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A new method of anomeric protection and activation based on the conversion of glycosyl azides into glycosyl fluorides

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ABSTRACT

Glycosyl azides provide reliable anomeric protection stable to conditions for hydrolytic removal of ester groups, for reductive opening or release of acetalic diol protection, for the introduction of ether-type protection, and for glycosylation processes. The utility of this anomeric protection is further enhanced as glycosyl azides may be converted into glycosyl fluorides, which can be activated for glycosylation reactions. To this end, glycosyl azides have been subjected to 1,3-dipolar cycloaddition with di-*tert*-butyl acetylenedicarboxylate. On treatment with hydrogen fluoride–pyridine complex the N-glycosyl triazole derivatives directly give glycosyl fluorides.

INTRODUCTION

Owing to the important roles which complex carbohydrates exhibit in biological recognition processes, the synthesis of these compounds is receiving increased attention. A number of these natural carbohydrates, such as, i- and I-antigen, proteoglycans, or oligomeric Lewis antigens, contain repeating units consisting of di- or tri-saccharide structures (for a review, see, for example, ref 1). An efficient and economic synthesis of such oligosaccharides demands a maximum of convergent and a minimum of linear synthetic transformations. For oligosaccharides containing repeating units, this principle suggests the use of repeating di- or tri-saccharides as building blocks. By this strategy, the manipulations of protecting groups can be transferred to the mono- or di-saccharide level, whereas the chain-extending reactions only require the deblocking and glycosylation of one hydroxyl group. In the course of *N*-glycopeptide syntheses[2], we found that the azido group provides a valuable anomeric protection and a precursor of the anomeric amino group finally required for the construction of the *N*-glycosylasparagine linkage[3,4]. For example, the *O*-acetylated *N*-acetylglucosaminyl azide **1**

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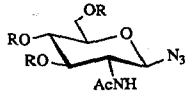
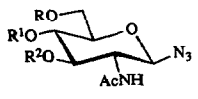
(ref 5) was subjected to Zemplén transesterification to give **2**, subsequent introduction of the 4,6-(4-methoxybenzylidene) acetal protection to yield **3**, acetylation at 3-OH, and regioselective reductive opening of the acetal[6] to form compound **4**. All these conversions were realized without affecting the anomeric azido group[4].



1 R = Ac

2 R = H



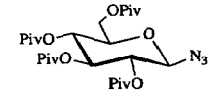
3 R, R^1 = >HC-(4-MeO-C$_6$H$_4$) ; R^2 = H

4 R = $-H_2C$-(4-MeO-C$_6$H$_4$); R^1 = H, R^2 = Ac

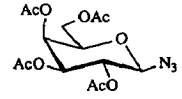
The use of glycosyl azides as anomerically protected glycosyl acceptors in block-condensation strategies demands, besides the stability just noted, their efficient transformation into glycosyl donors having activatable leaving groups. In this sense, we here report on the conversion of glycosyl azides into glycosyl fluorides.

RESULTS AND DISCUSSION

Synthesis and protecting-group manipulations on glycosyl azides.—Glycosyl azides are readily accessible from glycosyl halides[7], in particular, via phase-transfer catalysis[4,8]. They may also be obtained from glycosyl phosphates[9]. An efficient synthesis of *O*-acetylated glycosyl azides consists in the treatment of peracetylated mono- or di-saccharides with trimethylsilyl azide in the presence of tin tetrachloride[10]. According to or by analogy to this method, 2,3,4,6-tetra-*O*-pivaloyl-β-D-glucopyranosyl azide[11,12] (**5**), 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl azide[10] (**6**). 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide[3,4] (**7**), and (2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl azide[13] (**8**) were synthesized.



5 (Piv = Me_3C-CO)



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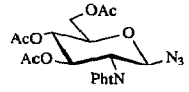

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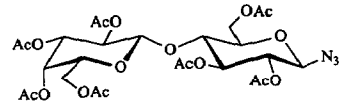
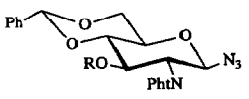
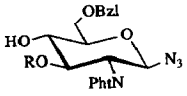


8

The *N*-phthaloyl protected glucosamide azide **7** served as the starting material for the synthesis of lactosamine azides carrying different protecting groups in both

the galactose and the glucosamine portion. To this end, compound **7** was subjected to Zemplén deacetylation using catalytic amounts of sodium methoxide in 2:3 methanol–dichloromethane and subsequently treated with benzaldehyde dimethyl acetal in the presence of tetrafluoroboric acid to give the 4,6-*O*-benzylidene-protected glycosyl azide **9**. Alkylation of the 3-OH group of **9** was performed after deprotonation with sodium hydride. While the reaction with allyl bromide was conducted in the presence of tetrabutylammonium iodide in tetrahydrofuran at 60°C to give **10**, the benzylation was effected with benzyl bromide in dimethylformamide at room temperature to yield **11**.





9 R = H

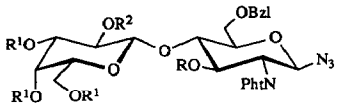
10 R = -CH_2-CH=CH_2 (All)

11 R = -CH_2-Ph (Bzl)

12 R = All

13 R = Bzl

Regioselective opening of the benzylidene acetal[6] of **10** or **11** using sodium cyanoborohydride in tetrahydrofuran in the presence of hydrogen chloride afforded the 2-phthalimido glucosyl azides **12** or **13**, respectively. The anomeric azido group remained stable during all of these transformations. Glycosylation of the glycosyl acceptor **12**, regioselectively deblocked at 4-OH, using tetra-*O*-acetyl-α-D-galactopyranosyl fluoride[14] in the presence of boron trifluoride[15,16] furnished the lactosamine azide **14**.



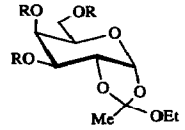
14 R = All, $R^1 = R^2$ = Ac

15 R = All, R^1 = Bzl, R^2 = Ac

16 R = R^1 = Bzl, R^2 = Ac

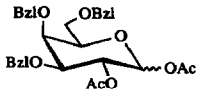
For syntheses of lactosamine azides **15** and **16** bearing selectively removable acetyl protection at the 2′-position, a suitable glycosyl donor is required. This was obtained from penta-*O*-acetyl-D-galactopyranose by analogous application of a procedure reported by Itoh et al.[17] for the corresponding glucose derivatives. On treatment with hydrogen bromide in acetic acid and subsequent reaction with ethanol–2,6-lutidine in nitromethane of the resultant crude galactosyl bromide, the penta-*O*-acetylgalactose was transformed into the orthoester **17**. Crude **17** was subjected to deacetylation using methanolic sodium methoxide and subsequent benzylation by using benzyl bromide–sodium hydride in *N*,*N*-dimethylformamide to give **18**. Hydrolysis of the orthoester with dilute sulfuric acid and acetylation of

the crude product with acetic acid anhydride in pyridine furnished the 1,2-di-*O*-acetylgalactose derivative **19** as a mixture of anomers.

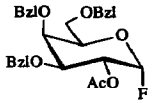


17 R = Ac

18 R = Bzl



19

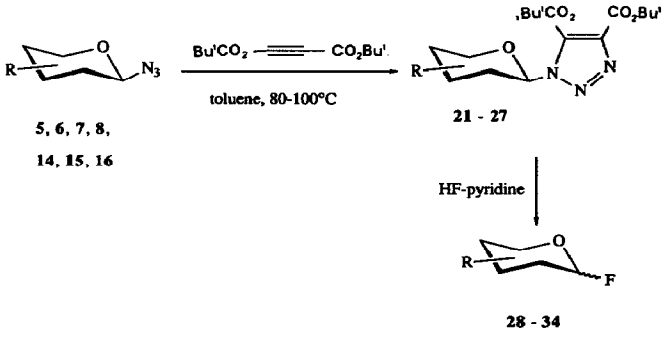


20

Treatment of **19** with hydrogen fluoride–pyridine complex[18] gave the required galactosyl fluoride **20**. Activation of the galactosyl fluoride **20** with boron trifluoride in dichloromethane[15,16] and reaction with the glycosyl acceptor **12** or **13** in the presence of molecular sieves (4 Å) resulted in the formation of the lactosamine derivatives **15** (35%) or **16** (41%), respectively.

Conversion of glycosyl azides into glycosyl fluorides.—Glycosyl azides undergo 1,3-dipolar cycloaddition reactions with alkynes to give the corresponding 1-*N*-glycosyltriazoles[19]. The reactions with di-*tert*-butyl acetylenedicarboxylate proceed in toluene at 80–100°C. Although the reaction time required was 2–4 days, neither the different protecting groups nor the intersaccharidic bonds present in the carbohydrates **5–8** and **14–16** were affected under these conditions.

The *N*-glycosyltriazole derivatives **21–27** were isolated in good yield and were fully characterized. Treatment of the *N*-glycosyltriazoles **21–27** with hydrogen fluoride-pyridine complex[18] furnished the corresponding glycosyl fluorides **28–34** (Table I). These conversions usually were performed at ~ 0°C. The acyl protecting groups and also benzyl and allyl ethers or intersaccharide bonds remained unaffected under these conditions. It is noteworthy that intersaccharidic bonds of saccharide units which predominantly carry ether-type protection and are usually sensitive to acids[3] proved to be stable towards the treatment with hydrogen fluoride–pyridine.



