Carbohydrate Research, 255 (1994) 61–85
Elsevier Science B.V., Amsterdam

Synthesis of hyaluronic acid-related di-, tri-, and tetra-saccharides having an *N*-acetylglucosamine residue at the reducing end *

Ted M. Slaghek [a,b,†], Yoshiaki Nakahara [b], Tomoya Ogawa [b,c], Johannis P. Kamerling [a] and Johannes F.G. Vliegenthart [a]

[a] *Bijvoet Center, Department of Bio-Organic Chemistry, Utrecht University, P.O. Box 80.075, NL-3508 TB Utrecht (Netherlands)*
[b] *The Institute of Physical and Chemical Research (RIKEN), Wako-shi, Hirosawa 2-1, Saitama, 351-01 (Japan)*
[c] *Faculty of Agriculture, University of Tokyo, Yayoi, Bunkyo-ku, Tokyo, 113 (Japan)*

(Received March 26th, 1993; accepted August 10th, 1993)

ABSTRACT

The synthesis is reported of 4-methoxyphenyl *O*-(β-D-glucopyranosyluronic acid)-(1 → 3)-2-acetamido-2-deoxy-β-D-glucopyranoside (**1**), 4-methoxyphenyl *O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 4)-*O*-(β-D-glucopyranosyluronic acid)-(1 → 3)-2-acetamido-2-deoxy-β-D-glucopyranoside (**5**), and 4-methoxyphenyl *O*-(β-D-glucopyranosyluronic acid)-(1 → 3)-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 4)-*O*-(β-D-glucopyranosyluronic acid)-(1 → 3)-2-acetamido-2-deoxy-β-D-glucopyranoside (**10**), which are structural elements of the extracellular polysaccharide hyaluronic acid. 6-*O*-Levulinoyl-2,3,4-tri-*O*-*p*-toluoyl-α-D-glucopyranosyl trichloroacetimidate (**3**) was condensed with 4-methoxyphenyl 2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-D-glucopyranoside (**4**). De-isopropylidenation and acetylation of the obtained disaccharide derivative yielded 4-methoxyphenyl *O*-(6-*O*-levulinoyl-2,3,4-tri-*O*-*p*-toluoyl-β-D-glucopyranosyl)-(1 → 3)-4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside, and subsequent delevulinoylation, oxidation, complete deprotection, and *N*-acetylation gave **1**. Coupling of 4-*O*-allyloxycarbonyl-6-*O*-levulinoyl-2,3-di-*O*-*p*-toluoyl-α-D-glucopyranosyl trichloroacetimidate with **4** followed by de-isopropylidenation, acetylation, and deallyloxycarbonylation of the obtained disaccharide derivative gave **8**. Condensation of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate with **8** afforded trisaccharide derivative 4-methoxyphenyl *O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1 → 4)-*O*-(6-*O*-levulinoyl-2,3-di-*O*-*p*-toluoyl-β-D-glucopyranosyl)-(1 → 3)-4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside, and subsequent delevulinoylation, oxidation, complete deprotection, and *N*-acetylation gave **5**. 3-*O*-Allyloxycarbonyl-2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate was coupled with disaccharide acceptor **8**, and deallyloxycarbonylation of the obtained trisaccharide derivative yielded **12**. Condensation of **3** with **12** followed by de-isopropylidenation and acetylation of the obtained tetrasaccharide derivative gave 4-methoxyphenyl *O*-(6-*O*-levulinoyl-2,3,4-tri-*O*-*p*-toluoyl-β-D-glucopyranosyl)-(1 → 3)-*O*-(4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1 →

* Part 2 of the series, "Synthesis of Oligosaccharides Related to Hyaluronic Acid". For part 1 see ref 1.
† Corresponding author.

SSDI 0008-6215(93)E0384-D

4)-*O*-(6-*O*-levulinoyl-2,3-di-*O*-*p*-toluoyl-β-D-glucopyranosyl)-(1 → 3)-4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside, and delevulinoylation, oxidation, complete deprotection, and *N*-acetylation yielded **10**.

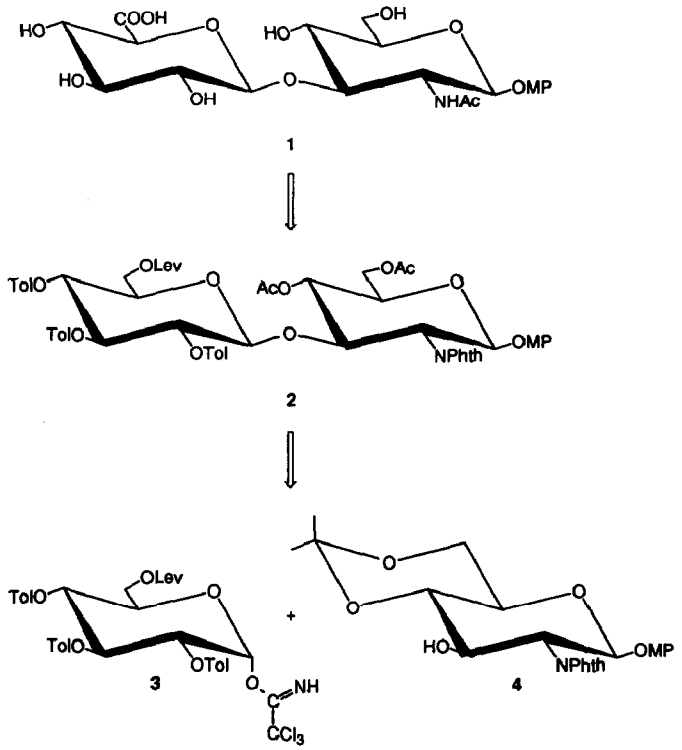
INTRODUCTION

Hyaluronic acid[2] (HA) is a linear extracellular carbohydrate polymer consisting of disaccharide repeating units of 2-acetamido-2-deoxy-D-glucose and D-glucuronic acid, namely[3], [4)-β-D-Glc*p*A-(1 → 3)-β-D-Glc*p*NAc-(1 →]$_n$. HA is synthesised by a membrane-bound hyaluronic acid synthetase at the inner side of plasma membranes, and is then extruded to the cell surface[4]. It plays an important role in cell migration[5], the repair of fetal wounds[6,7], and the regulation of cell locomotion[8]. The interaction of HA with the cell surface is organised via a receptor glycoprotein, which has a receptor binding site that coordinates at least a hexasaccharide fragment of HA[9]. A high concentration of HA inhibits vascularisation[10], while medium-sized oligosaccharide fragments of HA, generated by digestion with, for example, testicular hyaluronidase or *Streptomyces* hyaluronidase, stimulate the formation of new capillary blood vessels[11]. Therefore it appears that HA is an important angiogenic factor[11,12].

The finding of the stimulating effect of enzymically generated HA oligosaccharides of the type [4)-β-D-Glc*p*A-(1 → 3)-β-D-Glc*p*NAc-(1 →]$_{3-10}$ on capillary blood vessel formation led to the initiation of a synthetic program focused on the preparation of a wide range of medium-sized oligosaccharide fragments with 2-acetamido-2-deoxy-D-glucose or D-glucuronic acid units at the reducing position. This series of carbohydrates, being more diverse than the enzymically prepared series, will make it possible to study this highly interesting biological phenomenon in more detail. The present report describes the stereoselective synthesis of a di- (**1**), tri- (**5**), and tetra-saccharide (**10**) fragment having a 4-methoxyphenyl 2-acetamido-2-deoxy-D-glucopyranose residue at the reducing end.

RESULTS AND DISCUSSION

For the syntheses of the three oligosaccharides **1**, **5**, and **10** a series of suitable coupling synthons, namely **3**, **4**, **7**, **9**, and **13**, were designed, which in principle would serve for extension to higher oligosaccharides. 6-*O*-Levulinoyl-2,3,4-tri-*O*-*p*-toluoyl-α-D-glucopyranosyl trichloroacetimidate (**3**) and 4-*O*-allyloxycarbonyl-6-*O*-levulinoyl-2,3-di-*O*-*p*-toluoyl-α-D-glucopyranosyl trichloroacetimidate (**9**) are precursors for the D-glucuronic acid element in nonreducing terminal and internal positions, respectively, whereas 4-methoxyphenyl 2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-D-glucopyranoside (**4**), 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate (**7**), and 3-*O*-allyloxycarbonyl-2-deoxy-4,6-

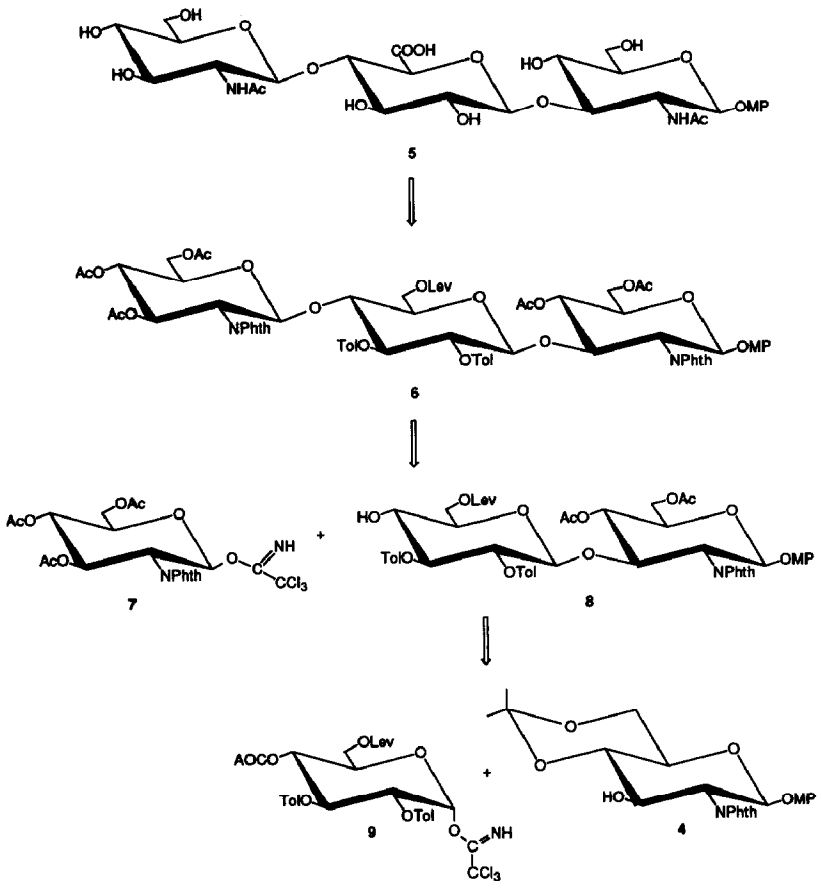


Lev = Levulinoyl; MP = 4-methoxyphenyl; Tol = *p*-toluoyl; Phth = phthaloyl

Scheme 1. Retrosynthetic analysis of disaccharide structure **1**.

O-isopropylidene-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate (**13**) are the precursors for the 2-acetamido-2-deoxy-D-glucose element in glycosidic, nonreducing terminal, and internal positions, respectively. Of the 5 synthons, only monosaccharide derivative **7** has been synthesised before[13]. The preparation of the remaining 4 compounds will be presented first.

1,2,3,4,6-Penta-*O*-acetyl-β-D-glucopyranose (**14**) was glycosylated with 4-methoxyphenol in dichloromethane, using trimethylsilyl trifluoromethanesulfonate as a promoter (→ **15**, 95%). Then conventional saponification (→ **16**) and 4,6-*O*-benzylidenation with benzaldehyde dimethyl acetal in the presence of *p*-toluenesulfonic acid gave **17** (88%). The HO-2 and -3 groups of **17** were *p*-toluoylated with *p*-toluoyl chloride in pyridine (→ **18**, 99%), and after acid hydrolysis of the benzylidene group (→ **19**, 88%), the primary hydroxyl group was selectively protected using levulinic acid in the presence of 2-chloro-1-methylpyridinium iodide and 1,4-diazabicyclo[2.2.2]octane[14,15] (→ **20**, 96%). *p*-Toluoylation of HO-4 of **20** (→ **21**, 90%), followed by removal of the 4-methoxyphenyl group with ammonium cerium(IV)nitrate[16] (→ **22**, 88%) and subsequent imidation with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene[17] gave **3** (89%). On the

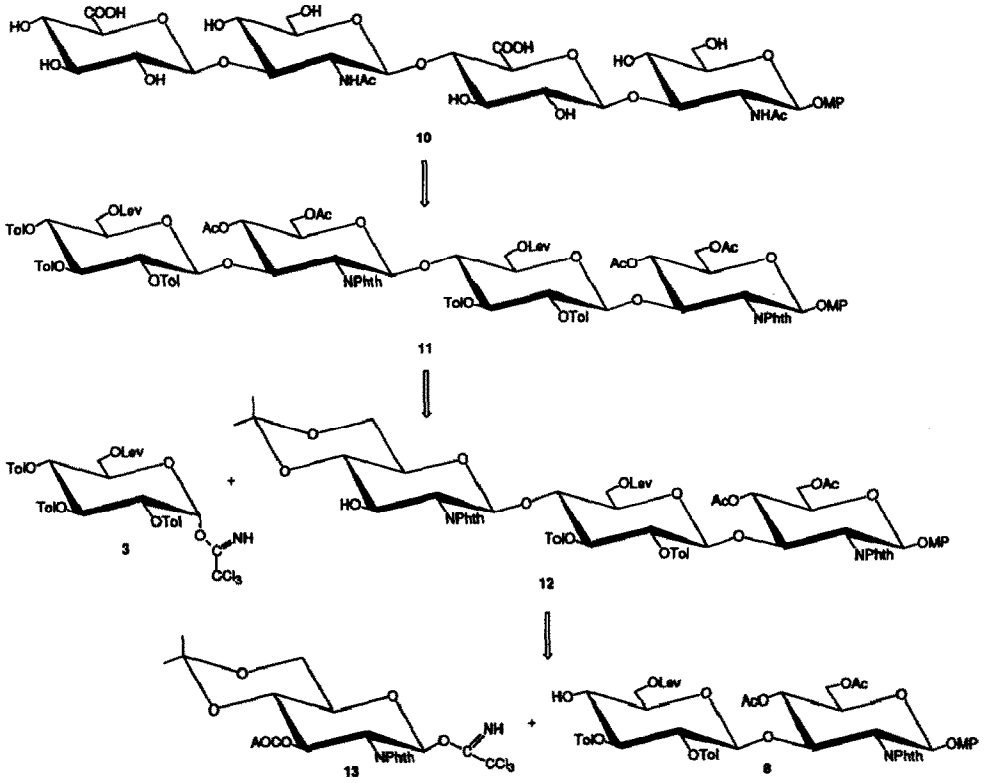


Scheme 2. Retrosynthetic analysis of trisaccharide structure **5**.

