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# CHROMIC ACID OXIDATION IN THE SYNTHESIS OF URONIC ACIDS. USE OF THE *O*-LEVULINOYL GROUP TO MINIMIZE ACYL MIGRATION

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ABSTRACT

In the chromate oxidation of a partially acylated sugar derivative to form the corresponding uronic acid, acyl migration to the primary alcohol group is a frequent cause of interference. In contrast to more commonly employed ester substituents, the *O*-levulinoyl group is far less prone to migration during oxidations with Jones reagent (chromic–sulfuric acids). Examples described here include levulinoyl at O-5 of acyclic and furanose derivatives, and both *eq* and *ax* O-4 of pyranose derivatives. It is also shown that, because of the acidity of the Jones reagent, use of the *O*-levulinoyl group, in combination with a primary *p*-anisyldiphenylmethyl substituent, permits sequential rapid hydrolysis of the latter and oxidation of the newly exposed alcohol group, which favors high overall yields. In contrast to its immobility in these oxidation reactions, when the levulinoyl group is on O-2 of an aldosyl bromide, it participates in 1,2-orthoester formation as rapidly as *O*-acetyl. The 2,3,4,6-tetraacetate of either anomer of methyl D-glucopyranoside is oxidized to a uronic acid in moderate yield, by chromic acid in 5:1 acetic acid–water.

## INTRODUCTION

Methods[1–3] for the oxidative conversion of aldosides into the corresponding uronic acid glycosides are of prime importance in the synthesis of oligosaccharides structurally related to many polysaccharides, including the glycosaminoglycans. Oxidation of the primary alcohol group of an unprotected aldoside may be effected selectively in some instances, most notably[4] with oxygen and a platinum catalyst. Such oxidants as chromate or permanganate are used with appropriately substituted derivatives in which only the primary alcohol group is unprotected. In applying chromate oxidation to prepare uronic acids from some partially acetylated compounds, acyl migration was found to interfere with the intended course of the reaction, as has been observed[5,6] in a number of other reactions of partially esterified carbohydrates. However, this problem was largely eliminated by replacement of the migrating *O*-acetyl substituents with *O*-levulinoyl groups, as reported here. Other aspects of the oxidation and acyl-migration reactions are also described.

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## RESULTS AND DISCUSSION

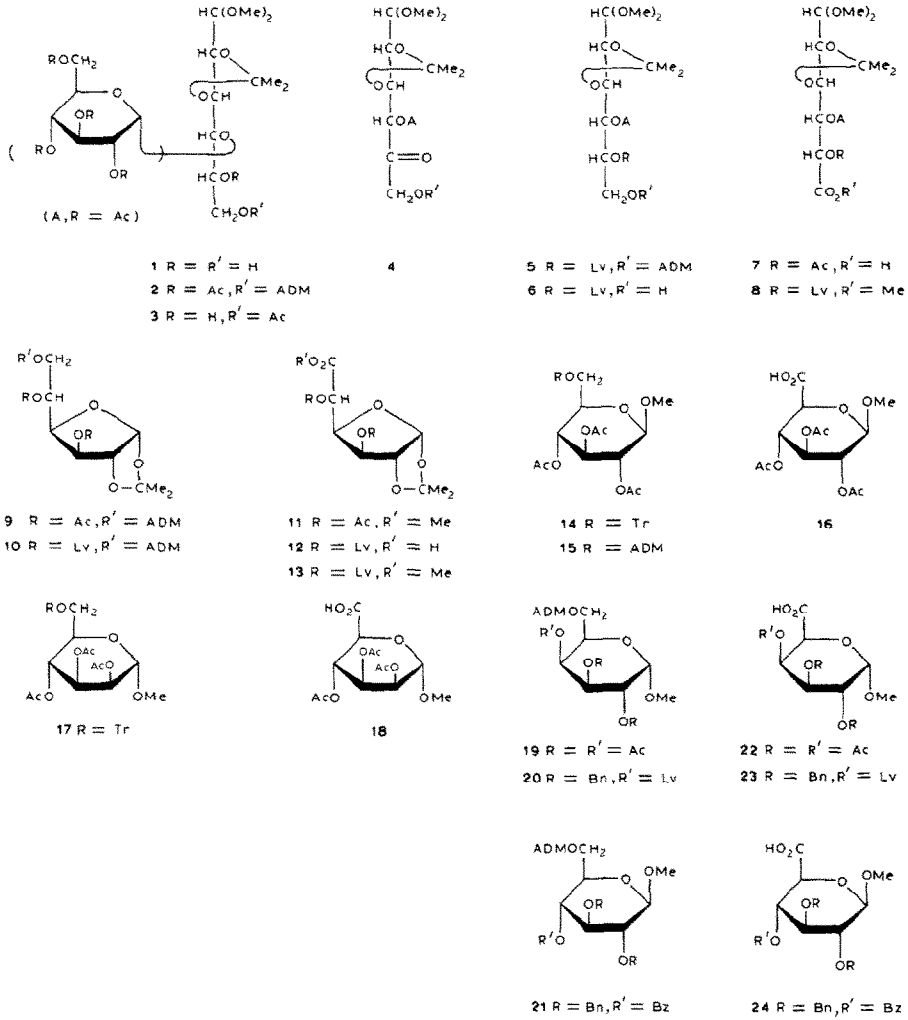
During experiments[7] designed to transform maltose into disaccharides structurally related to heparin and heparan sulfate, the acyclic acetal derivative **1** was obtained. In attempting to prepare the corresponding pseudoaldobiouronic acid, through oxidation of the primary alcohol group of **1**, the 6-*O*-*p*-anisyldiphenylmethyl (ADM) derivative[8] was formed and then acetylated at OH-5, to yield **2**. However, removal of the ADM substituent with aqueous acetic acid, prior to the oxidation step, was accompanied by migration of the 5-*O*-acetyl group to O-6, giving **3**. These changes were evident from the fact that the H-6,6′ signals of the latter were 0.6 p.p.m. downfield, and its H-5 signal 1.2 p.p.m. upfield, of their positions relative to those in the spectrum of **2**. Also consistent with structure **3** was its smooth oxidation by pyridinium dichromate to ketone **4**, the $^{13}C$ spectrum of which exhibited a characteristic signal at $\delta$ 200.4, and downfield shifts of 3 and 6 p.p.m., respectively, for its C-4 and C-6 resonances, relative to those of **3**.

To test the possibility that the rate of hydrolysis of the ADM group of **2** might substantially exceed the rate of subsequent migration by the 5-*O*-acetyl group, and permit oxidation directly to **7**, compound **2** was treated with the strongly acidic Jones reagent[9] (chromium trioxide–sulfuric acid in aqueous acetone). Acid **7** was, indeed, formed, although in admixture with other products, including **3**, and it was isolated in a yield of only 30%. A slightly higher yield (47%) of uronic acid was obtained from the hydrolysis–oxidation of 3,5-di-*O*-acetyl-6-*O*-*p*-anisyldiphenylmethyl-1,2-*O*-isopropylidene-$\alpha$-D-glucofuranose (**9**) with the Jones reagent (3 h, 0°), furnishing **11**. The corresponding 5-*O*-acetyl-3-*O*-benzyl derivative had been obtained[10] similarly in 51% yield. In all three instances, it is likely that migration of the 5-*O*-acetyl group to O-6 was a yield-limiting factor.

