J. CARBOHYDRATE CHEMISTRY, 13(1), 1-25 (1994)

SYNTHESIS OF STRUCTURAL ELEMENTS OF THE CAPSULAR POLYSACCHARIDE OF *STREPTOCOCCUS PNEUMONIAE* TYPE 14

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Received April 4, 1993 - Final Form August 27, 1993

ABSTRACT

The synthesis is reported of methyl *O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-*O*- [β-D-galactopyranosyl-(1→4)] -*O*-2-acetamido-2-deoxy-β-D-glucopyranoside (**13**), methyl *O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-*O*-[β-D-galactopyranosyl-(1→4)] -*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (**28**), and *O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-*O*-[β-D-galactopyranosyl-(1→4)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranose (**38**), representing fragments of the capsular polysaccharide of *Streptococcus pneumoniae* type 14 ({ →3)-β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→6)-[β-D-Gal*p*-(1→4)] -β-D-Glc*p*NAc-(1→}$_n$). 4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (**6**) was coupled regio- and stereoselectively with HO-6 of methyl 3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**4**) in dichloromethane, using boron trifluoroetherate as a promoter. Coupling of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl trichloroacetimidate (**8**) with HO-4 of the resulting trisaccharide derivative (**9**) in dichloromethane, using boron trifluoroetherate as a promoter, afforded methyl 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-6-*O*- [4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl] -3-*O*-benzyl-2-deoxy-2-phthalimido-β-

D-glucopyranoside (**10**). Debenzylation of **10**, followed by dephthaloylation, *N*,*O*-acetylation, and de-*O*-acetylation gave tetrasaccharide methyl glycoside **13**. Disaccharide derivative **6** was also coupled with HO-6 of allyl 3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**16**) in dichloromethane using trimethylsilyl trifluoromethanesulfonate as a promoter. Coupling of **8** with HO-4 of the resulting trisaccharide derivative (**17**) in dichloromethane, using trimethylsilyl trifluoromethanesulfonate as a promoter, afforded allyl 4-*O*-(2,3,4,6 -tetra-*O*-acetyl-β-D-galactopyranosyl)-6-*O*- [4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl) -2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl] -3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**18**). Deallylation of **18**, followed by imidation gave an activated tetrasaccharide (**20**), which was coupled to both methyl (**24**) and benzyl (**33**) 2,3,6-tri-*O*-benzyl-4-*O*- (2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside in dichloromethane, using trimethylsilyl trifluoromethanesulfonate as a promoter, to give the corresponding hexasaccharide derivatives **25** and **34**. Debenzylation of **25**, followed by dephthaloylation, *N*,*O*-acetylation, and de-*O*-acetylation gave hexasaccharide methyl glycoside **28**. Dephthaloylation of **34**, followed by *N*,*O*-acetylation, debenzylation, re-*O*-acetylation and de-*O*-acetylation gave hexasaccharide **38**.

INTRODUCTION

Streptococcus pneumoniae is a gram-positive bacterium which can induce infections such as pneumonia, otitis media, and meningitis in human beings. At the moment 85 different serotypes of *S. pneumoniae* are known. A polyvalent vaccine[1] (Pneumovax® 23) against pneumococcal diseases is available, which contains the capsular polysaccharides from 23 species of *S. pneumoniae*. The vaccine has some disadvantages, since polysaccharides are not very immunogenic in people at high risk and do not induce a long-lasting immunological memory, whereas the induction of tolerance is a severe problem.[2] In the framework of our investigations on the development of synthetic oligosaccharide vaccines against infections by *S. pneumoniae* serotypes, based on neoglycoproteins, attention has been focused on the preparation of oligosaccharide fragments related to different types of pneumococcal polysaccharides.[3-8]

The structure of *S. pneumoniae* type 14 capsular polysaccharide has been characterised[9] as:

$$[\rightarrow 3)\text{-}\beta\text{-D-Gal}p\text{-}(1\rightarrow 4)\text{-}\beta\text{-D-Glc}p\text{-}(1\rightarrow 6)\text{-}\beta\text{-D-Glc}p\text{NAc-}(1\rightarrow]_n \qquad \textbf{(1)}$$

$$\begin{array}{c} 4 \\ \uparrow \\ 1 \\ \beta\text{-D-Gal}p \end{array}$$

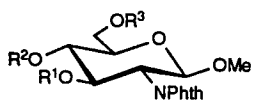
Several oligosaccharides related to the capsular polysaccharide of type 14 have been synthesised, i.e. the tetrasaccharide β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→6)-[β-D-Gal*p*-(1→4)]-D-Glc*p*NAc[10] and the benzyl β-glycoside of β-D-Gal*p*-(1→4)-β-D-Glc*p*NAc-(1→3)-β-D-Gal*p*-(1→4)-D-Glc*p*.[11] During our investigations focused on the synthesis of type 14 oligosaccharide fragments, parallel reports appeared in the literature. Using a two-plus-two approach, the propyl β-glycoside of β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→6)-[β-D-Gal*p*-(1→4)]-D-Glc*p*NAc was prepared,[12] and as an extension of this work, 3-OMe-Gal variants of a tetrasaccharide[13] and an octasaccharide[13] consisting of two tetrasaccharide repeating units. Furthermore, by using a one-plus-two-plus-one approach, the 7-methoxycarbonyl-3,6-dioxaheptyl and 8-azido-3,6-dioxaoctyl β-glycosides of β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→6)-[β-D-Gal*p*-(1→4)]-D-Glc*p*NAc were prepared.[14] Finally, a polysaccharide fragment was prepared, with a polymerisation degree of about 10 tetrasaccharide units.[15]

Here we report on the synthesis of methyl *O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-*O*-[β-D-galactopyranosyl-(1→4)] -*O*-2-acetamido-2-deoxy-β-D-glucopyranoside (**13**), methyl *O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-*O*-[β-D-galactopyranosyl-(1→4)] -*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (**28**), and *O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-*O*-[β-D-galactopyranosyl-(1→4)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3) -*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranose (**38**).

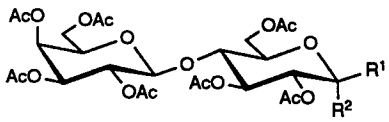
RESULTS AND DISCUSSION

For the synthesis of tetrasaccharide methyl glycoside **13**, methyl 3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**4**), 4-*O*-(2,3,4,6 -tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (**6**), and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl trichloroacetimidate (**8**) were chosen as synthons. The synthesis of hexasaccharide methyl glycoside **28** involved the use of allyl 3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**16**), **6**, **8**, and methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**24**). In the case of hexasaccharide **38**, also **16**, **6**, and **8** were used, but **24** was replaced by benzyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**33**).

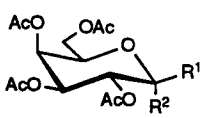
Isopropylidenation of methyl 2-deoxy-2-phthalimido-β-D-glucopyranoside,[16] using 2,2-dimethoxypropane and *p*-toluenesulfonic acid (→**2**, 82%), and subsequent benzylation in tetrahydrofuran at reflux temperature for 1 h, using a slight excess of benzyl bromide, afforded **3** (75%). The choice for a benzylation of HO-3 instead of an esterification is based on the observation that an ester function at this position decreases the reactivity of the aimed acceptor **9** dramatically.[17] Then acid-catalysed deisopropylidenation of **3** gave **4** (>98%). Peracetylated lactose was deacetylated at C-1 using hydrazine acetate[18] (→**5**, 99%), and the product was treated with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene[19] to yield imidate **6** (75%). Only the α-anomer could be detected. The galactosyl imidate **8** was prepared in a similar way, starting from peracetylated galactose (overall yield 75%), and again only the α-anomer was detected. It has to be noted that using sodium, instead of 1,8-diazabicyclo[5.4.0]undec-7-ene, in both cases α/β-mixtures are obtained.[14]



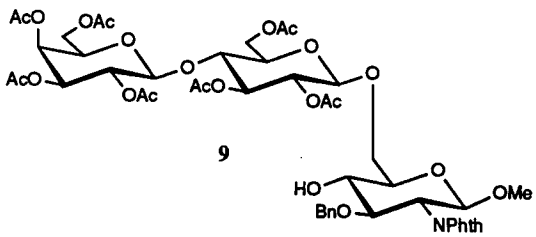
2 R^1 = H; R^2,R^3 = CMe_2
3 R^1 = Bn; R^2,R^3 = CMe_2
4 R^1 = Bn; R^2 = R^3 = H



5 R^1,R^2 = H,OH
6 R^1 = H; R^2 = $OCNHCCl_3$



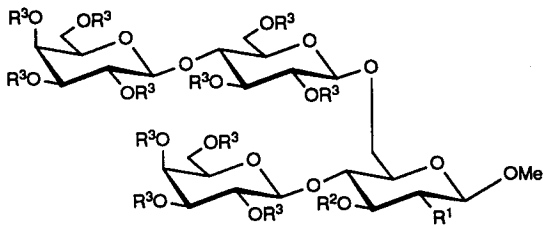
7 R^1,R^2 = H,OH
8 R^1 = H; R^2 = $OCNHCCl_3$



9

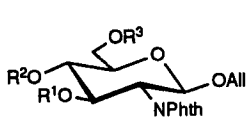
Regio- and stereoselective coupling of **6** with **4** (HO-6) in dichloromethane using boron trifluoroetherate[20] as a promoter gave trisaccharide derivative **9** (66%), and condensation of **9** with **8** in dichloromethane in the presence of boron trifluoroetherate gave tetrasaccharide derivative **10** (64%). Reductive debenzylation of **10** (→**11**, quantitatively), followed by consecutive dephthaloylation using hydrazine hydrate in ethanol,[21]

peracetylation (→**12**, 48%), and de-*O*-acetylation afforded tetrasaccharide methyl glycoside **13** (97%).

