# SYNTHESIS AND ACID-CATALYZED HYDROLYSIS OF SOME 3-(4-METHOXYPHENYL)PROPYL GLUCURONATES

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3-(4-Methoxyphenyl)propyl D-glucuronate, 3-(4-methoxyphenyl)propyl methyl 4-*O*-methyl-α-Dglucopyranosiduronate, 3-(4-methoxyphenyl)propyl 1,2,3,4-tetra-*O*-acetyl-α-D-glucopyranuronate and 3-(4-methoxyphenyl)propyl 1,2-(*S*):3,5-di-*O*-benzylidene-α-D-glucofuranuronate were prepared as a model substances for the ester lignin–saccharide bonds. Rates of acid-catalyzed hydrolysis of the prepared compounds in 1 M HCl in acetonitrile–water 3 : 1 at 20 °C have been measured by LC-DAD analysis and it showed the low stability of the ester bonds towards acid hydrolysis.

**Key words**: Carbohydrates; Glucuronates; Esters; Hydrolysis; Reaction kinetics; Lignins; Uronates; Uronic acids.

The formation and stability of benzyl esters between lignin and polysaccharides during lignin biosynthesis was investigated by examining the reaction between D-glucuronic acid and quinone methide[1] and the first lignin–carbohydrate complex (LCC) benzyl ester model was synthesized[2]. Other studies demonstrated that a part of glucuronic acid residues is esterified in the lignified wood cell walls[3–7]. To the model compounds containing benzyl-type esters of D-glucuronic acid and some benzylalcohols and binding site analysis of ester linkages between lignin and glucuronoxylan[3] the conjugate acid oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and trifluoroacetic acid was applied.

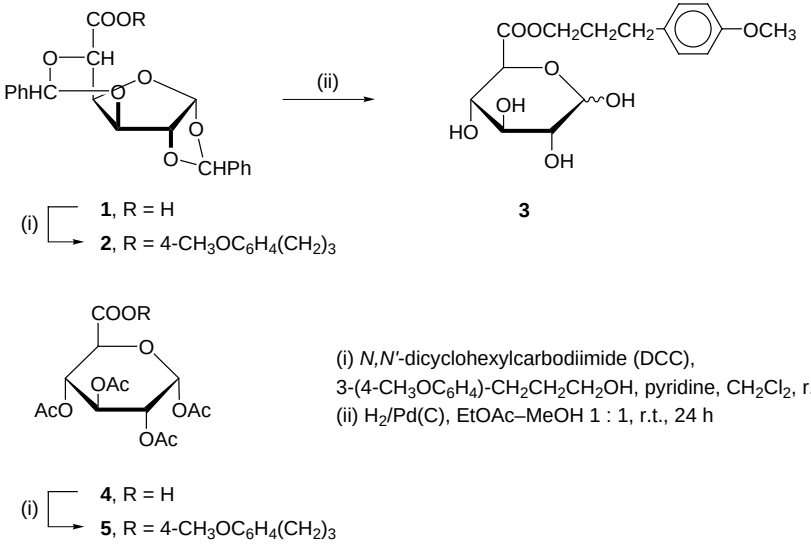
As generally known, some alkyl and benzyl esters of glucuronic acid are sensitive to alkaline hydrolysis, but considerably resistant towards acid-catalyzed hydrolysis[4–7]. Stability of other esters of glucuronic acid with respect to the rate of hydrolysis has not been studied so far.

In connection with the study of the character and properties of the ester bonds between lignin and polysaccharides in wood and model compounds

we prepared (4-alkoxyphenyl)propyl esters of D-glucuronic acid, the aromatic component of which represents one of structural types of the lignin units. It was, therefore, convenient to investigate the stability of the synthesized 3-(4-methoxyphenyl)propyl esters of D-glucuronic acid towards acid catalyzed hydrolysis.