The levulinate ester group[11,12] has rarely been used[12,13] as a carbohydrate substituent. It is readily introduced by the use of levulinic anhydride or of levulinic acid and *N,N*-dicyclohexylcarbodiimide, and offers the advantage[11,12] of its facile removal in the presence of other ester groups (*O*-acetyl, *O*-benzoyl) by the action of hydrazine. For the present purpose, it was found to be more suitable than *O*-acetyl as a blocking group for OH-5, because it was less prone to migration.

Formation of the 5-*O*-levulinoyl derivative corresponding to **2**, namely **5**, was evidenced by the appearance of characteristic n.m.r. methyl and methylenic $^1H$ resonances as well as the ketone ($\delta$ 206) and ester ($\delta$ 173) $^{13}C$ resonances. Acid-catalyzed removal of the ADM group of **5** afforded **6**. The fact that the levulinoyl group was retained at O-5 was apparent from the strongly deshielded location of the H-5 signal ($\delta$ 5.1), the upfield location of the H-6,6′ signals ($\delta$ 3.83–4.05), and the detection of coupling between H-6 and a hydroxyl proton. Oxidation of **6** with pyridinium dichromate in the presence[14] of acetic anhydride afforded the pseudoaldobiouronic acid, isolated as its methyl ester (**8**).

Another example that demonstrated the lesser propensity of the levulinoyl group to migrate from O-5 to primary O-6 was found in the combined hydrolysis–

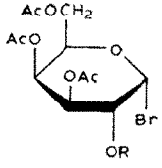



oxidation reaction of the 6-*O*-*p*-anisyldiphenylmethyl-3,5-di-*O*-levulinoyl derivative **10**. In marked contrast to the low yield of uronic acid (47%, identified as methyl ester **11**) obtained with its 3,5-di-*O*-acetyl analog (**9**), compound **10** was converted by chromic acid (Jones) oxidation (3 h, 0°) into **12** in 85% yield, the product being characterized as its methyl ester **13**.

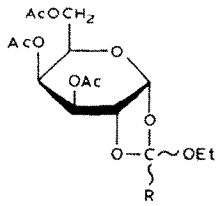
Parallel experiments with 6-*O*-ADM derivatives **9** and **10** showed, indeed, that hydrolysis for 18 h at 25° with $H_2SO_4$ in aqueous acetone (no $CrO_3$ present) was accompanied by ~50% migration from O-5 to O-6 for the 3,5-diacetate, whereas ≤10% migration was observed for the 3,5-dilevulinate. It is worth noting, however, that virtually no migration was observed with either compound when removal of the ADM group was effected with Amberlite IR-120 ($H^+$) resin in methanol for 18 h at 25°.

To increase the solubility of **9** and **10** in the oxidizing medium, the proportion of acetone used was six-fold that in the conventional Jones reagent. Although this lowered the concentration of chromic anhydride to 0.82M, the reaction rates were sufficiently high to allow for complete oxidation in 2.5–3 h at 0°. This modified reagent was also less strongly acidic, being only 0.38M with respect to sulfuric acid. Undoubtedly for this reason, it gave rise to a marked difference when the ADM substituent and the more-stable *O*-trityl substituent were compared as blocking groups at O-6, for example, in the oxidations of methyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-β-D-glucopyranoside (**14**) with that of the corresponding 6-*O*-ADM derivative **15**. Although both afforded the same uronic acid (**16**), the yield obtained from **15** was 88%, whereas that from **14** was only 46%. Furthermore, because the rate of oxidation of **14** was so low, the temperature was raised to 20° and the time increased to 24 h. As *O*-acetyl migration from O-4 to OH-6 has been observed[6,15] in some reactions of partially acylated D-glucopyranosides, the co-occurrence of this type of rearrangement under the more-drastic reaction conditions may account for the decreased yield of **16** from **14**. In another oxidation involving concomitant hydrolysis of an *O*-trityl group which, again, required a reaction temperature of 20° and a time of 24 h, methyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-mannopyranoside (**17**) gave a 42% yield of the corresponding mannuronic acid (**18**).

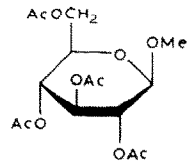
The use of the 6-*O*-ADM substituent and the less-drastic oxidation conditions associated with it did not, however, always guarantee a high yield of uronic acid. Thus, in the *galacto* series, a yield of only 58% of methyl 2,3,4-tri-*O*-acetyl-α-D-galactopyranosiduronic acid (**22**) was obtained from the corresponding 6-*O*-ADM glycoside (**19**). Whether or not acyl migration took place from axial O-4 to the OH-6 group liberated *in situ*, was not determined. Nevertheless, in a parallel experiment, employing a 4-*O*-levulinoyl substituent, the oxidation of methyl 6-*O*-*p*-anisyldiphenylmethyl-2,3-di-*O*-benzyl-4-*O*-levulinoyl-α-D-galactopyranoside (**20**) appeared to take place without acyl migration. Thus, only the formation of the uronic acid derivative **23** was observed by t.l.c. and n.m.r. monitoring of the reaction, although concomitant oxidation of *O*-benzyl groups also occurred (as evidenced by the formation of benzoic acid). As a result, the isolated yield of **23**




25 R = Ac
26 R = Lv




27 R = Me
28 R = $MeCOCH_2CH_2$–




29

was only 30% under the conditions used*. However, with a fourfold decrease in the proportion of oxidant, and a doubling of the reaction time, the yield of **23** was enhanced to 60% (and less benzoic acid was produced). These observations, which show that the concentrations of chromate should be kept low with such compounds as *O*-benzyl ethers, are consistent with reports on the oxidation of other *O*-benzyl derivatives.

*Neighboring-group participation by the* O-*levulinoyl substituent.* — One possibility suggested by the evidence that an *O*-levulinoyl migrates less readily than *O*-acetyl, is that it has less affinity to form an orthoacid intermediate, required[5,6] for migration. In attempting to compare the potential affinity of these two esters, we measured the relative rates of formation of 1,2-orthoesters by 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**25**) and its 2-*O*-levulinoyl analog **26** (the latter was synthesized in two steps from 1,3,4,6-tetra-*O*-acetyl-D-galactose). Thus, the conversion of an equimolar mixture of **25** and **26** into the corresponding ethyl ortho esters (**27** and **28**) was monitored[16] by $^1$H-n.m.r. spectroscopy. Contrary to expectation, products **27** and **28** were produced at the same rate and, in addition, the ratios of their *exo* and *endo* diastereomeric forms were the same (~17:1). Consequently, this facile neighboring-group participating ability of the *O*-levulinoyl substituent at the anomeric centre, although under relatively basic conditions, contrasts markedly with its stability towards migration (in acid). It is also worth noting that, on the basis of molecular modelling, the hypothetical 1,2-orthoacid formed from an *O*-levulinoyl group would be of approximately the same energy as that from an *O*-acetyl group. Apparently, a different basis for rationalization is required.