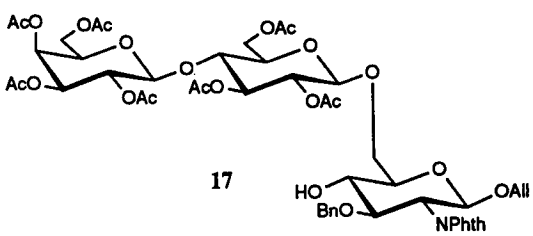


10 R^1 = NPhth; R^2 = Bn; R^3 = Ac
11 R^1 = NPhth; R^2 = H; R^3 = Ac
12 R^1 = NHAc; R^2 = R^3 = Ac
13 R^1 = NHAc; R^2 = R^3 = H

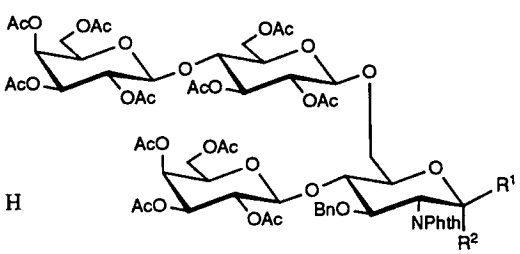
Isopropylidenation of allyl 2-deoxy-2-phthalimido-β-D-glucopyranoside,[22] using 2,2-dimethoxypropane and *p*-toluenesulfonic acid, gave **14** (88%). Benzylation of **14** in tetrahydrofuran at reflux temperature for 3 h, using 1.1 equivalent of benzyl bromide (→**15**, 82%), and subsequent acid-catalysed deisopropylidenation gave **16** (76%). Regio- and stereoselective coupling of the lactosyl imidate **6** with **16** (HO-6) in dichloromethane at -40 °C, using trimethylsilyl trifluoromethanesulfonate as a promoter, afforded trisaccharide derivative **17** (61%), and condensation of **17** with galactosyl imidate **8**, using almost the same conditions, gave tetrasaccharide derivative **18** (66%). Deallylation of **18**, achieved in a one-pot reaction by sonication in aqueous 96% acetic acid in the presence of palladium (II) chloride and sodium acetate[19] (→**19**, 85%), and subsequent imidation of HO-1, using trichloroacetonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene, yielded block synthon **20** (86%).



14 R^1 = H; R^2,R^3 = CMe_2
15 R^1 = Bn; R^2,R^3 = CMe_2
16 R^1 = Bn; R^2 = R^3 = H

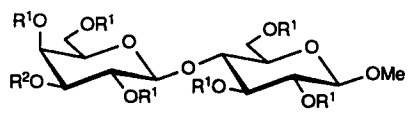


17



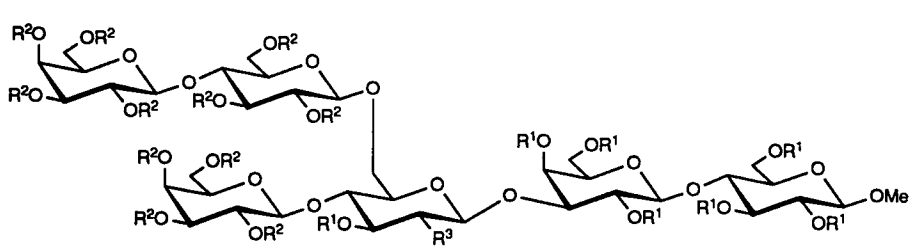
18 R^1 = OAll; R^2 = H
19 R^1,R^2 = H,OH
20 R^1 = $OCNHCCl_3$; R^2 = H

Synthesis of the hexasaccharides requires the condensation of **20** with lactose derivatives having a free HO-3' group. Taking into account that ether functions in the aglycon increase the reactivity of the acceptor,[23] two lactose derivatives with benzyl groups as permanent protecting groups were synthesised. Several examples in the literature[21,24-28] describe the synthesis of galactose residues with a free HO-3 group.



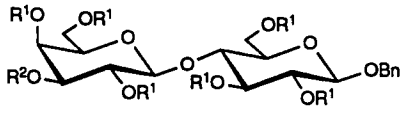
21 $R^1 = R^2 = H$
22 $R^1 = H$; $R^2 = MBn$
23 $R^1 = Bn$; $R^2 = MBn$
24 $R^1 = Bn$; $R^2 = H$

First, methyl 4-*O*-β-D-galactopyranosyl-β-D-glucopyranoside[29] (**21**) in benzene was treated with dibutyl tinoxide,[30] followed by tetrabutylammonium iodide and 4-methoxybenzyl chloride, to give **22**. Benzylation of the remaining hydroxyl groups (→**23**, 47%) and de-4-methoxybenzylation with 5% trifluoroacetic acid in dichloromethane, afforded **24** (98%). Coupling of **20** with the lactoside **24** in dichloromethane at -70 °C, using trimethylsilyl trifluoromethanesulfonate as a promoter, gave hexasaccharide derivative **25** (53%). Debenzylation of **25** (→**26**), followed by dephthaloylation with hydrazine monohydrate, and re-*N,O*-acetylation afforded the fully protected hexasaccharide methyl *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→6)-*O*- [(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)]-*O*-(2-acetamido-3-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*- (2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (**27**, 42%). Finally, de-*O*-acetylation with sodium methoxide in methanol gave the hexasaccharide methyl glycoside **28** (44%).

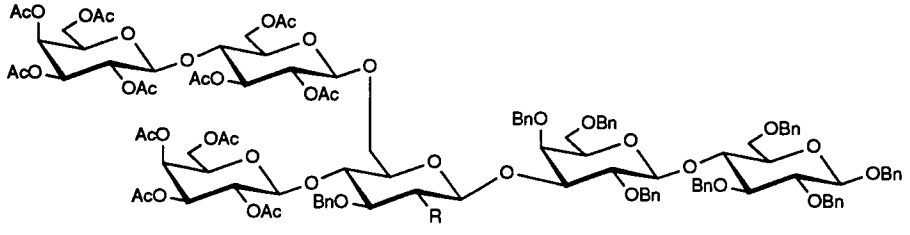


25 $R^1 = Bn$; $R^2 = Ac$; $R^3 = NPhth$
26 $R^1 = H$; $R^2 = Ac$; $R^3 = NPhth$
27 $R^1 = R^2 = Ac$; $R^3 = NHAc$
28 $R^1 = R^2 = H$; $R^3 = NHAc$

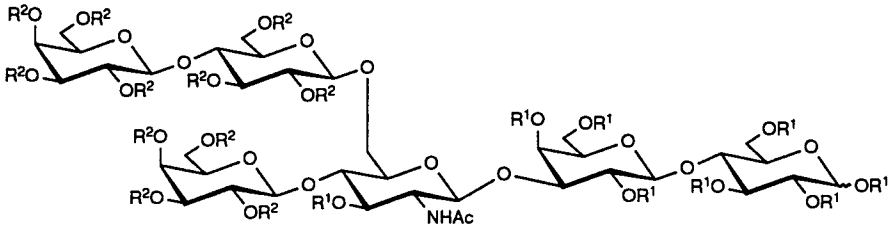
Secondly, benzyl 4-*O*-β-D-galactopyranosyl-β-D-glucopyranoside[31] (**29**) was chosen as starting compound. Using the same reaction sequence as for **23**, the 3'-*O*-(4-methoxybenzyl)-derivative **30** was prepared. However, removal of the O-3' protecting group was accompanied by degradation, and therefore the 4-methoxybenzyl group was replaced by an allyl group. Introduction of the allyl group was achieved by treating **29** in methanol with dibutyl tinoxide, followed by tetrabutylammonium bromide and allyl bromide in benzene (instead of toluene[32]) to give **31** (61%). Benzylation of **31** (→**32**, 90%), and subsequent deallylation, using potassium *tert*-butoxide,[33] in two steps, gave benzyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside (→**33**, 59%). Coupling of **20** and **33** in dry dichloromethane at -50 °C using trimethylsilyl trifluoromethanesulfonate as a promoter, gave hexasaccharide derivative **34** (61%). Dephthaloylation of **34**, using hydrazine monohydrate, and re-*N,O*-acetylation afforded **35** (61%). Debenzylation of **35** (→**36**), and subsequent re-*O*-acetylation gave the fully acetylated hexasaccharide derivative **37** (84%). Finally, de-*O*-acetylation, using ammonia in water, afforded hexasaccharide **38** (97%).



29 $R^1 = R^2 = H$
30 $R^1 = Bn$; $R^2 = MBn$
31 $R^1 = H$; $R^2 = All$
32 $R^1 = Bn$; $R^2 = All$
33 $R^1 = Bn$; $R^2 = H$



34 R = NPhth
35 R = NHAc



36 $R^1 = H$; $R^2 = Ac$
37 $R^1 = R^2 = Ac$
38 $R^1 = R^2 = H$

The synthetic compounds will be used in different immunological inhibition experiments. Furthermore, the developed synthetic strategies will be followed for the preparation of spacer-linked higher oligosaccharides, which can be coupled with proteins, yielding neoglycoproteins.