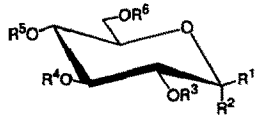
other hand, allyloxycarbonylation of HO-4 of **20** with allyl chloroformate in 1:1 pyridine–dichloromethane at −35°C[18] afforded **23** (71%), which, after removal of the 4-methoxyphenyl group with ammonium cerium(IV) nitrate (→ **24**, 88%), was converted into the trichloroacetimidate **9** (81%) using trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene.

4-Methoxyphenyl 2-deoxy-2-phthalimido-β-D-glucopyranoside[19] (**25**) was 4,6-*O*-isopropylidenated with 2,2-dimethoxypropane in *N*,*N*-dimethylformamide using a catalytic amount of *p*-toluenesulfonic acid to give **4** (86%). Allyloxycarbonylation of HO-3 of **4** with allyl chloroformate in 1:1 pyridine–dichloromethane at −35°C (→ **26**, 96%), followed by removal of the 4-methoxyphenyl group with ammonium cerium(IV) nitrate (→ **27**, 76%), and subsequent imidation as described above yielded **13** (92%).

As a first step in the synthesis of disaccharide 4-methoxyphenyl glycoside **1**, the

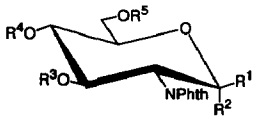


Scheme 3. Retrosynthetic analysis of tetrasaccharide structure **10**.



	R^1	R^2	R^3	R^4	R^5	R^6
14	OAc	H	Ac	Ac	Ac	Ac
15	OMP	H	Ac	Ac	Ac	Ac
16	OMP	H	H	H	H	H
17	OMP	H	H	H	CHPh	
18	OMP	H	Tol	Tol	CHPh	
19	OMP	H	Tol	Tol	H	H
20	OMP	H	Tol	Tol	H	Lev
21	OMP	H	Tol	Tol	Tol	Lev
22	H,OH		Tol	Tol	Tol	Lev
23	OMP	H	Tol	Tol	AOC	Lev
24	H,OH		Tol	Tol	AOC	Lev

Scheme 4.

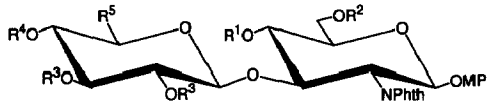


	R1	R2	R3	R4	R5
25	OMP	H	H	H	H
26	OMP	H	AOC	$\widetilde{CMe_2}$	
27	$\widetilde{H,OH}$		AOC	$\widetilde{CMe_2}$	

Scheme 5.

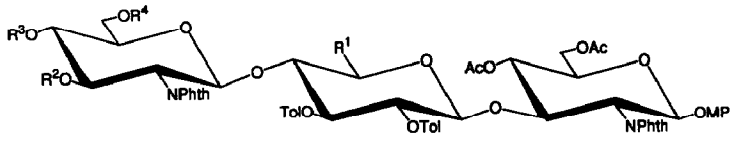
condensation of **3** and **4** in dichloromethane at 0°C, using trimethylsilyl trifluoromethanesulfonate as a promoter, afforded disaccharide derivative **28** (81%). Then de-isopropylidenation of **28** with aqueous trifluoroacetic acid in dichloromethane (→ **29**, 84%), subsequent conventional acetylation (→ **2**, 97%), and delevulinoylation using hydrazine acetate in 1:2 toluene–ethanol[20,21] gave **30** (98%). The oxidation of the primary hydroxyl group of the glucose unit in **30** was conducted in two stages, namely first a Swern oxidation with oxalyl chloride and dimethyl sulfoxide[22], then a treatment with sodium chlorite[23], giving **31** in 70% yield. To obtain **1**, **31** was treated with methylamine[24] in ethanol followed by selective *N*-acetylation using acetic anhydride in methanol. However, because ^{1}H NMR showed the presence of an *O*-acetyl group, an additional treatment with sodium methoxide in methanol was necessary to yield **1** (65%).

The synthesis of trisaccharide 4-methoxyphenyl glycoside **5** was carried out as follows. Condensation of glycosyl imidate **9** with acceptor **4** in dichloromethane at 0°C, using trimethylsilyl trifluoromethanesulfonate as a promoter, gave disaccharide derivative **32** (87%). Then de-isopropylidenation of **32** using aqueous trifluoroacetic acid in dichloromethane (→ **33**, 88%), subsequent conventional acetylation (→ **34**, 98%), and de-allyloxycarbonylation with tetrakis(triphenylphosphine) palladium[25,26] in tetrahydrofuran and morpholine gave disaccharide acceptor **8**



	R1	R2	R3	R4	R5
28	$\widetilde{CMe_2}$		Tol	Tol	CH_2OLev
29	H	H	Tol	Tol	CH_2OLev
30	Ac	Ac	Tol	Tol	CH_2OH
31	Ac	Ac	Tol	Tol	COOH
32	$\widetilde{CMe_2}$		Tol	AOC	CH_2OLev
33	H	H	Tol	AOC	CH_2OLev
34	Ac	Ac	Tol	AOC	CH_2OLev

Scheme 6.



	R^1	R^2	R^3	R^4
35	CH_2OH	Ac	Ac	Ac
36	COOH	Ac	Ac	Ac
37	CH_2OLev	AOC	CMe_2	

Scheme 7.

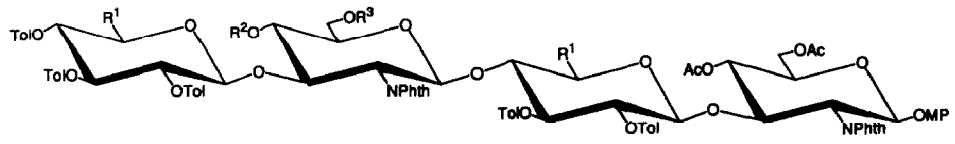
(95%). Condensation of **8** with glycosyl imidate **7** in dichloromethane at 25°C, using boron trifluoride etherate as a promoter, gave trisaccharide derivative **6** (81%). After removal of the levulinoyl group with hydrazine acetate in 1:2 toluene–ethanol (→ **35**, 88%), a Swern oxidation with oxalyl chloride and dimethyl sulfoxide followed by an oxidation with sodium chlorite afforded **36** (95%). Finally, **36** was deacylated with methylamine in methanol, followed by selective *N*-acetylation with acetic anhydride in methanol to give **5** (79%).

For the synthesis of tetrasaccharide 4-methoxyphenyl glycoside **10** disaccharide acceptor **8** was condensed with donor **13** in dichloromethane at 25°C, using boron trifluoride etherate as a promoter, to give trisaccharide derivative **37** (88%). After removal of the allyloxycarbonyl group with tetrakis(triphenylphosphine)palladium in tetrahydrofuran and morpholine (→ **12**, 95%), the product was condensed with glucose donor **3** in dichloromethane at 0°C, using trimethylsilyl trifluoromethanesulfonate, to give tetrasaccharide **38** (87%). Then de-isopropylidenation of **38** with aqueous trifluoroacetic acid in dichloromethane (→ **39**, 85%), followed by conventional acetylation (→ **11**, 96%), and de-levulinoylation with hydrazine acetate in 1:2 toluene–ethanol, gave **40** (76%). Subsequent Swern oxidation with oxalyl chloride and dimethyl sulfoxide in dichloromethane followed by an oxidation with sodium chlorite afforded **41** (86%). Finally, **41** was deacylated with methylamine in methanol, followed by selective *N*-acetylation with acetic anhydride in methanol, to afford **10** (82%).

The three synthesised oligosaccharides will be tested in biological systems.

EXPERIMENTAL

General methods.—The ^1H (300 and 500 MHz) and ^{13}C (75 and 100 MHz), including APT (attached proton test) experiments NMR spectra were recorded at 25°C with a GNM-GSX-500, a JEOL GX-400, a Bruker AC 300 or a Bruker AC 500 spectrometer, for solutions in $CDCl_3$ unless stated otherwise. Chemical shifts (δ) are given in ppm relative to the signal for internal Me_4Si ($CDCl_3$) or sodium 4,4-dimethyl-4-silapentane-1-sulfonate (D_2O, measured from internal acetone at δ



	R^1	R^2	R^3
38	CH_2OLev	CMe_2	
39	CH_2OLev	H	H
40	CH_2OH	Ac	Ac
41	COOH	Ac	Ac

Scheme 8.

2.225) for ^1H, and relative to the signal for internal Me_4Si ($CDCl_3$, measured from $CDCl_3$ at δ 76.9) or external Me_4Si (D_2O, measured from internal acetone at δ 31.55) for ^{13}C. Column chromatography was performed on Kieselgel 60 (Merck, 230–400 mesh), and fractions were monitored by TLC on Kieselgel 60 F_{254} (Merck) by detection with UV light and then charring with H_2SO_4. Optical rotations were measured on solutions in CH_2Cl_2, unless stated otherwise, at 20°C with a Perkin–Elmer 241 polarimeter, using a 10-cm, 1-mL cell. Melting points were determined with a Mettler FP-51 instrument. Solvents were evaporated under reduced pressure at 40°C (bath). All solvents were distilled from the appropriate drying agents.

4-Methoxyphenyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**15**).—To a solution of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**14**; 50.0 g, 128.2 mmol) and 4-methoxyphenol (24.0 g) in 1,2-dichloroethane (400 mL) was added $CF_3SO_3SiMe_3$ (2.5 mL) at 0°C. The mixture was stirred for 4.5 h, diluted with EtOAc (600 mL), washed with aq satd $NaHCO_3$ (2 × 200 mL) and water (2 × 200 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Crystallisation from 2-propanol and purification of the mother liquor by column chromatography (2:1 toluene–EtOAc) yielded **15** (55.3 g, 95%); $[\alpha]_D$ −21° (*c* 1); R_f 0.66; mp 102°C. ^1H NMR data: δ 2.032, 2.041, 2.076, and 2.083 (4 s, 12 H, 4 Ac), 3.775 (s, 3 H, $C_6H_4OCH_3$), 4.168 (dd, 1 H, $J_{6a,5}$ 2.2, $J_{6a,6b}$ − 12.1 Hz, H-6a), 4.288 (dd, 1 H, $J_{6b,5}$ 5.1 Hz, H-6b), 4.953 (d, 1 H, $J_{1,2}$ 7.3 Hz, H − 1), 6.817 and 6.946 (2 d, 4 H, $C_6H_4OCH_3$). Anal. Calcd for $C_{21}H_{26}O_{11}$: C, 55.50; H, 5.77. Found: C, 55.48; H, 5.76.

4-Methoxyphenyl 4,6-O-benzylidene-β-D-glucopyranoside (**17**).—To a solution of **15** (5.07 g, 11.16 mmol) in MeOH (50 mL) was added 0.1 M methanolic NaOMe (5.0 mL), and the mixture was stirred overnight, when TLC (10:2:1 EtOAc–EtOH–H_2O) showed the deacetylation to be complete (**16**; R_f 0.71). Then Amberlyst-15 resin was added to neutralise the mixture and it was filtered and concentrated to give crude **16**. The residue was dissolved in DMF (56 mL), and benzaldehyde dimethyl acetal (2.6 mL) and *p*-TsOH were added. The mixture was stirred overnight, when TLC (5:1 CH_2Cl_2–acetone) showed the benzylidenation to be complete (**17**; R_f 0.65). Amberlyst-21 resin was added to neutralise the acid,

and the mixture was filtered and concentrated. Column chromatography (5:1 CH_2Cl_2–acetone) of the residue gave **17**, isolated as a syrup (3.69 g, 88%); $[\alpha]_D$ −48° (*c* 1, MeOH). ^1H NMR data: δ 3.791 (s, 3 H, $C_6H_4OCH_3$), 4.903 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 5.587 (s, 1 H, C_6H_5CH), 6.851 and 7.049 (2 d, 4 H, $C_6H_4OCH_3$), 7.36–7.37 and 7.48–7.52 (2 m, 5 H, C_6H_5CH). Anal. Calcd for $C_{20}H_{22}O_7$: C, 64.16; H, 5.92. Found: C, 63.98; H, 5.89.

4-Methoxyphenyl 4,6-O-benzylidene-2,3-di-O-p-toluoyl-β-D-glucopyranoside (**18**). —To a solution of **17** (3.18 g, 8.49 mmol) in pyridine (40 mL) was added *p*-toluoyl chloride (3.5 mL) and 4-dimethylaminopyridine (5 mg). When TLC (95:5 CH_2Cl_2–EtOAc) showed the reaction to be complete (**18**; R_f 0.89), the mixture was diluted with EtOAc (100 mL) and washed with aq satd $NaHCO_3$ (20 mL) and water (20 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (3:2 hexane–EtOAc) of the residue yielded **18**, isolated as a syrup (5.16 g, 99%); $[\alpha]_D$ +65° (*c* 1). ^1H NMR data: δ 2.344 and 2.351 (2 s, 6 H, 2 $COC_6H_4CH_3$), 3.736 (s, 3 H, $C_6H_4OCH_3$), 3.774 (m, 1 H, H-5), 5.232 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 5.562 (s, 1 H, C_6H_5CH), 5.684 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 5.812 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 6.768 and 6.920 (2 d, 4 H, $C_6H_4OCH_3$), 7.163 (4 H), 7.858, and 7.874 (3 d, 8 H, 2 $COC_6H_4CH_3$), and 7.31–7.41 (m, 5 H, C_6H_5CH). Anal. Calcd for $C_{36}H_{34}O_9$: C, 70.80; H, 5.61. Found: C, 70.15; H, 5.57.