*Solvents effects on chromium trioxide oxidations.* — In contrast to oxidations with Jones reagent, chromium trioxide in acetic acid acts[17] stereoselectively on acetylated methyl glycosides so as to induce ring-opening. Thus, methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**29**) (although not its α anomer) is converted into methyl 2,3,4,6-tetra-*O*-acetyl-D-*xylo*-hexulosonate. By contrast, **29** was found to be unaffected in 24 h at 25° by the Jones reagents used in the present study. Angyal and James[17] have suggested that the actual oxidizing agent in acetic acid is chromyl acetate, because the reaction did not take place with chromic acid in water or pyridine. Presumably, then, the oxidant should be modified in mixtures of acetic acid and water, and at some appropriate solvent composition ketoester formation would cease. Experimentally with **29**, we observed no ketoester at water levels of 15% and above. Under these conditions, however, another reaction occurred. It appeared that the 6-*O*-acetyl group of **29** was hydrolysed slowly, and then oxidation followed, because in 24 h at 25° a 25% yield of methyl 2,3,4-tri-*O*-acetyl-β-D-glucuronic acid (**16**) was found in the mixture. As a similar result was obtained with the α-glycoside, no stereoselectivity was evident. Nevertheless, the regioselectivity

*Similarly, the uronic acid **24** obtained from the corresponding 4-*O*-benzoyl-D-*gluco* analog **21** was isolated in 30% yield.

observed is not unexpected, inasmuch as facile hydrolysis of the primary acetoxyl groups of these compounds is favored. Attempts to increase the yields of uronic acids in these oxidations, by use of more prolonged periods or of a higher proportion of the oxidant, were unsuccessful, because of a progressive increase in the importance of unidentified side-reactions.

## EXPERIMENTAL

*General methods.* — Melting points were recorded with a Fisher–Johns melting-point apparatus and are uncorrected. Optical rotations were measured with a Jasco digital polarimeter. $^1$H-N.m.r. spectra were recorded with Varian XL-200 and XL-300 n.m.r. spectrometers, using chloroform-*d* as the solvent and $Me_4Si$ as the internal standard. Proton-decoupled $^{13}$C-n.m.r. spectra were recorded with a Varian XL-300 spectrometer, using chloroform-*d* as the solvent and internal standard. Thin-layer chromatography (t.l.c.) was performed on Merck precoated plates. Flash chromatography was routinely used to purify the products, using Silica Gel as adsorbent and light petroleum–ethyl acetate mixtures in different proportions as indicated. Mass spectrometry was performed with a Dupont unit, or an HP5980A spectrometer of the Biomedical Mass Spectrometry Unit, McGill. Microanalyses were provided by Guelph Chemical Laboratories, Guelph, ON.

*5-O-Acetyl-6-O-p-anisyldiphenylmethyl-2,3-O-isopropylidene-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)*-aldehydo-D-*glucose dimethyl acetal* (**2**). — *p*-Anisyldiphenylchloromethane (112 mg, 0.36 mmol) was added to a solution of **1** (200 mg, 0.34 mmol) in $C_5H_5N$ (2 mL) at 0°. After 16 h at room temperature, $Ac_2O$ (0.5 mL) was added, and 5 h later, the solvents were removed by evaporation. Chloroform was added to the residue and the resulting solution washed with $NaHCO_3$ solution and water, then dried, and evaporated. The residue was chromatographed (1:2 EtOAc–hexane) to give **2** (280 mg, 0.31 mmol, 90%); $^1$H-n.m.r.: δ 1.24, 1.30 (2 s, 6 H, $CMe_2$), 2.00, 2.01, 2.018, 2.09, 2.15 (5 s, 15 H, OAc), 3.36, 3.43 (2 s, 6 H, OMe), 3.38–3.49 (m, 2 H, H-6a,6b), 3.79 (dd, 1 H, $J_{4,5}$ 1.4 Hz, H-4), 3.80 (s, 3 H, PhOMe), 3.84 (ddd, 1 H, H-5′), 3.91 (dd, 1 H, $J_{6a',6b'}$ 12.6 Hz, H-6a′), 3.97 (dd, 1 H, $J_{3,4}$ 6.6 Hz, H-3), 4.15 (dd, 1 H, $J_{2,3}$ 6.6 Hz, H-2), 4.18 (dd, 1 H, H-6b′), 4.28 (d, 1 H, $J_{1,2}$ 6.6 Hz, H-1), 4.80 (dd, 1 H, $J_{2',3'}$ 10.6 Hz, H-2′), 5.04 (dd, 1 H, $J_{4',5'}$ 10.2 Hz, H-4′), 5.13 (d, 1 H, $J_{1',2'}$ 3.5 Hz, H-1′), 5.23 (dd, 1 H, $J_{3',4'}$ 10.2 Hz, H-3′), 5.43 (ddd, 1 H, $J_{5,6a}$ 2.8, $J_{5,6b}$ 8.8 Hz, H-5), and 6.85–7.47 (m, 14 H, Ph).

*Anal.* Calc. for $C_{47}H_{58}O_{18}$: C, 61.97; H, 6.42. Found: C, 61.48; H, 6.81.

*6-O-Acetyl-2,3-O-isopropylidene-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)*-aldehydo-D-*glucose dimethyl acetal* (**3**). — A solution of **2** (610 mg, 0.67 mmol) in 80% aq. AcOH (5 mL) was stirred for 10 h, until t.l.c. (EtOAc) showed the complete loss of starting material. The solvent was evaporated off and the residue chromatographed (1:1 EtOAc–hexane) to give **3** (330 mg, 0.52 mmol, 78%), rather than the expected 5-*O*-acetyl product; $[\alpha]_D^{20}$ +54° (*c* 4.4, $CHCl_3$);

$^1$H-n.m.r.: δ 1.43, 1.51 (2 s, 6 H, $CMe_2$), 2.01, 2.04, 2.09, 2.10 (4 s, 15 H, OAc), 3.44, 3.46 (2 s, 6 H, OMe), 3.70 (dd, 1 H, $J_{4,5}$ 2 Hz, H-4), 4.05 (dd, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 4.12 (dd, 1 H, $J_{6a',6b'}$ 12.5 Hz, H-6a'), 4.13–4.25 (m, 6 H, H-2,5,6a,6b,6b'), 4.28 (d, 1 H, $J_{1,2}$ 5.9 Hz, H-1), 4.45 (ddd, 1 H, $J_{5',6a'}$ 2.2, $J_{5',6b'}$ 4.6 Hz, H-5'), 4.91 (dd, 1 H, $J_{2',3'}$ 10.5 Hz, H-2'), 5.03 (dd, 1 H, $J_{4',5'}$ 10.5 Hz, H-4'), 5.15 (d, 1 H, $J_{1',2'}$ 3.9 Hz, H-1'), and 5.50 (dd, 1 H, $J_{3',4'}$ 9.5 Hz, H-3'); $^{13}$C-n.m.r.: δ 60.96 and 61.55 (C-6, C-6').

*Anal.* Calc. for $C_{27}H_{42}O_{17}$: mol. wt. 638. Found: *m/z* 744 (M + DEAH, 50) (F.a.b., DEA, diethanolamine).

