Monatshefte für Chemie 131, 1197–1205 (2000)

Monatshefte für Chemie
Chemical Monthly

Preparation of Some Benzyl *D*-Glucuronates from 4-Methoxybenzylidene Derivatives of *D*-Glucuronic Acid

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Summary. Because of the low stability of the benzyl ester linkage in benzyl 1,2:3,5-di-O-benzylidene-α-*D*-glucofuranuronate during the removal of the benzylidene groups by acid hydrolysis and/or hydrogenolysis, 4-methoxybenzylidene groups were used to block the free hydroxyl groups of *D*-glucuronic acid. Several benzyl esters of *D*-glucuronic acid were prepared, and their relative rates of acid catalyzed hydrolysis were determined by liquid-chromatographic separation of the reaction mixture and subsequent diode array detection.

Keywords. 1,2-(*R*,*S*):3,5-Di-O-(4-methoxybenzylidene)-α-*D*-glucofuranuronic acids; Benzyl esters of *D*-glucuronic acid; Lignin-carbohydrate complex.

Introduction

Preparation of glucuronic acid esters gives rise to problems concerning the choice of a protection group that can be easily removed under conditions favourable with respect to the stability of the ester bond. Fully acetylated glucuronic acid has been used for the preparation of benzyl esters [1–3] representing ester-like lignin-carbohydrate complexes (LCC), although without any possibility to split off the protecting acetyl groups. Syntheses of glucuronates from benzylated glucuronic acids have been described as well [4]. Acetal derivatives have been used as reactants for the synthesis of several esters of uronic acid [5, 6]. *Sippilä* has exploited the higher reactivity of the carboxylic group of *D*-glucuronic acid to yield benzyl *D*-glucuronate after reaction with a chinonmethide derivative [7].

Results and Discussion

It is well known that some of the acetal protection groups used in saccharide synthesis are removable by means of acid hydrolysis and hydrogenolysis [8]. For certain glucuronic acid benzyl esters, the cleavage of the benzyl ester bond takes place simultaneously under those conditions.

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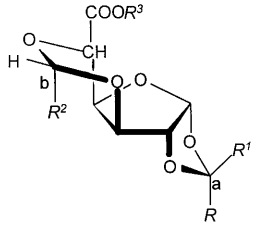

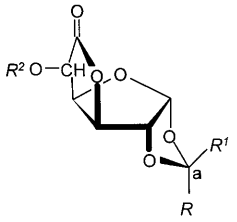

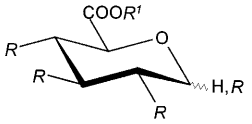

1: $R = R^3 = H$, $R^1 = R^2 = 4\text{-MeOPh}$
2: $R^1 = R^3 = H$, $R = R^2 = 4\text{-MeOPh}$
3: $R = R^2 = H$, $R^1 = 4\text{-MeOPh}$
4: $R^1 = R^2 = H$, $R = 4\text{-MeOPh}$
5: $R = H$, $R^1 = 4\text{-MeOPh}$, $R^2 = Ac$
6: $R = H$, $R^1 = R^2 = 4\text{-MeOPh}$, $R^3 = CH_2Ph$
7: $R = H$, $R^1 = R^2 = 4\text{-MeOPh}$, $R^3 = 4\text{-MeOPhCH}_2$
8: $R = H$, $R^1 = R^2 = 4\text{-MeOPh}$, $R^3 = -CH_2-C_6H_3(OCH_3)-CH_2-C_6H_5$
9: $R = OH$, $R^1 = CH_2Ph$
10: $R = OH$, $R^1 = 4\text{-MeOPhCH}_2$
11: $R = OH$, $R^1 = -CH_2-C_6H_3(OCH_3)-CH_2-C_6H_5$
12: $R = OAc$, $R^1 = CH_2Ph$
13: $R = OAc$, $R^1 = 4\text{-MeOPhCH}_2$
14: $R = OAc$, $R^1 = -CH_2-C_6H_3(OCH_3)-CH_2-C_6H_5$
15: $R = R^2 = Ph$, $R^1 = H$, $R = CH_2Ph$