4-Methoxyphenyl 2,3-di-O-p-toluoyl-β-D-glucopyranoside (**19**).—A solution of **18** (6.02 g, 9.86 mmol) in acetic acid (39.2 mL) and water (9.8 mL) was stirred at 80°C until TLC (4:1 CH_2Cl_2–acetone) showed the conversion of **18** into **19** (R_f 0.76). Then the solution was concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 100 mL) were evaporated from the residue. Column chromatography (4:1 CH_2Cl_2–acetone) of the residue gave **19**, isolated as a syrup (4.54 g, 88%); $[\alpha]_D$ + 132° (*c* 1). ^1H NMR data: δ 2.352 and 2.361 (2 s, 6 H, 2 $COC_6H_4CH_3$), 3.742 (s, 3 H, $C_6H_4OCH_3$), 5.180 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 5.418 and 5.639 (2 t, 2 H, H-2,3), 6.771 and 6.909 (2 d, 4 H, $C_6H_4OCH_3$), 7.164, 7.179, 7.856, and 7.871 (4 d, 8 H, 2 $COC_6H_4CH_3$). Anal. Calcd for $C_{29}H_{30}O_9$: C, 66.65; H, 5.79. Found: C, 66.55; H, 5.82.

4-Methoxyphenyl 6-O-levulinoyl-2,3-di-O-p-toluoyl-β-D-glucopyranoside (**20**).—To a solution of **19** (16.10 g, 30.82 mmol) in 1,2-dichloroethane (500 mL) was added levulinic acid (6.31 mL) and 2-chloro-1-methylpyridinium iodide (20.3 g). The mixture was stirred for 15 min, then, 1,4-diazabicyclo[2.2.2]octane (13.36 g) was added, and the stirring was continued for another 20 min, when TLC (6:1 CH_2Cl_2–acetone) revealed the levulinoylation to be complete (**20**; R_f 0.86). Then the mixture was filtered through Celite, diluted with EtOAc (400 mL), and washed with aq 5% NaCl (2 × 200 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (95:5 CH_2Cl_2–acetone) of the residue gave **20**, isolated as a syrup (18.46 g, 96%); $[\alpha]_D$ + 76° (*c* 1). NMR data: ^1H, δ 2.187 (s, 3 H, $COCH_2CH_2COCH_3$), 2.353 and 2.364 (2 s, 6 H, 2 $COC_6H_4CH_3$), 2.64–2.78 (m, 4 H, $COCH_2CH_2COCH_3$), 3.514 (d, 1 H, $J_{OH,4}$ 4.4 Hz, OH), 3.744 (s, 3 H, $C_6H_4OCH_3$), 3.787 (m, 1 H, H-5), 3.962 (dt, 1 H, $J_{4,3} = J_{4,5} = 9.5$ Hz, H-4),

4.457 (dd, 1 H, $J_{6a,5}$ 2.2, $J_{6a,6b}$ −12.1 Hz, H-6a), 4.545 (dd, 1 H, $J_{6b,5}$ 5.1 Hz, H-6b), 5.121 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 5.43 (t, 1 H, $J_{3,2}$ 9.2 Hz, H-3), 5.640 (dd, 1 H, H-2), 6.768 and 6.930 (2 d, 4 H, $C_6H_4OCH_3$), 7.165, 7.180, 7.857, and 7.883 (4 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 21.5 ($COC_6H_4CH_3$), 28.0, 29.6, and 37.9 ($COCH_2CH_2COCH_3$), 55.5 ($C_6H_4OCH_3$), 63.3 (C-6), 100.7 (C-1), 114.5 (2 C), 118.8 (2 C), 151.3, and 155.7 ($C_6H_4OCH_3$), 165.3 and 166.9 (2 $COC_6H_4CH_3$), 172.8 ($COCH_2CH_2COCH_3$), and 206.6 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{34}H_{36}O_{11}$: C, 65.79; H, 5.85. Found: C, 65.36; H, 5.82.

4-Methoxyphenyl6-O-levulinoyl-2,3,4-tri-O-p-*toluoyl-β*-D-*glucopyranoside* (**21**).—To a solution of **20** (5.13 g, 8.26 mmol) in pyridine (41 mL) was added *p*-toluoyl chloride (1.64 mL). The solution was stirred overnight, when TLC (9:1 CH_2Cl_2–acetone) showed the formation of **21** (R_f 0.92). Then EtOAc (200 mL) was added, the mixture was washed with aq satd $NaHCO_3$ (50 mL) and water (50 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (98:2 CH_2Cl_2–acetone) of the residue yielded **21**, isolated as a syrup (5.47 g, 90%); $[\alpha]_D$ + 22° (*c* 1). NMR data: ^1H, δ 2.160 (s, 3 H, $COCH_2CH_2COCH_3$), 2.289 and 2.348 (6 H) (2 s, 9 H, 3 $COC_6H_4CH_3$), 2.676 (m, 4 H, $COCH_2CH_2CO$-CH_3), 3.744 (s, 3 H, $C_6H_4OCH_3$), 4.102 (m, 1 H, H-5), 5.231 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 5.578 and 5.894 (2 t, 2 H, H-3,4), 5.704 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 6.779 and 6.961 (2 d, 4 H, $C_6H_4OCH_3$), 7.080, 7.162 (4 H), 7.740, 7.809, and 7.853 (5 d, 12 H, 3 $COC_6H_4CH_3$); ^{13}C, δ 21.2 ($COC_6H_4CH_3$), 27.5, 29.3, and 37.5 ($COCH_2CH_2$-$COCH_3$), 55.2 ($C_6H_4OCH_3$), 63.0 (C-6), 100.5 (C-1), 114.2 (2 C), 118.5 (2 C), 150.8, and 155.4 ($C_6H_4OCH_3$), 164.8, 164.9, and 165.4 (3 $COC_6H_4CH_3$), 171.8 ($COCH_2$-CH_2COCH_3), and 205.8 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{42}H_{42}O_{12}$: C, 68.28; H, 5.73. Found: C, 68.35; H, 5.82.

6-O-Levulinoyl-2,3,4-tri-O-p-*toluoyl-α/β*-D-*glucopyranose* (**22**).—To a solution of **21** (5.47 g, 7.40 mmol) in 1:1:1 toluene–MeCN–water (600 mL) was added while stirring ammonium cerium(IV) nitrate (40.7 g). After 30 min TLC (9:1 CH_2Cl_2–acetone) showed the conversion of **21** into **22** (R_f 0.19). Then the mixture was diluted with EtOAc (500 mL) and washed with aq satd $NaHCO_3$ (50 mL) and water (100 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (9:1 CH_2Cl_2–acetone) of the residue yielded **22**, isolated as a syrup (4.11 g, 88%); $[\alpha]_D$ + 24° (*c* 1) (α:β 2.7:1). ^1H NMR data: δ 2.170 (s, 3 H, $COCH_2CH_2COCH_3$), 2.266, 2.325, and 2.334 (3 s, 9 H, 3 COC_6H_4-CH_3), 2.658 (m, 4 H, $COCH_2CH_2COCH_3$), 4.664 (d, 0.27 H, $J_{1,2}$ 8.1 Hz, H-1β), and 5.733 (d, 0.73 H, $J_{1,2}$ 3.3 Hz, H-1α). Anal. Calcd for $C_{35}H_{35}O_{11}$: C, 66.44; H, 5.74. Found: C, 66.16; H, 5.82.

6-O-Levulinoyl-2,3,4-tri-O-p-*toluoyl-α*-D-*glucopyranosyl trichloroacetimidate* (**3**).—To a solution of **22** (2.45 g, 3.88 mmol) in CH_2Cl_2 (11.1 mL) and trichloroacetonitrile (4.1 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (140 μL). The mixture was stirred overnight and purified by column chromatography (95:5 CH_2Cl_2–acetone) to yield **3**, isolated as a syrup (2.70 g, 89%); R_f 0.58; $[\alpha]_D$ + 38° (*c* 1). ^1H NMR data: δ 2.179 (s, 3 H, $COCH_2CH_2COCH_3$), 2.292, 2.341, and 2.356

(3 s, 9 H, 3 $COC_6H_4CH_3$), 2.61–2.74 (m, 4 H, $COCH_2CH_2COCH_3$), 5.545 (dd, 1 H, $J_{2,1}$ 3.7, $J_{2,3}$ 10.3 Hz, H-2), 5.662 and 6.200 (2 t, 2 H, H-3,4), 6.795 (d, 1 H, H-1), 7.086, 7.147, 7.168, 7.748, and 7.832 (4 H) (5 d, 12 H, 3 $COC_6H_4CH_3$), and 8.631 (s, 1 H, NH). Anal. Calcd for $C_{37}H_{36}Cl_3NO_{11}$: C, 57.18; H, 4.67. Found: C, 56.76; H, 4.68.

*4-Methoxyphenyl 4-O-allyloxycarbonyl-6-O-levulinoyl-2,3-di-*O-p-*toluoyl-β-*D-*glucopyranoside* (**23**)—To a solution of **20** (7.71 g, 12.42 mmol) in 1:1 CH_2Cl_2–pyridine (140 mL) at −35°C was added allyl chloroformate (3 × 2 mL, at intervals of 10 min). When TLC (85:15 toluene–acetone) showed the conversion of **20** into **23** (R_f 0.41), the mixture was diluted with EtOAc (200 mL) and washed with aq satd $NaHCO_3$ (50 mL) and water (50 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (98:2 CH_2Cl_2–acetone) of the residue yielded **23**, isolated as a syrup (6.23 g, 71%); $[\alpha]_D$ + 65° (*c* 1). NMR data: ^1H, δ 2.192 (s, 3 H, $COCH_2CH_2COCH_3$), 2.354 and 2.358 (2 s, 6 H, 2 $COC_6H_4CH_3$), 2.61–2.81 (m, 4 H, $COCH_2CH_2COCH_3$), 3.739 (s, 3 H, $C_6H_4OCH_3$), 4.342 (dd, 1 H, $J_{6a,5}$ 2.6, $J_{6a,6b}$ −13.2 Hz, H-6a), 4.395 (dd, 1 H, $J_{6b,5}$ 5.1 Hz, H-6b), 5.164 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 5.638 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-2), 6.763 and 6.925 (2 d, 4 H, $C_6H_4OCH_3$), 7.165 (4 H), 7.835, and 7.851 (3 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 21.6 ($COC_6H_4CH_3$), 27.9, 29.7, and 37.9 ($COCH_2CH_2CO-CH_3$), 55.6 ($C_6H_4OCH_3$), 62.4 (C-6), 100.9 (C-1), 114.5 (2 C), 119.0 (2 C), 151.0, and 155.9 ($C_6H_4OCH_3$), 119.0 ($COOCH_2CH=CH_2$), 131.0 ($COOCH_2CH=CH_2$), 153.8 ($COOCH_2CH=CH_2$), 165.1 and 165.6 (2 $COC_6H_4CH_3$), 172.2 ($COCH_2-CH_2COCH_3$), and 206.1 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{38}H_{40}O_{13}$: C, 64.76; H, 5.72. Found: C, 64.92; H, 5.77.

*4-O-Allyloxycarbonyl-6-O-levulinoyl-2,3-di-*O-p-*toluoyl-α/β-*D-*glucopyranose* (**24**). —To a suspension of **23** (6.23 g, 8.84 mmol) in 3:4:3 toluene–MeCN–water (500 mL) was added ammonium cerium(IV) nitrate (48.6 g). After stirring for 40 min TLC (95:5 CH_2Cl_2–acetone) showed the conversion of **23** into **24** (R_f 0.17). Then the mixture was diluted with EtOAc (300 mL) and washed with aq satd $NaHCO_3$ (50 mL) and water (100 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (9:1 CH_2Cl_2–acetone) of the residue gave **24**, isolated as a syrup (4.22 g, 88%); $[\alpha]_D$ + 101° (*c* 1) (α:β 2.3:1). ^{13}C NMR data: δ 21.6 ($COC_6H_4CH_3$), 28.0, 29.7, and 38.0 ($COCH_2CH_2COCH_3$), 62.4 (C-6), 90.4 (C-1α), 95.8 (C-1β), 118.8 ($COOCH_2CH=CH_2$), 131.0 ($COOCH_2CH=CH_2$), 154.0 ($COOCH_2CH=CH_2$), 172.4 ($COCH_2CH_2COCH_3$), and 207.0 ($CO-CH_2CH_2COCH_3$). Anal. Calcd for $C_{31}H_{34}O_{12}$: C, 62.20; H, 5.73. Found: C, 62.20; H, 5.78.

*4-O-Allyloxycarbonyl-6-O-levulinoyl-2,3-di-*O-p-*toluoyl-α-*D-*glucopyranosyl trichloroacetimidate* (**9**).—To a solution of **24** (3.41 g, 6.26 mmol) in CH_2Cl_2 (18 mL) was added trichloroacetonitrile (6.7 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (240 μL). The mixture was stirred overnight and purified by column chromatography (93:7 CH_2Cl_2–acetone) to yield **9**, isolated as a syrup (3.78 g, 81%); R_f 0.88; $[\alpha]_D$ + 105° (*c* 1). NMR data: ^1H, δ 2.170 (s, 3 H, $COCH_2CH_2COCH_3$), 2.345 and

2.360 (2 s, 6 H, 2 $COC_6H_4CH_3$), 2.66–2.79 (m, 4 H, $COCH_2CH_2COCH_3$), 5.057 and 5.171 (2 m, 2 H, $COOCH_2CH{=}CH_2$), 5.472 (dd, 1 H, $J_{2,1}$ 3.7, $J_{2,3}$ 10.3 Hz, H-2), 5.695 (m, 1 H, $COOCH_2CH{=}CH_2$), 6.732 (d, 1 H, H-1), 7.147, 7.175, 7.831, and 7.851 (4 d, 8 H, 2 $COC_6H_4CH_3$), and 8.607 (s, 1 H, NH); ^{13}C, δ 21.6 ($COC_6H_4CH_3$), 27.9, 29.8, and 37.9 ($COCH_2CH_2COCH_3$), 61.7 (C-6), 90.1 ($CNHCCl_3$), 93.1 (C-1), 119.1 ($COOCH_2CH{=}CH_2$), 130.8 ($COOCH_2CH{=}CH_2$), 153.8 ($COOCH_2CH{=}CH_2$), 160.2 ($CNHCCl_3$), 165.4 ($COC_6H_4CH_3$), 172.2 ($COCH_2CH_2COCH_3$), and 205.0 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{33}H_{34}Cl_3NO_{12}$: C, 53.34; H, 4.61. Found: C, 53.38; H, 4.64.