5, 6, 7, 8,

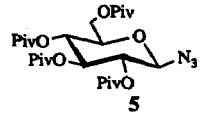
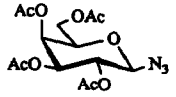
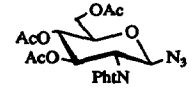
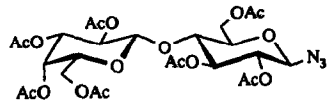
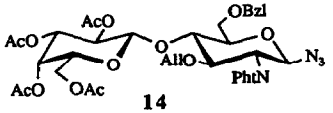
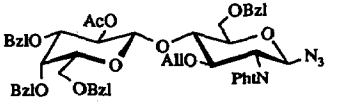
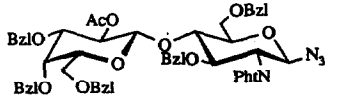
14, 15, 16

21 - 27

28 - 34

TABLE I

Synthesis of glycosyl fluorides from glycosyl azides via glycosyl triazoles

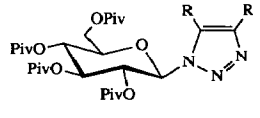
Glycosyl azide R-N_3	Glycosyl triazole Yield (%)	Glycosyl fluoride reaction	
		Temp./Time	Yield (%)
 **5**	**21** (71)	−30 → −10°C 2 h	28 (71) pure β
 **6**	**22** (75)	−30 → −10°C 2 h	**29** (60) pure β
 **7**	**23** (68)	5°C 16 h	**30** (72) $\alpha:\beta$ 1:1
 **8**	**24** (72)	0°C, 16 h −10°C, 10 h	**31** (74) pure α (51) α/β 2:1
 **14**	**25** (83)	0°C 16 h	**32** (72) α/β 3:1
 **15**	**26** (62)	0°C 16 h	**33** (41) α/β 4:1
 **16**	**27** (70)	0°C 16 h	**34** (61) α/β 3:2

The ratio of the α and β anomers of the resultant glycosyl fluorides depends upon the protecting-group pattern of the corresponding compounds, and on the reaction time and temperature. After short reaction-times at lower temperatures the β-fluorides were obtained. In this sense, the more-reactive glycosyl triazoles **21**

and **22** gave pure β-fluorides. Longer reaction-times and higher temperatures, often required for a complete conversion of the less-reactive glycosyl triazoles, correspond to the preferred formation of the thermodynamically more stable α-fluorides. The transformation of triazoles into glycosyl fluorides normally proceeds without side reactions as long as moisture is excluded. If impure or aged samples of the reagent were applied, a decrease in the yield was observed, which in the case of the lactosamine derivative **25** was mainly caused by cleavage of the 6-benzyl ether.

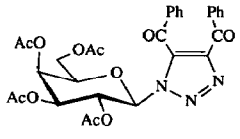
The stability of the intersaccharide bonds of the disaccharide derivatives **24–27** during treatment with hydrogen fluoride–pyridine is obviously due to the presence of phthaloyl and acetyl groups, as already observed in the course of the synthesis of fucosyl chitobiose glycopeptides[3]. In this sense, the *N*-phthalimido group and the 2′-*O*-acetyl group in compound **25** could also indirectly protect the 3-allyl ether. The conversions of the glycosyl triazoles **26** and **27** with prevailing benzyl ether protection in the galactose portion were less effective, probably because of partial cleavage of benzyl ether groups.

The efficiency of the conversion of *N*-glycosyltriazoles **21–27** into the corresponding glycosyl fluorides **28–34** depends decisively on the *tert*-butyl ester groups. This was demonstrated by treatment of the electronically similar *N*-glycosyltriazoles **35–37** with hydrogen fluoride–pyridine.



35 R = COOMe

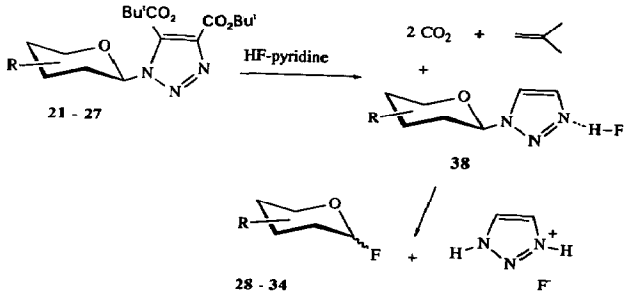
36 R = CO-Ph



37

The dimethyl ester **35** (ref 19), corresponding to **21**, and also the 4,5-dibenzoyltriazole derivatives **36** and **37** synthesized from **5** (refs 11 and 12) or **6** (ref 10), respectively, and dibenzoylacetylene[20] did not react with hydrogen fluoride–pyridine complex under conditions identical to those applied for the di-tert-butyl esters **21** and **22**.

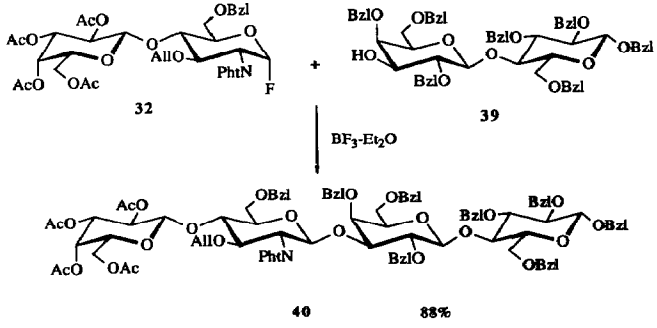
These results, at first sight surprising, may throw light on the mechanistic pathway of the conversion of the *N*-glycosyltriazoles **21–27** into the glycosyl fluorides **23–34**. Probably, hydrogen fluoride first cleaves the *tert*-butyl ester groups of **21–27**. After decarboxylation, the corresponding unsubstituted *N*-glycosyltriazoles **38** are formed. Because of their enhanced basicity, they are subject to an efficient remote activation by protonation at N-3 and subsequent elimination of triazole. The latter is immediately protonated, while the glycosyl cation (or acyloxonium ion) formed traps fluoride to furnish the glycosyl fluoride. According to this interpretation the triazole moiety operates as the leaving group in a manner that parallels its function in the phosphoramidite procedure for the oligonucleotide synthesis[21].



Synthesis of neo-lactotetraose: glycosylation using glycosyl fluorides.—The *O*-pivaloyl protected *N*-glucosyltriazole derivative **21** was demonstrated to be a useful glycosyl donor in the synthesis of glycosides and disaccharides[19]. Its activation is achieved by application of two equivalents of trimethylsilyltrifluoromethanesulfonate in dichloromethane at room temperature. The dimethyl and diisopropyl esters corresponding to **21** were less suitable, since they undergo accompanying transesterification reactions[19].

In contrast, the glycosyl fluorides, accessible from glycosyl azides via the corresponding glycosyl di-*tert*-butyl triazole-4,5-dicarboxylates, are powerful glycosylating agents under homogeneous conditions, if they are activated with boron trifluoride etherate[15,16]. In this manner, the lactosamine-derived disaccharide fluoride **32** was coupled with the benzyl lactoside **39** (ref 22) selectively deblocked in the 3′-position to furnish the neo-lacto tetraose **40** in high yield.

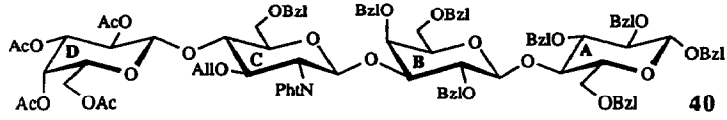
The formation of the tetrasaccharide occurred with complete β-selectivity. Very small amounts of hydrolyzed glycosyl donor **32** were found as the only side product. Compound **40** carries a protecting-group pattern that makes it susceptible to selective deprotection and coupling of further saccharide units. From this viewpoint, the synthesis of the regioselectively deprotectable neo-lactotetraose **40** illustrates the efficiency of the methodology consisting in the use of the azide group as an anomeric protection which is convertible via *N*-glycosyltriazoles into to glycosyl fluorides. Because of the stability of the anomeric azide, a versatile



exchange and modification of protecting groups of the prospected glycosyl donor may be realized. The glycosyl fluorides as the ultimate glycosylation agents provide an efficient glycosylation reaction under homogeneous conditions.

EXPERIMENTAL

General methods.—Melting points were determined with a Büchi apparatus (Dr. Tottoli) and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. IR spectra were recorded with a Perkin–Elmer FTIR spectrometer with a resolution of 2 cm^{-1}. ^1H NMR spectra (200 and 400 MHz) and ^{13}C NMR spectra (50.3 and 100.6 MHz) were recorded with Bruker WT 200 and AM 400 spectrometers, respectively. The values of δ are expressed relative to the signal of Me_4Si in $CDCl_3$, unless otherwise noted. For the assignment of NMR signals of oligosaccharides, the monosaccharide units are indicated as A, B, C and D, beginning at the reducing terminus, i.e.:



40

TLC was carried out with Silica Gel 60 F_{254} (Merck) or on RP-18 glass plates (Merck) with detection by UV fluorescence (λ 254 nm) or spraying with a 1:1 mixture of 1 M H_2SO_4 and a 0.3% solution of resorcinol monomethyl ether in MeOH. Flash chromatography was performed on columns of Silica Gel 60 (Merck, 0.04–0.06 mm). Solvents were used in freshly dried and distilled form[23].

4,6-O-Benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide (**9**).—To a solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide[4] (11.9 g, 25 mmol) in a mixture of CH_2Cl_2 (75 mL) and MeOH (50 mL) was added a 0.1 M solution of NaOMe in MeOH (25 mL). The mixture was stirred for 1.5 h at room temperature. After neutralization with an excess of AcOH (0.3 mL, 5 mmol) and evaporation of the solvent, toluene (100 mL) was distilled twice from the residue. The remainder was taken up in dry MeCN (100 mL) and treated with benzaldehyde dimethyl acetal (7 mL, 50 mmol) and etheral HBF_4 (0.68 ml, 54%) for 1 h at room temperature. The mixture was neutralized with Et_3N and the solvent was removed in vacuo. Sirupy **9** was purified by flash chromatography (3:1 light petroleum–EtOAc) to give amorphous **9** (9.5 g, 90%); $[\alpha]_D^{22} - 48.3°$ (*c* 1.0, $CHCl_3$); R_f 0.70 (1:1 light petroleum–EtOAc); ^{13}C NMR [$(CD_3)_2SO$]: δ 167.4 (C=O Pht), 137.3, 134.8, 130.9, 128.8, 127.9, 126.3, 123.3 (C_{arom}), 100.7 (C_6H_5)-*C*H), 85.6 (C-1), 80.6, 68.3, 67.0 (C-3, C-4, C-5), 67.4 (C-6), 56.8 (C-2); ^1H NMR: δ 7.95–7.87 (m, 4 H, Pht-H), 7.46–7.36 (m, 5 H, Ph-H), 5.85 (d, 1-H, $J_{OH,3}$ 5.1 Hz,

OH-3), 5.67 (s, 1 H, Ph-CH), 5.53 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 4.37 (ddd, 1 H, $J_{2,3}$ 9.7, $J_{3,4}$ 9.2 Hz, H-3), 4.29 (dd, 1 H, $J_{5,6a}$ 4.6, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.87 (dd, 1 H, H-2), 3.85 (dd, 1 H, $J_{5,6b}$ 9.7 Hz, H-6b), 3.74 (ddd, 1 H, $J_{4,5}$ 9.3 Hz, H-5), 3.66 (dd, 1 H, H-4). Anal. Calcd for $C_{21}H_{18}N_4O_6$: C, 59.71; H, 4.30; N, 13.26. Found: C, 59.83; H, 4.55; N, 13.39.