Scheme 1

The high sensitivity of 4-methoxybenzylidene [9] as well as 4-methoxybenzyl derivatives of methyl α-*D*-glucopyranoside [10] to acidic hydrolysis guided us to prepare the *D*-glucuronic acid di-4-methoxybenzylidene derivative. In comparison with the zinc chloride catalyzed reaction of *D*-glucuronic acid with benzaldehyde rendering only 11% of 1,2:3,5-di-O-benzylidene α-*D*-glucofuranuronic acid [11], the acid catalyzed transacetalization reaction of *D*-glucuronic acid with 4-methoxybenzaldehyde dimethyl acetal gives the 1,2-(*R*,*S*):3,5-di-O-(4-methoxybenzylidene)-α-*D*-glucofuranuronic acids **1** and **2** in satisfactory yields. ^{1}H NMR analysis of the product mixture showed two doublets for H-1 ($\delta = 6.19$ and 6.24 ppm, $J \approx 4$ Hz) and two singlets ($\delta = 5.92$ and 6.11 ppm, H(Ca)) due to two isomers at the acetal centre of the 1,3-dioxolane ring. After two crystallization steps, the isomer with *R* configuration of the 4-methoxyphenyl group on the 1,2-benzylidene ring was obtained. Formation of the isomer **1** reflects initial kinetic control [12]. Its analysis by ^{1}H NMR spectroscopy afforded one doublet ($\delta = 6.19$ ppm, $J \approx 4$ Hz, H-1) and one singlet ($\delta = 5.92$ ppm, H(Ca)). The by-product of this reaction, 1,2-O-(*R*)-(4-methoxybenzylidene)-α-*D*-glucofuranurono-6,3-lactone (**3**), indicated the same orientation of the 4-methoxyphenyl group on the 1,2-benzylidene ring ($\delta = 6.16$ (H-1) and 5.94 (H(C_a)) ppm).

The phenyl group attached to the 1,3-dioxolane ring is the thought to be positioned equatorially in the case of both the (*S*) and the (*R*) phenyl isomer, as studies of benzylidene derivatives of xylose [13] and glucuronic acid [11] have shown. Nevertheless, these compounds can exist with the phenyl ring in either of two slightly distorted conformations (O inside or H inside). Therefore, this assumption does not permit a configurational assignment at the second benzylidene centre. However, resemblance of *Shah*'s H-4 and H-5 signals in the ^{1}H NMR spectra of either isomers of **1** and **2** [11] and a coupling constant of $J_{23} < 1$ confirmed the ''O-inside'' conformation.

Esterification of the carboxylic group of *D*-glucuronic acid with substituted benzyl alcohols by means of an equimolar amount of N,N′-dicyclohexylcarbodiimide [4, 14] in dichloromethane catalyzed by pyridine provided benzyl 1,2-(*R*):3,5-di-O-(4-methoxybenzylidene)-α-*D*-glucofuranuronate (**6**), 4-methoxybenzyl 1,2-(*R*):3,5-di-O-(4-methoxybenzylidene)-α-*D*-glucofuranuronate (**7**), and (3-methoxy-4-benzyloxy) benzyl 1,2-(*R*):3,5-di-O-(4-methoxybenzylidene)-α-*D*-glucofuranuronate (**8**) in high yields. Compound **6** and benzyl 1,2-(*S*):3,5-di-O-benzylidene-α-*D*-glucofuranuronate (**15**) were also prepared by reaction of N,N′-dimethylformamide dibenzyl acetal with the corresponding acids (**1** and 1,2:3,5-di-O-benzylidene-α-*D*-glucofuranuronic acid).

It is commonly known that uronic acid alkyl esters are sensitive to alkaline hydrolysis, but relatively stable towards acids [15]. In the present work, the benzyl ester bond of **15** was found to be approximately equally stable as the 3,5-acetal bond when acid-catalyzed hydrolysis by means of 1 *N* hydrochloric acid at ambient temperature was performed. Under these experimental conditions, the ester bond was hydrolyzed, whereas the benzylidene acetal group in 1,2-position showed a remarkably better stability; the free benzyl *D*-glucuronate could thus not be prepared by hydrolysis of both benzylidene acetal protection groups.

On the basis of the stability comparison of all functional groups in **15**, we found that $k_{\text{1,2-O-benzylidene}} \gg k_{\text{3,5-O-benzylidene}} \approx k_{\text{benzyl ester}}$. Treatment of the diacetal ester **15** with hydrogen did not yield the free benzyl *D*-glucuronate because of simultaneous removal of the benzyl ester group.

To achieve an intermediate blockage of the *D*-glucuronic acid hydroxyl groups, the benzylidene protection groups were changed to 4-methoxybenzylidene groups. Thus, the release of the free benzyl ester was achieved by the decrease of the acetal's stability to acid-catalyzed hydrolysis due to the polar influence of the 4-methoxy group [9, 16]. Acetal groups of the 4-methoxybenzylidene derivatives **6**, **7**, and **8** were removed by relatively mild acid hydrolysis.

The properties of acetal and ester bonds towards acid-catalyzed hydrolysis led to the experimental conditions necessary for the preparation of the corresponding free esters. To use 0.25 *N* hydrochloric acid in aqueous acetonitrile at 40°C for 2 h turned out to work best for removing the 4-methoxybenzylidene groups. Kinetic monitoring of the hydrolyses was carried out at 40°C with aqueous acetonitrile (acetonitrile:water = 3:1), which was 0.25 *N* in hydrochloric acid. The course of the hydrolysis was determined by LC-DAD analysis. It was possible to distinguish the course of hydrolysis of acetal and ester bonds simultaneously.