*6-O-Acetyl-2,3-O-isopropylidene-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)*-aldehydo-D-*xylo-hexos-5-ulose dimethyl acetal* (**4**). — To a stirred suspension of **3** (133 mg, 0.2 mmol) in $Me_2CO$ (5 mL) at −10° was added Jones reagent (77% $CrO_3$ in 3.5M aq. $H_2SO_4$) (0.4 mL). After 18 h, EtOAc was added, and the mixture washed with $NaHCO_3$ solution and water, dried and evaporated. The clear residue was chromatographed (1:1 EtOAc–hexane) to give **4** (76 mg, 70%); $[\alpha]_D^{20}$ +54° (*c* 1.9, $CHCl_3$); $^1$H-n.m.r.: δ 1.40, 1.47 (2 s, 6 H, $CMe_2$), 2.02, 2.04, 2.08, 2.10, 2.17 (5 s, 15 H, OAc), 3.44, 3.47 (2 s, 6 H, OMe), 4.0–4.46 (m, 7 H, H-1,2,3,4,5',6a',6b'), 4.83 (d, 1 H, $J_{6a,6b}$ 17.2 Hz, H-6a), 4.99 (dd, 1 H, $J_{2',3'}$ 10.3 Hz, H-2'), 5.05 (d, 1 H, H-6b), 5.10 (dd, 1 H, $J_{4,5}$ 9.5 Hz, H-4'), 5.13 (d, 1 H, $J_{1',2'}$ 4.1 Hz, H-1'), and 5.56 (dd, 1 H, $J_{3',4'}$ 10.2 Hz, H-3'); $^{13}$C-n.m.r. data: δ 20.57, 20.79 (OAc), 26.62, 27.10 ($CMe_2$), 55.37, 57.15 (OMe), 62.00 (C-6'), 67.24 (C-6), 68.48, 69.13, 70.10, 70.91 (C-2',3',4',5'), 76.25, 78.13 (C-2,3), 83.48 (C-4), 98.96 (C-1'), 105.86 (C-1), 111.10 ($CMe_2$), 169.90, 170.17, 170.33, 170.81 (OAc), and 200.43 (C-5).

*Anal.* Calc. for $C_{27}H_{40}O_{17}$ (636): Found: *m/z* 742 (M + DEAH, 30), (f.a.b., DEA).

*5-O-Acetyl-2,3-O-isopropylidene-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)*-aldehydo-D-*glucuronic acid dimethyl acetal* (**7**). — To a stirred solution of **2** (420 mg, 0.46 mmol) in $Me_2CO$ (20 mL) at 0°, was added Jones reagent. After 16 h, EtOAc was added and the mixture filtered. The filtrate was concentrated, dissolved in $CHCl_3$, and the resulting solution washed with water, dried and re-evaporated. The final residue was chromatographed (2% MeOH in $CHCl_3$) to give **7** (96 mg, 0.15 mmol, 33%); $[\alpha]_D^{20}$ +73° (*c* 1.4, $CHCl_3$); $^1$H-n.m.r.: δ 1.98 (s, 6 H, $CMe_2$), 1.98, 2.01, 2.04, 2.08, 2.14 (5 s, 15 H, OAc), 3.44, 3.46 (2 s, 6 H, OMe), 3.96 (d, 1 H, H-4), 4.0–4.12 (m, 2 H, H-2,6a'), 4.29–4.35 (m, 2 H, H-5',6'), 4.43 (d, 1 H, $J_{1,2}$ 5.4 Hz, H-1), 4.46 (dd, 1 H, H-3), 4.82 (dd, 1 H, $J_{2',3'}$ 10.3 Hz, H-2'), 5.36 (d, 1 H, $J_{1',2'}$ 3.4 Hz, H-1'), 5.36 (dd, 1 H, $J_{3',4'}$ 9.8 Hz, H-3'), and 5.48 (s, 1 H, H-5); $^{13}$C-n.m.r.: δ 20.55, 20.61, 20.68, 20.73, 20.83 (OAc), 26.77, 27.04 ($CMe_2$), 54.24, 56.88 (OMe), 61.34 (C-6'), 67.58 (C-5'), 68.06 (C-4'), 69.78 (C-3'), 70.62 (C-2'), 72.88, 77.26, 78.43 (C-2,3,5), 80.62 (C-4), 97.13 (C-1'), 104.77 (C-1), 110.51 ($CMe_2$), 169.79, 169.97, 170.07, 170.13, 170.36, and 170.89 (OAc, $CO_2H$).

*Anal.* Calc. for $C_{27}H_{40}O_{18}$ (652): Found: *m/z* 758 (M + DEAH, 70), (f.a.b., DEA).

*6-O-p-Anisyldiphenylmethyl-2,3-O-isopropylidene-5-O-levulinoyl-4-O-(2,3,-4,6-tetra-O-acetyl-α-D-glucopyranosyl)*-aldehydo-D-*glucose dimethyl acetal* (**5**). — As described in the procedure for **2**, the 6-*O*-*p*-anisyldiphenylmethyl derivative was prepared, and purified by the same chromatographic process. The recovered syrup (450 mg, 0.5 mmol) was dissolved in tetrahydrofuran (15 mL) containing *N,N'*-dimethylaminopyridine (~10 mg), *N,N'*-dicyclohexylcarbodiimide (200 mg, 0.97 mmol) and levulinic acid (0.3 mL, 2.9 mmol) were added, and the mixture was stirred for 1 h. The tetrahydrofuran was removed by evaporation, the residue dissolved in $CHCl_3$ and the resulting mixture washed with $NaHCO_3$ solution, and water, dried and concentrated. Chromatography (2:3 EtOAc–hexane) provided **5** (420 mg, 0.43 mmol, 86%); $^1$H-n.m.r.: δ 1.25, 1.30 (2 s, 6 H, $CMe_2$), 1.99, 2.01, 2.07, 2.18 (4 s, 15 H, OAc, Lv-$CH_3$), ~2.6, 2.8 (m, 4 H, Lv-$CH_2$), 3.35, 3.41 (2 s, 6 H, OMe), 3.3–3.5 (m, 3 H, H-4,6a,6b), 3.79 (s, 3 H, PhOMe), 3.85 (m, 1 H, H-5'), 3.5–3.92 (m, 2 H, H-3,6a'), 4.13 (dd, 1 H, $J_{2,3}$ 6 Hz, H-2), 4.19 (dd, 1 H, $J_{6b',6a'}$ 12.5 Hz, H-6b'), 4.27 (dd, 1 H, $J_{1,2}$ 5.9 Hz, H-1), 4.81 (dd, 1 H, $J_{2',3'}$ 10 Hz, H-2'), 5.04 (dd, 1 H, $J_{4',5'}$ 10 Hz, H-4'), 5.13 (d, 1 H, $J_{1',2'}$ 3.9 Hz, H-1'), 5.22 (dd, 1 H, $J_{3',4'}$ 10 Hz, H-3'), 5.4 (m, 1 H, H-5), and 6.8–7.4 (Ph). $^{13}$C-n.m.r.: δ 20.57–27.52 (OAc, Lv-$CH_3$, $CMe_2$), 54.27, 56.91 (OMe), 55.15 (PhOMe), 61.04 (C-6'), 61.79 (C-6), 67.76, 67.85 (C-4',5'), 69.71 (C-3'), 70.44 (C-2'), 74.31, 76.10, 78.45 (C-2,3,5), 81.75 (C-4), 86.30 (MMT-C), 97.66 (C-1'), 105.47 (C-1), 110.14 ($CMe_2$), 113.08–158.52 (Ph), and 169.58–172.60 (OAc, Lv-$CO_2^-$).

*Anal.* Calc. for $C_{50}H_{62}O_{19}$: C, 62.10; H, 6.46. Found: C, 61.56; H, 6.60.