3-O-Allyl-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide (**10**). —Allyl bromide (10.2 ml, 120 mmol) was added to a stirred mixture of 80% NaH (3.6 g, 120 mmol) and Bu_4NI (22.2 g, 60 mmol) in dry THF (200 mL). To this suspension a solution of **9** (25 g, 59.2 mmol) in dry THF (200 mL) was slowly added and the mixture was then heated to 60°C for 3 h. After adding MeOH (10 mL) the solvent was removed, the remaining residue was dissolved in CH_2Cl_2, washed with aq $NaHCO_3$ and dried with $MgSO_4$. Evaporation and flash chromatography (5:1 light petroleum–EtOAc) gave amorphous **10** (25 g, 91%); $[\alpha]_D^{22}$ −23.3° (*c* 1.0, $CHCl_3$); R_f 0.73 (2:1 light petroleum–EtOAc); ^{13}C NMR: δ 137.1, 134.2, 131.5, 129.0, 128.2, 126.0 (C_{arom}, H_2C=*C*H-CH_2), 117.2 (H_2C=CH-CH_2), 101.3 (C_6H_5-*C*H), 86.3 (C-1), 82.4, 74.8, 68.4 (C-3, C-4, C-5), 73.2 (H_2C=CH-*C*H_2), 68.4 (C-6), 55.3 (C-2); ^1H NMR: δ 7.87, 7.75 (m_c, 2 H, Pht-H), 7.47 (m_c, 2 H, Ph-H), 7.37 (m_c, 3 H, Ph-H), 5.59 (s, 1 H, Ph-CH), 5.52 (m_c, 1 H, H_2C=C*H*-CH_2), 5.45 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 5.00 (ddd, 1 H, $J_{vic(trans)}$ 17.2 Hz, *H*$_2$C=CH-CH_2), 4.85 (ddd, 1 H, $J_{vic(cis)}$ 10.4 Hz, *H*$_2$C=CH-CH_2), 4.43 (dd, 1 H, $J_{3,4}$ 8.1, $J_{4,5}$ 10.5 Hz, H-4), 4.42 (dd, 1 H, $J_{2,3}$ 10.2 Hz, H-3), 4.26 (ddt, 1 H, J_{gem} 13.1, J_{vic} 5.1 Hz, H_2C=CH-C*H*$_2$), 4.15 (dd, 1 H, H-2), 3.95 (ddt, 1 H, J_{vic} 6.3 Hz, H_2C=CH-C*H*$_2$), 3.84 (dd, 1 H, $J_{5,6a}$ 10.0, $J_{6a,6b}$ 12.0 Hz, H-6a), 3.77–3.72 (m, 2 H, H-5, H-6b). Anal. Calcd for $C_{24}H_{22}N_4O_6$: C, 62.33; H, 4.80; N, 12.11. Found: C, 62.43; H, 4.80; N, 12.21.

3-O-Benzyl-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide (**11**).—To a suspension of NaH (80%, 0.9 g, 30 mmol) in dry DMF (50 mL) were added benzyl bromide (3.6 mL, 30 mmol) and then, dropwise a solution of **9** (5.6 g, 15 mmol) in DMF (50 mL). After 12 h at room temperature MeOH (3 mL) was added and the solvent was evaporated in high vacuum. The residue was dissolved in CH_2Cl_2 (500 mL), the solution was washed with satd $NaHCO_3$ (250 mL) and dried with $MgSO_4$. After evaporation of the solvent and purification of the residue by flash chromatography (4:1 light petroleum–EtOAc) on silica gel (140 g) **11** was isolated as an amorphous solid (5.6 g, 73%); $[\alpha]_D^{22}$ +42.6° (*c* 1.0, $CHCl_3$); R_f 0.52 (2:1 light petroleum–EtOAc); ^{13}C NMR: δ 167.6 (C=O Pht), 137.5–123.4 (C_{arom}), 101.2 (Ph-CH), 86.0 ($J_{C,H}$ 166 Hz, C-1), 82.5, 74.1, 68.1 (C-3, C-4, C-5), 74.0 (Ph-CH_2), 68.2 (C-6), 55.0 (C-2); ^1H NMR: δ 7.84–7.64 (m, 4H, Pht-H), 7.53–7.35, 6.98–6.85 (m, 5 H, Ph-H), 5.63 (s, 1 H, Ph-CH), 5.41 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 4.44 (dd, 1 H, $J_{5,6a}$ 4.7, $J_{6a,6b}$ 10.0 Hz, H-6a), 4.43 (dd, 1 H, $J_{2,3}$ 9.7 Hz, H-2), 4.12 (dd, 1 H, $J_{3,4}$ 9.4 Hz, H-3), 3.85 (dd, 1 H, $J_{5,6b}$ 9.7 Hz, H-6b), 3.82 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 3.73 (ddd, 1 H, H-5). Anal. Calcd for $C_{28}H_{24}N_4O_6$: C, 65.62; H, 4.72; N, 10.93. Found: C, 65.25; H, 4.66; N, 10.90.

3-O-Allyl-6-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide (**12**).—Diethyl ether saturated with HCl was added at room temperature to a mixture of

compound **10** (2.9 g, 6.3 mmol), $NaCNBH_3$ (4.0 g, 63 mmol) and 3 Å molecular sieves in THF (125 mL) until the mixture was acidic. The mixture was stirred for 1.5 h at room temperature and then filtered through Celite. The solvent was removed in vacuo and the resulting syrup was diluted with CH_2Cl_2. This solution was washed with aq $NaHCO_3$, dried, and evaporated. Purification by flash chromatography (6:1 light petroleum–EtOAc) gave syrupy **12** (1.6 g, 55%); $[\alpha]_D^{22}$ −6.5° (*c* 1.0, $CHCl_3$); R_f 0.43 (2:1 light petroleum–EtOAc); ^{13}C NMR: [$(CD_3)_2SO$]: δ 167.8, 167.2 (C=O Pht), 138.4, 135.1, 135.0, 130.8, 128.2, 127.4, 123.5 (C_{arom}, H_2C=*C*H-CH_2), 115.9 (H_2C=CH-CH_2), 85.1 (C-1), 79.7, 78.5, 70.7 (C-3, C-4, C-5), 72.6, 72.3 (H_2C=CH-CH_2, Ph-CH_2), 68.9 (C-6), 54.7 (C-2); ^1H NMR: δ 7.95–7.87 (m, 4 H, Pht-H), 7.36–7.25 (m, 5 H, Ph-H), 5.65 (d, 1 H, $J_{OH,4}$ 6.9 Hz, OH-4), 5.54–5.43 (m, 1 H, H_2C=C*H*-CH_2), 5.45 (d, 1 H, $J_{1,2}$ 9.4 Hz, H-1), 4.90 (dd, 1 H, $J_{vic(trans)}$ 17.2 Hz, H_2C=CH-CH_2), 4.74 (dd, 1 H, $J_{vic(cis)}$ 10.4 Hz, H_2C=CH-CH_2), 4.56 (s, 2 H, Ph-CH_2), 4.22 (dd, 1 H, J_{gem} 13.2, J_{vic} 4.9 Hz, H_2C=CH-CH_2), 4.04 (dd, 1 H, $J_{2,3}$ 10.6, $J_{3,4}$ 8.7 Hz, H-3), 3.85 (ddt, 1 H, J_{vic} 6.9 Hz, H_2C=CH-CH_2), 3.84 (d, 1 H, $J_{6a,6b}$ 10.8 Hz, H-6a), 3.78 (d, 1 H, H-6b), 3.72–3.62 (m, 2 H, H-2, H-5), 3.45 (m_c, 1 H, H-4). Anal. Calcd for $C_{24}H_{24}N_4O_6$: C, 62.06; H, 5.21; N, 12.06. Found: C, 62.13; H, 5.23; N, 11.85.

*3,6-Di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl azide* (**13**).—Under dry Ar a solution of **11** (3.2 g, 6.2 mmol) and $NaCNBH_3$ (3.9 g, 62 mmol) in THF (125 mL) was stirred with 3 Å molecular sieves at room temperature. Within 30 min a solution of HCl in diethyl ether was added dropwise until evolution of gas ceased. After 3 h the solution was filtered through silica, which was then washed with THF. The combined THF solutions were evaporated in vacuo, the remaining oil was dissolved in CH_2Cl_2 (250 mL), washed with satd $NaHCO_3$ (250 mL), and dried with $MgSO_4$. The solvent was evaporated in vacuo and the residue purified by flash chromatography (5:1 light petroleum–EtOAc) on silica gel (140 g) to give **13** (2.3 g, 70%); amorphous solid; $[\alpha]_D^{22}$ +14.7° (*c* 1.0, $CHCl_3$); R_f 0.46 (2:1 light petroleum–EtOAc); ^{13}C NMR: δ 168.0 (C=O Pht), 137.9–123.6 (C_{arom}), 85.8 (C-1), 78.4, 76.2, 73.5 (C-3, C-4, C-5), 74.6, 73.8 (Ph-CH_2), 69.8 (C-6), 54.9 (C-2); ^1H NMR: δ 7.79 (s, 1 H, Pht-H), 7.69 (s, 3 H, Pht-H), 7.38–7.24 (m, 6 H, Ph-H), 7.03–7.01, 6.95–6.91 (m, 2 H, Ph-H), 5.36 (d, 1 H, $J_{1,2}$ 9.4 Hz, H-1), 4.73 (d, 1 H, J_{gem} 12.2 Hz, Ph-CH_2), 4.65, 4.58 (d, 1 H, J_{gem} 12.0 Hz, Ph-CH_2), 4.51 (d, 1 H, J_{gem} 12.2 Hz, Ph-CH_2), 4.24 (dd, 1 H, $J_{2,3}$ 10.6, $J_{3,4}$ 8.5 Hz, H-3), 4.06 (dd, 1 H, H-2), 3.86–3.69 (m, 4 H, H-4, H-5, H-6a, H-6b), 2.93 (d, 1 H, $J_{OH,4}$ 2.0 Hz, OH-4). Anal. Calcd for $C_{28}H_{26}N_4O_6$: C, 65.36; H, 5.09; N, 10.89. Found: C, 65.35; H, 4.94; N, 10.83.

