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Comparative Synthesis Studies Towards Methyl and Phenyl 4-Deoxy-β-L-*threo*-hex-4-enopyranosiduronic Acid as Model Compounds of Hexenuronic Acid Moieties in Hardwood Pulps

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Summary: The present study describes two approaches to synthesize hexenuronic acid model compounds in which the xylan backbone is replaced by a simple substituent, either methyl or phenyl. To general pathways towards the two products are offered: the first one, starting from glucuronic acid and involving formation and reopening of the 1,6-lactone, was especially suitable to afford the phenyl derivative **8**. The second one, by contrast, is more appropriate for the methyl compound **12**; it starts from galactose and involves TEMPO oxidation and conversions of the intermediate 1,3-lactone. Both pathways were optimized on a mg scale and subsequently upscaled to afford the targets in gram amounts. The ''detour'' via the methyl glucopyranosiduronate – instead of using the free acid – proved to be crucial in boosting the yield in the elimination step.

Keywords: chromophore formation; hexenuronic acid; pulping; synthesis; xylan

Introduction

4-O-Methylglucuronic acids, $1 \rightarrow 2$-α-glycosidically linked to xylopyranan chains, are key structural motifs in hardwood xylans. Undergoing elimination of methanol under basic conditions, such as those prevailing in kraft pulping, 4-O-methylglucuronic acids are the precursors of 4-deoxy-β-L-threo-hex-4-enopyranosiduronic acid residues (''hexenuronic acids'', HexA) that have evoked a surge of interest since their contribution to the pool of oxidizable structures in pulp (as measured by the kappa number) has been established in the late 1990ies.[1–3] Since then, the role of hexenuronic acids in bleaching, yellowing, and brightness reversion, their removal by acid treatments, and reliable methods for their determination are hot topics in pulping and bleaching as well as in polysaccharide chemistry.

We are interested in the chemistry of HexA from two points of view: the mechanisms of chromophore formation, and their determination in pulps relative to molecular weight – analogous to the profiling of carbonyl and carboxyl groups according to the CCOA[4–5] and FDAM[6] methods.

Working directly with xylan imposes some analytical problems due to the polymeric nature of the material, especially if mechanistic studies are envisioned. Thus, we preferred to use model compounds of HexA, in which the xylan backbone is replaced by a simple substituent. The first obvious choice was a methyl α-glycoside, the second target was the corresponding phenyl α-glycoside. In the case of the latter compound, the UV detectability of all derivatives and intermediates with still intact glycosidic bond was a definite benefit with regard to analytical issues (TLC, HPLC). One requirement set for the

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synthesis approaches was the ability to provide the target compounds in sufficiently large amounts for reactivity and chromophore formation studies, i.e. on a gram scale.

In this paper, we would like to communicate the synthesis of the two HexA model compounds phenyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid (**8**) and methyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid (**12**), the optimization of the two respective approaches, and their comparative evaluation with regard to yield and large-scale applicability.