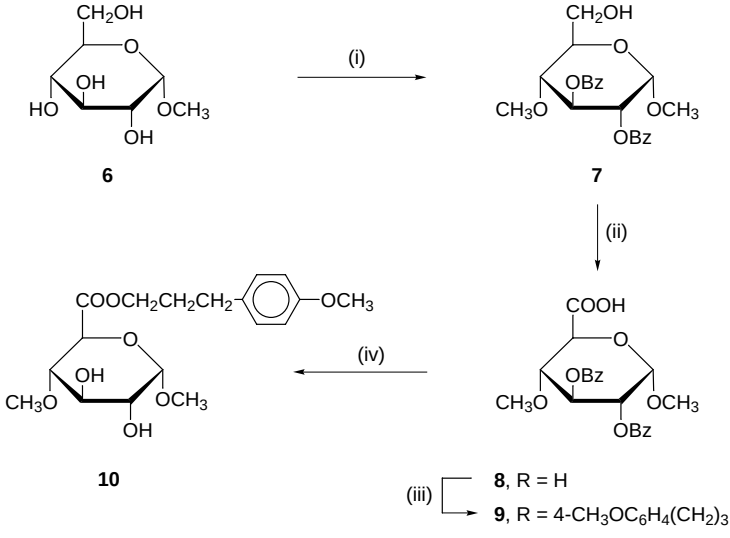
## RESULTS AND DISCUSSION

The compounds examined (Scheme 1) were prepared as described in Experimental. $^1$H NMR analysis of the product mixture after acetalization reaction (preparation of compound **1**) showed two doublets for H-1 (δ 6.27 and 6.23 ppm, $J \approx 4$, H-1 (*S*)/(*R*)) and two singlets (δ 6.18 and 5.94 ppm, 1,2-PhC**H** (*S*)/(*R*)) due to two isomers at the acetal centre of the 1,3-dioxolane ring. Its $^1$H NMR analysis afforded one doublet (δ 6.27 ppm, $J = 3.6$, H-1) and one singlet (δ 6.18 ppm, 1,2-PhC**H**), which were characteristic for isomer with *S* configuration of the phenyl group on the 1,2-benzylidene ring. Isomers with the *S*-phenyl and *R*-phenyl group orientation were distinguished by characteristic different for hydrogens on 1,2-benzylidene ring (0.24 ppm). The steric accessibility of carboxylic groups in substituted D-glucuronic acids [acid **1**, methyl 2,3-di-*O*-benzyl-4-*O*-methyl-α-D-glucopyranosiduronic acid (**8**) and 1,2,3,4-tetra-*O*-acetyl-α-D-glucopyranuronic acid (**4**)] for ester formation were demonstrated: the acids were condensed with




SCHEME 1

3-(4-methoxyphenyl)propanol and corresponding 3-(4-methoxyphenyl)-propyl esters in appropriate yields were obtained. Benzylidene groups of 3-(4-methoxyphenyl)propyl 1,2-(*S*):3,5-di-*O*-benzylidene-α-D-glucofuranuronate (**2**) and benzyl groups of 3-(4-methoxyphenyl)propyl methyl 2,3-di-*O*-benzyl-4-*O*-methyl-α-D-glucopyranosiduronate (**9**) were removed by hydrogenolysis at room temperature and atmospheric pressure in the presence of palladium-on-carbon catalyst in EtOAc–MeOH, affording quantitative yields of 3-(4-methoxyphenyl)propyl D-glucuronate (**3**) and 3-(4-methoxyphenyl)propyl methyl 4-*O*-methyl-α-D-glucopyranosiduronate (**10**). Compound **3** was obtained as mixture α and β anomers, which was confimed by $^{13}C$ NMR data (94.0 C-1α and 98.7 C-1β). Its acetylation afforded of the mixture tetraacetates in ratio the 1 : 2.5. A key step in synthesis of methyl 2,3-di-*O*-benzyl-4-*O*-methyl-α-D-glucopyranosiduronic acid (**8**) was oxidation of the primary hydroxyl group of compound **7** to carboxylic acid (Scheme 2). It was achieved by 2,2,6,6-tetramethylpiperidine-oxy free radical (TEMPO)-catalyzed oxidation (TEMPO, NaOCl, $Bu_4NBr$, KBr,




(i) 1. $PhCH(OCH_3)_2$, 4-toluenesulfonic acid monohydrate, DMF, 60 °C, 2 h; 2. $PhCH_2Cl$, KOH, $H_2O$, 90–100 °C, 2 h; 3. 1M HCl, $(CH_3)_2CO$–$H_2O$ 5 : 1, reflux; 4. $Ph_3CCl$, pyridine, 100 °C, 5 h; MeI, $Ag_2O$, $CH_2Cl_2$, r.t., 24 h; 5. $CH_3COOH$, 90–100 °C, 2 h; (ii) TEMPO, NaOCl (5% aq. solution), KBr, $NaHCO_3$, $Bu_4NBr$, $CH_2Cl_2$, 0 °C, 30 min; (iii) DCC, 3-(4-$CH_3OC_6H_4$)-$CH_2CH_2CH_2OH$, pyridine, $CH_2Cl_2$, r.t., 5 h; (iv) $H_2$/Pd(C), EtOAc–MeOH 1 : 1, r.t., 24 h