*2,3-O-Isopropylidene-5-O-levulinoyl-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)*-aldehydo-D-*glucose dimethyl acetal* (**6**). — A solution of **5** (290 mg, 0.3 mmol) in 80% aq. AcOH (3 mL) was stirred for 18 h. Removal of the solvents under high vacuum, followed by chromatography (2:1 EtOAc–hexane) of the residue, gave **6** (123 mg, 0.18 mmol, 60%) as an oil; $[\alpha]_D^{20}$ +86° (*c* 1.2, $CHCl_3$); $^1$H-n.m.r.: δ 1.40, 1.42 (2 s, 6 H, $CMe_2$), 2.02, 2.06, 2.08, 2.11, 2.20 (5 s, OAc, Lv-$CH_3$), ~2.6, 2.8 (m, 4 H, Lv-$CH_2$), 3.46, 3.49 (2 s, 6 H, OMe), 3.83–4.03 (m, 2 H, H-6a,6b), 3.91 (dd, 1 H, $J_{4,5}$ 2.2 Hz, H-4), 4.10–4.20 (m, 3 H, H-2,3,6a'), 4.26 (ddd, 1 H, $J_{5',6a'}$ 2.7, $J_{5',6b'}$ 2.7 Hz, H-5'), 4.33 (dd, 1 H, H-6b'), 4.36 (d, 1 H, $J_{1,2}$ 5.4 Hz, H-1), 4.91 (dd, 1 H, $J_{2',3'}$ 10.5 Hz, H-2'), ~5.1 (H-5), 5.14 (dd, 1 H, $J_{4',5'}$ 9.2 Hz, H-4'), 5.32 (d, 1 H, $J_{1',2'}$ 3.9 Hz, H-1'), and 5.47 (dd, 1 H, $J_{3',4'}$ 9.2 Hz, H-3').

*Anal.* Calc. for $C_{30}H_{46}O_{18}$ (694): Found: *m/z* 800 (M + $DEAH^+$, 60), (f.a.b., DEA).

*Methyl 2,3-O-isopropylidene-5-O-levulinoyl-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)*-aldehydo-D-*glucuronate dimethyl acetal* (**8**). — To a stirred solution of **6** (1.15 g, 1.66 mmol) in $CH_2Cl$ (75 mL) was added pyridinium dichromate (2.82 g) and $Ac_2O$ (0.7 mL). After 16 h, the solvents were removed by evaporation, and the residue chromatographed (10% MeOH in $CHCl_3$) to give a crude brown product (800 mg), presumably the acid. A small portion (120 mg) in $CH_2Cl_2$ (2 mL) was treated with ethereal diazomethane. After removal of the solvents, the residue

was chromatographed (2:1 EtOAc–hexane) to give **8** (100 mg; 78% from **6**); $[\alpha]_D^{20}$ +66° (*c* 3.9, $CHCl_3$); $^1$H-n.m.r.: δ 1.36 (s, 6 H, $CMe_2$), 1.98, 2.01, 2.02, 2.08, 2.17 (5 s, 15 H, OAc, Lv-$CH_3$), ~2.6, 2.8 (m, 4 H, Lv-$CH_2$), 3.41, 3.45 (OMe), 3.82 ($CO_2Me$), 3.94 (dd, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 3.99 (dd, 1 H, $J_{2,3}$ 6.3 Hz, H-2), 4.08 (dd, 1 H, $J_{6a',6b'}$ 12 Hz, H-6a'), 4.06–4.37 (m, 5 H, H-1,3,5',6'), 4.75 (dd, 1 H, $J_{2',3'}$ 10.1 Hz, H-2'), 5.08 (dd, 1 H, $J_{4',5'}$ 9.8 Hz, H-4'), 5.36 (dd, 1 H, $J_{3',4'}$ 10 Hz, H-3'), 5.40 (d, 1 H, $J_{1',2'}$ 3.9 Hz, H-1'), and 5.57 (d, 1 H, H-5). $^{13}$C-n.m.r.: δ 20.63–37.59 (OAc, Lv-$CH_3$, Lv-$CH_2$, $CMe_2$), 52.54 ($CO_2Me$), 53.73, 56.96 (OMe), 61.47 (C-6'), 67.71 (C-5'), 67.99 (C-4'), 69.44 (C-3'), 70.56 (C-2'), 72.59 (C-5), 77.27 (C-2), 78.19 (C-3), 80.17 (C-4), 96.76 (C-1'), 105.06 (C-1), 110.40 ($CMe_2$), and 167.43–171.80 (OAc, Lv-$CO_2$, $CO_2Me$).

*6-O-p-Anisyldiphenylmethyl-1,2-O-isopropylidene-α-D-glucofuranose*. — 1,2-*O*-Isopropylidene-α-D-glucofuranose (1.6 g, 7.27 mmol) was suspended in dry $CH_2Cl_2$ (45 mL). Pyridine (15 mL) was added, followed by the addition of *p*-anisylchlorodiphenyl methane (2.5 g; 8.12 mmol) and a catalytic amount of dimethylaminopyridine (15 mg). The mixture was stirred at room temperature for 18 h, evaporated, and the residue was dissolved in $CH_2Cl_2$ (100 mL) and washed successively with 5% HCl (20 mL), 5% $NaHCO_3$ (20 mL), and 20% NaCl (20 mL). The washings were re-extracted with $CH_2Cl_2$, the combined extract was dried over anhydrous $MgSO_4$, and evaporated, giving the chromatographically pure compound in 93% yield (3.3 g), as an oil. (Its stability was enhanced by the presence of a small proportion of $C_5H_5N$). $^1$H-N.m.r.: δ 1.30 and 1.46 (2 s, 6 H, $CHe_2$), 3.32 (dd, 1 H, $J_{6,6'}$ 9.8, $J_{5,6'}$ 6.0 Hz, H-6'), 3.45 (dd, 1 H, $J_{5,6}$ 4.4 Hz, H-6), 3.80 (s, 3 H, OMe), 4.10 (dd, 1 H, $J_{3,4}$ 2.2, $J_{4,5}$ 5.6 Hz, H-4), 4.22 (m, 1 H, H-5), 4.31 (d, 1 H, $J_{3,4}$ 2.0 Hz, H-3), 4.51 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-2), 5.95 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), and 6.60–7.51 (m, 14 H, Ph).

*3,5-Di-O-acetyl-6-O-p-anisyldiphenylmethyl-1,2-O-isopropylidene-α-D-glucofuranose* (**9**). — To a solution of 6-*O*-*p*-anisyldiphenylmethyl-1,2-*O*-isopropylidene-α-D-glucofuranose (300 mg, 0.6 mmol) in $C_5H_5N$ (3 mL) at 0°, was added $Ac_2O$ (1 mL). After 18 h, workup gave a solid product in 97% yield (341 mg); m.p. 136–137°; $^1$H-n.m.r.: δ 1.31 and 1.53 (2 s, 6 H, $CMe_2$), 2.02 and 2.03 (2 s, 6 H, 2 OAc), 3.29 (dd, 1 H, $J_{5,6'}$ 5.4, $J_{6,6'}$ 10.5 Hz, H-6'), 3.39 (dd, 1 H, $J_{5,6}$ 2.1, $J_{6,6'}$ 10 Hz, H-6), 3.79 (s, 3 H, OMe), 4.47 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-2), 4.62 (dd, 1 H, $J_{3,4}$ 2.8, $J_{4,5}$ 9.7 Hz, H-4), 5.24 (m, 1 H, H-5), 5.36 (d, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 5.89 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), and 6.82–7.45 (m, 14 H, Ph).

*Anal.* Calc. for $C_{33}H_{36}O_9$: mol. wt. 576.23607. Found: *m/z* 576.23593 ($M^+$).