Results and Discussion

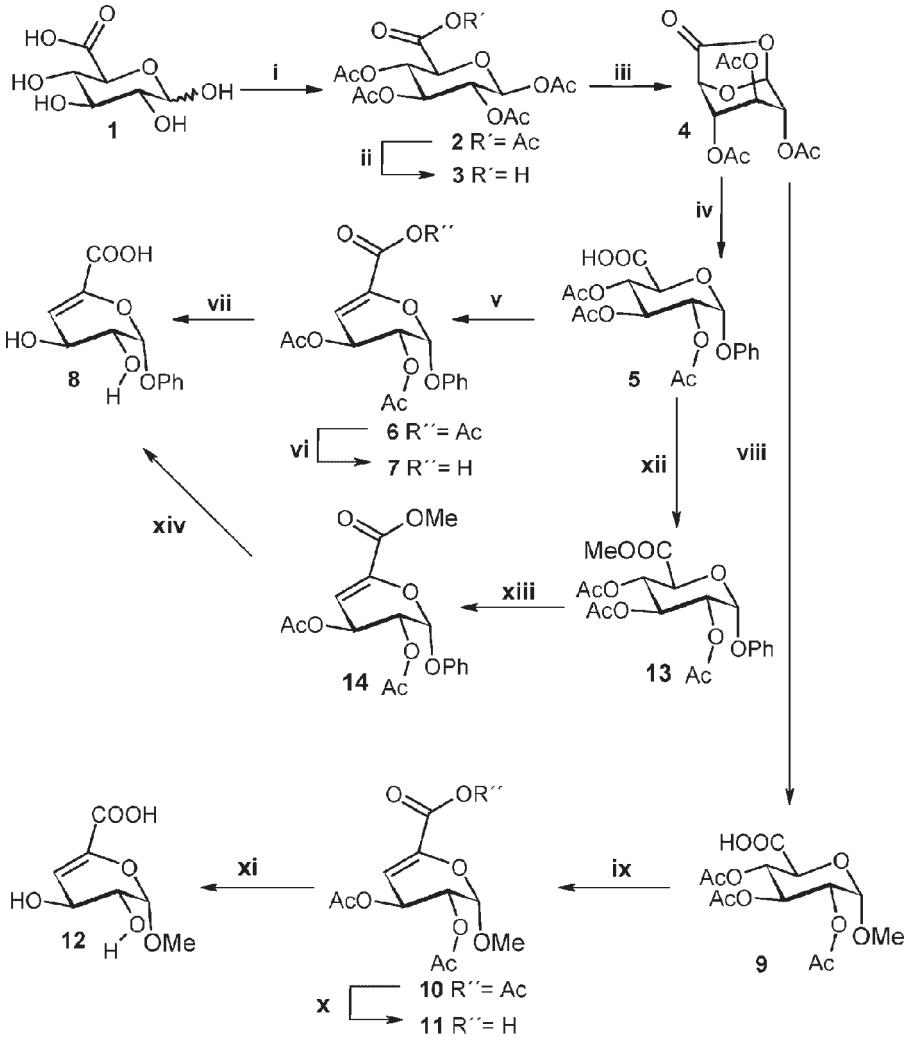
Glucuronic Acid Approach

The first pathway towards the target compounds phenyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid (**8**) and methyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid (**12**) started from commercially available D-glucuronic acid (Scheme 1).[7–8] It comprised seven steps: acetylation, deprotection of the carboxylic function, lactone formation, lactone opening, β-elimination followed by a second deprotection of carboxylic function and finally removal of all protecting groups. The lactone intermediate **4** was prepared without the need for chromatographic separations at any previous stage.

In the first step, D-glucopyranosiduronic acid (**1**) was converted into the peracetylated mixed anhydride **2** by reaction with acetic anhydride in the presence of iodine. Under these conditions, lactone formation is avoided. Subsequent cleavage of the anhydride into peracetylated D-glucopyranosiduronic acid (**3**) proceeded readily in a water-THF mixture (1:2). The subsequent treatment with $SnCl_4$ in dry dichloromethane under argon atmosphere was the key step in the reaction sequence, causing regioselective formation of the 1,6-lactone **4** under inversion of the chair conformation of the pyranose ring. The glycosidation reactions of uronic acid donors is often non-efficient due to their low reactivity. Due to the axial configuration of the oxycarbonyl substituent in position 1 of the lactone, subsequent ring opening by alkoxy- or aroxy- nucleophiles affords glycosides exclusively in α-configuration, i.e. the aglycon being in axial position after another ring inversion.

As lactone-ring opening with alcohols was generally limited by low yields, after extensive screening of nucleophiles and conditions, the usage of phenoxytrimethylsilane and methoxytrimethylsilane, respectively, in the presence of $SnCl_4$ was found to work best leading to higher yields (59%) without loss of stereoselectivity. The following step, elimination of the 4-substituent, was optimized thoroughly as well. Among the bases and conditions tested, working in acetic anhydride-pyridine (1:1) and catalytic amounts of DMAP at room temperature for 3 d was most convincing, although we failed to increase the yield beyond 25%, which clearly made this conversion the yield-limiting step in the sequence. The unfavorable outcome can be explained by the elimination from the disfavored synclinal conformation. However, in order to overcome this problem, an alternative approach included the methylation of **5**[10] which was then subjected to elimination reaction in the presence of DBU.[11] This way, the yield was significantly improved up to 83%. Easy purification and one-step deprotection[9] of the obtained elimination product **14** to the target **8** showed this elimination reaction to be more advantageous and convenient than working with the derivatives of the free glucuronic acid.