SCHEME 2

$NaHCO_3$), which was very effective for selective transformation of hydroxyl group of carbohydrate **7** and quickly produced acid **8** in 80% yield of pure compound after extraction reaction mixture without further purification. $^{13}C$ NMR analysis of acid **8** showed presence new signal in carboxylic region (173.4 ppm) and C-6 primary hydroxyl carbon peak (≈62 ppm) disappeared. Protecting groups of **7** were intacted during reaction[8]. Further, for monitoring acid-catalyzed hydrolysis α-anomer of 1,2,3,4-tetra-*O*-acetyl-D-glucopyranuronic acid (**4**) was esterified (δ 6.41 ppm, H-1). All esterified compounds (**2**, **3**, **5**, **9** and **10**) were characterized by multiplet for terminal $CH_2$ group of alcohol linked to carboxyl of corresponding D-glucuronic acid (δ 4.12–4.30 ppm).

Very few measurements of the hydrolysis rates of uronic acid esters and so the present work was undertaken in an attempt to determine the effect of various configurations on the hydrolysis of 3-(4-methoxyphenyl)propyl D-glucuronates and in particular to compare the rates for differently substituted carboxylic part of esters.

The hydrogen ion-catalyzed hydrolysis and formation of esters have been carefully studied[9–12]. These reactions are reversible, so if the mechanism is known for one of them, that for the reversible reaction can be inferred by means of the principle of microscopic reversibility. For most esters in aqueous acid solution the evidence is consistent with the $A_{AC}2$ pathway, the reaction rates being first order in substrate an in hydrogen ion[9,13,14]. The effects of steric hidrance produced by bulky substituents in the ester should have a serious retarding effect for the $A_{AC}2$ mechanism. Ingold[9] has stressed that the unimolecular mechanism is favoured when the bimolecular mechanism is retarded by steric hindrance.

In the present work quantitative measurements have been made of the rates of acid-catalyzed hydrolysis of the ester bond of the D-glucuronates (**2**, **3**, **5** and **10**) are given in Table I.

The hydrolyses were carried out at 20 °C with 1 M HCl in acetonitrile–water 3 : 1. The course of hydrolysis was checked by LC-DAD analysis. This method seems to be appropriate, because the hydrolysis mixture is analysed by direct introducing the sample and separation of the components. The method gives valuable information about the products of hydrolysis and parent compounds. The results obtained were accurate and reproducible. These observations had ability to distinguish the hydrolysis of acetal and ester bonds in the studied compounds simultaneously. The analytical measurements were treated in standard fashion. The first-order rate constants were calculated from Eq. (*1*):

$$k = \frac{2.303}{t} \log \frac{c_\infty - c_0}{c_\infty - c_t}, \qquad (1)$$

where $c_0$, $c_t$ and $c_\infty$ are concentrations of the reaction solution initially, after a time $t$ and at infinite time.

Concentrations of all the components of the hydrolyzed mixture were measured within the predetermined time scale, the half-life of the reaction and the values were found, using a calibration curve. Rate constants for hydrolysis of 3-(4-methoxyphenyl)propyl D-glucuronates (**2**, **3**, **5** and **10**) were calculated from the increase in concentration of 3-(4-methoxyphenyl)-propanol in the hydrolysis mixture as well as from the decrease in concentration of the starting ester. In the case of benzylidene derivative **2**, the hydrolysis rate of the 3,5-benzylidene group was determined from the increase in concentration benzaldehyde. The hydrolysis of each compound was examined in duplicate and the differences between the mean values of the rate constants never differing more than 3%.

The results from the kinetic study of hydrolysis showed that ester bond of all study compounds hydrolyze under relatively mild conditions at similar rates. The observed small differences are due to the influence of the glucuronic acid moieties only. The effect of substituents in the acyl moiety is evident but small. The highest reaction rate of nonsubstituted ester **3** is only 1.7 times higher than that of the lowest **10**. The experiments indicated that in the case of ester **10** no cleavage of the glycosidic bond occurred. Moreover, the acid-catalyzed hydrolysis of the 1,2-benzylidene acetal group is virtually not observed under the conditions of the ester bond hydrolysis in the benzylidene derivative of α-D-glucofuranuronate **2**, while ester and 3,5-benzylidene acetal group were hydrolyzed approximately at the same