O-*(2,3,4,6-Tetra-*O*-acetyl-β-*D*-galactopyranosyl)-(1 → 4)-3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl azide* (**14**).—A mixture of **12** (1.28 g, 2.75 mmol), 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl fluoride[14] (2.9 g, 8.28 mmol) and 4 Å molecular sieves in dry CH_2Cl_2 (100 mL) was stirred at 5°C for 1 h under dry Ar. Then a solution of $BF_3 \cdot OEt_2$ (6.2 mL) in CH_2Cl_2 (25 mL) was slowly added. After 1 h the ice-bath was removed. The mixture was stirred for 2 h at

room temperature and then filtered through Celite. The solution was washed with aq $NaHCO_3$, dried and evaporated. Flash chromatography (4:1 light petroleum–EtOAc) gave amorphous **14** (1.66 g, 76%); $[\alpha]_D^{22}$ −1.2° (*c* 1.0, $CHCl_3$); R_f 0.74 (1:1 light petroleum–EtOAc); ^{13}C NMR: δ 170.2, 170.0, 169.8, 169.0 (C=O Ac), 137.7, 134.6, 134.1, 131.6, 128.5, 127.9, 123.4 (C_{arom}, $H_2C=CH\text{-}CH_2$), 116.7 (H_2C=CH-CH_2), 100.3 (C-1B), 85.8 (C-1A), 77.2, 76.8, 71.0, 70.5, 69.5 (C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C5-B), 73.7, 73.4 (H_2C=CH-CH_2, Ph-CH_2), 67.3, 60.9 (C-6A, C-6B), 55.2 (C-2A), 20.6, 20.5, 20.4 (CH_3 Ac); ^1H NMR: δ 7.85–7.84, 7.75–7.71 (m, 2 H, Pht-H), 7.41–7.30 (m, 5 H, Ph-H), 5.51–5.41 (m, 1 H, H_2C=C*H*-CH_2), 5.34 (d, 1 H, $J_{1,2}$ 9.3 Hz, H-1A), 5.27 (d, 1 H, $J_{3,4}$ 3.4 Hz, H-4B), 5.07 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.4 Hz, H-2B), 4.95 (dd, 1 H, $J_{vis(trans)}$ 17.2 Hz, H_2C=CH-CH_2), 4.82 (dd, 1 H, H-3B), 4.78 (d, 1 H, J_{gem} 12.1 Hz, Ph-CH_2), 4.74 (dd, 1 H, $J_{vis(cis)}$ 10.9 Hz, H_2C=CH-CH_2), 4.54 (d, 1 H, H-1B), 4.49 (d, 1 H, Ph-CH_2), 4.25 (dd, 1 H, J_{gem} 12.8, J_{vic} 5.1 Hz, H_2C=CH-CH_2), 4.18 (dd, 1 H, $J_{2,3}$ 10.6, $J_{3,4}$ 8.6 Hz, H-3A), 4.08 (dd, 1 H, H-2A), 4.04 (m_c, 2 H, H-6Ba, H-6Bb), 3.99 (dd, 1 H, $J_{4,5}$ 9.9 Hz, H-4A), 3.82 (dd, 1 H, J_{vic} 6.5 Hz, H_2C=CH-CH_2), 3.76 (d, 2 H, $J_{5,6a/b}$ 2.0 Hz, H-6Aa, H-6Ab), 3.66 (dd, 1 H, $J_{5,6a} = J_{5b,6b}$ = 6.8 Hz, H-5B), 3.58 (dt, 1 H, H-5A), 2.07, 2.01, 1.97, 1.95 (s, 3 H, CH_3Ac). Anal. Calcd for $C_{38}H_{42}N_4O_{15}$: C, 57.43; H, 5.33; N, 7.05. Found: C, 58.03; H, 5.49; N, 6.71.

O-(*2-O-Acetyl-3,4,6-tri-O-benzyl-β-D-galactopyranosyl)-(1 → 4)-3-O-allyl-6-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide* (**15**).—To dry **12** (0.81 g, 2.3 mmol) and galactosyl fluoride **20** (1.14 g, 8.28 mmol) in CH_2Cl_2 (100 mL) were added 4 Å molecular sieves and, dropwise under Ar at 0°C, a solution of $BF_3 \cdot OEt_2$ (1.2 ml, 9.6 mmol) in CH_2Cl_2 (20 mL) within 15 min. After 1 h at 0°C and 3 h at room temperature the solution was filtered through celite, which was washed with CH_2Cl_2. The combined organic solutions were washed with aq $NaHCO_3$, dried with $MgSO_4$, and the solvent was evaporated in vacuo. The residue was purified by flash chromatography (8:1 light petroleum–EtOAc) to give amorphous **15** 562 mg, 35%); $[\alpha]_D^{22}$ +11.3° (*c* 1.0, $CHCl_3$); R_f 0.51 (1:1; light petroleum–EtOAc); ^{13}C NMR: δ 169.2 (Ac-C=O), 138.8, 138.1, 138.0 (Bzl-C_{ipso}), 134.9, 134.2 (Pht-C-4/5, $H_2C=CH\text{-}CH_2$), 131.6 (Pht-C-1/2), 128.5–127.3 (Bzl-C_{arom}), 123.5 (Pht-C-3/6), 116.3 (H_2C=CH-CH_2), 100.7 (C-1B), 85.8 (C-1A), 80.4, 77.4, 77.2, 77.0, 73.4, 72.7, 72.0 (C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C5-B), 74.4, 73.9, 73.6, 71.8 (H_2C=CH-CH_2, Ph-CH_2), 68.3, 67.6 (C-6A, C-6B), 55.4 (C-2A), 21.1 (Ac-CH_3); ^1H NMR: δ 7.84 (bs, 2 H, Pht-H), 7.74–7.71 (m, 2 H, Pht-H), 7.36–7.16 (m, 20 H, Ph-H), 5.40–5.36 (m, 1 H, H_2C=C*H*-CH_2), 5.33 (d, 1 H, $J_{1,2}$ 9.4 Hz, H-1A), 5.25 (dd, 1 H, $J_{1,2}$ 7.9, $J_{2,3}$ 10.0 Hz, H-2B), 4.89 (d, 1 H, J_{gem} 11.5 Hz, Ph-CH_2), 4.88 (dd, 1 H, $J_{vic(trans)}$ = 17.4 Hz, H_2C=CH-CH_2), 4.72 (d, 1 H, J_{gem} 12.1 Hz, Ph-CH_2), 4.65–4.62 (m, 2 H, Ph-CH_2, H_2C=CH-CH_2), 4.51 (d, 1 H, J_{gem} 11.5 Hz, Ph-CH_2), 4.48 (d, 1 H, J_{gem} 12.1 Hz, Ph-CH_2), 4.45 (d, 1 H, H-1B), 4.43 (d, 1 H, J_{gem} 12.5 Hz, Ph-CH_2), 4.41, 4.48 (d, 1 H, J_{gem} 11.7 Hz, Ph-CH_2), 4.31 (dd, 1 H, J_{gem} 12.9, J_{vic} 5.1 Hz, H_2C=CH-CH_2), 4.17 (dd, 1 H, $J_{2,3}$ 10.6, $J_{3,4}$ 8.5 Hz, H-3A), 4.06 (dd, 1 H, H-2A), 3.94–3.90 (m, 2 H, H-4A, H-4B), 3.78 (dd, 1 H,

J_{vic} 6.3 Hz, H_2C=CH-CH_2), 3.75 (d, 1 H, $J_{5,6}$ 2.2 Hz, H-6Aa, H-6Ab), 3.62–3.58 (m, 2 H, H-5A, H-6Ba), 3.54 (dd, 1 H, $J_{5,6b}$ 5.2, $J_{6a,6b}$ 9.0 Hz, H-6Bb), 3.42 (dd, 1 H, $J_{5,6a}$ 7.7 Hz, H-5B), 3.33 (dd, 1 H, $J_{3,4}$ 2.8 Hz, H-3B), 1.96 (s, 3 H, Ac-CH_3). Anal. Calcd for $C_{53}H_{54}N_4O_{12}$: C, 67.79; H, 5.80; N, 5.97. Found: C, 67.72; H, 5.87 N, 5.72.

O-(2-O-*Acetyl-3,4,6-tri*-O-*benzyl*-β-D-*galactopyranosyl*)-(1 → 4)-3,6-*di*-O-*benzyl*-2-*deoxy*-2-*phthalimido*-β-D-*glucopyranosyl azide* (**16**).—The lactosamine azide derivative **16** was prepared, analogously to the synthesis of **15**, from **13** (1.5 g, 2.1 mmol) and the galactosyl fluoride **20** (1.2 g, 2.5 mmol) in CH_2Cl_2 (100 mL) by promotion with $BF_3 \cdot OEt_2$ (1.4 mL, 11.1 mmol) dissolved in CH_2Cl_2 (20 mL). After working up as described for **15**, **16** was purified by flash chromatography (6:1 light petroleum–EtOAc) to give pure **16** as an amorphous solid (881 mg, 41%); $[\alpha]_D^{22}$ +22.5° (*c* 1, $CHCl_3$); R_f 0.50 (1:1 light petroleum–EtOAc); ^{13}C NMR: δ 169.1 (C=O Ac), 138.6–123.3 (C_{arom}), 100.6 (C-1B), 85.7 (C-1A), 80.3, 77.2, 77.2, 76.6, 72.7, 71.9 (C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C5-B), 74.6, 74.3, 73.5, 73.3, 71.7 (Ph-CH_2), 68.1, 67.4 (C-6A, C-6B), 55.2 (C-2A), 20.9 (CH_3Ac); ^1H NMR: δ 7.79 (bs, 1 H, Pht-H), 7.66 (bs, 3 H, Pht-H), 7.37–7.02 (m, 21 H, Ph-H), 6.95–6.91, 6.87–6.78 (m 2 H, Ph-H), 5.34 (dd, 1 H, $J_{1,2}$ 7.9, $J_{2,3}$ 10.1 Hz, H-2B), 5.32 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1A), 4.90 (d, 1 H, J_{gem} 11.6 Hz, Ph-CH_2), 4.84 (d, 1 H, J_{gem} 12.4 Hz, Ph-CH_2), 4.74 (d, 1 H, J_{gem} 12.1 Hz, Ph-CH_2), 4.65 (d, 1 H, J_{gem} 12.2 Hz, Ph-CH_2), 4.51–4.47 (m, 3 H, Ph-CH_2), 4.41 (d, 1 H, J_{gem} 12.2 Hz, Ph-CH_2), 4.34 (d, 1 H, J_{gem} 11.7 Hz, Ph-CH_2), 4.29–4.24 (m, 2 H, H-3A, Ph-CH_2), 4.08 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2A), 4.02 (dd, 1 H, $J_{3,4}$ 8.7, $J_{4,5}$ 9.9 Hz, H-4A), 3.92 (d, 1 H, $J_{3,4}$ 2.8 Hz, H-4B), 3.78 (s, 2 H, H-6Aa, H-6Ab), 3.61 (d, 1 H, H-5A), 3.44–3.38 (m, 3 H, H-5B, H-6Ba, H-6Bb), 3.34 (dd, 1 H, H-3B), 2.00 (s, 3 H, CH_3Ac). Anal. Calcd for $C_{57}H_{56}N_4O_{12}$: C, 69.22; H, 5.71; N, 5.66. Found: C, 69.26; H, 5.75 N, 5.56.