In an attempt to avoid this problem, the second synthesis approach (see below) was designed, starting from galacto-configuration which entails more favored antiperiplanar elimination. The resulting protected α,β-unsaturated carboxylic acid was deprotected in two steps: hydrolysis of the mixed anhydride function in neutral aqueous medium and deacetylation by LiOH in MeOH/water. Both Zemplen conditions for deacetylation (cat. NaOMe/MeOH) and the use of alternative alkali hydroxides



i) Ac_2O / I_2, 99%[7] **ii)** H_2O/THF (v/v=1/2), 72%[7] **iii)** $SnCl_4$, CH_2Cl_2, 66%[7]
iv) $SnCl_4$ / CH_2Cl_2, TMSOPh, 59%[8], **v)** Ac_2O/Py/DMAP, r.t., 3d, 20%[7],
vi) H_2O/THF (v/v=1:1), 46%[7], **vii)** LiOH/MeOH/H_2O/THF, 99%[7],
viii) $SnCl_4$ / CH_2Cl_2, TMSOMe, 43%[7], **ix)** Ac_2O/Py/DMAP, r.t., 3d,19%[7],
x) H_2O/THF (v/v=1:1), 79%[7], **xi)** LiOH/MeOH/H_2O/THF, 99%[7], **xii)** TMS-CHN_2
DMAc, r.t., 50%[10], **xiii)** DBU, dry CH_2Cl_2, mol. sieves, 83%[11], **xiv)** LiOH/MeOH/
H_2O/THF, 99%[9]

Scheme 1.
Synthesis of phenyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid (**8**) and methyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid (**12**) starting from glucopyranosiduronic acid (**1**).

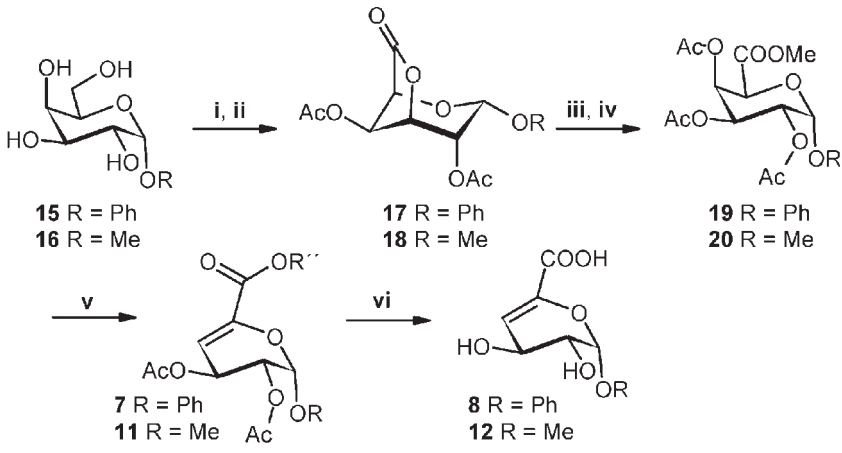
were inferior by giving significantly lower yields.

Galactoside Approach

The alternative approach (Scheme 2) towards the two targets used the respective galactosides (**15**, **16**), which, on the one hand, promised better yields in the elimination step to the unsaturated acid. On the other hand, it involved an initial TEMPO oxidation step with its inherent difficulties to provide the product galactopyranosiduronic acids (**15**, **16**) in analytical purity and free of salts. These problems were overcome by directly subjecting the lyophilized reaction mixture to acetylation, which gave rise to the 1,3-lactones (**17**, **18**) under inversion of the pyran ring. Transesterification with methanol and reacetylation of the liberated 3-OH afforded the peracetylated galactopyranosiduronates (**19**, **20**), which subsequently underwent elimination to the α,β-unsaturated acids **7** and **11**, which proceeded in more than threefold yield as compared to the analogous elimination step in Scheme 1. Final deacetylation provided the model compounds **8** and **12.** The sequence starting from **15**, which had been published previously[9], was optimized towards yields and larger-scale practicability: only one column chromatography step was necessary, a run with 5 gram of starting material was viable, and the final product (**8**) was obtained in 32% overall yield, and in 30% for g-scale preparations.

The same reaction scheme was carried out with the cheaper gluco analogues, but with inferior yield (11%), once more due to yield penalties in the elimination step.