*3,5-Di-O-acetyl-1,2-O-isopropylidene-α-D-glucofuranuronic acid methyl ester* (**11**). — Compound **9** was oxidized with the Jones reagent and the acid product isolated (47%) was converted into the methyl ester (**11**); $[\alpha]_D$ +4.0° (*c* 1.2 $CHCl_3$); $^1$H-n.m.r.: δ 1.31 and 1.52 (2 s, 6 H, $CMe_2$), 2.07 and 2.09 (2 s, 6 H, OAc), 3.81 (s, 3 H, OMe), 4.52 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-2), 4.56 (dd, 1 H, $J_{3,4}$ 3.1 Hz, $J_{4,5}$ 9.3 Hz, H-4), 5.09 (d, 1 H, H-5), 5.37 (d, 1 H, H-3), and 5.97 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1);

$^{13}$C-n.m.r.: δ 20.3 and 20.6 ($Me_2$), 26.2 and 26.7 (2 COMe), 68.4, 75.2, 77.2, 82.9 (C-2,3,4,5), 105.4 (C-1), 112.9 ($CMe_2$), 169.4, 169.5, and 171.9 (3 CO).

*Anal.* Calc. for $C_{14}H_{20}O_9$: mol. wt. 332. Found: 332 ($M^+$).

*6-O-p-Anisyldiphenylmethyl-1,2-O-isopropylidene-3,5-di-O-levulinoyl-α-D-glucofuranose* (**10**). — 6-*O*-*p*-Anisyldiphenylmethyl-1,2-*O*-isopropylidene-α-D-glucofuranose (400 mg, 0.8 mmol) was dissolved in dry tetrahydrofuran (9.5 mL), *N,N'*-dicyclohexylcarbodiimide (640 mg, 3.1 mmol) was added, followed by the addition of levulinic acid (357 mg, 3.08 mmol) and a catalytic amount of dimethylaminopyridine (12 mg). The mixture was stirred for 18 h at room temperature. Separated solid was filtered off, and washed with tetrahydrofuran (10 mL), and the filtrate was evaporated. The residue was dissolved in $CH_2Cl_2$ (75 mL), washed with 5% $NaHCO_3$ (15 mL) and 20% NaCl, the washings were extracted with $CH_2Cl_2$ (50 mL), and the extracts were combined and dried over anhydrous $MgSO_4$. On evaporation of the solvent, the crude product obtained was chromatographed on a short column, giving **10** in 85% yield. $^1$H-N.m.r.: δ 1.30 and 1.52 (2 s, 6 H, $CMe_2$), 2.15 (s, 3 H, COMe), 2.18 (s, 3 H, $COCH_3$ group), 2.52–2.76 (m, 8 H, 4 × $LvCH_2$), 3.29 (dd, 1 H, $J_{6,6'}$ 10.5 Hz, H-6'), 3.40 (dd, 1 H, $J_{6,6'}$ 10.5 Hz, H-6), 3.79 (s, 3 H, $OCH_3$), 4.49 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-2), 4.64 (dd, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 5.21 (m, 1 H, H-5), 5.27 (d, 1 H, $J_{3,4}$ 3.2, H-3), 5.86 (d, 1 H, $J_{1,2}$ 3.9, H-1), and 6.82–7.45 (m, 14 H, Ph).

*Anal.* Calc. for $C_{39}H_{44}O_{10}$: mol. wt. 672. Found: *m/z* 672 ($M^+$).

*1,2-O-Isopropylidene-3,5-di-O-levulinoyl-α-D-glucofuranuronic acid* (**12**), *and its methyl ester* (**13**). — To a solution of **10** (800 mg, 1.2 mmol) in acetone (45 mL) at 0°, was added dropwise a solution of $CrO_3$ (4.15 g, 41.5 mmol) in 3.5M $H_2SO_4$ (5.4 mL). After 3 h at 0°, the solution was diluted with water (25 mL), extracted with $CH_2Cl_2$ (2 × 100 mL), the extract was washed with 20% NaCl (20 mL), dried over anhydrous $MgSO_4$, and evaporated. The residue was purified by chromatography (9:1 $CHCl_3$–MeOH), affording acid **12** in 85% yield (439 mg); $^1$H-n.m.r. data for **12**: δ 1.30 and 1.51 (2 s, 6 H, $CMe_2$), 2.16 and 2.17 (2 s, 6 H, 2 LvMe), 2.54–2.85 (m, 8 H, 4 $LvCH_2$), 4.55 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-2), 4.62 (dd, 1 H, $J_{4,5}$ 9.2 Hz, H-4), 5.13 (d, 1 H, $J_{4,5}$ 9.2 Hz, H-5), 5.35 (d, 1 H, $J_{3,4}$ 2.6, H-3), and 6.0 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1).

A solution of acid **12** (70 mg) in $CH_2Cl_2$ (10 mL) was quantitatively converted into syrupy methyl ester **13** by treatment with ethereal diazomethane; $[\alpha]_D$ −9.2° (*c* 1.0, $CHCl_3$); $^1$H-n.m.r. data for **13**: δ 1.3 and 1.51 (2 s, 6 H, $CMe_2$), 2.16 and 2.18 (2 s, 6 H, 2 LvMe), 2.55–2.80 (m, 8 H, 4 $LvCH_2$), 3.82 (s, 3 H, $CO_2Me$), 4.54 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-2), 4.56 (dd, 1 H, $J_{3,4}$ 3.1 Hz, H-4), 5.04 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-5), 5.33 (d, 1 H, H-3), and 5.98 (d, 1 H, H-1); $^{13}$C-n.m.r. data for **13**: δ 26.1 and 26.6 ($Me_2$), 27.4 and 27.7 (2 LvMe), 29.5, 29.6, 37.6, 37.7 (4 $LvCH_2$), 52.7 (OMe), 69.1, 75.3, 77.2, 82.6 (C-2,3,4,5), 105.3 (C-1), 168.9, 171.2, and 171.3 (3 OCO), 205.8 and 206.3 (2 CO).

*Anal.* Calc. for $C_{20}H_{28}O_{11}$: mol.wt. 444.17098. Found (c.i.): *m/z* 445.17089 (M + H).

*Methyl 2,3,4-tri-*O*-acetyl-β-*D*-glucosiduronic acid,* (**16**) *and its methyl ester.* — Methyl 2,3,4-tri-*O*-acetyl-6-*O*-*p*-anisyldiphenylmethyl-β-D-glucopyranoside (**15**, 1 g, 1.7 mmol) was prepared (as for **9**) from methyl β-D-glucopyranoside, and its oxidation carried out as described for **12**. Isolated in 88% yield (0.5 g), acid **16** had m.p. 130–131° (lit.[18] 128–128.5°). It was converted into its methyl ester with diazomethane; $^1$H-n.m.r. data for the ester: δ 2.02, 2.03, and 2.05 (3 s, 9 H, 3 OAc), 3.53 (s, 3 H, OMe), 3.77 (s, 3 H, $CO_2Me$), 4.04 (d, 1 H, $J_{4,5}$ 9.7 Hz, H-5), 4.48 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 5.01 (dd, 1 H, $J_{2,3}$ 9.4 Hz, H-2), 5.22 (dd, 1 H, $J_{3,4}$ 8.9 Hz, $J_{4,5}$ 9.7 Hz, H-4), 5.26 (dd, 1 H, $J_{2,3}$ 9.4 Hz, H-3).

The correspnding 6-trityl ether (**14**), when oxidized at 25° for 24 h, afforded **16** in 39% yield.

*Methyl 2,3,4-tri-*O*-acetyl-α-*D*-mannopyranosiduronic acid* (**18**). — Methyl 2,3,4-tri-*O*-acetyl-6-*O*-triphenylmethyl-α-D-mannopyranoside (**17**) was oxidized with the Jones reagent for 24 h at room temperature. The uronic acid formed was isolated as its syrupy methyl ester[19] in 57% yield; $^1$H-n.m.r.: δ 2.01, 2.05, and 2.15 (3 s, 9 H, OAc), 3.45 (s, 3 H, OMe), 3.77 (s, 3 H, $CO_2Me$), 4.30 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-5), 4.82 (d, 1 H, $J_{1,2}$ 2.2 Hz, H-1), 5.24 (dd, 1 H, $J_{2,3}$ 3.0 Hz, H-2), and 5.40 (m, 2 H, H-3,4).