1,2-Di-O-*acetyl*-3,4,6-*tri*-O-*benzyl*-D-*galactopyranose* (**19**).—A solution of HBr in AcOH (33%, 120 mL) was slowly added to a stirred solution of penta-*O*-acetyl-β-D-galactopyranose (30 g, 77 mmol) in CH_2Cl_2 (200 mL) at 0°C. After 1 h the solvent was removed in vacuo and toluene (250 mL) was distilled off three times from the residue. This was taken up in $MeNO_2$ (200 mL) and, after addition of 2,6-lutidine (18 mL), EtOH (15 mL), and tetrabutylammonium bromide (2.5 g), heated to 40°C for 20 h. The solution was partitioned between EtOAc and aq $NaHCO_3$. The organic layer was dried with $MgSO_4$ and evaporated. The resulting syrupy residue of orthoester **17** was dissolved in MeOH (500 mL) and a 0.1 M solution of NaOMe in MeOH (80 mL) was added. After stirring for 1 h at room temperature, the solvent was evaporated and toluene was distilled from the residue. To a solution of this oily residue in DMF (300 mL), 80% NaH (10.4 g) and benzyl bromide (41 mL) were added. After stirring at room temperature for 15 h, MeOH (20 mL) was added dropwise. The mixture was diluted with EtOAc (1000 mL), washed with aq $NaHCO_3$ and water, dried and evaporated in vacuo. To a solution of the resulting residue of the orthoester **18** in 1,4-dioxane (250 mL),

water (50 mL), and concd H_2SO_4 (5 mL) were added. The mixture was refluxed for 2 h, cooled and then neutralized by adding $NaHCO_3$. The solvent was removed in vacuo and the residue was partitioned between EtOAc and water. The organic layer was dried with $MgSO_4$ and evaporated. After silica gel filtration (1:1 light petroleum–EtOAc) the syrupy residue was dissolved in a mixture of pyridine (250 mL) and Ac_2O (100 mL) and stirred for 16 h at room temperature. After removing the solvent in vacuo the resulting residue was taken up in CH_2Cl_2 washed with 2 M H_2SO_4 and aq $NaHCO_3$, and dried with $MgSO_4$. Evaporation of the solvent and flash chromatography (2:1 light petroleum–EtOAc) gave syrupy **19** (29.5 g, 72%) as a mixture of the anomers; $[\alpha]_D^{22}$ +52.5° (*c* 1.0, $CHCl_3$); R_f 0.50 (2:1 light petroleum–EtOAc); ^{13}C NMR: δ 169.9, 169.5, 169.2 (C=OAc), 138.4–127.4 (C_{arom}), 92.7 (C-1β), 90.6 (C-1α), 80.2, 77.4, 72.4, 70.4 (C-2β, C-3β, C-4β, C-5β), 76.6, 74.1, 72.1, 69.5 (C-2α, C-3α, C-4α, C-5α), 74.9, 74.7, 73.7, 73.6, 72.6, 72.2 (Ph-CH_2), 68.3 (C-6α), 68.0 (C-6β), 21.0, 20.9, 20.8 (CH_3Ac); ^1H NMR: δ 7.37–7.22 (m, Ph-H), 6.32 (d, $J_{1\alpha,2\alpha}$ 3.7 Hz, H-1α), 5.56 (d, $J_{1\beta,2\beta}$ 8.2 Hz, H-1β), 5.50 (dd, $J_{2\alpha,3\alpha}$ 10.5 Hz, H-2α), 5.47 (dd, $J_{2\beta,3\beta}$ 9.5 Hz, H-2β), 4.94–4.37 (Ph-CH_2), 4.06 (d, $J_{3\alpha,4\alpha}$ 2.7 Hz, H-4α), 4.04 (dd, $J_{5\alpha,6\alpha a} = J_{5\alpha,6\alpha\beta} = 6.2$ Hz, 5a-H-5α), 4.00 (d, $J_{3b,4b}$ 2.4 Hz, H-4β), 3.90 (dd, H-3α), 3.70 (dd, $J_{5\beta,6\beta a} = J_{5\beta,6\beta b} = 6.4$ Hz, H-5β), 3.64–3.51 (m, H-3β, H-6αa, H-6αb, H-6bα, H-6bβ), 2.08, 2.00 (s, $CH_3Ac\alpha$), 2.05, 1.99 (s, $CH_3Ac\beta$). Anal. Calcd for $C_{31}H_{34}O_8$: C, 69.65; H, 6.41. Found: C, 69.75; H, 6.73.

2-O-Acetyl-3,4,6-tri-O-benzyl-α-D-galactopyranosyl fluoride (**20**).—To a solution of **19** (6 g, 11.2 mmol) in dry CH_2Cl_2 (150 mL) was added HF–pyridine (50 mL) at 0°C. The mixture was vigorously stirred for 3 h at 0°C, and then carefully poured into a Teflon separation funnel filled with CH_2Cl_2 (250 mL), satd $NaHCO_3$ (250 mL), and ice (100 g). After careful shaking the organic layer was separated, washed with 1 M H_2SO_4 (250 mL), satd $NaHCO_3$ (twice 250 mL), and dried with $MgSO_4$. After addition of silica gel the solvent was evaporated in vacuo and the pure α anomer **20** (3.8 g, 68%) was isolated as an oil by flash chromatography (6:1 light petroleum–EtOAc) on silica gel (300 g); $[\alpha]_D^{22}$ +51.1° (*c* 1.0, $CHCl_3$); R_f 0.56 (4:1 light petroleum–EtOAc), ^{13}C NMR: δ 170.2 (C=OAc), 138.2–127.4 (Bzl-C_{arom}), 105.1 ($J_{C,F}$ 238 Hz, C-1), 76.1, 73.8, 71.9 (C-3, C-4, C-5), 74.8, 73.5, 72.7 (Ph-CH_2), 70.5 ($J_{C,F}$ 24 Hz, C-2), 68.1 (C-6), 20.8 (CH_3Ac); ^1H NMR: δ 7.38–7.24 (m, 15 H, Ph-H), 5.76 (dd, 1 H, $J_{F,1}$ 54.5, $J_{1,2}$ 2.8 Hz, H-1), 5.36 (ddd, 1 H, $J_{F,2}$ 24.8, $J_{2,3}$ 10.5 Hz, H-2), 4.94 (d, 1 H, J_{gem} 11.4 Hz, Ph-CH_2), 4.71, 4.65 (d, 1 H, J_{gem} 12.1 Hz, Ph-CH_2), 4.57 (d, 1 H, J_{gem} 11.4 Hz, Ph-CH_2), 4.49, 4.43 (d, 1 H, J_{gem} 11.8 Hz, Ph-CH_2), 4.12 (t, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 4.06 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-4), 3.94 (dd, 1 H, H-3), 3.58 (d, 2 H, H-6a, H-6b), 2.09 (s, 3 H, CH_3Ac). Anal. Calcd for C8d2$_9H_{31}FO_6$: C, 70.43; H, 6.32; Found: C, 70.55; H, 6.38.

*1-(2,3,4,6-Tetra-O-pivaloyl-β-D-glucopyranosyl)-4,5-di-*tert*-butyloxycarbonyl-1,2,3-triazole* (**21**).—A solution of 2,3,4,6-tetra-*O*-pivaloyl-β-D-glucopyranosyl azide **5** (ref. 11) (6 g, 11 mmol) and di-tert-butyl acetylenedicarboxylate (2.5 g, 11 mmol) in dry toluene (25 mL) was kept for 3 days at 100°C. The cooled mixture was evaporated to dryness. Flash chromatography (6:1 light petroleum–EtOAc) of the

residue and crystallization from heptane gave crystalline **21** (6 g, 71%); mp 144°C; $[\alpha]_D^{22}$ −13.6° (*c* 1.0, $CHCl_3$); R_f 0.60 (4:1 light petroleum–EtOAc) ^{13}C NMR: δ 178.0, 177.2, 176.2, 175.4 (C=O Piv), 159.1, 157.0 (C=O triazole), 141.8, 131.0, (C=C triazole) 85.4 [$OC(CH_3)_3$], 84.9 (C-1), 83.2 [$OC(CH_3)_3$], 75.7, 72.8, 69.6, 67.2 (C-2, C-3, C-4, C-5), 61.4 (C-6), 38.8–38.6 [$C(CH_3)_3$ Piv] 28.1–26.7 [$C(CH_3)_3$]; ^1H NMR: δ 6.14 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 6.03 (dd, 1 H, $J_{3,4}$ 9.8, $J_{4,5}$ 10.0 Hz, H-4), 5.47 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-2), 5.13 (dd, 1 H, H-3), 4.17 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 12.6 Hz, 4.06 (dd, 1 H, $J_{5,6b}$ 5.1 Hz, H-6b), 3.97 (ddd, 1 H, H-5), 1.59, 1.57 [s, 9 H, $OC(CH_3)_3$], 1.16, 1.14, 1.11, 0.92 (s, 9 H, OPiv). Anal. Calcd for $C_{38}H_{61}N_3O_{13}$: C, 59.44; H, 8.01; N, 5.47. Found: C, 59.79; H, 7.93; N, 5.43.