TABLE I
Rates of hydrolysis of 3-(4-methoxyphenyl)propyl esters of D-glucuronic acid at 20 ± 0.1 °C in acetonitrile–water 3 : 1, 1 M HCl

| Compound | $10^6 k$, $s^{-1}$ | Relative rate |
|---|---|---|
| **3** | 15.1 ± 0.02 | 1.70 |
| **2** | 9.28 ± 0.1 | 1.04 |
| **5** | 9.49 ± 0.04 | 1.07 |
| **10** | 8.90 ± 0.03 | 1 |

rates. The slower rate of hydrolysis of 1,2-acetal group and glycoside *vs* ester in studied substance was caused probably slower reaction in the generally accepted mechanism for acetals and glycosides, involves a fast, pre-equilibrium protonation, followed by rate-determining heterolysis of the protonated intermediate to an alcohol and a carbonium ion[10,11].

Steric effects are negligible for the unimolecular decomposition of a protonated ester. The bimolecular reaction is characterized by a small electronic effect of different substituents in the acyl group. The rate of heterolysis of the acyl–oxygen bond in the $A_{AC}1$ mechanism is very sensitive to changes in the electronic structure of the protonated ester. The $A_{AC}2$ mechanism should show specific hydrogen-ion catalyst and not general acid catalysis[15]. The experimental evidence suggests that the bimolecular mechanism is the commonest for the hydrolysis of simple esters in aqueous acid solutions.

## EXPERIMENTAL

Melting points were determined on a Kofler hot-stage. Optical rotations were measured at 20 °C using a Perkin–Elmer automatic polarimeter, model 141; $[\alpha]_D$ values are given in $10^{-1}$ deg cm$^2$ g$^{-1}$. $^1$H NMR and $^{13}$C NMR spectra in chloroform-*d* and acetone-$d_6$ were recorded with a Bruker AM-300 spectrometer ($^1$H at 300 MHz, $^{13}$C at 75 MHz). Chemical shifts, given in ppm (δ-scale) were distinguished by HETCOR. Coupling constants (*J*) are given in Hz. Mass spectra: LC/PB-MS was performed on a HP 5989 B MS Engine apparatus equipped with a HP 59980B PB interface and a "high energy dynode" (HED) detector (Hewlett–Packard). Liquid Chromatography/Particle Beam-Mass Spectrometer was connected with a 50 cm × 0.12 mm i.d. stainless-steel capillary. The system was controlled and data were acquired by a HP MS ChemStation G1034C software running on a Vectra Series 4 computer. Thin layer chromatography on silica gel (Merck $PF_{254}$) coated glass plates was carried out using systems A (ethyl acetate–methanol 10 : 1), B (benzene–ethyl acetate 8 : 1), C (benzene–methanol 40 : 1) as eluents, and column chromatography on columns of dry packed silica gel (product No. 9385, Merck) was carried out using the same systems. Detection was performed by charring with 5% sulfuric acid in ethanol. D-Glucuronic acid, *N*,*N*′-dicyclohexylcarbodiimide and 3-(4-methoxyphenyl)propanol were commercial products (Fluka).

*Solvents and chemicals.* LiChrospher RP-18 analytical column 250 mm long with 4.0 mm i.d., packed with 5 μm octadecylsilica, was used for separation of analytes present in the reaction mixture. HPLC gradient-grade acetonitrile was obtained from Merck (Merck, Germany). Ultra-pure water was prepared by ultrafiltration with a Milli-Q system (Millipore, U.S.A.).

*Instrumentation*. The LC analyses were performed with a HP 1090 Series II liquid chromatograph (Hewlett–Packard, Germany) equipped with a PV5 ternary solvent delivery system (SDS) and injection valve with a 25 μl 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 nm with a bandwidth of 4 nm. During recording absorption spectra the optical slit of diode width was 4 nm and a sampling interval for recording of the spectra was 320 ms with

a peak width of 0.053 min. Absorption spectra were recorded from 190 to 600 nm. Data from the DA detector were collected and evaluated by the ChemStation software C.03.03 (Hewlett–Packard).

The mobile phase consisted of water (A)–acetonitrile (B) gradient mixture. The gradient started at 70% A and decreased linearly to 0% A after 12 min, remained kept at 0% A for 6 min and returned to 70% A in 1 min. The total run-time was thus 19 min, while the flow rate was constantly set at 0.4 ml $min^{-1}$.