Comparing both approaches, the attractivity of the first one lies in the avoidance of the TEMPO oxidation which might involve problems with regard to purification and work-up, especially when carried out on a gram scale on low-molecular weight carbohydrate compounds. Its drawback are the inferior yields in the elimination step, which are caused by the usage of gluco-derivatives. In the second approach these pros and cons are ''inverted'', the elimination proceeds in acceptable yields due to the galacto-configuration, but a TEMPO oxidation step is contained. In summary,



i) TEMPO oxidation, ii) Ac_2O, NaOAc, iii) MeOH / DBU, iv) Ac_2O/ Py/DBU,
v) DBU/CH_2Cl_2, vi) LiOH/MeOH/H_2O/THF
total yield **12**: 32%

Scheme 2.
Alternative synthesis of phenyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid (**8**) and methyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid (**12**) starting from phenyl α-D-galactoside (**13**) and methyl α-D-galactoside (**14**), respectively.

the sequence in Scheme 1 can be recommended to obtain the phenyl-substituted HexA model compound (phenyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid, **8**), but it gives lower yields for the methyl analogue (methyl 4-deoxy-β-L-*threo*-hex-4-enopyranosiduronic acid, **12**). Inversely, the sequence in Scheme 2 appeared appropriate to synthesize **12**, but less suitable for the phenyl derivative **8**.

Experimental Part

General Methods

Commercial chemicals were of the highest grade available and were used without further purification. Reagent-grade solvents were used for all extractions and workup procedures. Distilled water was used for all aqueous extractions and for all aqueous solutions. n-Hexane, diethyl ether, ethyl acetate and petroleum ether used in chromatography were distilled before use. All reactions involving non-aqueous conditions were conducted in oven-dried (140 °C, overnight) or flame-dried glassware under an argon or nitrogen atmosphere. TLC was performed using Merck silica gel 60 F254 pre-coated plates. Flash chromatography was performed using Baker silica gel (40 μm particle size). All products were purified to homogeneity by TLC/GCMS analysis. The use of brine refers to saturated NaCl(aq). All given yields refer to isolated, pure products.

Melting points, determined on a Kofler-type micro hot stage with Reichert-Biovar microscope, are uncorrected. Elemental analyses were performed at the Microanalytical Laboratory of the Institute of Physical Chemistry at the University of Vienna. All compounds showed satisfactory microanalytical data within the limits of 0.3%.

^{1}H NMR spectra were recorded at 300.13 MHz (400.13 MHz, respectively) for ^{1}H and at 75.47 MHz (100 MHz, respectively) for ^{13}C NMR in $CDCl_3$ as the solvent if not otherwise stated. Chemical shifts, relative to TMS as internal standard, are given in δ values, coupling constants in Hz. ^{13}C peaks were assigned by means of APT, HMQC and HMBC spectra.

In the following, preparation of the common precursor **4** is described in g scale. For the following conversions leading to **8** and **12** the amounts used in the optimized small scale runs are given. Those experiments were repeated with up to the 100fold amount of starting material without yield losses beyond 3%.

Synthesis of Hexenuronic Acid Model Compound 8 (Phenyl Glycoside), According to Scheme 1

D-Glucuronic acid (**1**) (5.0 g, 25.75 mmol) was suspended in acetic anhydride (75 ml) and stirred at 0 °C for 15 min. Iodine (350 mg, 1.65 mmol) was added slowly. The reaction mixture was stirred for 2 h under cooling with an ice/water mixture and 3 h at r. t. Excess acetic anhydride was removed *in vacuo*. After dilution with dichloromethane (70 ml), the organic phase was washed three times with cold $Na_2S_2O_3$ (1 M, 80 ml), dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure. The crude product **2** was used without further purification for the next step (10.34g, 25.57 mmol, 99%). TLC: dichloromethane/methanol = 9:1, R_f = 0.24. ^{1}H NMR (300 MHz): δ 5.82 (d, 1H, $J_{1,2}$ = 6.9 Hz, H-1), 5.39 (t, 1H, J = 9.0, H-4), 5.30 (t, 1H, J = 8.3, H-3), 5.13 (dd, 1H, H-2), 4.33 (d, 1H, H-5), 2.29 (s, 3H, CH_3 in anhydride), 2.15, 2.06, 2.05, 2.04 (4 s, each 3H, acetoxy).