*1-(2,3,4,6-Tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4,5-di-*tert*-butyloxycarbonyl-1,2,3-triazole* (**22**).—A solution of 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl azide **6** (ref 10) (3.8 g, 10 mmol) and di-*tert*-butyl acetylene–dicarboxylate (2.5 g, 11 mmol) in dry toluene (100 mL) was heated for 3 days at 100°C. The cooled mixture was evaporated to dryness. Crystallization of the resulting residue from EtOH gave **22** (4.5 g, 75%); mp 171°C; $[\alpha]_D^{22}$ −14.9° (*c* 1.0, $CHCl_3$); R_f 0.10 (2:1 light petroleum–EtOAc); ^{13}C NMR: δ 170.12, 170.06, 169.90, 168.24 (C=O Ac), 158.9, 156.9 (C=O triazole), 141.5, 131.4 (C=C triazole), 85.6 (C-1), 85.1, 83.0 [$OC(CH_3)_3$], 74.1, 71.4, 67.0, 66.8 (C-2, C-3, C-4, C-5), 61.0 (C-6), 28.0, 27.8 [$C(CH_3)_3$], 20.52, 20.47, 20.39, 20.28 (CH_3Ac); ^1H NMR: δ 6.16 (dd, 1 H, $J_{1,2}$ 9.3, $J_{2,3}$ 10.1 Hz, H-2), 6.04 (d, 1 H, H-1), 5.48 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 5.19 (dd, 1 H, H-3), 4.17–4.04 (m, 3 H, H-5, H-6a, H-6b), 2.19, 2.01, 1.98, 1.87 (s, 3 H, CH_3Ac), 1.59, 1.58 [s, 9 H, $C(CH_3)_3$]. Anal. Calcd for $C_{26}H_{37}N_3O_{13}$: C, 52.08; H, 6.22; N, 7.01. Found: C, 52.01; H, 6.25; N, 7.08.

*1-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-4,5-di-*tert*-butyloxycarbonyl-1,2,3-triazole* (**23**).—3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide **7** (ref 4) (4.6 g, 10 mmol) and di-tert-butyl acetylenedicarboxylate (2.5 g, 11 mmol) were heated in dry toluene (25 mL) for 4 days at 100°C. Evaporation of the solvent and flash chromatography (3:1 light petroleum–EtOAc) gave amorphous **23** (4.7 g, 68%); $[\alpha]_D^{22}$ +39.6° (*c* 1.0, $CHCl_3$); R_f 0.21 (2:1 light petroleum–EtOAc); ^{13}C NMR: δ 170.4, 170.0, 169.1 (C=O Ac), 158.7, 156.4 (C=O triazole), 141.4 (C=C triazole), 134.4 (Pht), 131.6, 131.0 (Pht, C=C triazole), 123.7 (Pht), 85.4, 83.1 [$OC(CH_3)_3$], 82.0 (C-1), 75.1, 71.1, 68.0 (C-3, C-4, C-5), 61.6 (C-6), 52.1 (C-2), 27.9, 27.8 [$C(CH_3)_3$], 20.5, 20.4, 20.2 (CH_3Ac); ^1H NMR: δ 7.75, 7.67 (m_c, 2 H, Pht-H), 7.12 (d, 1 H, $J_{1,2}$ 9.9 Hz, H-1), 5.87 (dd, 1 H, $J_{2,3}$ 9.5, $J_{3,4}$ 10.1 Hz, H-3), 5.50 (dd, 1 H, $J_{4,5}$ 10.2 Hz, H-4), 5.32 (dd, 1 H, H-2), 4.27 (dd, 1 H, $J_{5,6a}$ 4.7, $J_{6a,6b}$ 12.6 Hz, H-6a), 4.13 (dd, 1 H, $J_{5,6b}$ 1.9 Hz, H-6b), 4.10 (ddd, 1 H, H-5), 2.05, 2.03, 1.86 (s, 3 H, CH_3Ac), 1.62, 1.52 [s, 9 H, $C(CH_3)_3$]. Anal. Calcd for $C_{32}H_{38}N_4O_{13}$: C, 55.97; H, 5.58; N, 8.16. Found: C, 55.97; H, 5.68; N, 8.13.

*1-[O-(2,3,4,6-Tetra-*O*-acetyl-β-*D*-galactopyranosyl)-(1 → 4)-(2,3,6-tri-*O*-acetyl-β-*D*-glucopyranosyl)]-4,5-di-*tert*-butyloxycarbonyl-1,2,3-triazole* (**24**).—Heating of 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-acetyl-β-D-gluco-pyranosyl azide (ref 13) (6.6 g, 10 mmol) with di-*tert*-butyl acetylenedicarboxylate (2.5

g, 11 mmol) in dry toluene (100 mL) for 2 days at 100°C, yielded after evaporation of the solvent and flash chromatography (2:1 light petroleum–EtOAc) amorphous **24** (6.4 g, 72%); $[\alpha]_D^{22}$ −26.5° (*c* 1.0, $CHCl_3$); R_f 0.08 (RP-18, 1:1 MeCN–water); ^{13}C NMR: δ 170.2, 170.1, 170.0, 169.9, 169.8, 169.0, 168.5 (C=O Ac), 158.9, 156.7 (C=O triazole), 141.8, 130.9 (C=C triazole), 100.9 (C-1B), 85.2, 83.2 [$OC(CH_3)_3$], 84.1 (C-1A), 75.7, 75.4, 73.3, 70.8, 70.7, 69.5, 69.1, 66.6 (C-2A, C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C5-B), 61.6, 60.8 (C-6A, C-6B), 28.0, 27.8 [$C(CH_3)_3$], 20.6, 20.5, 20.4, 20.3 (CH_3Ac); ^1H NMR: δ 6.09 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1A), 5.95 (dd, 1 H, $J_{2,3}$ 9.4 Hz, H-2A), 5.34 (dd, 1 H, $J_{3,4}$ 9.3 Hz, H-3A), 5.32 (d, 1 H, $J_{3,4}$ 3.4 Hz, H-4B), 5.10 (dd, 1 H, $J_{1,2}$ 7.9, $J_{2,3}$ 10.4 Hz, H-2B), 4.93 (dd, 1 H, H-3B), 4.49 (d, 1 H, H-1B), 4.42 (dd, 1 H, $J_{5,6a}$ 1.7, $J_{6a,6b}$ 12.2 Hz, H-6Aa), 4.13–4.07 (m, 2 H, H-6Ba, H-6Bb), 4.04 (dd, 1 H, $J_{5,6b}$ 5.1 Hz, H-6Ab), 3.95 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4A), 3.88–3.82 (m, 2 H, H-5A, H-5B), 2.13, 2.05, 2.02, 1.93, 1.85 (s, 3 H, CH_3Ac), 2.04 (s, 6 H, 2 CH_3Ac_3), 1.57, 1.56 [s, 9 H, $C(CH_3)_3$]. Anal. Calcd for $C_{38}H_{53}N_3O_{21}$: C, 51.41; H, 6.02; N, 4.73. Found: C, 51.56; H, 6.06; N, 4.95.

1-[O-*(2,3,4,6-Tetra-*O*-acetyl-β-*D*-galactopyranosyl)-(1 → 4)-(3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)]-4,5-di-*tert*-butyloxycarbonyl-1,2,3-triazole* (**25**).—A solution of **14** (795 mg, 1 mmol) and di-tert-butyl acetylenedicarboxylate (452 mg, 2 mmol) in toluene (15 mL) was heated to 100°C for 2 days under dry Ar. Evaporation of the solvent and flash chromatography (3:1 light petroleum–EtOAc) gave amorphous **25** (847 mg, 83%); $[\alpha]_D^{22}$ +12.9° (*c* 1.0, $CHCl_3$); R_f 0.40 (RP-18, 4:1 MeCN–water); ^{13}C NMR: δ 170.3, 170.0, 169.8, 169.0 (C=O Ac), 165.9 (C=O Pht), 158.9, 156.7 (C=O triazole), 141.0 (C=C triazole), 137.4, 134.3, 134.2, 131.6, 131.4, 128.5, 128.0, 123.7, 123.1 (Bzl-C_{arom}, triazole C=C, H_2C=*C*H-CH_2), 116.9 (H_2C=CH-CH_2), 100.2 (C-1B), 85.1, 82.5 [$OC(CH_3)_3$], 82.5 (C-1A), 78.0, 77.4, 76.8, 70.9, 70.5, 69.4, 66.9 (C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C5-B), 73.6, 73.5 (H_2C=CH-*C*H_2, Ph-CH_2), 67.2, 60.9 (C-6A, C-6B), 55.3 (C-2A), 27.0, 27.8 [$C(CH_3)_3$], 20.6, 20.5, 20.43, 20.38 (CH_3Ac); ^1H NMR: δ 7.77–7.73, 7.69–7.65 (m, 2 H, Pht-H), 7.37–7.24 (m, 5 H, Ph-H), 6.82 (d, 1 H, $J_{1,2}$ 10.1 Hz, H-1A), 5.48–5.38 (m, 1 H, H_2C=C*H*-CH_2), 5.27 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4B), 5.26 (dd, 1 H, $J_{2,3}$ 10.1 Hz, H-2A), 5.08 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.4 Hz, H-3B), 4.96 (dd, 1 H, $J_{vic(trans)}$ 17.2 Hz, H_2C=CH-CH_2), 4.82 (dd, 1 H, H-3B), 4.71 (dd, 1 H, $J_{vic(cis)}$ 10.9 Hz, H_2C=CH-CH_2), 4.67 (d, 1 H, J_{gem} 12.0 Hz, Ph-CH_2), 4.57 (d, 1 H, H-1B), 4.27 (dd, 1 H, J_{gem} 12.8, J_{vic} 5.1 Hz, H_2C=CH-CH_2), 4.24 (dd, 1 H, $J_{3,4}$ 8.8 Hz, H-3A), 4.15–4.00 (m, 4 H, H-4A, H-5B, H-6Ba, H-6Bb), 3.84 (dd, 1 H, J_{vic} 6.7 Hz, H_2C=CH-CH_2), 3.77–3.65 (m, 3 H, H-5A, H-6Aa, H-6Ab), 2.07, 2.03, 1.98, 1.98 (s, 3 H, CH_3Ac), 1.57, 1.52 [s, 9 H, $C(CH_3)_3$]. Anal. Calcd for $C_{50}H_{60}N_4O_{19}$: C, 58.82; H, 5.92; N, 5.49. Found: C, 58.24; H, 5.67; N, 5.33.