*Procedure for rate measurements*. A solutions of the 3-(4-methoxyphenyl)propyl esters of D-glucuronic acid (**2**, **3**, **5** and **10**) were 8 mM in acetonitrile. From this solution, 3 ml were placed under nitrogenous atmosphere in a thermostat maintained at 20 ± 0.1 °C. When the solution had attained thermostat temperature, 4 M aqueous hydrochloric acid (1 ml) was added (resulting concentration of HCl was 1 mol $l^{-1}$). The portions (25 µl) of reaction mixture were subsequently withdrawn according for suitable time schedule and added to acetonitrile (0.950 ml). Afterwords, the solution was immediately neutralized with 1 M aqueous NaOH (25 µl), cooled to about 0 °C. The 10 µl aliquot was used for LC-DAD analyses.

1,2-(*S*):3,5-Di-*O*-benzylidene-α-D-glucofuranuronic Acid (**1**)

Compound **1** was prepared acetalization reaction of D-glucuronic acid with benzaldehyde according to ref.[16] and mixture of isomeric 1,2-(*RS*):3,5-di-*O*-benzylidene-α-D-glucofuranuronic acids were obtained. After two recrystallization steps from chloroform–heptane (5 : 1) acid **1** was obtained. M.p. 186–189 °C, $[\alpha]_D$ +31.0 (*c* 1.0, pyridine); ref.[16] gives m.p. 195–196 °C, $[\alpha]_D$ +48.6 (*c* 1.01, pyridine). $^1$H NMR ($CDCl_3$): 6.27 d, 1 H, *J*(1,2) = 3.6 (H-1); 6.18 s, 1 H (1,2-PhCH); 5.85 s, 1 H (3,5-PhCH); 5.06 s, 1 H (H-5); 4.82 d, 1 H, *J*(2,3) < 1 (H-2); 4.66 d, 1 H, *J*(3,4) = 2.1 (H-3); 4.60 d, 1 H, *J*(4,5) = 1 (H-4). $^{13}$C NMR ($CDCl_3$): 172.6 ($COO^-$); 129.7, 128.4, 127.8, 126.5 (C-arom.); 106.2 (1,2-PhCH); 105.3 (C-1); 96.3 (3,5-PhCH); 84.4 (C-2); 77.7 (C-3); 74.3 (C-4); 73.4 (C-5). For $C_{20}H_{18}O_7$ (370.4) calculated: 64.85% C, 4.90% H; found: 65.00% C, 4.82% H.

3-(4-Methoxyphenyl)propyl 1,2-(*S*):3,5-Di-*O*-benzylidene-α-D-glucofuranuronate (**2**)

A solution of compound **1** (0.18 g, 0.5 mmol) in dichloromethane (10 ml) was added gradually to 3-(4-methoxyphenyl)propanol (0.08 g, 0.5 mmol), *N*,*N*′-dicyclohexylcarbodiimide (0.10 g, 0.5 mmol) and dry pyridine (0.1 ml) in dichloromethane (10 ml), and left standing at room temperature for 5 h. *N*,*N*′-Dicyclohexylurea was filtered off and the solvent was evaporated to dryness. The residue was treated with ether and a second crop of *N*,*N*′-dicyclohexylurea was removed. The etheral filtrate was evaporated and the residue was crystallized from methanol. Yield 0.21 g (80%) of **2**, m.p. 98–100 °C, $[\alpha]_D$ +27.0 (*c* 1.0, chloroform). $^1$H NMR ($CDCl_3$): 7.52–7.43 m, 10 H (H-arom. from acetals); 7.08 d, 2 H, *J* = 8.5 (H-arom. from ester); 6.83 d, 2 H (H-arom.); 6.26 d, 1 H, *J*(1,2) = 3.6 (H-1); 6.17 s, 1 H (1,2-PhCH); 5.87 s, 1 H (3,5-PhCH); 4.96 s, 1 H (H-5); 4.81 d, 1 H, *J*(2,3) < 1 (H-2); 4.63 d, 1 H, *J*(3,4) = 2 (H-3); 4.53 d, 1 H, *J*(4,5) = 1 (H-4); 4.28 m, 2 H ($COOC\mathbf{H}_2CH_2CH_2$); 3.78 s, 3 H ($OCH_3$); 2.67 t, 2 H ($COOCH_2CH_2C\mathbf{H}_2$); 2.03 m, 2 H ($COOCH_2C\mathbf{H}_2CH_2$). $^{13}$C NMR ($CDCl_3$): 168.2 (COOR); 129.7, 128.8, 126.1 (C-arom); 106.1 (1,2-PhCH); 105.3 (C-1); 95.9 (3,5-PhCH); 84.4 (C-2); 76.6 (C-3); 74.8 (C-4); 73.7 (C-5); 65.3 ($COOCH_2CH_2CH_2$); 55.3 ($OCH_3$); 31.2, 30.3 ($COOCH_2CH_2CH_2$). EI-MS, *m/z* (%): 518 (12, $[M]^+$), 369 (20), 263 (35), 166 (15), 148 (38), 121 (29), 105 (27), 77 (18). For $C_{30}H_{30}O_8$ (518.6) calculated: 69.46% C, 5.84% H; found: 69.58% C, 5.76% H.

