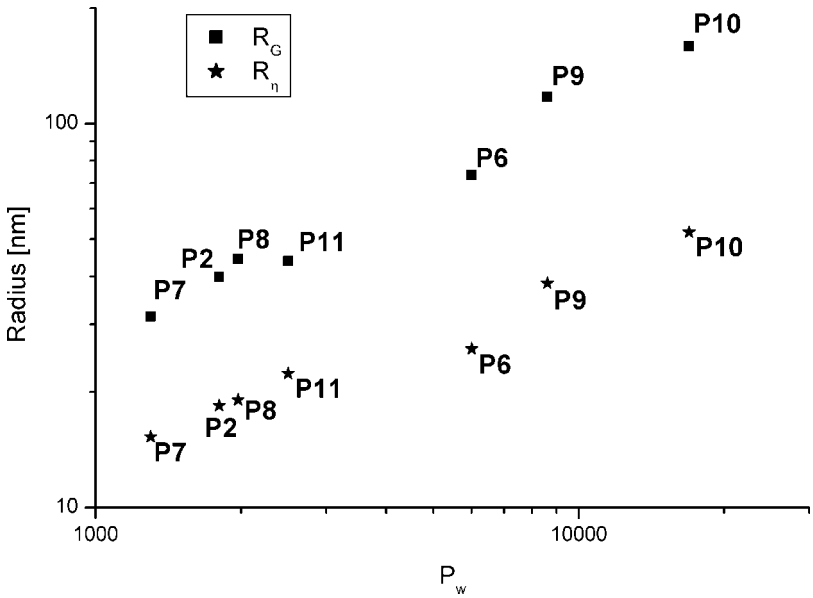

Figure 4. R_G and R_η of the copolymers with high molecular weight vs. degree of polymerization.

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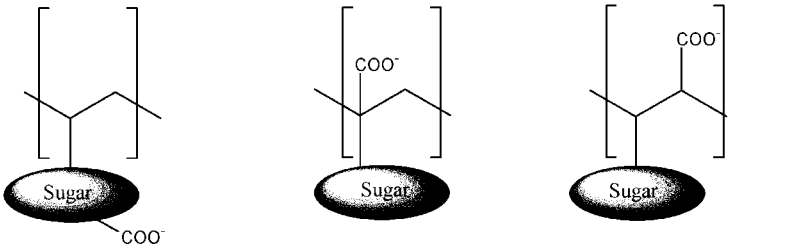

Carboxylated Poly(vinylsaccharide)[3] Poly(1-sugaracrylic acid)[12] Poly(maleicamido saccharide)

Figure 5. Different anionic glycopolymers.

CONCLUSION

New anionic saccharide monomers were synthesized by a convenient conversion of different amino carbohydrates with maleic anhydride in water. These maleicamido saccharides could be easily copolymerized with N-vinylamides to form a new class of anionic glycopolymers. In comparison to former works on this field,[3,12] the usage of maleic anhydride as the polymerizable compound led to a so far unknown position of the carboxy group within the polymer (Fig. 5). Another commonly used anhydride of an unsaturated dicarboxylic acid is itaconic anhydride, which could be used to form similar anionic glycopolymers. First attempts with this reagent showed encouraging results, and will be of interest for following publications.

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