1-[O-*(2-O-Acetyl-3,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl-(1 → 4)-3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)]-4-5-di-*tert*-butyloxycarbonyl-1,2,-3-triazole* (**26**).—A solution of **15** (464 mg, 0.49 mmol) and di-*tert*-butyl acetylenedicarboxylate in toluene (100 mL) was kept at 100°C for 3 days. The yellow oil remaining after evaporation of the solvent was purified by flash chro-

matography (4:1 light petroleum–EtOAc) on silica gel (16 g) to give **26** as an amorphous solid (359 mg, 62%); $[\alpha]_D^{22} = +20.4°$ (*c* 1.0, $CHCl_3$); R_f 0.37 (1:1 light petroleum–EtOAc); ^{13}C NMR: δ 169.2 (Ac-C=O), 168.2, 166.0 (Pht-C=O), 158.9, 156.5 (triazole C=O), 140.8 (triazole C=C), 137.9, 137.8, 137.7 (Bzl-C_{ipso}), 134.5, 134.1, 133.9 (Pht-C-4/5, H_2C=*C*H-CH_2), 131.9, 131.4 (Pht-C-1/2, triazole C=C), 128.4–127.2 (Bzl-C_{arom}), 123.7, 123.1 (Pht-C-3/6), 116.6 (H_2C=CH-CH_2), 100.6 (C-1B), 85.2, 82.8 [triazole *C*$(CH_3)_3$], 82.6 (C-1B), 80.2, 78.3, 77.6, 76.6, 73.3, 72.6, 71.9 (C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C5-B), 74.2, 73.9, 73.5, 71.6 (H_2C=CH-CH_2, Ph-CH_2), 68.2, 67.5 (C-6A, C-6B), 53.4 (C-2A), 28.0, 27.9 [triazole C(*C*$H_3)_3$], 20.9 (Ac-CH_3); ^1H NMR: δ 7.75 (bs, 2 H, Pht-H), 7.68–7.65 (m, 2 H, Pht-H), 7.35–7.17 (m 20 H, Ph-H), 6.81 (d, 1 H, $J_{1,2}$ 10.0 Hz, H-1A), 5.40–5.30 (m, 1 H, H_2C=C*H*-CH_2), 5.28–5.22 (m, 2 H, H-2A, H-2B), 4.91–4.87 (m, 2 H, Ph-CH_2, H_2C=CH-CH_2), 4.65–4.59 (m, 3 H, 2 Ph-CH_2, H_2C=CH-CH_2), 4.52–4.36 (m, 6 H, H-1B, Ph-CH_2), 4.32 (dd, 1 H, J_{gem} 12.9, J_{vic} 5.1 Hz, H_2C=CH-CH_2), 4.22 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 8.8 Hz, H-3A), 4.05 (dd, 1 H, $J_{4,5}$ 9.0 Hz, H-4A), 3.93 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-4B), 3.81 (dd, 1 H, J_{vic} 6.6 Hz, H_2C=CH-CH_2), 3.74–3.66 (m, 3 H, H-5A, H-6Aa, H-6Ab), 3.60 (dd, 1 H, $J_{5,6a}$ 7.7, $J_{6a,6b}$ 9.1 Hz, H-6Ba), 3.55 (1 H, $J_{5,6b}$ 9.1 Hz, H-6Bb), 3.43 (dd, 1 H, H-5B), 3.34 (dd, 1 H, $J_{2,3}$ 10.1 Hz, H-3B), 1.95 (s, 3 H, Ac-CH_3), 1.56, 1.52 [s, 9 H, triazole C$(CH_3)_3$]. Anal. Calcd for $C_{65}H_{72}N_4O_{16}$: C, 67.00; H, 6.23; N, 4.81. Found: C, 66.98; H, 6.24 N, 4.89.

1-[O-(*2-O-Acetyl-3,4,6-tri-O-benzyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)]-4,5-di-*tert*-butyloxycarbonyl-1,2,3-triazole* (**27**).—Under dry Ar the glycosylazide **16** (773 mg, 0.78 mmol) and di-*tert*-butyl acetylenedicarboxylate (334 mg, 1.56 mmol) in toluene (50 mL) were kept at 100°C for 3 days. After evaporation of the solvent the product was purified by flash chromatography (4:1 light petroleum–EtOAc) to give **27** as an amorphous solid (649 mg, 68%); $[\alpha]_D^{22}$ +29.5° (*c* 1, $CHCl_3$); R_f 0.36 (1:1 light petroleum–EtOAc); ^{13}C NMR: δ 169.2 (C=OAc), 167.9, 166.0 (C=O Pht), 158.9, 156.6 (C=O triazole), 140.9 (C=C triazole), 138.6–123.2 (C_{arom}, C=C triazole), 100.6 (C-1B), 85.1, 82.8 [O*C*$(CH_3)_3$], 82.6 (C-1B), 80.3, 78.2, 77.2, 76.8, 73.3, 72.6, 71.9 (C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C5-B), 74.7, 74.3, 73.5, 73.4, 71.6 (Ph-CH_2), 68.0, 67.4 (C-6A, C-6B), 53.3 (C-2A), 28.0, 27.8 [C(*C*$H_3)_3$], 21.0 (CH_3Ac); ^1H NMR: δ 7.68 (m_c, 1 H, Pht-H), 7.62–7.54 (m, 3 H, Pht-H), 7.36–7.14 (m, 21 H, Ph-H), 6.93–6.90 (m, 2 H, Ph-H), 6.83–6.72 (m, 3 H, H-1A, Ph-H), 5.34 (dd, 1 H, $J_{1,2}$ 7.9, $J_{2,3}$ 10.1 Hz, H-2B), 5.26 (dd, 1 H, $J_{1,2}$ 10.3, $J_{2,3}$ 10.2 Hz, H-2A), 4.89 (d, 1 H, J_{gem} 11.7 Hz, Ph-CH_2), 4.85 (d, 1 H, J_{gem} 12.3 Hz, Ph-CH_2), 4.64 (d, 1 H, J_{gem} 11.4 Hz, Ph-CH_2), 4.61 (d, 1 H, J_{gem} 11.6 Hz, Ph-CH_2), 4.33–4.26 (m, 3 H, H-3A, Ph-CH_2), 4.15 (dd, 1 H, $J_{3,4}$ 9.0, $J_{4,5}$ 9.6 Hz, H-4A), 3.91 (d, 1 H, $J_{3,4}$ 2.8 Hz, H-4B), 3.79–3.73 (m, 2 H, H-6Aa, H-6Ab), 3.67 (dd, 1 H, $J_{5,6a}$ 9.8 Hz, H-5A), 3.43–3.38 (m, 3 H, H-5B, H-6Ba, H-6Bb), 3.34 (dd, 1 H, H-3B), 1.99 (s, 3 H, CH_3Ac), 1.55, 1.52 [s, 9 H, C$(CH_3)_3$]. Anal. Calcd for $C_{69}H_{74}N_4O_{16}$: C, 68.19; H, 6.14; N, 4.61. Found: C, 68.04; H, 6.20 N, 4.38.

2,3,4,6-Tetra-O-pivaloyl-β-D-glucopyranosyl fluoride (**28**).—HF–pyridine[18] (3 mL) was added to a stirred solution of **21** (800 mg, 1.04 mmol) in dry CH_2Cl_2 (25 mL) at −30°C under N_2. The solution was allowed to warm up to −10°C within 2 h and then added to a mixture of CH_2Cl_2 (100 mL), ice (50 g), and aq $NaHCO_3$ (100 mL). The organic layer was washed with 1 M H_2SO_4, aq $NaHCO_3$, dried and evaporated in vacuo. Flash chromatography (8:1 light petroleum–EtOAc) gave **28** (366 mg, 71%) which was crystallized from EtOH; mp 122°C; $[\alpha]_D^{22}$ +21.9° (*c* 1.0, $CHCl_3$); R_f 0.64 (4:1 light petroleum–EtOAc); ^{13}C NMR: δ 178.0, 177.1, 176.5, 176.2 (C=O Piv), 106.8 (d, $J_{C,F}$ 219 Hz, C-1), 72.5, 71.4, 66.9 (C-3, C-4, C-5), 71.3 (d, $J_{C,F}$ 33.1 Hz, C-2), 61.4 (C-6), 38.87, 38.78, 38.74, 38.70 [*C*$(CH_3)_3$Piv], 27.1, 27.0 [C(*C*$H_3)_3$Piv]; ^1H NMR: δ 5.29 (dd, 1 H, $J_{F,1}$ 52, $J_{1,2}$ 6.7 Hz, H-1), 5.27 (dd, 1 H, $J_{2,3}$ 8.3, $J_{3,4}$ 9.3 Hz, H-3), 5.23 (dd, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 5.10 (ddd, 1 H, $J_{F,2}$ 11.7 Hz, H-2), 4.22 (dd, 1 H, $J_{5,6a}$ 1.9, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.10 (dd, 1 H, $J_{5,6b}$ 4.7 Hz, H-6b), 3.85 (ddd, 1 H, H-5), 1.20, 1.15, 1.12, 1.09 [s, 9 H, C$(CH_3)_3$Piv]. Anal. Calcd for $C_{26}H_{43}FO_9$: C, 60.21; H, 8.36. Found: C, 60.08; H, 8.02.

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl fluoride (**29**).—Treatment of **22** (615 mg, 1.03 mmol) with HF–pyridine (2 mL), as described for the synthesis of **28**, yielded after flash chromatography (2:1 light petroleum–EtOAc) **29** (249 mg, 69%) which was crystallized from EtOH; mp 96°C (lit.[7] mp 98–99°C); $[\alpha]_D^{22}$ +21.8° (*c* 1.0, MeOH) {lit.[7] $[\alpha]_D^{22}$ +22° (*c* 1.0, MeOH)}; R_f 0.18 (2:1 light petroleum–EtOAc).