4-Methoxyphenyl 2-deoxy-4,6-O-isopropylidene-2-phthalimido-β-D-glucopyranoside (**4**).—To a solution of 4-methoxyphenyl 2-deoxy-2-phthalimido-β-D-glucopyranoside[19] (**25**; 8.03 g, 28.0 mmol) in DMF (140 mL) and 2,2-dimethoxypropane (28 mL) was added a catalytic amount of *p*-TsOH. After overnight stirring TLC (2:1 toluene–EtOAc) showed the conversion of **25** into **4** (R_f 0.28). Then the mixture was neutralised with Amberlyst-21 resin, filtered, and concentrated. Column chromatography (3:1 toluene–EtOAc) of the residue yielded **4**, isolated as a syrup (11.02 g, 86%); $[\alpha]_D$ + 3° (*c* 1). ^1H NMR data: δ 1.38 and 1.51 [2 s, 6 H, $C(CH_3)_2$], 3.67 (s, 3 H, $C_6H_4OCH_3$), 5.73 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 6.63–6.88 (m, 4 H, $C_6H_4OCH_3$), and 7.60–7.86 (m, 4 H, Phth). Anal. Calcd for $C_{24}H_{25}NO_8$: C, 63.29; H, 5.53; N, 3.08. Found: C, 63.64; H, 5.56; N, 3.04.

4-Methoxyphenyl 3-O-allyloxycarbonyl-2-deoxy-4,6-O-isopropylidene-2-phthalimido-β-D-glucopyranoside (**26**).—To a solution of **4** (3.97 g, 8.72 mmol) in CH_2Cl_2 (48 mL) and pyridine (48 mL) at −35°C was added allyl chloroformate (3 × 1.4 mL, at intervals of 10 min). When TLC (9:1 toluene–EtOAc) showed a complete conversion of **4** into **26** (R_f 0.34), the mixture was diluted with EtOAc (200 mL) and washed with satd aq $NaHCO_3$ (50 mL) and water (50 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (9:1 toluene–EtOAc) of the residue yielded **26**, isolated as a syrup (4.52 g, 96%); $[\alpha]_D$ + 22° (*c* 1). NMR data: ^1H, δ 1.417 and 1.521 [2 s, 6 H, $C(CH_3)_2$], 3.708 (s, 3 H, $C_6H_4OCH_3$), 4.30–4.43 (m, 2 H, $COOCH_2CH{=}CH_2$), 4.560 (dd, 1 H, $J_{2,1}$ 8.4, $J_{2,3}$ 9.5 Hz, H-2), 4.969 and 5.083 (2 m, 2 H, $COOCH_2CH{=}CH_2$), 5.869 (d, 1 H, H-1), 6.722 and 6.816 (2 d, 4 H, $C_6H_4OCH_3$), and 7.73–7.85 (m, 4 H, Phth); ^{13}C, δ 19.0 and 28.9 [$C(CH_3)_2$], 55.2 and 55.6 ($C_6H_4OCH_3$ and C-2), 62.0 (C-6), 97.2 (C-1), 100.0 [$C(CH_3)_2$], 114.5 (2 C), 118.7 (2 C), 150.5, and 155.7 ($C_6H_4OCH_3$), 119.0 ($COOCH_2CH{=}CH_2$), 130.7 ($COOCH_2CH{=}CH_2$), and 154.3 ($COOCH_2CH{=}CH_2$). Anal. Calcd for $C_{28}H_{29}NO_{10}$: C, 62.33; H, 5.42; N, 2.60. Found: C, 62.10; H, 5.42; N, 2.58.

3-O-Allyloxycarbonyl-2-deoxy-4,6-O-isopropylidene-2-phthalimido-α/β-D-glucopyranose (**27**).—To a solution of **26** (1.00 g, 1.85 mmol) in toluene (78 mL) and MeCN (109 mL) was added water (78 mL) and ammonium cerium(IV) nitrate (10.2 g). After stirring for 20 min, TLC (6:1 CH_2Cl_2–acetone) showed a complete conversion into **27** (R_f 0.59). Then the mixture was diluted with EtOAc (200 mL) and washed with aq satd $NaHCO_3$ (50 mL) and water (50 mL), and the organic

layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (6:1 CH_2Cl_2–acetone) of the residue yielded **27**, isolated as a syrup (0.61 g, 76%); $[\alpha]_D$ −33.5° (*c* 1) (α/β 1:4). ^{13}C NMR data β anomer: δ 19.0 and 28.9 [$C(CH_3)_2$], 56.9 (C-2), 62.0 (C-6), 93.1 (C-1), 99.9 [$C(CH_3)_2$], and 118.6 ($COOCH_2CH{=}CH_2$): Anal. Calcd for $C_{21}H_{25}NO_9$: C, 58.19; H, 5.35. Found: C, 58.12; H, 5.21.

*3-O-Allyloxycarbonyl-2-deoxy-4,6-O-isopropylidene-2-phthalimido-β-*D*-glucopyranosyl trichloroacetimidate* (**13**).—To a solution of **27** (1.15 g, 2.65 mmol) in CH_2Cl_2 (7.6 mL) and trichloroacetonitrile (2.8 mL) was added 1,8-diazabicyclo-[5.4.0]undec-7-ene (100 μL). After overnight stirring TLC (9:1 CH_2Cl_2–acetone) showed a complete conversion of **27** into **13** (R_f 0.82), and the mixture was purified by column chromatography (9:1 CH_2Cl_2–acetone) to yield **13**, isolated as a syrup (1.42 g, 92%); $[\alpha]_D$ + 12° (*c* 1). NMR data: ^1H, δ 1.426 and 1.527 [2 s, 6 H, $C(CH_3)_2$], 4.618 (dd, 1 H, $J_{2,1}$ 8.8, $J_{2,3}$ 10.3 Hz, H-2), 5.007 and 5.119 (2 m, 2 H, $COOCH_2CH{=}CH_2$), 5.661 (m, 1 H, $COOCH_2CH{=}CH_2$), 6.635 (d, 1 H, H-1), 7.72–7.84 (m, 4 H, Phth), and 8.632 (s, 1 H, NH); ^{13}C, δ 19.0 and 28.9 [$C(CH_3)_2$], 54.2 (C-2), 61.8 (C-6), 94.0 (C-1), 100.1 [$C(CH_3)_2$], 118.7 ($COOCH_2CH{=}CH_2$), 131.0 ($COOCH_2CH{=}CH_2$), 154.3 ($COOCH_2CH{=}CH_2$), and 160.7 ($CNHCCl_3$).

*4-Methoxyphenyl O-(6-O-levulinoyl-2,3,4-tri-O-p-toluoyl-β-*D*-glucopyranosyl)-(1 → 3)-2-deoxy-4,6-O-isopropylidene-2-phthalimido-β-*D*-glucopyranoside* (**28**).—To a solution of **3** (2.67 g, 3.43 mmol) and **4** (1.35 g, 2.97 mmol) in CH_2Cl_2 (12 mL) containing powdered AW-300 molecular sieves (1.3 g) was added $CF_3SO_3SiMe_3$ (11.4 μL) at 0°C. The mixture was stirred for 30 min, when TLC (95:5 CH_2Cl_2–acetone) showed the disappearance of **4** and the formation of **28** (R_f 0.41). Then the mixture was neutralised with Et_3N, diluted with EtOAc (50 mL), filtered through Celite, and washed with water (15 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (97:3 CH_2Cl_2–acetone) of the residue yielded **28**, isolated as a syrup (2.57 g, 81%); $[\alpha]_D$ + 15° (*c* 1). NMR data: ^1H, δ 1.463 and 1.693 [2 s, 6 H, $C(CH_3)_2$], 2.131 (s, 3 H, $COCH_2CH_2COCH_3$), 2.251, 2.334, and 2.364 (3 s, 9 H, 3 $COC_6H_4CH_3$), 2.53–2.68 (m, 4 H, $COCH_2CH_2COCH_3$), 3.660 (s, 3 H, $C_6H_4OCH_3$), 5.204 (dd, 1 H, $J_{2',1'}$ 8.1, $J_{2',3'}$ 9.4 Hz, H-2′), 5.313 (d, 1 H, H-1′), 5.639 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 6.701 and 6.757 (2 d, 4 H, $C_6H_4OCH_3$), 7.067, 7.088, 7.226, 7.335, 7.551, and 7.772 (6 d, 12 H, 3 $COC_6H_4CH_3$); ^{13}C, δ 19.1 and 29.1 [$C(CH_3)_2$], 21.5 ($COC_6H_4CH_3$), 27.9, 29.1, and 37.8 ($COCH_2CH_2COCH_3$), 55.3 ($C_6H_4OCH_3$ and C-2), 98.1 (C-1), 99.7 [$C(CH_3)_2$], 100.2 (C-1′), 114.4 (2 C), 118.4 (2 C), 150.6, and 155.5 ($C_6H_4OCH_3$), 164.5, 165.0, and 165.5 (3 $COC_6H_4CH_3$), 172.1 ($COCH_2CH_2COCH_3$), and 206.0 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{59}H_{59}NO_{18}$: C, 66.22; H, 5.56; N, 1.31. Found: C, 65.45; H, 5.57; N, 1.29.

*4-Methoxyphenyl O-(6-O-levulinoyl-2,3,4-tri-O-p-toluoyl-β-*D*-glucopyranosyl)-(1 → 3)-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**29**).—To a solution of **28** (1.16 g, 1.09 mmol) in CH_2Cl_2 (19 mL) was added CF_3CO_2H (1.2 mL) and water (0.14 mL). After 45 min of stirring the de-isopropylidenation was complete as checked by TLC (**29**; R_f 0.33, 95:5 CH_2Cl_2–acetone). Then the mixture was concentrated,

and toluene, EtOH, and CH_2Cl_2 (each 3 × 100 mL) were evaporated from the residue. Column chromatography (85:15 CH_2Cl_2–acetone) of the residue yielded **29**, isolated as a syrup (939 mg, 84%); $[\alpha]_D$ + 28° (*c* 1). NMR data: ^1H, δ 2.218, 2.237, 2.321, and 2.335 (4 s, 12 H, 3 $COC_6H_4CH_3$ and $COCH_2CH_2COCH_3$), 2.64–2.80 (m, 4 H, $COCH_2CH_2COCH_3$), 3.673 (s, 3 H, $C_6H_4OCH_3$), 4.844 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1'), 5.480 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 6.653 and 6.683 (2 d, 4 H, $C_6H_4OCH_3$), 6.843, 6.970, 7.138, 7.342, 7.528, and 7.746 (6 d, 12 H, 3 $COC_6H_4CH_3$); ^{13}C, δ 21.5 ($COC_6H_4CH_3$), 27.7, 29.7, and 37.9 ($COCH_2CH_2CO-CH_3$), 54.8 and 55.4 ($C_6H_4OCH_3$ and C-2), 62.7 (C-6), 97.7 (C-1), 101.4 (C-1'), 114.5 (2 C), 118.2 (2 C), 150.7, and 155.4 ($C_6H_4OCH_3$), 172.2 ($COCH_2CH_2CO-CH_3$), and 206.4 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{56}H_{55}NO_{18}$: C, 65.30; H, 5.38; N, 1.36. Found: C, 64.99; H, 5.40; N, 1.31.

4-Methoxyphenyl O-(*6-O-levulinoyl-2,3,4-tri*-O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-4,6-di*-O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**2**).—To a solution of **29** (1.07 g, 1.04 mmol) in pyridine (10 mL) was added Ac_2O (10 mL) and 4-dimethylaminopyridine (5 mg). After overnight stirring, when TLC (9:1 CH_2Cl_2–acetone) showed the acetylation to be complete (**2**; R_f 0.93), the mixture was concentrated and toluene, EtOH, and CH_2Cl_2 (each 3 × 100 mL) were evaporated from the residue. Column chromatography (95:5 CH_2Cl_2–acetone) of the residue then yielded **2**, isolated as a syrup (1.13 g, 97%); $[\alpha]_D$ + 16° (*c* 1). NMR data: ^1H, δ 2.104, 2.145, and 2.175 (3 s, 9 H, 2 Ac and $COCH_2CH_2COCH_3$), 2.228, 2.319, and 2.381 (3 s, 9 H, 3 $COC_6H_4CH_3$), 2.60–2.74 (m, 4 H, $COCH_2-CH_2COCH_3$), 3.670 (s, 3 H, $C_6H_4OCH_3$), 4.526 (dd, 1 H, $J_{2,1}$ 8.4, $J_{2,3}$ 10.6 Hz, H-2), 4.691 (d, 1 H, $J_{1',2'}$ 8.1 Hz, H-1'), 5.256 (dd, 1 H, $J_{2',3'}$ 9.5 Hz, H-2'), 5.452 (d, 1 H, H-1), 6.651 and 6.693 (2 d, 4 H, $C_6H_4OCH_3$), 6.983, 7.028, 7.115, 7.457, 7.555, and 7.716 (6 d, 12 H, 3 $COC_6H_4CH_3$); ^{13}C, δ 20.8 ($COCH_3$), 21.3–21.6 (3 $COC_6H_4CH_3$), 27.8, 29.6, and 37.7 ($COCH_2CH_2COCH_3$), 55.4 ($C_6H_4OCH_3$ and C-2), 97.7 (C-1), 100.8 (C-1'), 114.4 (2 C), 118.4 (2 C), 150.6, and 155.6 ($C_6H_4OCH_3$), 164.8, 165.0, and 165.5 (3 $COC_6H_4CH_3$), 169.4 and 170.4 (2 $COCH_3$), 172.1 ($COCH_2CH_2COCH_3$), and 205.9 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{60}H_{59}NO_{20}$: C, 64.68; H, 5.34; N, 1.26. Found: C, 64.78; H, 5.42; N, 1.18.