The anhydride **2** (10.34g, 25.57 mmol) was dissolved in a mixture of water and THF (194 ml, 1:2) and stirred overnight. The reaction mixture was concentrated and the product extracted into dichloromethane, dried over $MgSO_4$, filtered and solvent was removed under reduced pressure to give crude product **3** which was used without further purification in the next step (6.70 g, 18.5 mmol, 72%). TLC: dichloromethane/methanol = 3:1, R_f = 0.55. ^{1}H NMR (300 MHz): δ 5.80 (d, 1H, $J_{1,2}$ = 7.5, H-1), 5.31 (m, 2H, H-3 and H-4), 5.15 (m, 1H, $J_{2,3}$ = 9.0, H-2), 4.26

(m, 1H, $J_{4,5} = 9.31$, H-5), 2.13, 2.06, 2.05, 2.04 (4 s, each 3H, acetoxy).

1,2,3,4-Tetra-*O*-acetyl-*β*-D-glucopyranosiduronic acid **3** (6.70 g, 18.5 mmol) was dissolved in dry dichloromethane (235 ml) under argon. $SnCl_4$ (1.12 ml, 0.5 eq) was added and the reaction mixture was stirred overnight at r. t. After completion of the reaction (TLC control), the solution was diluted with dichloromethane (50 ml) and an equal volume of saturated aqueous $NaHCO_3$ solution. The resulting viscous white emulsion was stirred for 30 min and filtered. The organic phase was washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$, and filtered. The solvent was removed in vacuo. Product **4** precipitated and was recrystallized from dichloromethane/hexane to give white crystals (3.71 g, 12.3 mmol, 66%). TLC: hexane/ethyl acetate = 1:3, $R_f = 0.8$. ^{1}H NMR (300 MHz): δ 5.92 (s, 1H, H-1), 4.96 (s, 1H, H-3), 4.82 (s, 1H, H-4), 4.78 (s, 1H, H-2), 4.60 (t, 1H, H-5), 2.19 (s, 6H, 2 acetoxy), 2.10 (s, 3H, acetoxy). ^{13}C NMR: δ 169.3, 169.2, 168.5 (CO in acetoxy), 167.7 (s, COO), 100.4 (s, C-1), 71.1, 68.9, 66.03, 65.8 (each s, C-2 – C-5), 20.7 (d.i.), 20.6 (acetyl).

Lactone **4** (120.89 mg, 0.40 mmol) was dissolved in dry dichloromethane (5 ml) in an atmosphere of argon. $SnCl_4$ (0.2 mmol, 0.5 eq) and TMSOPh (1 mmol, 2.5 eq) were then added and the reaction mixture was left to stir overnight. The mixture was then diluted with CH_2Cl_2 (10 ml) and saturated aqueous $NaHCO_3$ solution (15 ml) and was stirred for 30 min. The mixture was filtered through celite, the layers were separated, and the aqueous layer was acidified with acetic acid. The product was extracted with EtOAc, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel chromatography using chloroform/ethanol/water = 5:2:0.1 (47.6 mg, 0.12 mmol, 30%). TLC: chloroform/ethanol/water = 5:2:0.1. $R_f = 0.35$. ^{1}H NMR (300 MHz): δ 7.23 (dd, 2H, $J = 9.6$, $J = 7.6$, Ph), 7.01 (m, 3H, Ph), 5.82 (d, 1H, $J_{1,2} = 3.5$, H-1), 5.77 (t, 1H, $J = 9.7$, H-3), 5.31 (t, 1H, $J = 9.8$, H-4), 5.06 (dd, 1H, H-2), 4.48 (d, 1H, H-5), 2.06, 2.05, 2.04 (3 s, each 3H, acetoxy).