3-(4-Methoxyphenyl)propyl D-Glucuronate (**3**)

A mixture of **2** (0.16 g, 0.3 mmol) and 10% Pd/C (0.1 g) in ethyl acetate–methanol (1 : 1, 10 ml) was shaken in hydrogen under atmospheric pressure for 24 h. The catalyst was removed by filtration and washed with ethyl acetate. The solvent was removed and the crude product was purified by column chromatography (system A). Yield 0.10 g (100%) of title compound **3** (syrup). $^1$H NMR ($(CD_3)_2CO$): 7.11 d, 4 H, *J* = 8.7 (H-arom.); 6.85 d, 4 H (H-arom.); 5.26 d, 1 H, *J*(1,2) = 3.9 (H-1α); 4.72 d, 1 H, *J*(1,2) = 8.1 (H-1β); 4.32–3.24 m, 8 H (H-2, 3, 4, 5); 4.11 m, 4 H ($COOCH_2CH_2CH_2$); 3.79 s, 6 H ($OCH_3$); 2.61 t, 4 H ($COOCH_2CH_2CH_2$); 1.94–1.88 m, 4 H ($COOCH_2CH_2CH_2$). $^{13}$C NMR ($(CD_3)_2CO$): 170.6 (COOR); 98.7 (C-1β); 94.0 (C-1α); 77.4–72.8 (C-2, 3, 4, 5); 64.7, 64.5 ($COOCH_2CH_2CH_2$); 55.4 ($OCH_3$); 31.5–30.1 ($COOCH_2CH_2CH_2$). EI-MS, *m/z* (%): 342 (20, $[M]^+$), 282 (35), 252 (27), 193 (26), 166 (27), 148 (19), 121 (30), 77 (12). For $C_{16}H_{22}O_8$ (342.4) calculated: 56.11% C, 6.48% H; found: 55.87% C, 5.83% H.

1,2,3,4-Tetra-*O*-acetyl-α-glucopyranuronic Acid (**4**)

Title compound was prepared according to ref.[17], m.p. 151–152 °C, $[\alpha]_D$ +16.5 (*c* 0.5, chloroform); ref.[17] reported m.p. 152–154 °C, $[\alpha]_D^{20}$ +16.3 (*c* 0.5, chloroform).

3-(4-Methoxyphenyl)propyl 1,2,3,4-Tetra-*O*-acetyl-α-D-glucopyranuronate (**5**)

Compound **4** (0.18 g, 0.5 mmol) in dichloromethane (10 ml) was added gradually to 3-(4-methoxyphenyl)propanol (0.08 g, 0.5 mmol), *N*,*N*′-dicyclohexylcarbodiimide (0.10 g, 0.5 mmol) and dry pyridine (0.1 ml) in dichloromethane (5 ml), and left standing at room temperature for 5 h. *N*,*N*′-Dicyclohexylurea was filtered off and the solvent was evaporated to dryness. The residue was treated with ether and a second crop of *N*,*N*′-dicyclohexylurea was removed. The etheral filtrate was evaporated and the residue was purified by column chromatography (system B). Yield 0.21 g (82%) of **5** (syrup), $[\alpha]_D$ +56.0 (*c* 1.0, chloroform). $^1$H NMR ($CDCl_3$): 7.09 d, 2 H, *J* = 8.6 (H-arom.); 6.83 d, 2 H (H-arom.); 6.41 d, 1 H, *J*(1,2) = 3.6 (H-1); 5.55 t, 1 H, *J*(3,4) = 9.9, *J*(2,3) = 9.8 (H-3); 5.28 t, 1 H, *J*(3,4) = 9.9, *J*(4,5) = 10.0 (H-4); 5.12 dd, 1 H, *J*(2,3) = 9.8 (H-2); 4.42 d, 1 H, *J*(4,5) = 10.0 (H-5); 4.12 m, 2 H ($COOCH_2CH_2CH_2$); 3.78 s, 3 H ($OCH_3$); 2.62 t, 2 H ($COOCH_2CH_2CH_2$); 2.18, 2.11, 2.04, 2.01 4 × s, 4 × 3 H (4 × $OCOCH_3$); 1.93 m, 2 H ($COOCH_2CH_2CH_2$). $^{13}$C NMR ($CDCl_3$): 170.0 (COOR); 169.5–166.8 ($OCOCH_3$); 132.7, 129.2 (C-arom.); 88.8 (C-1); 73.1 (C-5); 72.0 (C-3); 70.6 (C-2); 69.1 ($COOCH_2CH_2CH_2$); 68.9 (C-4); 55.2 ($OCH_3$); 30.9, 30.1 ($COOCH_2CH_2CH_2$); 20.8, 20.6, 20.5, 20.3 (4 × $OCOCH_3$). EI-MS, *m/z* (%): 510 (17, $[M]^+$), 314 (19), 289 (40), 215 (18), 166 (29), 148 (35), 121 (21), 43 (34). For $C_{24}H_{30}O_{12}$ (510.5) calculated: 56.44% C, 5.93% H; found: 56.58% C, 5.96% H.