EXPERIMENTAL

General methods. ^1H NMR spectra were recorded at 300 MHz with a Bruker AC 300, at 360 MHz with a Bruker HX 360, and at 500 MHz with a Bruker AM 500 apparatus at 25 °C. Two-dimensional double-quantum-filtered ^1H-^1H correlation spectra (2D DQF ^1H-^1H COSY) were recorded in the phase-sensitive mode,[34] and two-dimensional homonuclear Hartmann-Hahn spectra (2D HOHAHA) with a 120 ms MLEV-17 mixing sequence.[35] ^{13}C NMR spectra (APT, 50 MHz) were recorded at 25 °C with a Bruker WP 200 spectrometer. Chemical shifts (δ) are given in ppm relative to the signal for internal Me_4Si ($CDCl_3$) or internal sodium 4,4-dimethyl-4-silapentane-1-sulfonate (D_2O; indirectly to internal acetone, δ 2.225) for ^1H, and to the signal for internal Me_4Si ($CDCl_3$; indirectly to $CDCl_3$, δ 76.9) or external Me_4Si (D_2O; indirectly to internal acetone, δ 31.55) for ^{13}C.

Column chromatography was performed on Kieselgel 60 (Merck, <230 mesh) and fractions were monitored by TLC on Kieselgel 60 F_{254} (Merck). Detection was effected by examination under UV light and by charring with aqueous 50 % sulfuric acid. Optical rotations were measured at 20 °C with a Perkin-Elmer 241 polarimeter, using a 10-cm 1-mL cell. In working-up procedures, washings were carried out three times with appropriate quantities of water or aqueous 10% sodium hydrogencarbonate unless indicated otherwise, and drying of organic solutions was performed with $MgSO_4$. Evaporations were conducted under reduced pressure at 40 °C. All solvents were distilled from appropriate drying agents.

Methyl 2-Deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-D-glucopyranoside (2). To a solution of methyl 2-deoxy-2-phthalimido-β-D-glucopyranoside[16] (4.11 g, 12.7 mmol) in acetone (20 mL) were added 2,2-dimethoxypropane (60 mL) and *p*-toluenesulfonic acid (20 mg). After 2 h, TLC indicated the reaction to be complete (**2** R_F 0.70, 9:1 dichloromethane-acetone), and solid sodium hydrogencarbonate was added, the mixture was filtered through Celite, and concentrated. Column chromatography (9:1 di-

chloromethane-acetone) of the residue gave **2** (3.79 g, 82%) as a white glass: $[\alpha]_D$ +18° (*c* 1, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 7.87-7.72 (m, 4H, Phth), 5.156 (d, 1H, H-1), 4.446 (t, 1H, H-3), 4.182 (dd, 1H, H-2), 3.995 (dd, 1H, H-6a), 3.850 (t, 1H, H-6b), 3.647 (t, 1H, H-4), 3.466 (m, 1H, H-5), 3.422 (s, 3H, OCH_3), 1.530 and 1.434 [2s, each 3H, $C(CH_3)_2$], $J_{1,2}$ = 8.5 Hz, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 9.1 Hz, $J_{4,5}$ = 9.4 Hz, $J_{5,6a}$ = 5.4 Hz, $J_{5,6b}$ = 10.5 Hz, $J_{6a,6b}$ = -10.6 Hz.

Anal. Calcd for $C_{18}H_{21}NO_7$: C, 59.50; H, 5.82. Found: C, 59.23; H, 5.93.

Methyl 3-*O*-Benzyl-2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-D-glucopyranoside (3). To a solution of **2** (2.22 g, 6.10 mmol) in freshly distilled tetrahydrofuran (35 mL) was added sodium hydride (150 mg, 6.25 mmol), and benzyl bromide (0.75 mL, 6.3 mmol) was added dropwise. After 1 h at reflux temperature the benzylation was complete (TLC 85:15 dichloromethane-ethyl acetate; **3** R_F 0.47), ethyl acetate (7 mL) was added, and the mixture was diluted with dichloromethane (25 mL), and concentrated. A solution of the residue in dichloromethane (25 mL) was washed with water, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. Column chromatography (9:1 dichloromethane-ethyl acetate) of the residue gave **3** (2.07 g, 75%) as a white glass: $[\alpha]_D$ +32° (*c* 1, dichloromethane); ^{13}C NMR ($CDCl_3$) δ 138.0 (Ph), 133.6, 131.5, and 123.1 (Phth), 127.8-127.1 (Ph), 99.6 (C-1), 99.2 [$C(CH_3)_2$], 75.7, 74.8, and 66.8 (C-3,4,5), 73.6 (OCH_2Ph), 62.1 (C-6), 56.7 and 55.5 (OCH_3, C-2).

Anal. Calcd for $C_{25}H_{27}NO_7$: C, 66.21; H, 6.00. Found: C, 66.15; H, 6.10.

Methyl 3-*O*-Benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (4). A suspension of **3** (2.0 g, 4.4 mmol) in aqueous 50% acetic acid (100 mL) was stirred for 2 h at 50 °C, when TLC showed a complete conversion into **4** (R_F 0.10, 9:1 dichloromethane-acetone). The mixture was concentrated, then co-concentrated with toluene (2 x 30 mL), ethanol (2 x 30 mL), and dichloromethane (2 x 30 mL). Column chromatography (75:25 dichloromethane-acetone) of the residue gave **4** (1.79 g, 99%) as a white glass: $[\alpha]_D$ +56° (*c* 1, dichloromethane), lit[16] +57.2° (*c* 1, chloroform); ^{13}C NMR ($CDCl_3$) δ 137.9 (Ph), 133.6, 131.4, and 123.1 (Phth), 127.9-127.1 (Ph), 99.1 (C-1), 78.8, 75.3, and 71.9 (C-3,4,5), 74.3 (OCH_2Ph), 61.8 (C-6), 55.6 and 55.3 (OCH_3, C-2); ^{1}H NMR ($CDCl_3$) δ 7.74-7.68 (m, 4H, Phth), 7.08-6.98 (m, 5H, Ph), 5.105 (d, 1H, H-1), 4.717 and 4.536 (2d, each 1H, OCH_2Ph), 4.271 (dd, 1H, H-3), 4.137 (dd, 1H, H-2), 3.970 (dd, 1H, H-6a), 3.904 (dd, 1H, H-6b), 3.829 (t, 1H, H-4), 3.542 (m, 1H, H-5), 3.393

(s, 3H, OC*H*$_3$), 2.992 and 1.849 (2bs, each 1H, 2O*H*), $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 10.7 Hz, $J_{3,4} \approx$ 9.0 Hz, $J_{4,5} \approx$ 9.0 Hz, $J_{5,6a}$ = 3.6 Hz, $J_{5,6b}$ = 4.1 Hz, $J_{6a,6b}$ = -11.8 Hz.

Anal. Calcd for $C_{22}H_{23}NO_7 \cdot 0.5H_2O$: C, 62.55; H, 5.73. Found: C, 62.97; H, 5.98.

4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (6). To a solution of peracetylated lactose (13.5 g, 19.9 mmol) in dry *N,N*-dimethylformamide (300 mL) was added hydrazine acetate (2.0 g, 21.7 mmol). After 2 h at 60 °C ethyl acetate (500 mL) was added, and the organic phase was washed with aqueous 5% sodium chloride and water, dried, filtered, and concentrated to give hepta-*O*-acetyl-α/β-D-lactose **5** (12.8 g, quantitative) as a syrup: R_F 0.63 (85:15 dichloromethane-acetone). To a solution of (**5**; 4.8 g, 7.5 mmol) and trichloroacetonitrile (7 mL, 70 mmol) in dry dichloromethane (50 mL) at 0 °C, was added 1,8-diazabicyclo[5.4.0]undec-7-ene (1.2 mL, 8.0 mmol). After stirring for 2 h at room temperature, the solution was concentrated and the residue was purified by column chromatography (9:1 dichloromethane-acetone) yielding **6** (4.4 g, 75%) as a brown solid: $[\alpha]_D$ +97° (*c* 1, dichloromethane); R_F 0.78 (85:15 dichloromethane-acetone); ^{13}C NMR ($CDCl_3$) δ 169.7-168.5 (*C*OCH$_3$), 160.2 (O*C*NHCCl$_3$), 100.5 (C-1'), 92.3 (C-1), 75.3, 70.5 (2C), 70.1, 69.4, 69.0, 68.6, and 66.3 (C-2,3,4,5,2',3',4',5'), 61.1 and 60.4 (C-6,6'), 20.2-19.9 (CO*C*H$_3$); ^{1}H NMR ($CDCl_3$) δ 8.666 (s, 1H, OCN*H*CCl$_3$), 6.491 (d, 1H, H-1), 5.562 (t, 1H, H-3), 5.360 (d, 1H, H-4'), 5.132 (dd, 1H, H-2'), 5.068 (dd, 1H, H-2), 4.978 (dd, 1H, H-3'), 4.531 (d, 1H, H-1'), 2.159, 2.112, 2.071, 2.067, 2.045, 2.011, and 1.969 (7s, each 3H, 7Ac), $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 9.5 Hz, $J_{1',2'}$ = 7.9 Hz, $J_{2',3'}$ = 10.4 Hz, $J_{3',4'}$ = 3.5 Hz.