From Table 1 it can be seen that the 1,2-O-(4-methoxybenzylidene) acetal bond in the ester **6** was hydrolyzed nearly 7.4 times faster and the 3,5-(4-methoxybenzylidene) acetal bond 75 times faster than the ester bond. Comparing the benzyl ester bond stabilities of **6** and **15**, it is obvious that the ester's benzyl part (in contrast to the acetal part) doesn't have a remarkable influence on the rate of hydrolysis. An increase of the hydrolysis rate of the ester bond by a factor of about 1.7 in 4-methoxybenzyl *D*-glucuronate (**10**) compared to **7** and **15** was caused by substitution of ester's acyl part.

The polar effect of the 4-methoxy group of the protonation rate is significant, because the extent of protonation defines the rate of the acid-catalyzed overall hydrolysis mechanism of the fission of benzylidene acetals [10]. On the other hand,

Table 1. Relative rates of hydrolysis of acetal and ester groups of **1**, **3**, **6**, **7**, **8**, **10**, and **15**

	Relative rates		
	1,2-O-ylidene	3,5-O-ylidene	ester
1	7.69	76.92	–
3	7.38	–	–
6	7.38	74.84	1.01
7	7.30	74.73	1.12
8	7.30	74.04	1.13
10	–	–	1.75
15	$\gg$	1.10	1

according to results obtained in our work, this effect is negligible for the hydrolysis of the ester bond the rate of which is predominantly affected by the steric factor in this case, corresponding to the bimolecular mechanism of the acid-catalyzed hydrolysis of certain esters which is accompanied by a molecule of water in the transition state [17].

In conclusion, high yields of benzyl *D*-glucuronates were achieved by the synthesis procedure chosen, *i.e*. transacetalization, esterification, and hydrolysis of the protection groups. 4-Methoxybenzylidene acetals can be utilized as intermediate products of the preparation of acid-labile types of *D*-glucuronates that represent lignin-saccharide model compounds with respect to their ester-bond linkages.

Experimental

General

Melting points were determined on a Kofler hotstage microscope. Optical rotations were measured using a Perkin-Elmer automatic polarimeter model 141. NMR spectra were recorded with a Bruker AM-300 spectrometer. Thin-layer chromatography on silica gel (Merck PF_{254}) coated glass plates was carried out using the systems A (benzene:methanol = 40:1) or B (ethyl acetate:methanol = 10:1). Detection was performed by charring with 5% H_2SO_4 in ethanol. Column chromatography on columns of dry-packed silica gel (product No. 9385, Merck) was carried out using the eluent system A. N,N′-Dicyclohexylcarbodiimide was a commercial product (Fluka). 4-Methoxybenzaldehyde dimethyl acetal was prepared according to Ref. [16]. LC analyses were performed with a HP 1090 Series II liquid chromatograph (Hewlett-Packard, Waldbronn, Germany) equipped with a PV5 ternary solvent-delivery system (SDS) and an injection valve with a 25×10^{-3} mm^3 loop and a built-in diode array detector equipped with a 10 mm flow cell. For single-wavelength monitoring the DA detector was set at 210 mm with a bandwidth of 4 nm. Data from the DA detector were collected and evaluated by the ChemStation software C.03.03 (Hewlett-Packard). The mobile phase consisted of a H_2O/CH_3CN gradient mixture. The gradient started at 70% H_2O and decreased linearly to 0% H_2O after 12 min, was kept at 0% H_2O for 6 min, and returned to 70% H_2O in 1 min. The total run-time was thus 19 minutes; the flow rate was constantly set at 0.4 cm^3/min.

Rate constant measurements

A weighed amount of hydrolyzed compound **1**, **3**, **6**, **7**, **8**, **10**, or **15** (8 mmol) was dissolved in 10 cm^3 acetonitrile. From these stock solutions, 3 cm^3 were placed under a N_2 atmosphere in a thermostat

maintained at 40±0.1°C. When the solution had attained thermostat temperature, 1 cm^3 of 4 *N* aqueous HCl was added (the resulting concentration was 1 *N* HCl in acetonitrile). At intervals, 25×10^{-3} cm^3 portions of the reaction mixture were withdrawn, 0.950 cm^3 acetonitrile were added, the mixture was neutralized with 25 mm^3 1 *N* aqueous NaOH, and cooled to about 0°C. 10×10^{-3} cm^3 samples were used for LC-DAD analyses.