4-Methoxyphenyl O-*(2,3,4-tri*-O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-4,6-di*-O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**30**).—To a solution of **2** (716 mg, 0.63 mmol) in EtOH (23 mL) and toluene (11.5 mL) was added $NH_2NH_2 \cdot$ AcOH (300 mg). The mixture was stirred for 40 min, when TLC (1:1 toluene–EtOAc) showed the conversion of **2** into **30** (R_f 0.63). Then the mixture was concentrated, and column chromatography (1:1 toluene–EtOAc) of the residue yielded **30**, isolated as a syrup (645 mg, 98%); $[\alpha]_D$ + 29° (*c* 1). NMR data: ^1H, δ 2.107 and 2.174 (2 s, 6 H, 2 Ac), 2.215, 2.324, and 2.369 (3 s, 9 H, 3 $COC_6H_4CH_3$), 3.665 (s, 3 H, $C_6H_4OCH_3$), 4.576 (dd, 1 H, $J_{2,1}$ 8.5, $J_{2,3}$ 10.9 Hz, H-2), 4.767 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 5.268 (dd, 1 H, $J_{2',3'}$ 9.6 Hz, H-2'), 5.461 (d, 1 H, H-1), 6.653 and 6.709 (2 d, 4 H, $C_6H_4OCH_3$), 6.981, 7.033, 7.136, 7.482, 7.577, and 7.771 (6 d,

12 H, 3 $COC_6H_4CH_3$); ^{13}C, δ 20.6 ($COCH_3$), 21.3 and 21.4 (2 C) (3 $COC_6H_4CH_3$), 55.3 ($C_6H_4OCH_3$ and C-2), 60.9 and 62.1 (C-6,6'), 97.5 (C-1), 100.0 (C-1'), 114.2 (2 C), 118.2 (2 C), 150.4, and 155.3 ($C_6H_4OCH_3$), 164.7, 165.5, and 166.0 (3 $COC_6H_4CH_3$), 169.8, and 170.6 (2 $COCH_3$). Anal. Calcd for $C_{55}H_{53}NO_{18}$: C, 64.97; H, 5.26. Found: C, 64.72; H, 5.32.

4-Methoxyphenyl O-*(2,3,4-tri*-O-p-*toluoyl-β-*D-*glucopyranosyluronic acid)-(1 → 3)-4,6-di*-O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**31**).—To a cold (−78°C) 2 M solution of oxalyl chloride in CH_2Cl_2 (0.5 mL) was added Me_2SO (150 μL). After 10 min of stirring a solution of **30** (103 mg, 101 μmol) in CH_2Cl_2 (1.7 mL) was added, and the mixture was stirred for 1 h at −78°C, whereby within 30 min a precipitate was formed. Diisopropylethylamine (739 μL) was added, and after 10 min the mixture was diluted with EtOAc (35 mL) and washed with M HCl (10 mL) and satd aq NaCl (10 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. To a solution of the residue in *t*-BuOH (4.2 mL), 2-methyl-2-butene (1.6 mL), and water (2.6 mL) were added NaH_2PO_4 (260 mg) and $NaClO_2$ (260 mg). After overnight stirring TLC (10:9:1 CH_2Cl_2–EtOAc–acetic acid) showed the conversion of **30** into **31** (R_f 0.51). Then the mixture was concentrated, and a solution of the residue in water was washed with hexane, acidified with M HCl, and extracted with EtOAc (3 × 20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (3:2 CH_2Cl_2–EtOAc followed by 10:9:1 CH_2Cl_2–EtOAc–acetic acid) of the residue yielded **31**, isolated as a pure (NMR) syrup (73 mg, 70%); $[\alpha]_D$ + 34° (*c* 1). NMR data: ^1H, δ 2.089 and 2.143 (2 s, 6 H, 2 Ac), 2.239, 2.315, and 2.372 (3 s, 9 H, 3 $COC_6H_4CH_3$), 3.667 (s, 3 H, $C_6H_4OCH_3$), 4.262 (d, 1 H, $J_{5',4'}$ 9.6 Hz, H-5'), 4.532 (dd, 1 H, $J_{2,1}$ 8.5, $J_{2,3}$ 10.8 Hz, H-2), 4.802 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1'), 5.281 (dd, 1 H, $J_{2',3'}$ 9.3 Hz, H-2'), 5.451 (d, 1 H, H-1), 6.642 and 6.689 (2 d, 4 H, $C_6H_4OCH_3$), 7.000, 7.009, 7.109, 7.463, 7.548, and 7.740 (6 d, 12 H, 3 $COC_6H_4CH_3$); ^{13}C, δ 20.6 ($COCH_3$), 21.4 and 21.5 (2 C) (3 $COC_6H_4CH_3$), 55.3 and 55.4 ($C_6H_4OCH_3$ and C-2), 62.6 (C-6), 97.4 (C-1), 100.5 (C-1'), 114.3 (2 C), 118.3 (2 C), 150.4, and 155.4 ($C_6H_4OCH_3$), 164.6, 165.1, and 165.4 (3 $COC_6H_4CH_3$), 169.4, 169.9, and 170.8 (2 $COCH_3$ and COOH). A small amount of **31** was esterified with diazomethane in ether, and analysed by ^1H NMR: δ 2.103 and 2.228 (2 s, 6 H, 2 Ac), 2.255, 2.340, and 2.389 (3 s, 9 H, 3 $COC_6H_4CH_3$), 3.650 (s, 3 H, $COOCH_3$), 3.679 (s, 3 H, $C_6H_4OCH_3$), 4.171 (d, 1 H, $J_{5',4'}$ 9.7 Hz, H-5'), 4.504 (dd, 1 H, $J_{2,1}$ 8.5, $J_{2,3}$ 10.9 Hz, H-2), 4.715 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 5.260 (dd, 1 H, $J_{2',3'}$ 9.6 Hz, H-2'), 5.413 (d, 1 H, H-1), 6.644 and 6.682 (2 d, 4 H, $C_6H_4OCH_3$), 7.015, 7.027, 7.134, 7.440, 7.591, and 7.740 (6 d, 12 H, 3 $COC_6H_4CH_3$).

4-Methoxyphenyl O-*(β-*D-*glucopyranosyluronic acid)-(1 → 3)-2-acetamido-2-deoxy-β-*D-*glucopyranoside* (**1**).—A solution of **31** (44 mg, 42 μmol) in ethanolic 30% methylamine (20 mL) was stirred for 3 days, when TLC (4:2:2:1 *n*-BuOH–EtOH–water–acetic acid) showed the conversion of the starting material into an intermediate amino compound (R_f 0.48). The mixture was concentrated, and a solution of the residue in MeOH (14.6 mL) and Ac_2O (204 μL) was stirred for 2 h

at 0°C, then concentrated, and 1:1 toluene–MeOH (3 × 15 mL) was evaporated from the residue. A solution of the residue in methanolic sodium methoxide (pH 10) was then stirred overnight at room temperature. After neutralisation with Amberlyst-15 the mixture was concentrated, and the residue was purified by gel filtration on Sephadex G-10 (water) to yield **1**, isolated after lyophilisation as an amorphous, white powder (14 mg, 65%); $[\alpha]_D$ −38° (*c* 0.5, H_2O). NMR data (D_2O): ^1H, δ 2.025 (s, 3 H, NHCOCH_3), 3.805 (s, 3 H, $C_6H_4OCH_3$), 4.573 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 5.066 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 6.962 and 7.053 (2 d, each 2 H, $C_6H_4OCH_3$); ^{13}C, δ 23.5 (NHCOCH_3), 55.7 ($C_6H_4OCH_3$ and C-2), 61.9 (C-6), 101.7 and 104.0 (C-1,1'), 116.5 (2 C), 119.7 (2 C), 152.3, and 156.2 ($C_6H_4OCH_3$), and 176.1 (*C*OOH and NH*C*OCH$_3$); FABMS *m/z* 504 $[M + H]^+$.

4-Methoxyphenyl O-*(4-O-allyloxycarbonyl-6-O-levulinoyl-2,3-di-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-2-deoxy-4,6-O-isopropylidene-2-phthalimido-β-*D-*glucopyranoside* (**32**).—To a solution of **9** (1.67 g, 2.24 mmol) and **4** (783 mg, 1.72 mmol) in CH_2Cl_2 (14 mL) containing powdered AW-300 molecular sieves (1.7 g) was added $CF_3SO_3SiMe_3$ (51 μL) at 0°C. When TLC (95:5 CH_2Cl_2–acetone) showed the disappearance of **4** and the formation of **32** (R_f 0.47), the mixture was diluted with EtOAc (50 mL), filtered through Celite, and washed with water (20 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (95:5 CH_2Cl_2–acetone) of the residue yielded **32**, isolated as a syrup (1.55 g, 87%); $[\alpha]_D$ + 68° (*c* 1). NMR data (CD_3COCD_3): ^1H, δ 1.471 and 1.677 [2 s, 6 H, C(CH_3)$_2$], 2.164 (s, 3 H, COCH$_2$CH$_2$COCH_3), 2.279 and 2.342 (2 s, 6 H, 2 $COC_6H_4CH_3$), 2.63–2.81 (m, 4 H, COCH_2CH_2COCH$_3$), 3.627 (s, 3 H, C_6H_4O-CH_3), 5.264 (d, 1 H, $J_{1',2'}$ 8.1 Hz, H-1'), 5.652 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 6.676 and 6.719 (2 d, 4 H, $C_6H_4OCH_3$), 7.045, 7.146, 7.331, and 7.652 (4 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 19.1 and 29.1 [C(*C*H$_3$)$_2$], 21.5 ($COC_6H_4CH_3$), 27.9, 29.7, and 37.8 (COCH_2CH_2COCH_3), 55.4 ($C_6H_4OCH_3$ and C-2), 98.0 (C-1), 99.6 [*C*(CH$_3$)$_2$], 100.1 (C-1'), 114.4 (2 C), 118.4 (2 C), 150.5, and 155.5 ($C_6H_4OCH_3$), 118.8 (COOCH$_2$CH=*C*H$_2$), 153.6 (*C*OOCH$_2$CH=CH$_2$), 164.4 and 165.3 (2 *C*O-$C_6H_4CH_3$), 172.2 (*C*OCH$_2$CH$_2$COCH$_3$), and 206.0 (COCH$_2$CH$_2$*C*OCH$_3$). Anal. Calcd for $C_{55}H_{57}NO_{19}$: C, 63.76; H, 5.55; N, 1.35. Found: C, 63.29; H, 5.58; N, 1.29.

4-Methoxyphenyl O-*(4-O-allyloxycarbonyl-6-O-levulinoyl-2,3-di-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**33**).—To a solution of **32** (1.65 g, 1.59 mmol) in CH_2Cl_2 (27.9 mL) was added water (0.2 mL) and CF_3CO_2H (1.7 mL). After 30 min of stirring TLC (9:1 CH_2Cl_2–acetone) showed the conversion of **32** into **33** (R_f 0.20). Then the mixture was concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 100 mL) were evaporated from the residue. Column chromatography (85:15 CH_2Cl_2–acetone) of the residue yielded **33**, isolated as a syrup (1.40 g, 88%); $[\alpha]_D$ + 92° (*c* 1). NMR data: ^1H, δ 2.230, 2.291, and 2.327 (3 s, 9 H, 2 $COC_6H_4CH_3$ and COCH$_2$CH$_2$COCH_3), 2.67–2.81 (m, 4 H, COCH_2CH_2COCH$_3$), 3.668 (s, 3 H, $C_6H_4OCH_3$), 4.666 (dd, 1 H, $J_{2,1}$ 8.4, $J_{2,3}$ 11.0 Hz, H-2), 4.768 (d, 1 H, $J_{1',2'}$ 8.1 Hz, H-1'), 5.358 (dd, 1 H, $J_{2',3'}$ 9.9

Hz, H-2'), 5.461 (d, 1 H, H-1), 5.662 (m, 1 H, $COOCH_2CH{=}CH_2$), 6.646 and 6.672 (2 d, 4 H, $C_6H_4OCH_3$), 6.851, 7.058, 7.352, and 7.635 (4 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 21.5 ($COC_6H_4CH_3$), 27.8, 29.7, and 37.9 ($COCH_2CH_2COCH_3$), 54.8 and 55.5 ($C_6H_4OCH_3$ and C-2), 97.7 (C-1), 101.3 (C-1'), 114.5 (2 C), 118.2 (2 C), 150.7, and 155.4 ($C_6H_4OCH_3$), 118.9 ($COOCH_2CH{=}CH_2$), 164.4 and 165.4 (2 $COC_6H_4CH_3$), 172.3 ($COCH_2CH_2COCH_3$), and 206.5 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{52}H_{53}NO_{19}$: C, 62.71; H, 5.36; N, 1.41. Found: C, 62.41; H, 5.37; N, 1.34.