*Anal.* Calc. for $C_{14}H_{20}O_{10}$: M − $OCH_3$ 317.0873. Found: *m/z* 317.0828 (M − $OCH_3$).

*Methyl 2,3,4-tri-*O*-acetyl-α-*D*-galactopyranosiduronic acid* (**22**). — Methyl 2,3,4-tri-*O*-acetyl-6-*O*-*p*-anisyldiphenylmethyl-α-D-galactopyranoside (**19**) was prepared from methyl α-D-galactopyranoside, and its oxidation carried out as described for **12**. The uronic acid produced (**22**) was isolated as its methyl ester in 59% yield; m.p. 95.5–96.5° (lit.[20] 95–96°); $^1$H-n.m.r.: δ 1.98, 2.08, 2.09 (3 s, 9 H, 3 OAc), 3.44 (s, 3 H, OMe), 3.74 (s, 3 H, $CO_2Me$), 4.60 (d, 1 H, $J_{4,5}$ 1.5 Hz, H-5), 5.13 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 5.20 (dd, 1 H, $J_{2,3}$ 10.8 Hz, H-2), 5.39 (dd, 1 H, $J_{3,4}$ 3.4, $J_{2,3}$ 10.8 Hz, H-3), and 5.76 (dd, 1 H, $J_{3,4}$ 3.4, $J_{4,5}$ 1.7 Hz, H-4).

*Anal.* Calc. for $C_{14}H_{20}O_{10}$: M − $OCH_3$ 317.0873. Found: *m/z* 317.0874 (M − $OCH_3$).

*Methyl 6-*O*-p-anisyldiphenylmethyl-2,3-di-*O*-benzyl-4-*O*-levulinoyl-α-*D*-galactopyranoside* (**20**). — To a solution of methyl 2,3-di-*O*-benzyl-α-D-galactopyranoside (283 mg, 0.75 mmol) in $CH_2Cl_2$ (10 mL) was added $C_5H_5N$ (2 mL), *N,N'*-dimethylaminopyridine (10 mg) and *p*-anisylchlorodiphenylmethane (320 mg; 1.04 mmol) and the mixture was stirred for 16 h at room temperature. The solvent and pyridine were evaporated off. The crude product, which was shown to be a single compound by t.l.c. and n.m.r. evidence, was dissolved in tetrahydrofuran (12 mL) and treated with *N,N'*-dicyclohexylcarbodiimide (1.0 g, 4.85 mmol), *N,N'*-dimethylaminopyridine (20 mg) and levulinic acid (450 mg, 3.87 mmol). After the mixture had been stirred for 15 h at room temperature, solid material was filtered off and washed with tetrahydrofuran. The filtrate was evaporated, dissolved in $CH_2Cl_2$ (100 mL), washed with 5% $NaHCO_3$ (20 mL), 20% NaCl (20 mL), the washings were extracted with $CH_2Cl_2$ (75 mL) and the extracts were combined,

dried over $MgSO_4$, and concentrated. The crude product was chromatographed on silica gel (9:1 petroleum–EtOAc) yielding pure **20** (350 mg, 0.47 mmol, 63%); $^1$H-n.m.r.: $\delta$ 2.06 (s, 3 H, LvMe), 2.42–2.55 (m, 4 H, 2 LvCH$_2$), 3.04 (dd, 1 H, $J_{6,6'}$ 9.5 Hz, $J_{5,6}$ 6.6 Hz, H-6), 3.27 (dd, 1 H, $J_{5,6'}$ 6.4 Hz, H-6'), 3.67 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 3.85–3.95 (m, 2 H, H-3 and H-5), 4.55, 4.74 (2d, 2 H, $J_{H,H'}$ 11.2 Hz, benzyl-CH$_2$), 4.64, 4.81 (2d, 2 H, $J_{H,H'}$ 12.1 Hz, benzyl-CH$_2$), 4.64 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 5.57 (d, 1 H, $J_{3,4}$ 2.9 Hz, H-4), and 6.82–7.43 (m, 14 H, Ph).

*Methyl 2,3-di-*O*-benzyl-4-*O*-levulinoyl-α-*D*-galactopyranosiduronic acid* (**23**) *and its methyl ester.* — Methyl 6-*O*-*p*-anisyldiphenylmethyl-2,3-di-*O*-benzyl-4-*O*-levulinoyl-α-D-galactopyranoside **20** (130 mg, 0.175 mmol) was dissolved in acetone (9 mL), and with stirring at 0° Jones reagent (1.04 mL) (prepared as in **13**) was slowly added. After 2 h, water was added, the mixture was extracted into $CH_2Cl_2$ (2 × 100 mL), the extract was concentrated to 50 mL and washed with 10% $NaHCO_3$ (20 mL). The aqueous layer was separated and acidified with HCl, extracted into $CH_2Cl_2$ (3 × 75 mL). The latter on being washed with 20% NaCl, dried, and evaporated, yielded acid (**23**), contaminated with benzoic acid (7:3 ratio as evidenced from the n.m.r. spectrum). Pure **23** was obtained by chromatography (9:1 $CHCl_3$–MeOH) (26 mg, 0.053 mmol, 30%), and converted into its methyl ester with diazomethane; $[\alpha]_D^{22}$ +57.9° (*c* 0.94, $CHCl_3$); $^1$H-n.m.r. data for acid **23**: $\delta$ 2.13 (s, 3 H, LvMe), 2.58–2.80 (m, 4 H, 2 LvCH$_2$), 3.42 (s, 3 H, OMe), 3.77 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 4.03 (dd, 1 H, $J_{3,4}$ 3.4 Hz, H-3), 4.52 (d, 1 H, H-5), 4.56, 4.77 (2d, 2 H, $J_{H,H'}$ 10.9 Hz, 2 benzyl-H), 4.64, 4.85 (2d, 2 H, $J_{H,H'}$ 12.1 Hz, 2 benzyl-H), 4.79 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.91 (dd, 1 H, $J_{4,5}$ 1.6 Hz, H-4), and 7.28–7.40 (m, 10 H, Ph). The $^1$H-n.m.r. spectrum of the ester showed a peak at 3.78 $\delta$ (s, 3 H) in addition to other peaks, as for **23**.

*Anal.* Calc. for $C_{27}H_{32}O_9$ (methyl ester): mol.wt. 500. Found (c.i.): 518 ($M + NH_4^+$).

*Methyl 4-*O*-benzoyl-2,3-di-*O*-benzyl-β-*D*-glucopyranosiduronic acid* (**24**) *and its methyl ester.* — Methyl 6-*O*-*p*-anisyldiphenylmethyl-4-*O*-benzoyl-2,3-di-*O*-benzyl-β-D-glucopyranoside (**21**) (97 mg, 0.13 mmol), dissolved in acetone (5.3 mL), was treated with Jones reagent (prepared as in **13**) (0.64 mL) at 0°. After 2.5 h, the mixture was diluted with water (25 mL) and extracted into $CH_2Cl_2$ (2 × 100 mL). The combined extract was washed with 20% NaCl, dried over $MgSO_4$, and evaporated. The residue was chromatographed (9:1 $CHCl_3$–MeOH) to obtain pure acid **24**, which was converted into the methyl ester, (21 mg, 0.04 mmol, 32%), m.p. 120–122°, $[\alpha]_D^{20}$ −41.6° (*c* 0.85, chloroform); $^1$H-n.m.r.: $\delta$ 3.60, 3.64 (2s, 6 H, OMe and $CO_2$Me), 3.82 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 4.05 (d, 1 H, H-5), 4.44 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.67, 4.79, 4.92 (3d, 4 H, $CH_2$), 5.40 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), and 7.03–7.98 (m, 15 H, Ph).