1,2-(R,S):3,5-Di-O-(4-methoxybenzylidene)-α-D-glucofuranuronic acids (**1**, **2**; $C_{22}H_{22}O_9$)

A mixture of 5.0 g *D*-glucuronic acid (25.8 mmol), 5.6 g 4-methoxybenzaldehyde dimethyl acetal (31 mmol), and 0.1 g toluene-*p*-sulfonic acid was stirred at 50°C for 30 min. After this time, the solution was cooled to room temperature, and the resulting yellow syrup was partitioned between 30 cm^3 $CHCl_3$ and 25 cm^3 aqueous $NaHCO_3$. The two layers were separated, and the aqueous phase was extracted with 3×15 cm^3 $CHCl_3$. The organic extracts were dried over Na_2SO_4 and concentrated. A mixture of **1** and **2** was obtained in 85% yield. Recrystallization from ethanol afforded 8.7 g (79%) **1**. The mother liquor was concentrated, and a mixture of the (*R*)/(*S*) isomers was isolated. ^{1}H NMR data: 6.19, 6.24 ppm (two doublets, $J_{12} \approx 4$ Hz, H-1 (*R*)/(*S*)); 5.92, 6.11 ppm (two singlets, H(C_a) (*R*)/(*S*)).

1,2-(R):3,5-Di-O-(4-methoxybenzylidene)-α-D-glucofuranuronic acid (**1**; $C_{22}H_{22}O_9$)

M.p.: 162–164°C; $[\alpha]_D^{20}$ ($CHCl_3$; $c = 0.5$): +70.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 3.79, 3.81 (2s, 2 OCH_3), 4.52 (d, $J_{34} = 2.4$ Hz, H-3), 4.61 (d, $J_{45} < 1.0$ Hz, H-4), 4.71 (d, $J_{23} < 1.0$ Hz, H-2), 5.02 (s, H-5), 5.77 (s, H(C_b)), 5.92 (s, H(C_a)), 6.19 (d, $J_{12} = 3.9$ Hz, H-1), 6.92, 7.42 (2d, H-arom (C_a), H-arom (C_b)) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 55.3, 55.4 (2 OCH_3), 72.3 (C-4), 73.2 (C-5), 77.8 (C-3), 84.6 (C-2), 96.3 (C_b), 104.9 (C_a), 105.0 (C-1), 113.9, 127.6, 129.1, 160.4 (C-arom), 173.1 (C-6) ppm.

1,2-O-(R,S)-(4-Methoxybenzylidene)-α-D-glucofuranurono-6,3-lactones (**3**, **4**; $C_{14}H_{14}O_7$)

A mixture of 1.0 g *D*-glucuronic acid (5.1 mmol), 1.11 g 4-methoxybenzaldehyde dimethyl acetal (6.12 mmol), and 0.1 g toluene-*p*-sulfonic acid was stirred at 50°C for 2 h. After cooling at room temperature, the mixture was diluted with 20 cm^3 $CHCl_3$ (the insoluble *D*-glucuronic acid was removed), and the organic layer was extracted with 10 cm^3 warm H_2O (for removing *D*-glucuronic acid), dried over Na_2SO_4, and concentrated, affording 68% of a mixture of **3** and **4**. Recrystallization from ethyl acetate/light petroleum (b.p.: 60–80°C) gave 0.87 g (58%) **3**. The mother liquor was concentrated, and a mixture of (*R*)/(*S*) isomers was obtained. ^{1}H NMR data: 6.16, 6.23 ppm (two doublets, H-1 (*R*)/(*S*)); 5.92, 6.07 ppm (two singlets, H (C_a) (*R*)/(*S*)).

1,2-O-(R)-(4-Methoxybenzylidene)-α-D-glucofuranurono-6,3-lactone (**3**; $C_{14}H_{14}O_7$)

M.p.: 181–183°C; $[\alpha]_D^{20}$ (MeOH, $c = 0.5$): +58.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 3.81 (s, OCH_3), 4.69 (d, $J_{45} = 4.4$ Hz, H-5), 4.95–5.08 (m, H-2, H-3, H-4), 5.94 (s, H(C_a)), 6.16 (d, $J_{12} = 3.7$ Hz, H-1), 6.93, 7.38 (2d, H-arom (C_a) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 55.3 (OCH_3), 72.5 (C-5), 79.1, 81.8, 83.1 (C-2, C-3, C-4), 104.7 (C_a), 105.1 (C-1), 113.6, 127.3, 128.1, 169.3 (C-arom), 186.8 (C-6) ppm.

5-O-Acetyl-1,2-O-(R)-(4-methoxybenzylidene)-α-D-glucofuranurono-6,3-lactone (**5**; $C_{16}H_{16}O_8$)

0.4 g **3** (1.4 mmol) were acetylated in the usual manner with pyridine and acetic anhydride. After crystallization from ethyl acetate/light petroleum (b.p.: 60–80°C), 0.46 g (98%) **5** were isolated.