4-Methoxyphenyl O-*(4-*O*-allyloxycarbonyl-6-*O*-levulinoyl-2,3-di-*O*-*p*-toluoyl-β-*D*-glucopyranosyl)-(1 → 3)-4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**34**).—To a solution of **33** (1.40 g, 1.40 mmol) in pyridine (10 mL) was added Ac_2O (10 mL) and 4-dimethylaminopyridine (5 mg). After overnight stirring, when TLC showed the acetylation to be complete (**34**; R_f 0.82, 9:1 CH_2Cl_2–acetone), the mixture was concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 100 mL) were evaporated from the residue. Column chromatography (95:5 CH_2Cl_2–acetone) then yielded **34**, isolated as a syrup (1.48 g, 98%); $[\alpha]_D$ + 79° (*c* 1). NMR data: ^1H, δ 2.101 and 2.122 (2 s, 6 H, 2 Ac), 2.206, 2.299, and 2.389 (3 s, 9 H, 2 $COC_6H_4CH_3$ and $COCH_2CH_2COCH_3$), 2.64–2.77 (m, 4 H, $COCH_2CH_2COCH_3$), 3.676 (s, 3 H, $C_6H_4OCH_3$), 4.603 (d, 1 H, $J_{1',2'}$ 8.1 Hz, H-1'), 5.427 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 6.648 and 6.682 (2 d, 4 H, $C_6H_4OCH_3$), 7.035, 7.073, 7.453, and 7.656 (4 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 20.7 ($COCH_3$), 21.6 ($COC_6H_4CH_3$), 27.8, 29.7, and 37.8 ($COCH_2CH_2COCH_3$), 55.5 ($C_6H_4OCH_3$ and C-2), 97.7 (C-1), 100.8 (C-1'), 114.4 (2 C), 118.4 (2 C), 150.6, and 155.5 ($C_6H_4OCH_3$), 118.8 ($COOCH_2CH{=}CH_2$), 131.0 ($COOCH_2CH{=}CH_2$), 153.7 ($COOCH_2CH{=}CH_2$), 164.7 and 165.4 (2 $COC_6H_4CH_3$), 169.3 and 170.5 (2 $COCH_3$), 172.2 ($COCH_2CH_2COCH_3$), and 206.0 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{56}H_{57}NO_{21}$: C, 62.27; H, 5.32; N, 1.30. Found: C, 62.36; H, 5.37; N, 1.22.

4-Methoxyphenyl O-*(6-*O*-levulinoyl-2,3-di-*O*-*p*-toluoyl-β-*D*-glucopyranosyl)-(1 → 3)-4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**8**).—To a solution of **34** (1.26 g, 1.17 mmol) in tetrahydrofuran (20 mL) and morpholine (0.7 mL) was added tetrakis(triphenylphosphine)palladium (233 mg). The mixture was stirred and boiled under reflux until the de-allyloxycarbonylation was complete (**8**; TLC R_f 0.38, 9:1 CH_2Cl_2–acetone). Then the mixture was diluted with EtOAc (100 mL) and washed with water (30 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (9:1 CH_2Cl_2–acetone) of the residue yielded **8**, isolated as a syrup (1.11 g, 95%); $[\alpha]_D$ + 86° (*c* 1). NMR data: ^1H, δ 2.159 and 2.181 (2 s, 6 H, 2 Ac), 2.294, 2.393, and 2.792 (3 s, 9 H, 2 $COC_6H_4CH_3$ and $COCH_2CH_2COCH_3$), 2.62–2.85 (m, 4 H, $COCH_2CH_2COCH_3$), 3.665 (s, 3 H, $C_6H_4OCH_3$), 4.852 (d, 1 H, $J_{1',2'}$ 8.1 Hz, H-1'), 5.072 (dd, 1 H, $J_{2',3'}$ 9.6 Hz, H-2'), 5.586 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 6.713 and 6.749 (2 d, 4 H, $C_6H_4OCH_3$), 7.103, 7.150, 7.419, and 7.664 (4 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 20.8 ($COCH_3$), 21.6 ($COC_6H_4CH_3$), 27.9, 29.7, and 37.9 ($COCH_2CH_2COCH_3$), 55.5 ($C_6H_4OCH_3$ and C-2), 62.5 and 63.1 (C-6,6'), 97.7 (C-1), 100.8 (C-1'), 114.4 (2 C), 118.4 (2 C),

150.7, and 155.6 ($C_6H_4OCH_3$), 165.0 and 166.0 (2 $COC_6H_4CH_3$), 169.4 and 170.7 (2 $COCH_3$), 173.1 ($COCH_2CH_2COCH_3$), and 206.8 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{52}H_{53}NO_{19}$: C, 62.71; H, 5.36; N, 1.41. Found: C, 62.74; H, 5.46; N, 1.32.

4-Methoxyphenyl O-*(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-(1 → 4)-*O*-(6-*O*-levulinoyl-2,3-di-*O*-*p*-toluoyl-β-*D*-glucopyranosyl)-(1 → 3)-4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**6**).—To a solution of **8** (114 mg, 0.114 mmol) and 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate[13] (**7**, 135 mg, 0.234 mmol) in CH_2Cl_2 (1.5 mL) containing powdered AW-300 molecular sieves (100 mg) was added a solution of M $BF_3 \cdot Et_2O$ in CH_2Cl_2 (70 μL). After 3 h stirring of the mixture at room temperature, TLC (1:1 toluene–acetone) showed the disappearance of **8** and the formation of **6** (R_f 0.24). Then Et_3N was added to neutralise the acids, the mixture was diluted with EtOAc (50 mL), filtered through Celite, and washed with water (10 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (1:1 toluene–acetone) of the residue yielded **6**, isolated as a syrup (130 mg, 81%); $[\alpha]_D$ + 51° (*c* 1). NMR data: ^1H, δ 1.772, 1.891, 1.901, 1.976, and 2.075 (5 s, 15 H, 5 Ac), 2.241 (s, 3 H, $COCH_2CH_2COCH_3$), 2.311 and 2.377 (2 s, 6 H, 2 $COC_6H_4CH_3$), 2.57–2.78 (m, 4 H, $COCH_2CH_2COCH_3$), 3.662 (s, 3 H, $C_6H_4OCH_3$), 4.433 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1'), 5.321 and 5.356 (2 d, 2 H, $J_{1,2} = J_{1'',2''} = 8.4$ Hz, H-1,1''), 6.626 and 6.648 (2 d, 4 H, $C_6H_4OCH_3$), 7.006, 7.069, 7.391, and 7.714 (4 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 20.2, 20.4, 20.6 (2 C), and 20.7 (5 $COCH_3$), 21.5 and 21.6 (2 $COC_6H_4CH_3$), 27.6, 29.6, and 37.8 ($COCH_2CH_2COCH_3$), 54.6, 55.2, and 55.6 ($C_6H_4OCH_3$ and C-2,2''), 61.4, 62.2, and 62.5 (C-6,6',6''), 97.5 and 97.6 (C-1,1''), 100.8 (C-1'), 114.2 (2 C), 118.3 (2 C), 150.5 and 155.4 ($C_6H_4OCH_3$), 164.9 and 165.0 (2 $COC_6H_4CH_3$), 169.2 (2 C), 169.9, 170.3, and 170.6 (5 $COCH_3$), 171.8 ($COCH_2CH_2COCH_3$), and 206.0 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{72}H_{72}N_2O_{28}$: C, 61.18; H, 5.14; N, 1.98. Found: C, 61.07; H, 5.18; N, 1.97.

4-Methoxyphenyl O-*(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)(1 → 4)-*O*-(2,3-di-*O*-*p*-toluoyl-β-*D*-glucopyranosyl)-(1 → 3)-4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**35**).—To a solution of **6** (231 mg, 0.163 mmol) in EtOH (23.3 mL) and toluene (11.7 mL) was added $NH_2NH_2 \cdot AcOH$ (75 mg). After 40 min of stirring TLC (1:1 toluene–EtOAc) showed the conversion of **6** into **35** (R_f 0.39). Then the mixture was concentrated, and column chromatography (1:1 toluene–EtOAc) of the residue yielded **35**, isolated as a syrup (189 mg, 88%); $[\alpha]_D$ + 57° (*c* 1). NMR data: ^1H, δ 1.785, 1.891, 1.924, 1.963, and 2.069 (5 s, 15 H, 5 Ac), 2.343 and 2.363 (2 s, 6 H, 2 $COC_6H_4CH_3$), 3.667 (s, 3 H, $C_6H_4OCH_3$), 4.643 (d, 1 H, $J_{1',2'}$ 7.3 Hz, H-1'), 5.388 and 5.494 (2 d, 2 H, $J_{1,2} = J_{1'',2''} = 8.4$ Hz, H-1,1''), 6.639 and 6.678 (2 d, 4 H, $C_6H_4OCH_3$), 7.027, 7.126, 7.462, and 7.744 (4 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 20.3, 20.5, 20.6, and 20.8 (2 C) (5 $COCH_3$), 21.6 ($COC_6H_4CH_3$), 54.9, 55.4, and 55.5 ($C_6H_4OCH_3$ and C-2,2''), 60.5, 61.2, and 62.2 (C-6,6',6''), 97.7 and 98.0 (C-1,1''), 99.7 (C-1'), 114.4 (2 C),

118.5 (2 C), 150.6, and 155.5 ($C_6H_4OCH_3$), 164.8 ($COC_6H_4CH_3$), 169.2, 169.6, 170.0, 170.4, and 170.6 (5 $COCH_3$). Anal. Calcd for $C_{67}H_{66}N_2O_{26}$: C, 61.18; H, 5.06; N, 2.13. Found: C, 61.58; H, 5.29; N, 2.02.

4-Methoxyphenyl O-*(3,4,6-tri*-O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl)-(1 → 4)*-O-*(2,3-di*-O-p-*toluoyl-β-*D-*glucopyranosyluronic acid)-(1 → 3)-4,6-di*-O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**36**).—To a cold (−78°C) 2 M solution of oxalyl chloride in CH_2Cl_2 (0.9 mL) was added Me_2SO (121 μL), and the solution was stirred for 10 min. Then a solution of **35** (122 mg, 93 μmol) in CH_2Cl_2 (2 mL) was added, and the mixture was stirred for 4 h at −78°C, whereby within 30 min a precipitate was formed. Diisopropylethylamine (656 μL) was added, and after 10 min the mixture was diluted with EtOAc (30 mL) and washed with M HCl (10 mL) and aq 5% NaCl (10 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. To a solution of the residue in *t*-BuOH (3.7 mL), 2-methyl-2-butene (1.4 mL), and water (2.3 mL) were added NaH_2PO_4 (230 mg) and $NaClO_2$ (230 mg). The mixture was stirred overnight, when TLC (10:9:1 CH_2Cl_2–EtOAc–AcOH) showed the complete conversion of **35** into **36** (R_f 0.24). Then the mixture was concentrated, and a solution of the residue in water was washed with hexane, acidified with M HCl, and extracted with EtOAc (3 × 20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (3:2 CH_2Cl_2–EtOAc followed by 10:9:1 CH_2Cl_2–EtOAc–AcOH) of the residue yielded **36**, isolated as a pure (NMR) syrup (118 mg, 95%); $[\alpha]_D$ + 16° (*c* 1). ^{1}H NMR data (1:1 $CDCl_3$–CD_3OD): δ 1.793, 1.866, 1.899, 1.927, and 2.085 (5 s, 15 H, 5 Ac), 2.316 and 2.399 (2 s, 6 H, 2 $COC_6H_4CH_3$), 3.669 (s, 3 H, $C_6H_4OCH_3$), 3.785 (d, 1 H, $J_{5',4'}$ 9.5 Hz, H-5'), 4.385 and 4.743 (2 dd, 2 H, H-2,2''), 4.551 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1'), 5.116 (dd, 1 H, $J_{2',3'}$ 9.5 Hz, H-2'), 5.352 and 5.384 (2 d, 2 H, $J_{1,2/1'',2''}$ 8.4 and 8.8 Hz, H-1,1''), 6.648 (m, 4 H, $C_6H_4OCH_3$), 7.003, 7.099, 7.346, and 7.705 (4 d, 8 H, 2 $COC_6H_4CH_3$). A small amount of **36** was esterified with diazomethane in ether, and analysed by ^{1}H NMR: δ 1.775, 1.883, 1.893, 1.905, and 2.070 (5 s, 15 H, 5 Ac), 2.322 and 2.381 (2 s, 6 H, 2 $COC_6H_4CH_3$), 3.554 (s, 3 H, $COOCH_3$), 3.664 (s, 3 H, $C_6H_4OCH_3$), 4.499 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1'), 4.888 and 5.356 (2 d, 2 H, $J_{1,2/1'',2''}$ 8.8 and 8.4 Hz, H-1,1''), 6.633 (m, 4 H, $C_6H_4OCH_3$), 6.999, 7.093, 7.378, and 7.717 (4 d, 8 H, 2 $COC_6H_4CH_3$).

4-Methoxyphenyl O-*(2-acetamido-2-deoxy-β-*D-*glucopyranosyl)-(1 → 4)*-O-*(β-*D-*glucopyranosyluronic acid)-(1 → 3)-2-acetamido-2-deoxy-β-*D-*glucopyranoside* (**5**).—A solution of **36** (30 mg, 23 μmol) in methanolic 40% methylamine (20 mL) was stirred for 4 days, when TLC (4:2:2:1 *n*-BuOH–EtOH–water–AcOH) showed a complete conversion of the starting material into the intermediate amino compound (R_f 0.48). The mixture was concentrated, and a solution of the residue in MeOH (5 mL) and Ac_2O (140 μL) was stirred for 2 h at 0°C. Then TLC (4:2:2:1 *n*-BuOH–EtOH–water–AcOH) showed the formation of **5** (R_f 0.50). The mixture was concentrated, and 1:1 toluene–MeOH (3 × 10 mL) was evaporated from the residue. Gel filtration on Sephadex G-10 (water) of the residue yielded **5**, isolated after lyophilisation as a white, amorphous powder (13 mg, 79%); $[\alpha]_D$ − 10.5° (*c*

0.5, H_2O). ^1H NMR data (1:1 D_2O–CD_3OD): δ 2.005 and 2.031 (2 s, 6 H, 2 $NHCOCH_3$), 3.372, 3.683, and 4.069 (3 dd, 3 H, H-2,2′,2″), 3.793 (s, 3 H, $C_6H_4OCH_3$), 4.494 and 4.525 (2 d, 2 H, $J_{1',2'/1'',2''}$ 8.1 and 8.4 Hz, H-1′,1″), 5.034 (d, 1 H, $J_{1,2}$ 8.8 Hz, H-1), 6.952 and 7.035 (2 d, 4 H, $C_6H_4OCH_3$); FABMS *m/z* 707 $[M + H]^+$.