Methyl 2,3-Di-*O*-benzyl-4-*O*-methyl-α-D-glucopyranoside (**7**)

The title compound was prepared according refs[18–21], starting from methyl α-D-glucopyranoside (**6**) in six steps in overall yield 31% (syrup), $[\alpha]_D$ +67.0 (*c* 1.0, chloroform).

Methyl 2,3-Di-*O*-benzyl-4-*O*-methyl-α-D-glucopyranosiduronic Acid (**8**)

To solution of **7** (0.39 g, 1 mmol) in dichloromethane (2 ml) containing TEMPO (2,2,6,6-tetramethylpiperidin-1-oxyl, 1 mg) a solution of saturated aqueous sodium hydrogen-

carbonate (2 ml) containing potassium bromide (11 mg) and tetrabutylammonium bromide (15 mg) was added. The mixture was cooled to 0 °C and solutions of 1.3 M sodium hypochlorite (3 ml) and sodium hydrogencarbonate (1 ml) were added dropwise over 30 min. The organic layer washed with water (5 × 10 ml). The combined aqueous extracts were acidified with 1 M hydrochloric acid and extracted with ethyl acetate (3 × 15 ml), dried and concentrated. Yield 0.32 g (80%) of **13** (syrup), $[\alpha]_D$ +39.0 (*c* 1.0, chloroform). $^1$H NMR ($CDCl_3$): 7.36–7.25 m, 10 H (H-arom.); 4.96–4.60 4 × d, 4 H, *J* = 10.9 (2 × $PhCH_2$); 4.81 d, 1 H, *J*(1,2) = 3.6 (H-1); 4.11 d, 1 H, *J*(4,5) = 10.1 (H-5); 3.90 t, 1 H, *J*(2.3) = 9.2, *J*(3,4) = 9.3 (H-3); 3.54 s, 3 H (4-$OCH_3$); 3.51 dd, 1 H, *J*(2,3) = 9.2 (H-2); 3.44 dd, 1 H, *J*(4,5) = 9.3 (H-4); 3.39 s, 3 H (1-$OCH_3$). $^{13}$C NMR ($CDCl_3$): 173.4 (COOR); 137.7–127.6 (C-arom.); 98.6 (C-1); 81.2, 81.1 (C-3, 4); 78.9 (C-2); 75.3, 73.6 (2 × $PhCH_2$); 69.4 (C-5); 60.8 (4-$OCH_3$); 55.7 (1-$OCH_3$). For $C_{22}H_{26}O_7$ (402.4) calculated: 65.64% C, 6.52% H; found: 65.85% C, 6.76% H.