M.p.: 115–116°C; $[\alpha]_D^{20}$ ($CHCl_3$, $c = 1.0$): +101.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 2.25 (s, 3H, $OCOCH_3$), 3.82 (s, 3H, OCH_3), 5.01 (d, $J_{23} < 1$ Hz, H-2), 5.05 (d, $J_{34} = 3.1$ Hz, H-3), 5.11 (t, $J_{45} = 4.3$ Hz, H-4), 5.51 (d, H-5), 5.97 (s, H(C_a)), 6.16 (d, $J_{12} = 3.6$ Hz, H-1), 6.90, 7.34 (2d, H-arom (C_a)) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 20.5 ($OCOCH_3$), 55.3 (OCH_3), 70.8 (C-5), 78.6 (C-4), 82.3 (C-3), 83.2 (C-2), 104.8 (C_a), 104.9 (C-1), 113.7, 126.6, 128.7, 160.1 (C-arom), 189.7 (C-6) ppm.

Reaction of acids with N,N′-dimethylformamide dibenzyl acetal

Acid **1** (1 mmol) or 1,2-(*S*):3,5-di-O-benzylidene-α-*D*-glucofuranuronic acid (1 mmol) [11], respectively, was dissolved in 10 cm^3 anhydrous CH_2Cl_2, and 0.33 g N,N′-dimethylformamide dibenzyl acetal (1.2 mmol) were added. The solution was kept at room temperature for 24 h under an N_2 atmosphere. After this time, TLC (system A) showed that the starting material was consumed. The mixture was diluted with 50 cm^3 $CHCl_3$ and washed with 2 × 25 cm^3 H_2O. The organic layer was dried over Na_2SO_4 and concentrated. After recrystallization from methanol, compounds **6** and **15** were obtained.

Benzyl 1,2-(R):3,5-di-O-(4-methoxybenzylidene)-α-D-glucofuranuronate (**6**; $C_{29}H_{28}O_9$)

Yield: 86%; m.p.: 124–126°C; $[\alpha]_D^{20}$ ($CHCl_3$, $c = 1.0$): +53.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 3.81, 3.82 (2s, 2 OCH_3), 4.48 (d, $J_{34} = 2.2$ Hz, H-3), 4.52 (d, $J_{45} < 1.0$ Hz, H-4), 4.67 (d, $J_{23} < 1.0$ Hz, H-2), 4.94 (s, H-5), 5.12, 5.23 (2d, $J_{CH_2} = 11.8$ Hz, $COOCH_2$), 5.75 (s, H(C_b)), 5.87 (s, H(C_a)), 6.17 (d, $J_{12} = 3.9$ Hz, H-1), 6.91, 7.36 (2d, H-arom (C_a), H-arom (C_b)), 7.30–7.48 (m, 5 H-arom) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 55.3, 55.4 (2 OCH_3), 67.5 ($COOCH_2$), 72.5 (C-4), 73.5 (C-5), 77.7 (C-3), 84.2 (C-2), 95.8 (C_b), 104.8 (C_a), 105.0 (C-1), 113.7, 127.7, 128.4, 158.3 (C-arom), 169.0 (C-6) ppm.

Benzyl 1,2-(S):3,5-di-O-benzylidene-α-D-glucofuranuronate (**15**; $C_{27}H_{24}O_7$)

Yield: 88%; m.p.: 126–128°C; $[\alpha]_D^{20}$ ($CHCl_3$, $c = 1.0$): +56.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 4.54 (d, $J_{45} < 1.0$ Hz, H-4), 4.59 (d, $J_{34} = 2.2$ Hz, H-3), 4.78 (d, $J_{23} < 1.0$ Hz, H-2), 4.99 (s, H-5), 5.20, 5.38 (2d, $J_{CH_2} = 12.1$ Hz, $COOCH_2$), 5.78 (s, H(C_b)), 6.14 (s, H(C_a)), 6.24 (d, $J_{12} = 3.6$ Hz, H-1), 7.29–7.50 (m, 15 H-arom) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 67.4 ($COOCH_2$), 72.7 (C-5), 74.4 (C-4), 77.7 (C-3), 84.4 (C-2), 96.3 (C_b), 106.3 (C_a), 105.3 (C-1), 114.7, 126.7, 127.4, 156.3 (C-arom), 168.9 (C-6) ppm.