4-Methoxyphenyl O-*(3-*O*-allyloxycarbonyl-2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-*D*-glucopyranosyl)-(1 → 4)-*O*-(6-*O*-levulinoyl-2,3-di-*O*-p-toluoyl-β-*D*-glucopyranosyl)-(1 → 3)-4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**37**). —To a solution of **13** (692 mg, 1.20 mmol) and **8** (477 mg, 0.48 mmol) in CH_2Cl_2 (6 mL) containing powdered AW-300 molecular sieves (0.4 g), 2 M $BF_3 \cdot Et_2O$ in CH_2Cl_2 (179 μL) was added at room temperature. After 1 h of stirring, when TLC (9:1 CH_2Cl_2–acetone) showed the disappearance of **8** and the formation of **37** (R_f 0.49), Et_3N was added to neutralise the mixture. Then the suspension was diluted with EtOAc (50 mL), filtered through Celite, and washed with water (10 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (9:1 CH_2Cl_2–acetone) of the residue yielded **37**, isolated as a syrup (598 mg, 88%); $[\alpha]_D$ + 27.5° (*c* 1). NMR data: ^1H, δ 1.129 and 1.234 [2 s, 6 H, $C(CH_3)_2$], 1.981 and 2.070 (2 s, 6 H, 2 Ac), 2.239 (s, 3 H, $COCH_2CH_2COCH_3$), 2.326 and 2.375 (2 s, 6 H, 2 $COC_6H_4CH_3$), 2.57–2.81 (m, 4 H, $COCH_2CH_2CO$-CH_3), 3.662 (s, 3 H, $C_6H_4OCH_3$), 4.322 (m, 2 H, $COOCH_2CH{=}CH_2$), 4.393 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1′), 4.961 and 5.053 (2 m, 2 H, $COOCH_2CH{=}CH_2$), 5.220 and 5.354 (2 d, 2 H, $J_{1,2/1'',2''}$ 8.1 and 8.4 Hz, H-1,1″), 5.580 (m, 1 H, $COOCH_2CH{=}CH_2$), 6.636 (m, 4 H, $C_6H_4OCH_3$), 7.020, 7.134, 7.421, and 7.744 (4 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 18.4 and 28.7 [$C(CH_3)_2$], 20.6 and 20.8 (2 $COCH_3$), 21.6 and 21.7 (2 $COC_6H_4CH_3$), 27.7, 29.9, and 37.8 ($COCH_2CH_2CO$-CH_3), 55.3 (2 C) and 55.6 ($C_6H_4OCH_3$ and C-2,2″), 60.8, 62.3, and 62.4 (C-6,6′,6″), 97.6 and 98.1 (C-1,1″), 99.5 [$C(CH_3)_2$], 100.8 (C-1′), 114.3 (2 C), 118.4 (2 C), 150.6, and 155.5 ($C_6H_4OCH_3$), 154.3 ($COOCH_2CH{=}CH_2$), 165.0 and 165.2 (2 $COC_6H_4CH_3$), 169.2 ($COCH_3$), and 171.9 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{73}H_{74}N_2O_{27}$: C, 62.16; H, 5.36; N, 1.99. Found: C, 61.56; H, 5.24; N, 1.94.

4-Methoxyphenyl O-*(2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-*D*-glucopyranosyl)-(1 → 4)-*O*-(6-*O*-levulinoyl-2,3-di-*O*-p-toluoyl-β-*D*-glucopyranosyl)-(1 → 3)-4,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**12**).—To a solution of **37** (598 mg, 0.42 mmol) in tetrahydrofuran (7 mL) and morpholine (280 μL) was added tetrakis(triphenylphosphine)palladium (85 mg). The mixture was boiled under reflux for 25 min, when TLC (9:1 CH_2Cl_2–acetone) showed the de-allyloxycarbonylation to be complete (**12**; R_f 0.37), then diluted with EtOAc (50 mL) and washed with water (10 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (85:15 CH_2Cl_2–acetone) of the residue yielded **12**, isolated as a syrup (535 mg, 95%); $[\alpha]_D$ + 34.5° (*c* 1). NMR data: ^1H, δ 1.160 and 1.261 [2 s, 6 H, $C(CH_3)_2$], 1.978 and 2.069 (2 s, 6 H, 2 Ac), 2.231 (s, 3 H, $COCH_2CH_2COCH_3$), 2.322 and 2.374 (2 s, 6 H, 2 $COC_6H_4CH_3$), 2.56–2.76 (m, 4 H, $COCH_2CH_2COCH_3$), 3.659 (s, 3 H, $C_6H_4OCH_3$), 3.998 and 4.426 (2 dd, 2 H,

H-2,2″), 4.399 (d, 1 H, $J_{1',2'}$ 8.1 Hz, H-1′), 5.124 and 5.359 (2 d, 2 H, $J_{1,2} = J_{1'',2''} = 8.4$ Hz, H-1,1″), 6.622 and 6.650 (2 d, 4 H, $C_6H_4OCH_3$), 7.019, 7.125, 7.420, and 7.737 (4 d, 8 H, 2 $COC_6H_4CH_3$); ^{13}C, δ 18.6 and 28.8 [$C(CH_3)_2$], 20.6, and 20.8 (2 $COCH_3$), 21.6 and 21.7 (2 $COC_6H_4CH_3$), 27.7, 29.7, and 37.8 ($COCH_2CH_2COCH_3$), 55.3, 55.4, and 56.7 ($C_6H_4OCH_3$ and C-2,2″), 60.9, 62.3, and 62.5 (C-6,6′,6″), 97.5 and 98.3 (C-1,1″), 99.5 [$C(CH_3)_2$], 100.8 (C-1′), 114.3 (2 C), 118.4 (2 C), 150.6, and 155.5 ($C_6H_4OCH_3$), 165.0 and 165.1 (2 $COC_6H_4CH_3$), 169.2 and 170.7 (2 $COCH_3$), and 171.8 ($COCH_2CH_2COCH_3$). Anal. Calcd for $C_{69}H_{70}N_2O_{25}$: C, 62.44; H, 5.32; N, 2.11. Found: C, 62.56; H, 5.32; N, 1.94.

4-Methoxyphenyl O-*(6-O-levulinoyl-2,3,4-tri-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-*O-*(2-deoxy-4,6-*O-*isopropylidene-2-phthalimido-β-*D-*glucopyranosyl)-(1 → 4)-*O-*(6-O-levulinoyl-2,3-di-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-4,6-di-*O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**38**).—To a solution of **3** (347 mg, 0.45 mmol) and **12** (118 mg, 89 μmol) in CH_2Cl_2 (2 mL) containing powdered AW-300 molecular sieves (0.1 g) 2.25 M $CF_3SO_3SiMe_3$ in CH_2Cl_2 (40 μL) was added at 0°C. After 2 h of stirring TLC (9:1 CH_2Cl_2–acetone) showed the disappearance of **12** and the formation of **38** (R_f 0.43). The mixture was neutralised with Et_3N, diluted with EtOAc (40 mL), filtered through Celite, and washed with water (10 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (9:1 CH_2Cl_2–acetone) of the residue yielded **38**, isolated as a syrup (151 mg, 87%); $[\alpha]_D$ + 5.5° (*c* 1). NMR data: ^1H, δ 1.216 and 1.302 [2 s, 6 H, $C(CH_3)_2$], 1.918 and 2.058 (2 s, 6 H, 2 Ac), 2.160 and 2.224 (2 s, 6 H, 2 $COCH_2CH_2COCH_3$), 2.238, 2.315, 2.326, and 2.370 (6 H) (4 s, 15 H, 5 $COC_6H_4CH_3$), 2.51–2.71 (m, 8 H, 2 $COCH_2CH_2COCH_3$), 3.657 (s, 3 H, $C_6H_4OCH_3$), 4.324 and 4.886 (2 d, 2 H, $J_{1',2'} = J_{1''',2'''} = 7.7$ Hz, H-1′,1‴), 4.967 and 5.337 (2 d, 2 H, $J_{1,2/1'',2''}$ 8.4 and 8.8 Hz, H-1,1″), 6.627 (m, 4 H, $C_6H_4OCH_3$), 6.962, 6.968, 7.012, 7.105, 7.132, 7.253, 7.401, 7.511, 7.709, and 7.733 (10 d, 20 H, 5 $COC_6H_4CH_3$); ^{13}C, δ 18.7 and 29.1 [$C(CH_3)_2$], 20.5 and 20.8 (2 $COCH_3$), 21.5–21.7 (5 $COC_6H_4CH_3$), 27.6, 27.9, 29.3, 29.7, 37.7, and 37.9 (2 $COCH_2CH_2COCH_3$), 55.2, 55.3, and 55.5 ($C_6H_4OCH_3$ and C-2,2″), 60.8, 62.2, 62.3, and 62.6 (C-6,6′,6″,6‴), 97.5 and 98.1 (C-1,1″), 99.2 [$C(CH_3)_2$], 100.1 and 100.8 (C-1′,1‴), 114.3 (2 C), 118.4 (2 C), 150.6 and 155.5 ($C_6H_4OCH_3$), 165.0 ($COC_6H_4CH_3$), 169.1 and 170.7 (2 $COCH_3$). Anal. Calcd for $C_{104}H_{104}N_2O_{35}$: C, 64.32; H, 5.40; N, 1.44. Found: C, 64.67; H, 5.76; N, 1.36.

4-Methoxyphenyl O-*(6-O-levulinoyl-2,3,4-tri-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-*O-*(2-deoxy-2-phthalimido-β-*D-*glucopyranosyl)-(1 → 4)-*O-*(6-O-levulinoyl-2,3-di-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-4,6-di-*O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**39**).—To a solution of **38** (111 mg, 57 μmol) in CH_2Cl_2 (1.5 mL) was added CF_3CO_2H (63.4 μL) and water (10 μL). After 2 h of stirring, when TLC (85:15 CH_2Cl_2–acetone) showed the de-isopropylidenation to be complete (**39**; R_f 0.33), the mixture was diluted with EtOAc (40 mL) and washed with aq satd $NaHCO_3$ (10 mL) and water (10 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (85:15 CH_2Cl_2–

acetone) of the residue yielded **39**, isolated as a syrup (93 mg, 85%); $[\alpha]_D$ + 19.5° (*c* 1). NMR data: ^{1}H, δ 1.925 and 2.066 (2 s, 6 H, 2 Ac), 2.159 and 2.234 (2 s, 6 H, 2 $COCH_2CH_2COCH_3$), 2.218, 2.323, 2.336, 2.342, and 2.381 (5 s, 15 H, 5 $COC_6H_4CH_3$), 2.53–2.73 (m, 8 H, 2 $COCH_2CH_2COCH_3$), 3.662 (s, 3 H, $C_6H_4OCH_3$), 4.353 and 4.670 (2 d, 2 H, $J_{1',2'/1''',2'''}$ 7.3 and 7.7 Hz, H-1',1'''), 4.916 and 5.358 (2 d, 2 H, $J_{1,2/1'',2''}$ 8.1 and 8.4 Hz, H-1,1''), 6.624 and 6.652 (2 d, 4 H, $C_6H_4OCH_3$), 6.845, 6.952, 7.016, 7.120, 7.138, 7.311, 7.389, 7.494, 7.711, and 7.727 (10 d, 20 H, 5 $COC_6H_4CH_3$); ^{13}C, δ 20.6 and 20.8 (2 $COCH_3$), 21.5, 21.6, and 21.7 (3 C) (5 $COC_6H_4CH_3$), 27.7, 29.3, 29.7, 29.9, 37.7, and 37.8 (2 $COCH_2CH_2COCH_3$), 54.8, 55.3, and 55.6 ($C_6H_4OCH_3$ and C-2,2''), 62.3 (2 C), 62.5, and 62.7 (C-6,6',6'',6'''), 97.5 and 97.7 (C-1,1''), 101.1 and 101.3 (C-1',1'''), 114.3 (2 C), 118.4 (2 C), 150.6, and 155.5 ($C_6H_4OCH_3$), 164.5, 165.0, 165.1, and 165.6 (2 C) (5 $COC_6H_4CH_3$), 169.2 and 170.7 (2 $COCH_3$), 171.8 and 172.2 (2 $COCH_2CH_2COCH_3$), 206.1 and 206.4 (2 $COCH_2CH_2COCH_3$). Anal. Calcd for $C_{101}H_{100}N_2O_{35}$: C, 63.78; H, 5.30; N, 1.47. Found: C, 63.46; H, 5.41; N, 1.42.