3-(4-Methoxyphenyl)propyl Methyl 2,3-Di-*O*-benzyl-4-*O*-methyl-α-D-gluco-pyranosiduronate (**9**)

Compound **8** (0.2 g, 0.5 mmol) in dichloromethane (10 ml) was added gradually to 3-(4-methoxyphenyl)propanol (0.08 g, 0.5 mmol), *N*,*N*′-dicyclohexylcarbodiimide (0.10 g, 0.5 mmol) and dry pyridine (0.1 ml) in dichloromethane (5 ml), and left standing at room temperature for 5 h. *N*,*N*′-Dicyclohexylurea was filtered off and the solvent was evaporated to dryness. The residue was treated with ether and a second crop of *N*,*N*′-dicyclohexylurea was removed. The etheral filtrate was evaporated and the residue was purified by column chromatography (system B). Yield 0.22 g (78%) of **9** (syrup), $[\alpha]_D$ +22.0 (*c* 1.0, chloroform). $^1$H NMR ($CDCl_3$): 7.39–7.21 m, 10 H (2 × $C_6\mathbf{H}_5CH_2$); 7.09 d, 2 H, *J* = 8.6 (H-arom.); 6.83 d, 2 H (H-arom.); 4.94–4.61 4 × d, 4 H, *J* = 12.3 (2 × $PhCH_2$); 4.59 d, 1 H, *J*(1,2) = 3.5 (H-1); 4.19 m, 2 H ($COOC\mathbf{H}_2CH_2CH_2$); 4.07 d, 1 H, *J*(4,5) = 10.1 (H-5); 3.87 t, 1 H, *J*(2.3) = 9.2, *J*(3,4) = 9.3 (H-3); 3.78 s, 3 H ($\mathbf{H}_3COC_6H_4$); 3.53 dd, 1 H, *J*(2,3) = 9.6 (H-2); 3.49 s, 3 H (4-$OCH_3$); 3.42 dd, 1 H, *J*(4,5) = 10.2 (H-4); 3.41 s, 3 H (1-$OCH_3$). $^{13}$C NMR ($CDCl_3$): 169.8 (COOR); 137.9, 129.8, 128.5, 127.7 (C-arom.); 98.8 (C-1); 81.4, 81.3 (C-3, 4); 79.1 (C-2); 75.8, 73.6 (2 × $PhCH_2$); 70.1 (C-5); 64.9 ($COOCH_2CH_2CH_2$); 60.7 (4-$OCH_3$); 55.7 (1-$OCH_3$); 55.2 ($H_3COC_6H_4$); 31.0, 30.3 ($COOCH_2CH_2CH_2$). For $C_{32}H_{38}O_8$ (550.6) calculated: 69.78% C, 6.97% H; found: 69.98% C, 6.84% H.

3-(4-Methoxyphenyl)propyl Methyl 4-*O*-Methyl-α-D-glucopyranosiduronate (**10**)

A mixture of **9** (0.16 g, 0.3 mmol) and 10% Pd/C (0.1 g) in ethyl acetate–methanol (1 : 1, 20 ml) was shaken in hydrogen under atmospheric pressure for 24 h. The catalyst was removed by filtration and washed with ethylacetate. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (system C). Yield 0.11 g (100%) of **10** (syrup), $[\alpha]_D$ +86.0 (*c* 0.5, chloroform). $^1$H NMR ($CDCl_3$): 7.09 d, 2 H, *J* = 8.4 (H-arom.); 6.83 d, 2 H (H-arom.); 4.82 d, 1 H, *J*(1,2) = 3.7 (H-1); 4.25 m, 2 H ($COOC\mathbf{H}_2CH_2CH_2$); 4.07 d, 1 H, *J*(4,5) = 9.8 (H-5); 3.79 s, 3 H ($\mathbf{H}_3COC_6H_4$); 3.72 t, 1 H, *J*(3,4) = *J*(2,3) = 9.4 (H-3); 3.59 dd, 1 H, *J*(2,3) = 9.4 (H-2); 3.52 s, 3 H (4-$OCH_3$); 3.46 s, 3 H (1-$OCH_3$); 3.40 dd, 1 H, *J*(3,4) = 9.2, *J*(4,5) = 9.5 (H-4). $^{13}$C NMR ($CDCl_3$): 169.6 ($COO^-$); 132.7, 130.9 (C-arom.); 99.4 (C-1); 80.8 (C-4); 74.5 (C-3); 72.1 (C-2); 70.2 (C-5); 65.0 ($COOCH_2CH_2CH_2$); 60.5 (4-$OCH_3$); 55.8 (1-$OCH_3$); 55.3 ($H_3COC_6H_4$); 31.1, 30.2 ($COOCH_2CH_2CH_2$). EI-MS, *m/z* (%): 370 (70, $[M]^+$), 321 (15), 251 (22), 222 (17), 166 (35),

148 (28), 121 (21), 77 (14). For $C_{18}H_{26}O_8$ (370.4) calculated: 58.33% C, 7.15% H; found: 58.58% C, 6.96% H.

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