Reaction of acids with alcohol in presence N,N′-dicyclohexylcarbodiimide; general procedure

Acid **1** (1 mmol) in 10 cm^3 CH_2Cl_2 was added to a mixture of the corresponding alcohol (1 mmol), N,N′-dicyclohexylcarbodiimide (1 mmol), and 0.1 cm^3 dry pyridine in 20 cm^3 CH_2Cl_2 and set aside at room temperature for 2 h. Dicyclohexylurea was filtered off, the solvent was evaporated to dryness, and the residue was crystallized from methanol to yield **6**, **7**, **8**, and **15**.

Benzyl 1,2-(R):3,5-di-O-(4-methoxybenzylidene)-α-D-glucofuranuronate (**6**; $C_{29}H_{28}O_9$)

Yield: 84%; analytical data were in all respects identical with those of the sample described above.

4-Methoxybenzyl 1,2-(R):3,5-di-O-(4-methoxybenzylidene)-α-D-glucofuranuronate (**7**; $C_{30}H_{30}O_{10}$)

Yield: 85%; m.p.: 154–157°C; $[\alpha]_D^{20}$ ($CHCl_3$; $c = 1.0$): +45.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 3.82, 3.83, 3.83 (3s, 3 OCH_3), 4.48 (d, $J_{34} = 2.2$ Hz, H-3), 4.53 (d, $J_{45} < 1.0$ Hz, H-4), 4.68 (d, $J_{23} < 1.0$ Hz, H-2), 4.94 (s, H-5), 5.16, 5.25 (2d, $J_{CH_2} = 11.7$ Hz, $COOCH_2$), 5.75 (s, H(C_b)), 5.86 (s,

H(C_a)), 6.17 (d, $J_{12} = 4.0$ Hz, H-1), 6.90, 7.38 (2d, H-arom (C_a), H-arom (C_b)), 7.28, 7.32 (2d, 4 H-arom) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 55.3, 55.4, 55.8 (3 OCH_3), 67.5 (COO*C*H_2), 72.4 (C-4), 73.5 (C-5), 77.8 (C-3), 84.3 (C-2), 95.7 (C_b), 104.8 (C_a), 104.9 (C-1), 113.7, 127.7, 128.4, 158.3 (C-arom), 169.1 (C-6) ppm.

(3-Methoxy-4-benzyloxy) benzyl 1,2-(R):3,5-di-O-(4-methoxybenzylidene)-α-D-glucofuranuronate (**8**; $C_{37}H_{36}O_{11}$)

Yield: 82%; m.p.: 111–114°C; $[\alpha]_D^{20}$ ($CHCl_3$, $c = 1.0$): +42.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 3.79, 3.82, 3.83 (3s, 3 OCH_3), 4.49 (d, $J_{34} = 2.1$ Hz, H-3), 4.55 (d, $J_{45} < 1.0$ Hz, H-4), 4.68 (d, $J_{23} < 1.0$ Hz, H-2), 4.95 (s, H-5), 5.12, 5.22 (2d, $J_{CH_2} = 12.0$ Hz, $COOCH_2$), 5.15 (s, 4-OCH_2Ph), 5.72 (s, H(C_b)), 5.86 (s, H(C_a)), 6.16 (d, $J_{12} = 4.0$ Hz, H-1), 6.89, 7.35 (2d, H-arom (C_a), H-arom (C_b)), 7.30–7.48 (m, 3 H-arom) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 55.3, 55.4, 56.0 (3 OCH_3), 67.7 (COO*C*H_2), 70.9 (OCH_2Ph), 72.5 (C-4), 73.6 (C-5), 77.6 (C-3), 84.5 (C-2), 95.9 (C_b), 104.7 (C_a), 104.9 (C-1), 113.7, 127.7, 128.4, 149.7, 158.3 (C-arom), 169.1 (C-6) ppm.

Benzyl 1,2-(S):3,5-di-O-benzylidene-α-D-glucofuranuronate (**15**; $C_{27}H_{24}O_7$)

Yield: 85%; analytical data were in all respects identical with those of the sample described above.

Preparation of benzyl D-glucuronates; general procedure

Esters **6**–**8** (0.25 mmol) were dissolved in 4 cm^3 acetone. 1 cm^3 of 1 *N* HCl was added, and the reaction mixture was kept at 40°C for 2 h. The mixture was cooled to room temperature, and the solvent was evaporated to dryness to yield benzyl *D*-glucuronate (**9**), **10**, and (3-methoxy-4-benzyloxy) benzyl *D*-glucuronate (**11**), which were purified by column chromatography (system B). $R_f = 0.20$–0.25 (system B).