2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl trichloroacetimidate (8). To a solution of peracetylated galactose (15.0 g, 38.4 mmol) in dry *N,N*-dimethylformamide (75 mL) was added hydrazine acetate (3.75 g, 40.7 mmol). After 2 h at 60 °C ethyl acetate (250 mL) was added, and the organic phase was washed with aqueous 5% sodium chloride and water, dried, filtered, and concentrated to give 2,3,4,6-tetra-*O*-acetyl-α/β-D-galactopyranose (**7**; 11.1 g, 83%) as a syrup: R_F 0.63 (85:15 dichloromethane-acetone). This product was used without further purification. To a solution of **7** (2.4 g, 6.9 mmol) and trichloroacetonitrile (4.3 mL, 42.9 mmol) in dichloromethane (25 mL) at 0 °C, was added 1,8-diazabicyclo[5.4.0]undec-7-ene (1 mL, 6.9 mmol). After 2 h at room tempera-

ture, the solution was concentrated and the residue was purified by column chromatography (9:1 dichloromethane-acetone) yielding **8** (2.7 g, 80%) as a light brown solid: $[\alpha]_D$ +42° (*c* 1, dichloromethane), lit[14] $[\alpha]_D$ +115.5° (chloroform); R_F 0.73 (85:15 dichloromethane-acetone); ^1H NMR ($CDCl_3$) δ 8.672 (s, 1H, OCN*H*CCl_3), 6.608 (d, 1H, H-1), 5.566 (dd, 1H, H-4), 5.433 (dd, 1H, H-3), 5.366 (dd, 1H, H-2), 4.466 (t, 1H, H-5), 4.172 (dd, 1H, H-6b), 4.087 (dd, 1H, H-6a), 2.031, 2.011, and 2.017 (3s, 3, 6, and 3H, 4Ac), $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.8 Hz, $J_{3,4}$ = 3.1 Hz, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 6.6 Hz, $J_{5,6b}$ = 6.7 Hz, $J_{6a,6b}$ = -11.3 Hz.

Methyl 6-*O*-[4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl]-3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (9). A mixture of **4** (0.49 g, 1.2 mmol), **6** (0.93 g, 1.2 mmol), and powdered molecular sieves (4Å, 0.5 g) in dry dichloromethane (3 mL) was stirred for 1 h at 0 °C. Then boron trifluoroetherate (150 μL, 1.2 mmol) in dichloromethane (0.8 mL) was added and the mixture was stirred overnight. TLC showed the disappearance of starting material and the formation of a new spot (R_F 0.35, 85:15 dichloromethane-acetone). The mixture was diluted with dichloromethane (4 mL), filtered through Celite, washed with aqueous 10% sodium hydrogencarbonate and water, dried, filtered, and concentrated. Column chromatography (9:1 dichloromethane-acetone) of the residue gave **9** (0.81 g, 66%) as a white solid: $[\alpha]_D$ +27° (*c* 1, dichloromethane); ^{13}C NMR ($CDCl_3$) δ 170.2-167.3 (*C*OCH_3, *C*O Phth), 137.6 (Ph), 133.4, 131.1, and 122.9 (Phth), 127.7-127.0 (Ph), 100.6 and 100.0 (C-1',1"), 98.7 (C-1), 78.5, 75.8, 74.8, 72.2 (2C), 71.1, 70.5, 70.2, 68.7, 66.3, and 66.2 (C-3,4,5,2',3',4',5',2",3",4",5"), 74.0 (O*C*H_2Ph), 68.3 (C-6), 61.6 and 60.5 (C-6',6"), 56.3 and 54.9 (O*C*H_3, C-2), 20.2-19.3 (CO*C*H_3); ^1H NMR ($CDCl_3$) δ 7.71-7.67 (m, 4H, Phth), 7.05-6.97 (m, 5H, Ph), 5.355 (d, 1H, H-4"), 5.200 (t, 1H, H-3'), 5.118 (dd, 1H, H-2"), 5.029 (d, 1H, H-1), 4.972 (dd, 1H, H-3"), 4.946 (dd, 1H, H-2'), 4.699 and 4.532 (2d, each 1H, OC*H*$_2$Ph), 4.684 (d, 1H, H-1'), 4.512 (d, 1H, H-1"), 4.227 (dd, 1H, H-2), 2.151, 2.067, 2.054, and 1.967 (4s, 6, 9, 3, and 3H, 7Ac), $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 10.8 Hz, $J_{1',2'}$ = 7.7 Hz, $J_{2',3'}$ = 9.2 Hz, $J_{1",2"}$ = 7.8 Hz, $J_{2",3"}$ = 10.4 Hz, $J_{3",4"}$ = 3.5 Hz.

Anal. Calcd for $C_{48}H_{57}NO_{24}$: C, 55.87; H, 5.57. Found: C, 55.85; H, 5.74.

Methyl 4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-6-*O*-[4-*O*-(2,3,4,6 -tetra-*O*-acetyl-β-D-galactopyranosyl) -2,3,6-tri-*O*-acetyl-β-D-glu-

copyranosyl]-3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (10). To a solution of **9** (110 mg, 0.11 mmol) and **8** (125 mg, 0.25 mmol) in dry dichloromethane (2 mL) was added boron trifluoroetherate (25 μL, 0.20 mmol) in dry dichloromethane (0.20 mL). The solution was stirred overnight at room temperature, after which TLC showed the complete disappearance of **9** and the formation of a new spot (R_F 0.43, 4:1 dichloromethane-acetone). The solution was diluted with dichloromethane (4 mL), washed with aqueous 10% sodium hydrogencarbonate and water, dried, filtered, and concentrated. Column chromatography (9:1 dichloromethane-acetone) of the residue afforded **10** (93 mg, 64%) as a white powder: $[\alpha]_D$ +8° (*c* 1, dichloromethane); ^{13}C NMR ($CDCl_3$) δ 170.0-168.7 (*C*OCH$_3$), 167.4 (*C*O Phth), 137.9 (Ph), 133.4, 131.2, and 122.9 (Phth), 127.5-126.7 (Ph), 100.7 (2C) and 100.0 (C-1',1'',1'''), 98.6 (C-1), 79.3, 76.5, 75.7, 74.6, 72.4 (2C), 71.4, 70.4, 70.3, 70.2 (2C), 69.2, 68.7, and 66.4 (2C) (C-3,4,5,2',3',4',5',2'',3'',4'',5'',2''',3''',4''',5'''), 74.3 (O*C*H$_2$Ph), 67.3 (C-6), 62.0, 60.5, and 60.3 (C-6',6'',6'''), 56.3 and 55.0 (O*C*H$_3$, C-2), 20.2 (CO*C*H$_3$); ^1H NMR ($CDCl_3$) δ 7.69-7.65 (m, 4H, Phth), 7.02-6.88 (m, 5H, Ph), 5.000 (d, 1H, H-1), 4.802 and 4.412 (2d, each 1H, OC*H*$_2$Ph), 4.730, 4.651, and 4.529 (3d, each 1H, H-1',1'',1'''), 3.375 (s, 3H, OC*H*$_3$), 2.150, 2.142, 2.097, 2.090, 2.073, 2.067, 2.057, 2.000, 1.981, and 1.965 (10s, 3, 3, 3, 3, 3, 6, 3, 3, 3, and 3H, 11Ac), $J_{1,2}$ = 8.4 Hz, $J_{1'2'}$, $J_{1'',2''}$, and $J_{1''',2'''}$ = 7.3, 7.8, and 7.9 Hz.

Anal. Calcd for $C_{62}H_{75}NO_{33}$: C, 54.67; H, 5.55. Found: C, 54.78; H, 5.80.

Methyl 2-Acetamido-3-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-6-*O*- [4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl]-2-deoxy-β-D-glucopyranoside (12). A solution of **10** (195 mg, 143 μmol) in 4:1 ethanol/ethyl acetate (20 mL) was hydrogenolysed using 10% palladium on charcoal (55 mg) at 4 kg/cm^2 for 40 h at room temperature. Then TLC showed the disappearance of **10** and the formation of a new spot (R_F 0.59, 4:1 dichloromethane-acetone), and filtration and concentration of the mixture afforded **11** (182 mg, quantitative). To a solution of **11** (182 mg, 143 μmol) in ethanol (10 mL) was added hydrazine monohydrate (5.5 mL, 113 mmol). After 1 h at 70 °C the mixture was concentrated and co-concentrated with toluene (2 x 7 mL) and ethanol (2 x 7 mL). The residue was dissolved in dry pyridine (10 mL), and acetic anhydride (5 mL) and a catalytic amount of *N*,*N*-dimethylaminopyridine were added. The mixture was stirred for 60 h, then con-

centrated, and co-concentrated with toluene (3 x 10 mL), ethanol (3 x 10 mL), and dichloromethane (3 x 10 mL). Column chromatography (97:3 dichloromethane-methanol) of the residue yielded **12** (84.1 mg, 48%) as a white powder: $[\alpha]_D$ +7° (*c* 1, dichloromethane); R_F 0.32 (85:15 dichloromethane-acetone); ^{1}H NMR ($CDCl_3$) δ 5.600 (d, 1H, N*H*Ac), 5.301 and 5.284 (2d, each 1H, H-4",4'''), 4.540 (d, 1H, H-1'), 4.437, 4.426, and 4.250 (3d, each 1H, H-1,1",1'''), 3.379 (s, 3H, OC*H*$_3$), 2.108, 2.085, 2.056, 1.993, 1.988, 1.981, 1.972, 1.906, and 1.898 (9s, 3, 6, 3, 3, 9, 6, 3, 3, and 3H, 12Ac and NHAc), $J_{1',2'}$ = 7.5 Hz, $J_{1,2}$, $J_{1'',2''}$, and $J_{1''',2'''}$ = 7.8, 7.5, and 7.0 Hz, $J_{2,NH}$ = 9.5 Hz.