2,3,4-Tri-*O*-acetyl-1-*O*-phenyl-*α*-D-glucopyranosiduronic acid (**5**) (308.5 mg, 0.78 mmol) was suspended in acetic anhydride/pyridine (1:1, 5.8 ml) and was stirred for 3 days at room temperature in presence of DMAP (5%) as a catalyst. The mixture was concentrated *in vacuo*, diluted with EtOAc, washed with water, dried over $MgSO_4$ and the solvent was evaporated. The crude product was purified by column chromatography ($CHCl_3$/EtOH = 2:1) to give unsaturated anhydride **6** (57.7 mg, 0.152 mmol, 20%). TLC: $CHCl_3$/EtOH = 2:1, $R_f = 0.40$. ^{1}H NMR (400 MHz): δ 7.30 (m, 2H, $J = 8.9$, Ph), 7.09 (m, 3H, Ph), 6.23 (d, 1H, $J_{3,4} = 3.0$, H-4), 5.87 (m, 2H, H-1 and H-3), 5.31 (dd, 1H, H-2), 2.16 (s, 3H, anhydride), 2.13, 2.11 (2 s, each 3H, acetoxy).

Intermediate **6** (57.7 mg, 0.152 mmol) was stirred in water and THF (1:2, 2.90 ml) for 3 h. The solvent was removed under reduced pressure and crude product was purified on a short column of silica gel (hexan/ethyl acetate = 1:4, one drop of AcOH) to give pure **7**, the acetyl-protected form of the target product (23.4 mg, 0.07 mmol, 46%). TLC: EtOAc/MeOH = 3:1, $R_f = 0.47$. ^{1}H NMR (400 MHz, MeOD): δ 7.31 (m, 2H, Ph), 7.10 (m, 3H, Ph), 6.11(d, 1H, $J_{3,4} = 3.2$, H-4), 5.87 (d, 1H, $J_{1,2} = 2.4$, H-1), 5.78 (dd, 1H, $J_{2,3} = 8.0$, H-3), 5.31 (dd, 1H, H-2), 2.10, 2.11 (2 s, each 3H, acetoxy).

Acetylated product **7** (20.1 mg, 0.06 mmol) was suspended in 3.14 ml of aqueous LiOH solution (0.1N in MeOH/H_2O/THF = 2.5/1.0/0.5) at 0 °C (ice bath) and was stirred for 2.5 h. The reaction mixture was diluted with water and acidified to pH 2 using cationic exchange resin Dowex 50 (H^+). The ion exchanger was removed by filtration, the mixture was concentrated and the crystalline precipitated lyophilized to dryness, affording product 8 as white crystals (15.01 mg, 0.0595 mmol, 99.6%). TLC: MeOH/CH_2Cl_2/H_2O = 5:10:1, $R_f = 0.49$. ^{1}H NMR (400 MHz, D_2O): δ 7 · 24 (dd, 2H, $J = 8.0$, J = 8.4, Ph), 7.01 (m, 3H, Ph), 6.03 (d, 1H, $J_{3,4} = 2.8$, H-4), 5.66 (d, 1H, $J_{1,2} = 2.6$, H-1), 4.43 (dd, 1H, H-3), 3.84 (dd, 1H, H-2). ^{13}C NMR (D_2O): δ 166.8 (COOH), 157.4 (Ph, C–O), 142.1 (s, C-5), 131.3, 125.2,

118.8 (Ph, CH), 113.8 (d, C-4), 99.7 (C-1), 71.1 (C-2), 67.2 (C-3).

Synthesis of Hexenuronic Acid Model Compound 12 (Methyl Glycoside), According to Scheme 1

Lactone **4** (241.8 mg, 0.80 mmol) was dissolved in dry (10 ml) in atmosphere of argon. $SnCl_4$ (0.26 mmol, 0.33 eq) and TMSOMe (0.53 mmol, 0.66 eq) were then added, and the reaction mixture was left for stirring overnight. The mixture was then diluted with CH_2Cl_2 (20 ml) and saturated with $NaHCO_3$ solution (30 ml) and stirred for 30 min. The mixture was filtered through celite, the layers were separated, and the aqueous layer was acidified with acetic acid. The product was extracted with EtOAc, dried over $MgSO_4$, and filtered. The reaction mixture was concentrated and the crude product **9** was purified by silica gel chromatography using chloroform/ethanol/water = 5:2:0.1 as eluant (114.1 mg, 0.34 mmol, 43%). TLC: $CHCl_3$/EtOH/H_2O = 5:2:0.1, R_f = 0.31. ^{1}H NMR (300 MHz): δ 8.8–7.9 (br s, 1H, COOH), 5.53 (dd, 1H, $J_{2,3}$ = 10.0, $J_{3,4}$ = 9.5, H-3), 5.22 (dd, 1H, $J_{4,5}$ = 10.1, H-4), 5.06 (d, 1H, $J_{1,2}$ = 3.5, H-1), 4.92 (dd, 1H, H-2), 4.32 (d, 1H, H-5), 3.46 (s, 3H, OCH_3), 2.08, 2.04, 2.02 (3 s, each 3H, acetoxy).