Benzyl D-glucuronate (**9**; $C_{13}H_{16}O_7$)

Yield: 80%; syrup; ^{1}H NMR (300 MHz, δ, acetone-d_6): 3.23–4.31 (m, H-2, H-3, H-4, H-5 (α,β)), 4.70 (d, $J_{12} = 7.9$ Hz, H-1β), 5.17–5.20 (4d, $J_{CH_2} = 12.2$ Hz, $COOCH_2$ (α,β)), 5.22 (d, $J_{12} = 4.0$ Hz, H-1α), 6.93–7.25 (m, 10 H-arom) ppm; ^{13}C NMR (75 MHz, δ, acetone-d_6): 67.5, 67.7 (COO*C*H_2 (α,β)), 72.5–77.3 (C-2, C-3, C-4, C-5), 94.1 (C-1α), 98.8 (C-1β), 128.3, 129.4, 130.7, 136.4 (C-arom), 170.3 (C-6) ppm.

4-Methoxybenzyl D-glucuronate (**10**; $C_{14}H_{18}O_8$)

Yield: 75%; syrup; ^{1}H NMR (300 MHz, δ, acetone-d_6): 3.24–4.35 (m, H-2, H-3, H-4, H-5 (α,β)), 3.80 (s, OCH_3), 4.69 (d, $J_{12} = 7.8$ Hz, H-1β), 5.15–5.21 (4d, $J_{CH_2} = 11.8$ Hz, $COOCH_2$ (α,β)), 5.24 (d, $J_{12} = 3.8$ Hz, H-1α), 6.94–7.15 (m, 8 H-arom) ppm; ^{13}C NMR (75 MHz, δ, acetone-d_6): 55.4 (OCH_3), 67.7, 67.9 (COO*C*H_2 (α,β)), 72.3–77.5 (C-2, C-3, C-4, C-5 (α,β)), 94.0 (C-1α), 98.6 (C-1β), 126.8, 127.8, 129.8, 132.4 (C-arom), 170.4 (C-6) ppm.

(3-Methoxy-4-benzyloxy-4) benzyl D-glucuronate (**11**; $C_{21}H_{24}O_9$)

Yield: 78%; syrup; ^{1}H NMR (300 MHz, δ, acetone-d_6): 3.27–4.35 (m, H-2, H-3, H-4, H-5) (α,β)), 3.81 (s, OCH_3), 4.68 (d, $J_{12} = 8.0$ Hz, H-1β), 5.10–5.19 (4d, $J_{CH_2} = 11.9$ Hz, $COOCH_2$ (α,β)), 5.14 (s, 4-OCH_2Ph), 5.26 (d, $J_{12} = 3.9$ Hz, H-1α), 6.98–7.45 (m, 16 H-arom) ppm; ^{13}C NMR (75 MHz, δ,

acetone-d_6): 55.8 (OCH_3), 67.5, 67.7 ($COOCH_2$ (α,β)), 70.8 (OCH_2Ph), 72.2–77.9 (C-2, C-3, C-4, C-5 (α,β)), 94.1 (C-1α), 99.0 (C-1β), 126.3, 127.5, 131.3, 134.8, 137.5 (C-arom), 170.7 (C-6) ppm.

A small sample of **9**, **10**, and **11**, respectively, was peracetylated for the NMR analysis as benzyl 1,2,3,4-tetra-O-acetyl-*D*-glucuronate (**12**), 4-methoxybenzyl 1,2,3,4-tetra-O-acetyl-*D*-glucuronate (**13**), and (3-methoxy-4-benzyloxy) benzyl 1,2,3,4-tetra-O-acetyl-*D*-glucuronate (**14**).

Benzyl 1,2,3,4-tetra-O-acetyl-D-glucuronate (**12**; $C_{21}H_{24}O_{11}$)

Syrup; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 1.78–2.13 (8s, 8 $OCOCH_3$), 4.21 (d, $J_{45} = 9.5$ Hz, H-5β), 4.45 (d, $J_{45} = 10.2$ Hz, H-5α), 5.09–5.29 (m, H-2 (α,β), H-3β, H-4 (α,β)), 5.12–5.20 (4d, $J_{CH_2} = 11.8$ Hz, $COOCH_2$ (α,β)), 5.48 (t, $J_{34} = 9.9$ Hz, H-3α), 5.78 (d, $J_{12} = 7.6$ Hz, H-1β), 6.29 (d, $J_{12} = 3.6$ Hz, H-1α), 7.23–7.41 (m, 10 H-arom) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 20.2–20.7 (8 $OCOCH_3$), 68.0 (C-4), 68.9, 69.1 ($COOCH_2$ (α,β)), 70.2, 70.5 (C-2), 71.9 (C-3), 73.1 (C-5), 88.8 (C-1α), 91.3 (C-1β), 128.6, 129.4, 131.2, 134.5 (C-arom), 167.3–169.4 (C-6 and $OCOCH_3$) ppm.