Methyl *O*-β-D-Galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-*O*-[β-D-galactopyranosyl-(1→4)]-*O*-2-acetamido-2-deoxy-β-D-glucopyranoside (13). To a solution of **12** (75 mg, 61 μmol) in dichloromethane (2 mL) were added dry methanol (5 mL) and a catalytic amount of sodium methoxide (pH 8-9). The solution was stirred until TLC (4:1 dichloromethane-methanol) showed the complete disappearance of **12**, then neutralised by filtration through a column of Dowex-50 (H^+) resin, yielding **13** (43 mg, 97%) as a white powder: $[\alpha]_D$ +1° (*c* 1, H_2O), lit[15] -4.4° (*c* 2.75, H_2O); ^{13}C NMR (D_2O) δ 176.0 (*C*OCH$_3$), 104.3, 104.1, 103.7, and 103.3 (C-1,1',1",1'''), 79.8, 79.2, 76.7, 76.6, 76.0, 75.6, 74.8, 74.0, 73.8 (3C), 72.3 (2C), and 69.9 (2C) (C-3,4,5, 2',3',4',5',2",3",4",5",2''',3''',4''',5'''), 68.7 (C-6), 62.3 (2C) and 61.4 (C-6',6",6'''), 58.6 and 56.3 (O*C*H$_3$, C-2), 23.5 (CO*C*H$_3$); ^{1}H NMR (COSY, HOHAHA) (D_2O) δ 4.563 (d, 1H, H-1'), 4.538 (d, 1H, H-1'''), 4.474 (d, 1H, H-1), 4.460 (d, 1H, H-1"), 4.311 (H-6a), 3.996 (H-6a'), 3.978 (H-6b), 3.933 (H-4"), 3.927 (H-4'''), 3.855 (H-4), 3.824 (H-6b'), 3.75 (H-2), 3.74 (H-5'''), 3.73 (3H, H-3,5,5"), 3.676 (H-3'), 3.674 (H-3'''), 3.671 (H-3"), 3.665 (H-5'), 3.616 (H-4'), 3.552 (H-2"), 3.549 (H-2'''), 3.510 (s, 3H, OC*H*$_3$), 3.388 (H-2'), 2.038 (s, 3H, NHAc), $J_{1,2}$ = 8.3 Hz, $J_{1',2'}$ = 8.0 Hz, $J_{1'',2''}$ = 8.0 Hz, $J_{1''',2'''}$ = 7.9 Hz.

Allyl 2-Deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-D-glucopyranoside (14). To a solution of allyl 2-deoxy-2-phthalimido-β-D-glucopyranoside[22] (9.7 g, 27.8 mmol) in acetone (80 mL) were added 2,2-dimethoxypropane (120 mL) and *p*-toluenesulfonic acid (40 mg). After stirring for 2 h the reaction was complete (TLC 85:15 dichloromethane-acetone; **14** R_F 0.69), and the mixture was neutralised with solid sodium hydrogencarbonate, filtered through Celite, and concentrated. Column chromatography (9:1 dichloromethane-acetone) of the residue gave **14** (9.5 g, 88%) as a glass: $[\alpha]_D$ +23°

(*c* 1, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 7.861 and 7.730 (2m, each 2H, Phth), 5.686 (m, 1H, $OCH_2CH{=}CH_2$), 5.269 (d, 1H, H-1), 5.122 and 5.031 (2m, each 1H, $OCH_2CH{=}CH_2$), 4.465 (m, 1H, H-3), 4.258 and 4.015 (2m, each 1H, $OCH_2CH{=}CH_2$), 4.229 (dd, 1H, H-2), 3.979 (dd, 1H, H-6a), 3.847 (t, 1H, H-6b), 3.642 (t, 1H, H-4), 3.457 (m, 1H, H-5), 2.320 (d, 1H, O*H*), 1.526 and 1.432 [2s, each 3H, $C(CH_3)_2$], $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 8.8 Hz, $J_{4,5}$ = 9.8 Hz, $J_{5,6a}$ = 5.5 Hz, $J_{5,6b}$ = 10.2 Hz, $J_{6a,6b}$ = -10.7 Hz, $J_{3,OH}$ = 3.4 Hz.

Anal. Calcd for $C_{20}H_{23}NO_7$: C, 61.69; H, 5.95. Found: C, 61.43; H, 6.04.

Allyl 3-*O*-Benzyl-2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-D-glucopyranoside (15). To a solution of **14** (9.5 g, 24.4 mmol) in freshly distilled tetrahydrofuran (300 mL) was added sodium hydride (1.4 g, 58.3 mmol), and benzyl bromide (3.2 mL, 26.9 mmol) was added dropwise. After 3 h at reflux temperature the mixture was treated with ethyl acetate (200 mL), filtered through Celite, and concentrated. A solution of the residue in dichloromethane (150 mL) was washed with water, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. Column chromatography (95:5 dichloromethane-ethyl acetate) of the residue yielded **15** (9.6 g, 82%) as a yellow solid: $[\alpha]_D$ +44° (*c* 1, dichloromethane); R_F 0.82 (9:1 dichloromethane-ethyl acetate); ^{13}C NMR ($CDCl_3$) δ 138.0 (Ph), 133.6, 131.4, and 123.1 (Phth), 133.2 ($OCH_2CH{=}CH_2$), 127.7-127.1 (Ph), 117.2 ($OCH_2CH{=}CH_2$), 99.2 [$C(CH_3)_2$], 97.7 (C-1), 75.6, 74.7, and 66.8 (C-3,4,5), 73.5 (OCH_2Ph), 69.7 ($OCH_2CH{=}CH_2$), 62.0 (C-6), 55.6 (C-2), 29.0 and 18.9 [$C(CH_3)_2$]; ^{1}H NMR ($CDCl_3$) δ 7.71-7.69 (m, 4H, Phth), 7.01-6.88 (m, 5H, Ph), 5.644 (m, 1H, $OCH_2CH{=}CH_2$), 5.193 (d, 1H, H-1), 5.083 and 4.992 (2m, each 1H, $OCH_2CH{=}CH_2$), 4.733 and 4.467 (2d, each 1H, OCH_2Ph), 3.972 (dd, 1H, H-6a), 3.452 (m, 1H, H-5), 1.531 and 1.460 [2s, each 3H, $C(CH_3)_2$], $J_{1,2}$ = 8.0 Hz, $J_{4,5} \approx J_{5,6b} \approx$ 10 Hz, $J_{5,6a}$ = 5.3 Hz, $J_{6a,6b}$ = -10.7 Hz.

Anal. Calcd for $C_{27}H_{29}NO_7$: C, 67.63; H, 6.10. Found: C, 67.32; H, 6.04.

Allyl 3-*O*-Benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (16). A solution of **15** (2.65 g, 5.53 mmol) in methanol (10 mL) and aqueous 50% acetic acid (75 mL) was stirred overnight at room temperature, after which TLC showed a complete conversion into **16** (R_F 0.45, 4:1 dichloromethane-acetone). The mixture was concentrated, and co-concentrated with toluene (3 x 25 mL), ethanol (3 x 25 mL), and dichloromethane (3 x 25 mL). Column chromatography (9:1 dichloromethane-acetone) of the residue af-

forded **16** (1.85 g, 76%) as a light yellow solid: $[\alpha]_D$ +39° (*c* 1, dichloromethane), lit[36] +40.3° (*c* 0.6, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.72-7.68 (m, 4H, Phth), 7.13-6.96 (m, 5H, Ph), 5.668 (m, 1H, OCH_2CH=CH_2), 5.217 (d, 1H, H-1), 5.089 and 5.009 (2m, each 1H, OCH_2CH=CH_2), 4.722 and 4.537 (2d, each 1H, OCH_2Ph), 3.083 and 2.460 (2bs, each 1H, 2O*H*), $J_{1,2}$ = 8.3 Hz.

Anal. Calcd for $C_{24}H_{25}NO_7 \cdot 0.5H_2O$: C, 64.28; H, 5.84. Found: C, 64.96; H, 5.93.