*Anal.* Calc. for $C_{29}H_{30}O_8 \cdot 0.5\ H_2O$: C, 67.55; H, 6.06. Found: C, 67.56; H, 5.84.

*1,3,4,6-Tetra-*O*-acetyl-2-*O*-levulinoyl-α-*D*-galactopyranose.* — Crystalline 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose (200 mg, 0.57 mmol) was dissolved in

dry tetrahydrofuran (8 mL), *N,N'*-dicyclohexylcarbodiimide (470 mg, 2.28 mmol), *N,N'*-dimethylaminopyridine (10 mg) and levulinic acid (198 mg, 1.71 mmol) were added, and the mixture was stirred for 4 h at room temperature. The solid was filtered off, washed with tetrahydrofuran, the filtrate was evaporated, and the residue was dissolved in $CH_2Cl_2$ (100 mL), washed with 5% $NaHCO_3$, 20% NaCl, and dried over $MgSO_4$. After removal of the solvent, the product was chromatographed (4:1 petroleum ether–EtOAc) to give the pure 2-levulinoyl derivative **25** (231 mg, 0.52 mmol, 91%); $^1$H-n.m.r.: $\delta$ 2.03, 2.16, 2.17 (3s, 15 H, 4 OAc and 1 LvMe), 2.40–2.92 (m, 4 H, 2 Lv$CH_2$), 4.12 (m, 2 H, H-6 and H-6'), 4.37 (t, 1 H, $J_{5,6} = J_{5,6'} = 6.3$ Hz, H-5), 5.37 (m, 2 H, H-2 and H-3), 5.52 (dd, 1 H, $J_{4,5}$ 1.3 Hz, $J_{3,4}$ 2.4 Hz, H-4), and 6.39 (d, 1 H, $J_{1,2}$ 2.9 Hz, H-1).

*3,4,6-Tri-*O*-acetyl-2-*O*-levulinoyl-α-*D*-galactopyranosyl bromide* (**26**). — 1,3,4,6-Tetra-*O*-acetyl-2-*O*-levulinoyl-α-D-galactopyranose (**25**, 85 mg, 0.19 mmol) was dissolved in 45% HBr in AcOH (0.7 mL), 0.02 mL of $Ac_2O$ was added, the mixture was stirred for 2 h, diluted with $CHCl_3$, washed with saturated $NaHCO_3$, and 20% NaCl, and dried over $MgSO_4$. Evaporation of the solvent yielded the bromo derivative **26** (80 mg, 0.17 mmol, 90%); $^1$H-n.m.r.: $\delta$ 2.04, 2.06, 2.16, 2.19 (4s, 12 H, 3 OAc and 1 LvMe), 2.63, 2.75 (2m, 4 H, 2 Lv$CH_2$), 4.10 (dd, 1 H, $J_{6,6'}$ 11.5 Hz, H-6), 4.19 (dd, 1 H, H-6'), 4.49 (t, $J_{5,6} = J_{5,6'} = 6.5$ Hz, H-5), 5.09 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 5.42 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 5.51 (dd, 1 H, $J_{4,5}$ 1.2 Hz, H-4), and 6.65 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1).

*3,4,6-Tri-*O*-acetyl-1,2-*O*-(1-ethoxy-4-oxopentyl)-α-*D*-galactopyranose* (**28**). — A solution of compound **26** (87 mg, 0.186 mmol) in $CH_2Cl_2$ (2.5 mL) was added to a well-stirred mixture of molecular sieves (3Å), collidine (0.31 mL), EtOH (0.36 mL) and $Bu_4NBr$ (285 mg). The mixture was stirred for 16 h at room temperature, and then filtered, and the filtrate was evaporated. A solution of the residue in $CH_2Cl_2$ (100 mL), was washed with M HCl, 5% $NaHCO_3$, and 20% NaCl, and dried over $MgSO_4$. The solvent was evaporated, and the product was chromatographed, affording orthoester **27** (46 mg, 0.106 mmol, 58%) as a 17:1 mixture of two diastereomers. $^1$H-N.m.r. data for the major diastereomer: $\delta$ 1.18 (t, 3 H, *J* 7.1 Hz, ethoxy-$CH_3$), 2.07, 2.12, 2.17 (3s, 12 H, 3 OAc and 1 4-oxopentyl $CH_3$), 2.20, 2.62 (2m, 4 H, 2 orthoester $CH_2$), 3.54 (q, 2 H, *J* 7.1 Hz, ethoxy $CH_2$), 4.10 (dd, 1 H, $J_{5,6}$ 6.7, $J_{6,6'}$ 11.3 Hz, H-6), 4.18 (dd, 1 H, $J_{5,6'}$ 6.7 Hz, H-6'), 4.32 (m, 2 H, H-2 and H-5), 5.06 (dd, 1 H, $J_{2,3}$ 6.6, $J_{3,4}$ 3.1 Hz, H-3), 5.46 (t, 1 H, $J_{4,5}$ 3.1 Hz, H-4), and 5.80 (d, 1 H, $J_{1,2}$ 4.7 Hz, H-1).

*Ortho-esters from 1,2,3,4,6-penta-*O*-acetyl-α-*D*-galactopyranose and 1,3,4,6-tetra-*O*-acetyl-2-*O*-levulinoyl-α-*D*-galactopyranose.* — Equimolar amounts of 1,2,3,4,6-penta-*O*-acetyl-α-D-galactopyranose (42 mg, 0.108 mmol) and 1,3,4,6-tetra-*O*-acetyl-2-*O*-levulinoyl-α-D-galactopyranose (48 mg, 0.108 mmol) were mixed and treated with 45% HBr in AcOH (0.7 mL) and $Ac_2O$ (0.015 mL) for 2 h at room temperature. The mixture was diluted with water, extracted into $CHCl_3$ (3 × 50 mL), and the extracts were washed with saturated $NaHCO_3$, 20% NaCl, and dried over $MgSO_4$. Evaporation of the solvent yielded a mixture of bromides in

equimolar amounts (82 mg; 87%). The presence of equivalent amounts of the two bromides was evidenced from integration of the H-1 signals at $\delta$ 6.70 (2-acetate) and $\delta$ 6.65 (2-levulinate). The crude product, in $CH_2Cl_2$ (2.5 mL), was added to a stirred mixture of $Bu_4NBr$ (300 mg), collidine (0.33 mL), EtOH (0.37 mL) and molecular sieves (3Å). Approximately one-third of the mixture was removed at 2, 4, and 6 h, respectively, and purified through a short column of silica gel. In the $^1$H-n.m.r. spectra of these three fractions, the H-1 signals of both starting bromides were found to decrease in intensity at the same rate, whereas the H-1 signals of the newly formed orthoesters at $\delta$ 5.81 (orthoester from the 2-acetate) and at $\delta$ 5.80 (orthoester from the 2-levulinate) were found to increase at the same rate over the intervals of 2, 4, and 6 h.

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