4-Methoxyphenyl O-*(6-O-levulinoyl-2,3,4-tri-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-*O-*(4,6-di-*O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl)-(1 → 4)-*O-*(6-O-levulinoyl-2,3-di-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-4,6-di-*O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**11**).—To a solution of **39** (60 mg, 31 μmol) in pyridine (2 mL) was added Ac_2O (2 mL) and 4-dimethylaminopyridine (5 mg). After overnight stirring at room temperature TLC (85 : 15 CH_2Cl_2–acetone) showed the acetylation to be complete (**11**; R_f 0.84). The mixture was concentrated and toluene, EtOH, and CH_2Cl_2 (3 × 20 mL) were evaporated from the residue. Column chromatography (9:1 CH_2Cl_2–acetone) then yielded **11**, isolated as a syrup (60 mg, 96%); $[\alpha]_D$ + 11.5° (*c* 1). NMR data: ^{1}H, δ 1.896, 1.919, 2.004, and 2.063 (4 s, 12 H, 4 Ac), 2.146 and 2.234 (2 s, 6 H, 2 $COCH_2CH_2COCH_3$), 2.222, 2.302, 2.315, 2.368, and 2.392 (5 s, 15 H, 5 $COC_6H_4CH_3$), 3.657 (s, 3 H, $C_6H_4OCH_3$), 4.355 and 4.550 (2 d, 2 H, $J_{1',2'} = J_{1''',2'''} = 7.7$ Hz, H-1',1'''), 4.934 and 5.349 (2 d, 2 H, $J_{1,2/1'',2''}$ 8.8 and 8.4 Hz, H-1,1''), 6.633 (m, 4 H, $C_6H_4OCH_3$), 6.967, 6.985, 7.017, 7.044, 7.100, 7.356, 7.410, 7.518, 7.676, and 7.683 (10 d, 20 H, 5 $COC_6H_4CH_3$); ^{13}C, δ 20.6, 20.7 (2 C), and 20.8 (4 $COCH_3$), 21.5, 21.6 (3 C), and 21.7 (5 $COC_6H_4CH_3$), 27.6, 27.7, 29.8, 29.9, and 37.8 (2 C) (2 $COCH_2CH_2COCH_3$), 55.3, 55.6, and 55.7 ($C_6H_4OCH_3$ and C-2,2''), 62.0, 62.3, 62.4, and 62.5 (C-6,6',6'',6'''), 97.5 and 97.7 (C-1,1''), 100.7 and 101.0 (C-1',1'''), 114.3 (2 C), 118.4 (2 C), 150.6, and 155.5 ($C_6H_4OCH_3$), 164.8, 164.9 (2 C), 165.0, and 165.7 (5 $COC_6H_4CH_3$), 169.1, 169.2, 170.5, and 170.7 (4 $COCH_3$), 171.8 and 172.2 (2 $COCH_2CH_2COCH_3$), 206.0, and 206.2 (2 $COCH_2CH_2COCH_3$). Anal. Calcd for $C_{105}H_{104}N_2O_{37}$: C, 63.50; H, 5.28; N, 1.41. Found: C, 63.27; H, 5.35; N, 1.35.

4-Methoxyphenyl O-*(2,3,4-tri-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-*O-*(4,6-di-*O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl)-(1 → 4)-*O-*(2,3-di-*O-p-*toluoyl-β-*D-*glucopyranosyl)-(1 → 3)-4,6-di-*O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**40**).—To a solution of **11** (93 mg, 47 μmol) in EtOH (7.0 mL) and toluene

(3.5 mL) was added $NH_2NH_2 \cdot AcOH$ (43.2 mg). After 45 min of stirring, when TLC (3:2 CH_2Cl_2–EtOAc) showed the de-levulinoylation to be complete (**40**; R_f 0.46), the mixture was concentrated, and column chromatography (3:2 CH_2Cl_2–EtOAc) of the residue yielded **40**, isolated as a syrup (64 mg, 76%); $[\alpha]_D$ + 30° (*c* 1). NMR data: ^1H, δ 1.917, 1.937, 2.018, and 2.060 (4 s, 12 H, 4 Ac), 2.228, 2.335 (6 H), 2.355, and 2.385 (4 s, 15 H, 5 $COC_6H_4CH_3$), 3.668 (s, 3 H, $C_6H_4OCH_3$), 4.559 and 4.603 (2 d, 2 H, $J_{1',2'/1''',2'''}$ 7.3 and 7.7 Hz, H-1',1'''), 5.084 and 5.371 (2 d, 2 H, $J_{1,2} = J_{1'',2''} = 8.4$ Hz, H-1,1''), 6.634 and 6.668 (2 d, 4 H, $C_6H_4OCH_3$), 6.978, 7.008, 7.036, 7.096, 7.131, 7.429, 7.446, 7.547, 7.695, and 7.745 (10 d, 20 H, 5 $COC_6H_4CH_3$); ^{13}C, δ 20.7 (2 C) and 20.8 (2 C) (4 $COCH_3$), 21.6 and 21.7 (4 C) (5 $COC_6H_4CH_3$), 55.4, 55.6, and 55.7 ($C_6H_4OCH_3$ and C-2,2''), 60.6, 61.1, 61.7, and 62.3 (C-6,6',6'',6'''), 97.7 and 98.0 (C-1,1''), 99.8 and 100.0 (C-1',1'''), 114.4 (2 C), 118.5 (2 C), 150.6, and 155.6 ($C_6H_4OCH_3$), 164.9 (3 C) and 165.7 (2 C) (5 $COC_6H_4CH_3$), 169.6, 169.8, 170.6, and 170.7 (4 $COCH_3$). Anal. Calcd for $C_{95}H_{92}N_2O_{33}$: C, 63.75; H, 5.18; N, 1.57. Found: C, 63.65; H, 5.48; N, 1.69.

4-Methoxyphenyl O-*(2,3,4-tri*-O-p-*toluoyl-β-*D-*glucopyranosyluronic acid)-(1 → 3)*-O-*(4,6-di*-O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl)-(1 → 4)*-O-*(2,3-di*-O-p-*toluoyl-β-*D-*glucopyranosyluronic acid)-(1 → 3)-4,6-di*-O-*acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranoside* (**41**).—To a cold (−78°C) 2 M solution of oxalyl chloride in CH_2Cl_2 (0.7 mL) was added Me_2SO (106 μL) and the mixture was stirred for 10 min. Then a solution of **40** (64 mg, 36 μmol) in CH_2Cl_2 (1 mL) was added and the mixture was stirred for 5 h, whereby in 30 min a precipitate was formed. Diisopropylethylamine (0.52 mL) was added, and after 10 min the mixture was diluted with EtOAc (20 mL) and washed with M HCl (10 mL) and satd aq NaCl (10 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. To a solution of the residue in *t*-BuOH (1.5 mL), 2-methyl-2-butene (0.56 mL), and water (0.92 mL) were added NaH_2PO_4 (92 mg) and $NaClO_2$ (92 mg). The mixture was stirred overnight, when TLC (10:9:1 CH_2Cl_2–EtOAc–AcOH) showed a complete conversion of **40** into **41** (R_f 0.10). Then the mixture was concentrated, and a solution of the residue in water was washed with hexane, acidified with M HCl, and extracted with EtOAc (3 × 20 mL), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (3:2 CH_2Cl_2–EtOAc followed by 10:5:1 EtOAc–CH_2Cl_2–AcOH) of the residue yielded **41**, isolated as a pure (NMR) syrup (56 mg, 86%); $[\alpha]_D$ + 9.5° (*c* 1). ^1H NMR data (1:1 $CDCl_3$–CD_3OD): δ 1.849, 1.959, 2.077 (6 H) (3 s, 12 H, 4 Ac), 2.252, 2.304, 2.337, 2.396, and 2.413 (5 s, 15 H, 5 $COC_6H_4CH_3$), 3.672 (s, 3 H, $C_6H_4OCH_3$), 4.115 and 4.184 (2 d, 2 H, $J_{5',4'/5''',4'''}$ 9.2 and 9.5 Hz, H-5',5'''), 4.342 and 4.682 (2 dd, 2 H, H-2,2''), 4.442 and 4.651 (2 d, 2 H, $J_{1',2'/1''',2'''}$ 7.7 and 8.1 Hz, H-1',1'''), 4.981 and 5.373 (2 d, 2 H, $J_{1,2/1'',2''}$ 8.1 and 8.8 Hz, H-1,1''), 5.056 and 5.194 (2 dd, 2 H, H-2',2'''), 6.647 (m, 4 H, $C_6H_4OCH_3$), 6.992, 7.014 (4 H), 7.062, 7.137, 7.320, 7.358, 7.535, 7.671, and 7.713 (9 d, 20 H, 5 $COC_6H_4CH_3$). A small amount of **41** was esterified with diazomethane in ether, and analysed by ^1H NMR: δ 1.852, 1.892, 2.064, and 2.091 (4 s, 12 H, 4 Ac), 2.241, 2.304, 2.332, 2.373, and 2.399 (5 s,

15 H, 5 $COC_6H_4CH_3$), 3.476 and 3.603 (2 s, 6 H, 2 $COOCH_3$), 3.663 (s, 3 H, $C_6H_4OCH_3$), 4.393 and 4.537 (2 d, 2 H, $J_{1',2'/1''',2'''}$ 7.3 and 7.7 Hz, H-1',1'''), 4.876 and 5.348 (2 d, 2 H, $J_{1,2/1'',2''}$ 8.1 and 8.4 Hz, H-1,1''), 6.632 (m, 4 H, $C_6H_4OCH_3$), 6.981, 6.997, 7.023, 7.055, 7.122, 7.345, 7.398, 7.564, 7.677, and 7.715 (10 d, 20 H, 5 $COC_6H_4CH_3$).

4-Methoxyphenyl O-(β-D-glucopyranosyluronic acid)-(1 → 3)-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 4)-O-(β-D-glucopyranosyluronic acid)-(1 → 3)-2-acetamido-2-deoxy-β-D-glucopyranoside (**10**).—A solution of **41** (22 mg, 12 μmol) in methanolic 40% methylamine (20 mL) was stirred for 4 days and then concentrated. A solution of the residue in methanolic 40% methylamine (20 mL) was stirred for another 4 days, and then the mixture was concentrated, and a solution of the residue in MeOH (2.5 mL) and Ac_2O (70 μL) was stirred for 2 h at 0°C. Then TLC (4:2:2:1 *n*-BuOH–EtOH–water–AcOH) showed the formation of **10** (R_f 0.18). The mixture was concentrated and 1:1 MeOH–toluene (3 × 20 mL) was evaporated from the residue. Gel filtration on Sephadex G-10 (water) of the residue yielded **10**, isolated after lyophilisation as a white, amorphous powder (9 mg, 82%); $[\alpha]_D$ − 19° (*c* 0.3, H_2O). ^1H NMR data (1:1 D_2O–CD_3OD): δ 2.004 and 2.015 (2 s, 6 H, 2 $NHCOCH_3$), 3.789 (s, 3 H, $C_6H_4OCH_3$), 4.444, 4.492, and 4.556 (3 d, 3 H, $J_{1',2'/1'',2''/1''',2'''}$ 7.9, 7.3, and 8.3 Hz, H-1',1'',1'''), 5.025 (d, 1 H, $J_{1,2}$ 8.6 Hz, H-1), 6.944 and 7.030 (2 d, 4 H, $C_6H_4OCH_3$). FABMS *m/z* 905 $[M + Na]^+$.

ACKNOWLEDGMENTS

The research of Dr. T.M. Slaghek has been made possible by a fellowship of the Science and Technology Agency of Japan and by a fellowship of the Royal Netherlands Academy of Art and Sciences. The authors would like to thank Dr. J. Uzawa and Mrs. T. Chijimitsu for recording the NMR spectra, Mr. Y. Esumi and Mrs. A.C.H.T.M. van der Kerk-van Hoof for recording the FABMS spectra, and Ms. M. Yoshida and her staff for the elemental analyses.

REFERENCES

1 T.M. Slaghek, Y. Nakahara, and T. Ogawa, *Tetrahedron Lett.*, 33 (1992) 4971–4974.
2 T.C. Laurent and J.R.E. Fraser, *FASEB J.*, 6 (1992) 2397–2404.
3 K. Meyer, *Fed. Proc.*, 17 (1958) 1075–1077.
4 P. Prehm, *Biochem. J.*, 200 (1984) 597–600; P. Prehm, in D. Evered and J. Whelan (Eds.), *The Biology of Hyaluronan*, Ciba Foundation Symposium 143, Wiley, Chichester, UK, 1989, pp 21–40.
5 I. Ellis, A.M. Grey, A.M. Schor, and S.L. Schor, *J. Cell. Sci.*, 102 (1992) 447–456.
6 B.A. Mast, J.H. Haynes, T.M. Krummel, R.F. Diegelmann, and I. Kelman-Cohen, *Plast. Reconst. Surg.*, 89 (1992) 503–509.
7 N.S. Adzick and M.T. Longaker, *Ann. Surg.*, 215 (1992) 3–7.
8 E.A. Turley, *Cancer Met. Rev.*, 11 (1992) 21–30.
9 A. Aruffo, I. Stamenkovic, M. Melnick, C.B. Underhill, and B. Seed, *Cell*, 61 (1990) 1303–1313.
10 R.N. Feinberg and D.C. Beebe, *Science*, 220 (1983) 1177–1179.
11 D.C. West and S. Kumar, in D. Evered and J. Whelan (Eds.), *The Biology of Hyaluronan*, Ciba Foundation Symposium 143, Wiley, Chichester, UK, 1989, pp 187–207.

12 D.C. West, I.N. Hampson, F. Arnold, and S. Kumar, *Science*, 228 (1985) 1324–1326.
13 G. Grundler and R.R. Schmidt, *Carbohydr. Res.*, 135 (1985) 203–218.
14 H.J. Koeners, J. Verhoeven, and J.H. van Boom, *Recl. Trav. Chim. Pays-Bas*, 100 (1981) 65–72.
15 K. Saigo, M.-H. Usui, K. Kikuchi, E. Shimada, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, 50 (1977) 1863–1866.
16 T. Fukuyama, A.A. Laird, and L.M. Hotchkiss, *Tetrahedron Lett.*, 26 (1985) 6291–6292.
17 R.R. Schmidt, J. Michel, and M. Roos, *Liebigs Ann. Chem.*, (1984) 1343–1357.
18 P. Boullanger, P. Chatelard, G. Descotes, M. Kloosterman, and J.H. van Boom, *J. Carbohydr. Chem.*, 5 (1986) 541–559.
19 T. Nakano, Y. Ito, and T. Ogawa, *Tetrahedron Lett.*, 31 (1990) 1597–1600.
20 J.H. van Boom and P.M.J. Burgers, *Tetrahedron Lett.*, (1976) 4875–4878.
21 N. Jeker and C. Tamm, *Helv. Chim. Acta*, 71 (1988) 1895–1903.
22 K. Omura and D. Swern, *Tetrahedron*, 34 (1978) 1651–1660.
23 B.O. Lindgren and T. Nilsson, *Acta Chem. Scand.*, 27 (1973) 888–890.
24 M.S. Motawia, J. Wengel, A.E.S. Abdel-Megid, and E.B. Pedersen, *Synthesis*, (1989) 384–387.
25 H. Kunz and H. Waldman, *Angew. Chem.*, 96 (1984) 49–50.
26 Y. Hayakawa, H. Kato, M. Uchiyama, H. Kajino, and R. Noyori, *J. Org. Chem.*, 51 (1986) 2400–2402.