Allyl 6-*O*-[4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl] -3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (17). A mixture of **16** (1.5 g, 3.41 mmol), **6** (2.7 g, 3.46 mmol), and molecular sieves (4Å, 3 g) in dry dichloromethane (15 mL) was cooled to -40 °C, and trimethylsilyl trifluoromethanesulfonate (0.65 mL, 3.58 mmol) was added. After stirring for 3 h at -40 °C, TLC showed the disappearance of **16** and the formation of a new spot (R_F 0.56, 85:15 dichloromethane-acetone). Pyridine (1 mL) was added, and the mixture was filtered through Celite, concentrated, and co-concentrated with toluene (3 x 15 mL), ethanol (3 x 15 mL), and dichloromethane (3 x 15 mL). A solution of the residue in dichloromethane (25 mL) was washed with water, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. Column chromatography (9:1 dichloromethane-acetone) of the residue gave **17** (2.2 g, 61%) as a white glass: $[\alpha]_D$ +12° (*c* 1, dichloromethane); ^{13}C NMR ($CDCl_3$) δ 170.4-168.9 ($COCH_3$, *C*O Phth), 137.9 (Ph), 133.7, 131.4, and 123.1 (Phth), 133.3 (OCH_2CH=CH_2), 128.0-127.3 (Ph), 117.2 (OCH_2CH=CH_2), 100.9 and 100.2 (C-1',1"), 97.1 (C-1), 78.6, 76.0, 74.6, 72.7, 72.6 (2C), 71.4, 70.8, 70.5, 68.9, and 66.5 (C-3,4,5,2',3',4',5',2",3",4",5"), 74.2 (OCH_2Ph), 69.6 (OCH_2CH=CH_2), 68.5 (C-6), 61.7 and 60.7 (C-6',6"), 55.2 (C-2), 20.6-20.3 ($COCH_3$); ^{1}H NMR ($CDCl_3$) δ 7.72-7.67 (m, 4H, Phth), 7.08-6.97 (m, 5H, Ph), 5.664 (m, 1H, OCH_2CH=CH_2), 5.354 (dd, 1H, H-4"), 5.200 (t, 1H, H-3'), 5.144 (d, 1H, H-1), 5.117 (dd, 1H, H-2"), 4.966 (dd, 1H, H-3"), 4.941 (dd, 1H, H-2'), 4.695 and 4.532 (2d, each 1H, OCH_2Ph), 4.673 (d, 1H, H-1'), 4.505 (d, 1H, H-1"), 4.242 (dd, 1H, H-2), 3.978 (m, 1H, OCH_2CH=CH_2), 2.633 (d, 1H, O*H*), 2.151, 2.067, 2.054, 2.053, and 1.966 (5s, 6, 6, 3, 3, and 3H, 7Ac), $J_{1,2}$ = 8.2 Hz, $J_{2,3}$ = 10.7 Hz, $J_{1',2'}$ = 7.7 Hz, $J_{2',3'}$ = 9.2 Hz, $J_{1",2"}$ = 7.8 Hz, $J_{2",3"}$ = 10.3 Hz, $J_{3",4"}$ = 3.4 Hz, $J_{4",5"}$ = 1.0 Hz, $J_{4,OH}$ = 3.8 Hz.

Anal. Calcd for $C_{50}H_{59}NO_{24}$: C, 56.76; H, 5.62. Found: C, 56.71; H, 5.85.

Allyl 4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-6-*O*-[4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl] -3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (18). A mixture of **17** (1.03 g, 0.97 mmol), **8** (0.95 g, 1.93 mmol), and molecular sieves (4Å, 3.2 g) in dichloromethane (20 mL) was cooled to -50 °C, and trimethylsilyl trifluoromethanesulfonate (0.17 mL, 0.94 mmol) was added dropwise. After stirring for 3 h at -50 °C, pyridine (1 mL) was added, and the mixture was filtered through Celite, concentrated, and co-concentrated with toluene (3 x 10 mL), ethanol (3 x 10 mL), and dichloromethane (3 x 10 mL). A solution of the residue in dichloromethane (15 mL) was washed with water, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. Column chromatography (9:1 dichloromethane-acetone) of the residue afforded **18** (0.9 g, 66%) as a white solid: $[\alpha]_D$ +8° (*c* 1, dichloromethane); R_F 0.51 (85:15 dichloromethane-acetone); ^{13}C NMR ($CDCl_3$) δ 170.3-169.6 ($COCH_3$, *C*O Phth), 138.2 (Ph), 133.6, 131.4, and 123.2 (Phth), 133.2 ($OCH_2CH=CH_2$), 127.8-127.0 (Ph), 117.4 ($OCH_2CH=CH_2$), 101.0 (2C) and 100.3 (C-1',1'',1'''), 96.9 (C-1), 79.6, 76.8, 76.0, 74.8, 72.7 (2C), 71.8, 70.9, 70.7, 70.5 (2C), 69.4, 68.9, 66.8, and 66.5 (C-3,4,5,2',3',4',5',2'',3'',4'',5'',2''',3''',4''',5'''), 74.8 (OCH_2Ph), 69.6 ($OCH_2CH=CH_2$), 67.4 (C-6), 62.2 and 60.7 (2C) (C-6',6'',6'''), 55.3 (C-2), 20.7-20.5 ($COCH_3$); ^1H NMR ($CDCl_3$) δ 7.67-7.63 (m, 4H, Phth), 7.02-6.84 (m, 5H, Ph), 5.660 (m, 1H, $OCH_2CH=CH_2$), 5.357 and 5.349 (2d, each 1H, H-4'',4'''), 5.223 (dd, 1H, H-2'''), 5.186 (t, 1H, H-3'), 5.118 (d, 1H, H-1), 4.795 and 4.414 (2d, each 1H, OCH_2Ph), 4.724 (d, 1H, H-1'), 4.633 (d, 1H, H-1'''), 4.509 (d, 1H, H-1''), 4.493 (dd, 1H, H-6a), 4.288 (d, 1H, H-2), 3.677 (m, 1H, H-5), 2.149, 2.141, 2.094, 2.084, 2.066, 2.060, 2.051, 2.000, 1.980, and 1.964 (10s, 3, 3, 3, 3, 6, 3, 3, 3, 3, and 3H, 11Ac), $J_{1,2}$ = 8.5 Hz, $J_{2,3}$ = 10.8 Hz, $J_{5,6a}$ = 1.8 Hz, $J_{6a,6b}$ = -12.0 Hz, $J_{1',2'}$ = 7.3 Hz, $J_{1'',2''}$ = 7.9 Hz, $J_{1''',2'''}$ = 7.9 Hz, $J_{2''',3'''}$ = 10.4 Hz, $J_{3'',4''}$ = $J_{3''',4'''}$ = 3.2 Hz.

4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-6-*O*- [4-*O*-(2,3,4,6-tetra- *O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri- *O*-acetyl-β-D-glucopyranosyl]-3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Trichloroacetimidate (20). A mixture of **18** (463 mg, 0.33 mmol), palladium (II) chloride (296 mg, 1.67 mmol), and sodium acetate trihydrate (227 mg, 1.67 mmol) in aqueous 96%

acetic acid (8 mL) was sonicated in an ultrasonic cleaner for 18 h. Then the mixture was filtered through Celite, diluted with dichloromethane (15 mL), and washed with water, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. Column chromatography (9:1 dichloromethane-acetone) of the residue gave **19** (382 mg, 85%) as a light coloured solid: $[\alpha]_D$ +3° (*c* 1, dichloromethane); R_F 0.11 and 0.23 (85:15 dichloromethane-acetone). To a solution of **19** (117 mg, 87 μmol) in dichloromethane (3 mL) at 0 °C, was added trichloroacetonitrile (70 μL, 700 μmol) and 1,8-diazabicyclo-[5.4.0]undec-7-ene (13 μL, 87 μmol). The mixture was stirred for 3.5 h at room temperature, then concentrated, and the residue was purified by column chromatography (900:100:1 dichloromethane-acetone-triethyl amine), yielding **20** (111 mg, 86%) as an amorphous white powder: $[\alpha]_D$ +34° (*c* 1, dichloromethane); R_F 0.45 (85:15 dichloromethane-acetone); ^{1}H NMR ($CDCl_3$) δ 8.640 (s, 1H, OCN*H*CCl_3), 7.67-7.65 (m, 4H, Phth), 7.04-6.87 (m, 5H, Ph), 6.357 (d, 1H, H-1), 5.367 (d, 1H, H-4‴), 5.352 (d, 1H, H-4″), 5.241 (dd, 1H, H-2‴), 5.158 (t, 1H, H-3′), 5.094 (dd, 1H, H-3‴), 5.093 (dd, 1H, H-2″), 4.947 (dd, 1H, H-3″), 4.916 (dd, 1H, H-2′), 4.830 and 4.456 (2d, each 1H, OC*H*$_2$Ph), 4.758 (d, 1H, H-1′), 4.667 (d, 1H, H-1‴), 4.473 (d, 1H, H-1″), 2.143, 2.099, 2.088, 2.078, 2.065, 2.056, 2.033, 2.019, 1.983, and 1.959 (10s, 6, 3, 3, 3, 3, 3, 3, 3, and 3H, 11Ac), $J_{1,2}$ = 8.3 Hz, $J_{1',2'}$ = 7.5 Hz, $J_{2',3'}$ = 9.2 Hz, $J_{1'',2''}$ = 7.8 Hz, $J_{2'',3''}$ = 10.4 Hz, $J_{3'',4''}$ = 3.4 Hz, $J_{1''',2'''}$ = 7.9 Hz, $J_{2''',3'''}$ = 10.5 Hz, $J_{3''',4'''}$ = 3.5 Hz.

Methyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2, 3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→6)-*O*-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)]-*O*-(3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (25). A mixture of methyl 4-*O*-β-D-galactopyranosyl-β-D-glucopyranoside[29] (**21**; 1.07 g, 3.00 mmol) and dibutyltin oxide (0.75 g, 3.01 mmol) in dry benzene (50 mL) was boiled under reflux in a Soxhlet apparatus containing molecular sieves (4Å). After 18 h tetrabutylammonium iodide (1.11 g, 3.00 mmol) and 4-methoxybenzyl chloride (1.0 mL, 7.4 mmol) were added, and boiling was continued for 6.5 h, when TLC showed the disappearance of **21** and the formation of a new product (4:1 dichloromethane-methanol; **22** R_F 0.47). After concentration, column chromatography (4:1 dichloromethane-methanol) of the residue gave **22** (1.0 g, 70%) as a syrup: ^{1}H NMR (CD_3OD) δ 7.30-7.08 (m, 4H, Ph), 3.68 (s, 3H, $OCH_2C_6H_4OCH_3$),

3.49 (s, 3H, OCH_3). To a solution of **22** (0.5 g, 1.05 mmol) in *N,N*-dimethylformamide (10 mL) was added sodium hydride (0.9 g, 60% dispersion in mineral oil, washed three times with hexane) and benzyl bromide (0.85 mL, 7.15 mmol). After stirring for 18 h, TLC showed the benzylation to be complete (95:5 dichloromethane-ethyl acetate; **23** R_F 0.70), and methanol was added to destroy the excess of sodium hydride. The mixture was poured into water (15 mL) and the solution was extracted with ether (3 x 5 mL). The combined extracts were washed with water, dried, filtered, and concentrated. Column chromatography (96:4 dichloromethane-ethyl acetate) of the residue gave **23** (0.50 g, 47%) as a syrup: ^{1}H NMR ($CDCl_3$) δ 7.30-6.60 (m, 34H, 7Ph), 3.72 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.51 (s, 3H, OCH_3). To a solution of **23** (0.50 g, 0.47 mmol) in dry dichloromethane (5 mL) was added 10% trifluoroacetic acid in dichloromethane (5 mL). After 30 min TLC showed the disappearance of **23** and the formation of a new spot (R_F 0.60, 95:5 dichloromethane-ethyl acetate). The mixture was co-concentrated with toluene (2 x 5 mL), ethanol (2 x 5 mL), and dichloromethane (2 x 5 mL). Flash chromatography (98:2 dichloromethane-acetone) of the residue yielded **24** (435 mg, 98%) as a syrup: ^{1}H NMR ($CDCl_3$) δ 7.40-7.00 (m, 30H, 6Ph), 3.54 (s, 3H, OCH_3). A mixture of **20** (111 mg, 74 μmol), **24** (93 mg, 103 μmol), and powdered molecular sieves (4Å, 1 g) in dichloromethane (8 mL) was stirred and cooled to -70 °C. Then a solution of trimethylsilyl trifluoromethanesulfonate (15 μL, 83 μmol) in dichloromethane (2 mL) was added dropwise. After 2 h at -70 °C the reaction was complete (TLC 9:1 dichloromethane-acetone; **25** R_F 0.52), pyridine (1 mL) was added, and the mixture was filtered through Celite, concentrated, and co-concentrated with toluene (3 x 5 mL), ethanol (3 x 5 mL), and dichloromethane (3 x 5 mL). A solution of the residue in dichloromethane (10 mL) was washed with water, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. Column chromatography (92:8 dichloromethane-acetone) of the residue gave **25** (87 mg, 53%) as an amorphous powder: $[\alpha]_D$ +1° (*c* 1, dichloromethane); ^{13}C NMR ($CDCl_3$) δ 170.1-167.3 (*C*OCH$_3$, *C*O Phth), 139.0-138.1 and 128.6-126.4 (Ph), 133.3, 131.0, and 123.0 (Phth), 104.3, 102.5, 101.0, 100.8 (2C), and 99.1 (C-1,1',1",1"', 1"",1""'), 61.9 and 60.5 (2C) (C-6"',6"",6""'), 56.7 and 56.0 (C-2", OCH$_3$), 20.7-20.3 (COCH$_3$); ^{1}H NMR ($CDCl_3$) δ 7.65-6.73 (m, 39H, 7Ph and Phth), 5.304 (d, 1H, H-1"), 5.276 and 5.250 (2d, each 1H, H-4"",4""'), 3.398 (s, 3H, OCH_3), 2.069, 2.050, 2.031, 2.022, 1.976, 1.938, 1.920, 1.916, 1.886, 1.883, and 1.852 (11s, each 3H, 11Ac), $J_{1",2"}$ = 8.3 Hz, $J_{3"",4""'}$ and $J_{3""',4""'}$ = 3.6 and 3.5 Hz.

Methyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→6)-*O*-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)]-*O*-(2-acetamido-3-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (27). A solution of **25** (67 mg, 30 μmol) in 5:3 ethanol/ethyl acetate (30 mL) was hydrogenolysed using 10% palladium on charcoal (30 mg) at 4 kg/cm^2 for 20 h at room temperature. Then TLC showed the debenzylation to be complete (R_F 0.42, 97:3 dichloromethane-methanol), and the mixture was filtered through Celite, concentrated, and co-concentrated with dichloromethane (2 x 5 mL), affording **26** (48 mg, quantitative). To a solution of **26** (48 mg, 30 μmol) in ethanol (10 mL) was added hydrazine monohydrate (1.1 mL, 22 mmol). After 1 h at 70 °C the mixture was concentrated, and co-concentrated with toluene (2 x 5 mL) and ethanol (2 x 5 mL). The residue was dissolved in pyridine (15 mL) and acetic anhydride (10 mL), and a catalytic amount of *N,N*-dimethylaminopyridine was added. After stirring for 40 h, TLC showed the disappearance of **26** and the formation of a new spot (R_F 0.78, 92:8 dichloromethane-methanol), and the solution was concentrated, and co-concentrated with toluene (3 x 5 mL), ethanol (3 x 5 mL), and dichloromethane (3 x 5 mL). Column chromatography (95:5 dichloromethane-methanol) of the residue afforded **27** (23 mg, 42%) as a white powder: $[\alpha]_D$ +5° (*c* 1, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 5.433 (d, 1H, N*H*Ac), 4.660, 4.631, 4.590, and 4.514 (4d, each 1H, 4 anomeric signals), 3.487 (s, 3H, OC*H*$_3$), 2.156, 2.143, 2.131, 2.103, 2.095, 2.064, 2.057, 2.046, 2.040, 2.030, 1.994, 1.959, 1.932, and 1.953 (14s, 3, 9, 6, 3, 3, 3, 6, 3, 3, 6, 3, 3, 3, and 3H, 18Ac and NHAc), $J_{2'',NH}$ = 8.9 Hz, $J_{1,2's}$ = 7.9, 5.3, 7.9, and 7.8 Hz.

Methyl *O*-β-D-Galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-*O*-[β-D-galactopyranosyl-(1→4)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (28). To a solution of **27** (23 mg, 12.6 μmol) in dichloromethane (1.5 mL) were added dry methanol (4 mL) and a catalytic amount of sodium methoxide (pH 9). The solution was stirred for 20 h, when TLC (5:1 dichloromethane-methanol) showed the complete disappearance of **27**, then filtered through a column of Dowex 50 (H^+) resin, and lyophilised, yielding **28** (6 mg, 44%) as a white solid: $[\alpha]_D$ +3° (*c* 1, H_2O); ^{1}H NMR (COSY, HOHAHA) (D_2O) δ 4.715 (d, 1H, H-1"), 4.554 (d, 1H, H-1'''), 4.533 (d, 1H, H-1''''), 4.455 (d, 1H, H-1''''), 4.429 (d, 1H, H-1'), 4.404 (d, 1H, H-1), 4.278 (dd, 1H, H-6"), 4.159 (d, 1H,

H-4'), 3.810 (H-2''), 3.724 (H-3'), 3.661 (H-3'''), 3.642 (H-3), 3.594 (H-2'), 3.572 (s, 3H, OCH_3), 3.376 (H-2'''), 2.036 (s, 3H, NHAc), $J_{1,2}$ = 8.0 Hz, $J_{1',2'}$ = 7.9 Hz, $J_{1'',2''}$ = 8.4 Hz, $J_{1''',2'''}$ = 8.0 Hz, $J_{1'''',2''''}$ = 7.8 Hz, $J_{1''''',2'''''}$ = 7.8 Hz, $J_{3',4'}$ = 3.2 Hz.

Benzyl 2,3,6-tri-*O*-Benzyl-4-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside (33). To a solution of benzyl 4-*O*-(3-*O*-allyl-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[37] (**32**; 1.4 g, 1.38 mmol) in dry *N*,*N*-dimethylformamide (20 mL) at 80 °C was added potassium *tert*-butoxide (300 mg, 2.67 mmol). After 2 h the mixture was cooled, dichloromethane (30 mL) was added, and the mixture was washed with water, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. A suspension of the residue in acetone (13.5 mL) and 0.1M hydrogen chloride (1.5 mL) was stirred for 45 min at reflux temperature. Then the mixture was neutralised with aqueous 25% ammonia, concentrated, and a solution of the residue in dichloromethane (20 mL) was washed with water, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. Column chromatography (20:1 toluene-acetone) of the residue afforded **33** (0.79 g, 59%) as a syrup: $[\alpha]_D$ -6° (*c* 0.5, dichloromethane), lit[37] -5° (*c* 1, chloroform); R_F 0.65 (20:1 toluene-acetone). ^{1}H NMR ($CDCl_3$) δ 7.38-7.15 (m, 35H, 7Ph), 2.170 (d, 1H, O*H*), $J_{3',OH}$ = 5.8 Hz.