4-Methoxybenzyl 1,2,3,4-tetra-O-acetyl-D-glucuronate (**13**; $C_{22}H_{26}O_{12}$)

Syrup; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 1.77–2.17 (8s, 8 $OCOCH_3$), 3.82 (s, OCH_3), 4.22 (d, $J_{45} = 9.5$ Hz, H-5β), 4.47 (d, $J_{45} = 10.0$ Hz, H-5α), 5.06–5.31 (m, H-2 (α,β), H-3β, H-4 (α,β)), 5.11–5.19 (4d, $J_{CH_2} = 11.7$ Hz, $COOCH_2$ (α,β)), 5.48 (t, $J_{3,4} = 9.8$ Hz, H-3α), 5.76 (d, $J_{12} = 7.5$ Hz, H-1β), 6.28 (d, $J_{1,2} = 3.6$ Hz, H-1α), 7.17–7.48 (m, 8 H-arom) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 20.1–20.9 (8 $OCOCH_3$), 55.3 (OCH_3), 68.1 (C-4), 68.8, 69.1 ($COOCH_2$ (α,β)), 70.2, 70.4 (C-2), 71.8 (C-3), 73.0 (C-5), 88.9 (C-1α), 91.5 (C-1β), 126.6, 127.6, 128.6, 132.5, 138.5 (C-arom), 167.1–169.8 (C-6 and $OCOCH_3$) ppm.

(3-Methoxy-4-benzyloxy) benzyl 1,2,3,4-tetra-O-acetyl-D-glucuronate (**14**; $C_{28}H_{30}O_{13}$)

Syrup; ^{1}H NMR (300 MHz, δ, $CDCl_3$): 1.72–2.12 (8s, 8 $OCOCH_3$), 3.89 (s, OCH_3), 4.21 (d, $J_{4,5} = 9.4$ Hz, H-5β), 4.48 (d, $J_{45} = 10.0$ Hz, H-5α), 5.06–5.31 (m, H-2 (α,β), H-3β, H-4 (α,β)), 5.11–5.19 (4d, $J_{CH_2} = 12.1$ Hz, $COOCH_2$ (α,β)), 5.12 (s, OCH_2Ph), 5.50 (t, $J_{34} = 9.8$ Hz, H-3α), 5.76 (d, $J_{12} = 7.7$ Hz, H-1β), 6.28 (d, $J_{12} = 3.5$ Hz, H-1α), 712–7.42 (m, 16 H-arom) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$): 20.1–20.8 (8 $OCOCH_3$), 55.8 (OCH_3), 68.0 (C-4), 68.2, 68.5 ($COOCH_2$ (α,β)), 70.1, 70.3 (C-2), 70.9 (OCH_2Ph), 71.7 (C-3), 73.2 (C-5), 88.9 (C-1α), 91.6 (C-1β), 126.3, 127.1, 128.6, 130.4, 132.5, 139.6 (C-arom), 167.0–169.9 (C-6 and $OCOCH_3$) ppm.

Acknowledgements

This work was supported by the Slovak Grant Agency (project No. 2/506098).

References

[1] Imamura T, Watanabe T, Kuwahara M, Koshijima T (1994) Phytochemistry **37**: 1165
[2] Takahashi N, Koshijima T (1988) Wood Sci Technol **22**: 231
[3] Watanabe T, Koshijima T (1988) Agric Biol Chem **52**: 2953
[4] Zissis E, Fletcher HG Jr (1970) Carbohydr Res **12**: 361
[5] Vogel C, Boye H, Kristen H (1990) Journal prakt Chem **332**: 28
[6] Joniak D (1995) Chem Pap **49**: 198
[7] Sippilä J, Brunow G (1991) Holzforschung **45**: 9
[8] De Bedler AN (1965) Adv Carbohydr Chem **20**: 219; De Bedler AN (1977) Adv Carbohydr Chem **34**: 179

[9] Joniak D, Košíková B, Kosáková L (1978) Collection Czechoslov Chem Commun **3**: 769
[10] Joniak D, Košíková B, Kosáková L (1980) Collect Czech Chem Commun **45**: 1959
[11] Shah RH (1970) Carbohydr Res **12**: 43
[12] Al-Jeboury FS, Baggett N, Foster AB, Webber JM (1965) Chem Comm **11**: 223
[13] Ferrier RJ, Hatton LR (1967) Carbohydr Res **5**: 132
[14] Pravdic N, Keglevic D (1965) Tetrahedron **21**: 1897
[15] Lundquist K, Simonson R, Tingsvik K (1983) Svensk Paperstidning **86**: R44
[16] Johansson R, Samuelsson B (1984) J Chem Soc Perkin I, 2371
[17] Ingold CK (1953) Structure and Mechanism in Organic Chemistry. Cornell Univ Press, Ithaca, NY, chap XIV

Received May 22, 2000. Accepted (revised) July 17, 2000