2,3,4-Tri-*O*-acetyl-1-*O*-methyl-α-D-glucopyranosiduronic acid (**9**, 190.4 mg, 0.57 mmol) was suspended in acetic anhydride/pyridine (1:1, 4.25 ml) and stirred for 3 days at room temperature in presence of DMAP (3%) as a catalyst. The solvent was removed *in vacuo*, the remainder diluted with EtOAc, washed with water, and dried over $MgSO_4$. The solvent was evaporated and the crude product was purified by column chromatography ($CHCl_3$/EtOH = 1:1) to afford unsaturated anhydride **10** (33.9 mg, 0.11 mmol, 19%). TLC: $CHCl_3$/EtOH = 1:1, R_f = 0.31. ^{1}H NMR (400 MHz): δ 6.14 (d, 1H, H-4), 5.63 (d, 1H, H-3), 5.29-5.18 (m, 2H, H-1, H-2), 3.53 (s, 3H, OMe), 2.18 (s, 3H, anhydride), 2.12, 2.09 (2 s, each 3H, acetoxy).

Intermediate **10** (33.9 mg, 0.11 mmol) was stirred in water and THF (1:2, 1.70 ml) for 3 h. The solvent was removed under reduced pressure and crude product was purified on a short column of silica gel (hexane/ethyl acetate 1:5, one drop of AcOH) to give pure **11**, the acetyl-protected form of the target product (23.4 mg, 0.07 mmol, 79%). TLC: EtOAc/MeOH = 3:1, R_f = 0.34. ^{1}H NMR (400 MHz, MeOD): δ 6.0 (d, 1H, $J_{3,4}$ = 3.2, H-4), 5.53 (dd, 1H, $J_{2,3}$ = 7.6, H-3), 5.15 (d, 1H, $J_{1,2}$ = 2.4, H-1), 5.12 (dd, 1H, H-2), 3.52 (s, 3H, OCH_3), 2.07, 2.06 (2 s, each 3H, acetoxy).

Acetylated product **11** (9.17 mg, 0.033 mmol) was suspended in 1.43 ml of aqueous LiOH solution (0.1N in MeOH/H_2O/THF = 2.5/1.0/0.5) at 0 °C (ice bath) and was stirred for 2.5 h. The reaction mixture was diluted with water and acidified to pH 2 using ion exchange resin Dowex 50 (H^+). The ion exchanger was removed by filtration, the mixture was concentrated and the precipitate lyophilized to dryness, affording **12** as colorless amorphous solid (6.29 mg, 0.033 mmol, 99%). TLC: MeOH/CH_2Cl_2/H_2O = 5:10:1, R_f = 0.6. ^{1}H NMR (400 MHz, D_2O): δ 5.95 (d, 1H, $J_{3,4}$ = 2.8, H-4), 4.95 (d, 1H, $J_{1,2}$ = 2.8, H-1), 4.21 (dd, 1H, $J_{2,3}$ = 7.6, H-3), 3.72 (dd, 1H, H-2), 3.44 (s, 3H, 1-OMe). ^{13}C NMR (D_2O): δ 166.3 (COOH), 141.1 (C-5), 111.6 (C-4), 100.5 (C-1), 69.6 (C-2), 65.6 (C-3), 56.8 (s, OMe).

Synthesis of Hexenuronic Acid Model Compounds 8 and 12 (Methyl and Phenyl Glycoside), According to Scheme 2

The synthesis was carried based on a previously published sequence.[9] Despite careful optimization, the yields given in the original literature – which seem to be astonishingly high in the light of analogous reactions – could not be reached in our hands. Analytical data of the products and intermediates were consistent with this reference, and are therefore not repeated here. The analytical data of intermediates (**7**, **11**) and products (**8**, **12**) were also identical to those given above for the corresponding compounds obtained according to the sequence in Scheme 1.

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