Anal. Calcd for $C_{61}H_{64}O_{11}$: C, 75.29; H, 6.63. Found: C, 75.34; H, 6.75.

Benzyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→6)-*O*-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)]-*O*-(3-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (34). A mixture of **20** (170 mg, 114 μmol), **33** (222 mg, 228 μmol), and molecular sieves (4Å, 8 g) in dichloromethane (23 mL) was stirred and cooled to -50 °C. After 30 min, a solution of trimethylsilyl trifluoromethanesulfonate (40 μL, 220 μmol) in dichloromethane (2 mL) was added, and the mixture was stirred for 2.5 h. Then pyridine (1 mL) was added, and the mixture was filtered through Celite, concentrated, and co-concentrated with toluene (3 x 5 mL) and ethanol (3 x 5 mL). A solution of the residue in dichloromethane (10 mL) was washed with water, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concen-

trated. Column chromatography (9:1 dichloromethane-acetone) of the residue gave **34** (161 mg, 61%) as a white solid: $[\alpha]_D$ -6° (*c* 1, dichloromethane); R_F 0.67 (85:15 dichloromethane-acetone); ^{13}C NMR ($CDCl_3$) δ 170.1-168.9 (*C*OCH_3, *C*O Phth), 139.1-137.4 and 128.3-126.5 (Ph), 133.4, 131.0, and 123.0 (Phth), 102.6, 102.2, 101.1 (2C), 100.8, and 99.1 (C-1,1',1",1‴,1⁗,1⁗'), 56.1 (C-2"), 20.7-20.5 (CO*C*H_3); ^1H NMR ($CDCl_3$) δ 7.29-6.80 (m, 44H, 8Ph and Phth), 5.369 (d, 1H, H-1"), 5.347 and 5.320 (2d, each 1H, H-4⁗,4⁗'), 2.136, 2.121, 2.100, 2.094, 2.039, 2.016, 1.989, 1.985, 1.960, 1.952, and 1.921 (11s, each 3H, 11Ac), $J_{1",2"}$ = 8.5 Hz, $J_{3⁗,4⁗}$ and $J_{3⁗',4⁗'}$ = 3.5 and 3.4 Hz.

Anal. Calcd for $C_{122}H_{135}NO_{43}$: C, 63.62; H, 5.91. Found: C, 63.32; H, 6.01.

Benzyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→6)-*O*-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)]-*O*-2-acetamido-3-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (35). To a solution of **34** (130 mg, 56.4 μmol) in methanol (25 mL) was added hydrazine monohydrate (0.4 mL, 8.2 mmol). After 18 h at reflux temperature, the mixture was concentrated, and co-concentrated with toluene (3 x 5 mL), ethanol (3 x 5 mL), and dichloromethane (3 x 5 mL). The residue, showing one new spot on TLC (R_F 0.10, 85:15 dichloromethane-acetone), was dissolved in pyridine (10 mL) and acetic anhydride (5 mL), and stirred overnight. Then TLC showed the disappearance of starting material and the formation of a new spot (R_F 0.22, 85:15 dichloromethane-acetone). The solution was concentrated, and co-concentrated with toluene (3 x 5 mL) and ethanol (3 x 5 mL), and a solution of the residue in dichloromethane (10 mL) was washed with water, 1M hydrogen chloride, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. Column chromatography (9:1 dichloromethane-acetone) of the residue afforded **35** (76 mg, 61%) as a white solid: $[\alpha]_D$ +2° (*c* 1, dichloromethane); ^{13}C NMR ($CDCl_3$) δ 170.2-169.0 (*C*OCH_3), 139.1-137.4 and 128.3-127.1 (Ph), 102.6, 102.5, 102.3, 101.1, 100.8, and 99.4 (C-1,1',1",1‴, 1⁗,1⁗'), 61.8 and 60.5 (2C) (C-6‴,6⁗,6⁗'), 52.3 (C-2"), 22.7 (NHCO*C*H_3), 20.7-20.4 (CO*C*H_3); ^1H NMR ($CDCl_3$) δ 7.35-7.10 (m, 40H, 8Ph), 5.399 and 5.341 (2d, each 1H, H-4⁗,4⁗'), 2.148, 2.043, 2.033, 2.029, 2.021, 2.003, 2.000, 1.982, and 1.962 (9s, 9, 6, 3, 3, 3, 3, 3, 3, and 3H, 11Ac and NHAc), $J_{3⁗,4⁗} \approx J_{3⁗',4⁗'} \approx$ 3.2 Hz.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→6)-*O*-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)]-*O*-(2-acetamido-3-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-1,2,3,6-tetra-*O*-acetyl-D-glucopyranose (37).** A solution of **35** (76 mg, 34 μmol) in ethyl acetate (25 mL) was hydrogenolysed using 10% palladium on charcoal (100 mg) at 1 kg/cm^2 for 2 h at room temperature. Then TLC showed the disappearance of **35** and the formation of a new spot (R_F 0.65, 4:1 dichloromethane-methanol), and the mixture was filtered through Celite, concentrated, and co-concentrated with dichloromethane (2 x 10 mL), affording **36** (32 mg, 63%) as a white powder. A solution of **36** (32 mg, 22 μmol) in pyridine (5 mL) and acetic anhydride (5 mL) containing a catalytic amount of *N,N*-dimethylaminopyridine was stirred for 40 h at 40 °C. Then TLC showed only one spot (R_F 0.66, 4:1 dichloromethane-acetone), and the solution was concentrated, and co-concentrated with toluene (3 x 5 mL) and ethanol (3 x 5 mL). A solution of the residue in dichloromethane (10 mL) was washed with water, 1M hydrogen chloride, aqueous 10% sodium hydrogencarbonate, and water, dried, filtered, and concentrated. Column chromatography (4:1 dichloromethane-acetone) of the residue gave **37** (33 mg, 84%) as a white powder: $[\alpha]_D$ -7° (*c* 1, dichloromethane); ^{13}C NMR ($CDCl_3$) δ 170.5-168.6 (*C*OCH_3), 101.5 (2C), 100.5 (2C), and 99.9 (C-1',1",1‴,1⁗,1⁗'), 91.4 (C-1β), 88.8 (C-1α), 54.1 (C-2"), 23.0 (NHCO*C*H_3), 20.6-19.6 (CO*C*H_3); ^{1}H NMR ($CDCl_3$) δ 6.264 (d, 0.5H, H-1α), 5.680 (d, 0.5H, H-1β), 4.878 (0.5H), 4.869 (0.5H), 4.657 (1H), 4.636 (0.5H), 4.631 (0.5H), 4.587 (0.5H), 4.580 (0.5H), 4.515 (0.5H), and 4.512 (0.5H) (9d, 5H, 5 anomeric signals), 2.217-1.930 (m, 60H, 19Ac and NHAc), $J_{1\alpha,2}$ = 3.7 Hz, $J_{1\beta,2}$ = 8.3 Hz, $J_{1,2's}$ = 8.8, 7.9, 5.3, 7.9, and 7.8 Hz.

***O*-β-D-Galactopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-*O*-[β-D-galactopyranosyl-(1→4)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranose (38).** To a solution of **37** (33 mg, 18 μmol) in dichloromethane (1 mL) and methanol (2 mL) was added a solution of ammonia in methanol (7M, 0.5 mL), and the mixture was stirred overnight, and concentrated. Because of incomplete de-*O*-acetylation, the residue was dissolved in water (2 mL) and aqueous 25% ammonia (0.2 mL) was added. After stirring overnight TLC showed the formation of only one new spot (R_F 0.30, 2:1:1 1-butanol-acetic acid-water),

and the mixture was concentrated, and co-concentrated twice with water (3 mL). The residue was lyophilised to yield **38** (18 mg, 97%) as a white solid: $[\alpha]_D$ +4° (*c* 1, H_2O). ^1H NMR (COSY, HOHAHA) (D_2O) δ 5.220 (d, H-1α), 4.719 and 4.716 (2d, 1H, H-1''), 4.662 (d, H-1β), 4.553 (d, 1H, H-1'''), 4.532 and 4.455 (2d, each 1H, H-1'''',1''''), 4.434 (d, 1H, H-1'), 4.278 (dd, 1H, H-6''), 4.159 (d, 1H, H-4'), 2.035 (s, 3H, NHAc), $J_{1\alpha,2}$ = 3.8 Hz, $J_{1\beta,2}$ = 8.0 Hz, $J_{1',2'}$ = 8.0 Hz, $J_{1'',2''}$ = 8.4 Hz, $J_{1''',2'''}$ = 8.0 Hz, $J_{1'''',2''''}$ = $J_{1'''',2''''}$ = 7.9 Hz, $J_{3',4'}$ = 3.3 Hz.

ACKNOWLEDGMENTS

This investigation was supported by the Netherlands Foundation for Chemical Research (SON/NWO), the Institute of Molecular Biology and Medical Biotechnology (IMB, Utrecht University), and the Netherlands Innovation Directed Programme for Biotechnology (IOP-b). We like to thank Drs. J. P. M. Lommerse and B. R. Leeflang for recording the 2D ^1H NMR spectra, and Drs. T. M. Slaghek, J. G. M. van der Ven, and A. M. P. van Steijn for recording the ^{13}C NMR spectra.

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