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranosyl fluoride (**30**).—HF–pyridine (2 mL) was added to a stirred solution of **23** (580 mg, 0.84 mmol) in dry CH_2Cl_2 (25 mL) at 5°C under dry Ar. The mixture was stirred for 16 h at 5°C and then added to a mixture of CH_2Cl_2 (100 mL), ice (50 g), and aq $NaHCO_3$ (100 mL). The organic layer was washed with 1 M H_2SO_4, aq $NaHCO_3$, dried and evaporated. Flash chromatography (2:1 light petroleum–EtOAc) gave an amorphous mixture of the anomers of **30** (226 mg, 62%, ratio α/β 1:1); R_f 0.55 (2:1 light petroleum–EtOAc); characteristic ^1H NMR: α anomer: δ 5.64 (dd, 1 H, $J_{F,1}$ 52.7, $J_{1,2}$ 2.8 Hz, H-1), 4.60 (ddd, 1 H, $J_{F,2}$ 29.5, $J_{2,3}$ 11.4 Hz, H-); β anomer: 6.07 (dd, 1 H, $J_{F,1}$ 52.3, $J_{1,2}$ 7.9 Hz, 1-H).

O-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-acetyl-α-D-glucopyranosyl fluoride (**31**).—HF–pyridine (2 mL) was added to a stirred solution of **24** (600 mg, 0.68 mmol) in dry CH_2Cl_2 (25 mL) at 0°C under dry Ar. The mixture was stirred for 16 h at 0°C and then added to a mixture of CH_2Cl_2 (100 mL), ice (50 g), and aq $NaHCO_3$ (100 mL). The organic layer was washed with 1 M H_2SO_4, aq $NaHCO_3$, dried and evaporated. Flash chromatography (3:1 light petroleum–EtOAc) gave amorphous **31** (319 mg, 74%); $[\alpha]_D^{22}$ +41.2° (*c* 1.0, $CHCl_3$) {lit.[24] $[\alpha]_D^{22}$ +40.3° (*c* 1.0, $CHCl_3$)}; R_f 0.32 (1:1 light petroleum–EtOAc).

O-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-3-O-allyl-6-O-benzyl-2-deoxy-2-phthalimido-D-glucopyranosyl fluoride (**32**).—HF–pyridine (3 mL) was added to a stirred solution of **25** (318 mg, 0.31 mmol) in dry CH_2Cl_2 (25 mL) at 0°C under dry Ar. The mixture was stirred for 16 h at 0°C and then added to a

mixture of CH_2Cl_2 (100 mL), ice (50 g), and aq $NaHCO_3$ (100 mL). The organic layer was washed with 1 M H_2SO_4, aq $NaHCO_3$, dried and evaporated. Flash chromatography (4:1 light petroleum–EtOAc) gave an amorphous mixture of the anomers of **32** (173 mg, 72%, ratio α/β 3:1); $[\alpha]_D^{22}$ +74.1° (*c* 1.0, $CHCl_3$); R_f 0.38 (2:1 light petroleum–EtOAc); NMR data of the α compound: ^{13}C, δ 170.1, 170.0 (C=O Ac), 168.9 (C=O Pht), 137.4, 135.3, 134.3, 131.6, 128.7, 128.3, 128.2, 123.4 (C_{arom}, H_2C=*C*H-CH_2), 115.6 (H_2C=CH-CH_2), 106.3 (d, $J_{C,F}$ 229 Hz, C-1A), 99.9 (C-1B), 73.7, 73.6 (H_2C=CH-*C*H_2, Ph-CH_2), 73.1, 73.0, 71.0, 70.5, 69.9 (C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C5-B), 69.8, 61.0 (C-6A, C-6B), 54.9 (d, $J_{C,F}$ 27 Hz, C-2A) 20.7, 20.6, 20.5 (CH_3Ac); ^1H, δ 7.86–7.83, 7.82–7.70 (m, 2 H, Pht-H), 7.42–7.32 (m, 5 H, Ph-H), 5.68–5.60 (m, 1 H, H_2C=C*H*-CH_2), 5.60 (dd, 1 H, $J_{F,1}$ 54.6, $J_{1,2}$ 2.6 Hz, H-1A), 5.26 (d, 1 H, $J_{3,4}$ 3.7 Hz, H-4B), 5.07 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.3 Hz, H-2B), 4.99 (dd, 1 H, $J_{vic(trans)}$ 17.2 Hz, H_2C=CH-CH_2), 4.93 (dd, 1 H, $J_{2,3}$ 11.3, $J_{3,4}$ 8.8 Hz, H-3A), 4.83 (d, 1 H, $J_{vic(cis)}$ 11.5 Hz, H_2C=CH-CH_2), 4.79 (d, 1 H, J_{gem} 12.3 Hz, Ph-CH_2), 4.77 (d, 1 H, H-3B), 4.47 (d, 1 H, H-1B), 4.44 (d, 1 H, Ph-CH_2), 4.36 (ddd, 1 H, $J_{F,2}$ 30.6 Hz, H-2A), 4.2 (m, 1 H, H_2C=CH-C*H*$_2$), 4.07–3.94 (m, 4 H, H-4A, H-5A, H-6Ba, H-6Bb), 3.8 (m, 1 H, H_2C=CH-C*H*$_2$), 3.79 (dd, 1 H, $J_{5,6a}$ 1.9, $J_{6a,6b}$ 11.0 Hz, H-6Aa), 3.67 (d, 1 H, H-6Ab), 3.63 (dd, 1 H, $J_{5,6a} = J_{5,6b} = 6.8$ Hz, H-5B), 2.08, 2.01, 1.96, 1.95 (s, 3 H, CH_3Ac). Anal. Calcd for $C_{38}H_{42}FNO_{15}$: C, 59.14; H, 5.49; N, 1.81. Found: C, 59.24; H, 5.58; N, 1.76.

O-(*2-O-Acetyl-3,4,6-tri-O-benzyl-β-D-galactopyranosyl-(1 → 4)-3-O-allyl-6-O-benzyl-2-deoxy-2-phthalimido-D-glucopyranosyl fluoride* (**33**).—To a solution of **26** (295 mg, 0.25 mmol) in CH_2Cl_2 at 0°C was added HF–pyridine (2 mL) under dry Ar. After stirring at 0°C for 16 h the mixture was poured into CH_2Cl_2 (100 mL), satd $NaHCO_3$ (100 mL), and ice (50 g). After cautious shaking, the organic layer was separated, washed with 1 M H_2SO_4 (100 mL) and satd $NaHCO_3$ (twice, 100 mL), and dried with $MgSO_4$. After evaporation of the solvent, the residue was purified by flash chromatography (4:1 light petroleum–EtOAc) to give **33** as a mixture (α/β 4:1) of anomers (95 mg, 41%); $[\alpha]_D^{22}$ +61.0° (*c* 1, $CHCl_3$); R_f 0.45 (1:1 light petroleum–EtOAc); NMR data of the α anomer: ^{13}C, δ 169.0 (Ac-C=O), 138.7, 138.0, 137.9, 137.7 (Bzl-C_{ipso}), 135.3, 134.1 (Pht-C-4/5, H_2C=*C*H-CH_2), 131.6 (Pht-C-1/2), 128.3–127.2 (Bzl-C_{arom}), 123.4, 123.3 (Pht-C-3/6), 115.5 (H_2C=CH-CH_2), 106.4 ($J_{C,F}$ 231 Hz, C-1A), 100.3 (C-1B), 80.3, 76.4, 73.3, 73.2, 72.7, 71.8 (C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C-5B), 74.3, 73.8, 73.6, 73.5 (H_2C=CH-*C*H_2, Ph-CH_2), 68.2, 67.1, C-6A, C-6B), 55.0 ($J_{C,F}$ 26.8 Hz, C-2A), 20.9 (Ac-CH_3); ^1H, δ 7.88–7.82, 7.76–7.67 (m, 2 H, Pht-H), 7.40–7.20 (m, 20 H, Ph-H), 5.63–5.55 (m, 1 H, H_2C=C*H*-CH_2), 5.61 (dd, $J_{F,1}$ 53.9, $J_{1,2}$ 2.6 Hz, H-1A), 5.30 (dd, 1 H, $J_{1,2}$ 7.9, $J_{2,3}$ 10.0 Hz, H-2B), 4.96–4.88 (m, 3 H, 2 Ph-CH_2, H_2C=CH-CH_2), 4.74–4.64 (m, 3 H, 2 Ph-CH_2, H_2C=CH-CH_2), 4.53–4.38 (m, 5 H, H-1B, Ph-CH_2), 4.32 (dd, 1 H, J_{gem} 11.4, J_{vic} 2.9 Hz, H_2C=CH-C*H*$_2$), 4.06–3.93 (m, 4 H, H-3A, H-4A, H-5A, H-4B), 3.84–3.76 (m, 3 H, H-2A, H-6Aa, H_2C=CH-C*H*$_2$), 3.68 (dd, 1 H, $J_{5,6b}$ 1.2, $J_{6a,6b}$ 11.0 Hz, H-6Ab), 3.65 (dd, 1 H, $J_{5,6a}$ 7.7, $J_{6a,6b}$ 9.2 Hz, H-6Ba), 3.58 (dd, 1 H, $J_{5,6b}$ 5.4 Hz, H-6Bb), 3.43 (dd, 1 H, H-5B), 3.32 (dd, 1 H,

$J_{3,4}$ 2.7 Hz, H-3B), 1.97 (s, 3 H, Ac-CH_3). Anal. Calcd for $C_{53}H_{54}FNO_{12}$: C, 69.50; H, 5.94; N, 1.53. Found: C, 69.19; H, 5.98 N, 1.54.

O-(*2-O-Acetyl-3,4,6-tri-O-benzyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-D-glucopyranosyl fluoride* (**34**).—To a solution of **27** (263 mg, 0.22 mmol) in dry CH_2Cl_2 (25 mL) under Ar at 0°C was added HF–pyridine (2 mL). After vigorous stirring for 16 h at 0°C, the mixture was poured into CH_2Cl_2 (100 mL), satd $NaHCO_3$ (100 mL), and ice (50 g) and shaken cautiously. The organic layer was separated, washed with 1 M H_2SO_4 (100 mL) and satd $NaHCO_3$ (twice 100 mL), and dried with $MgSO_4$. After evaporation of the solvent the residue was subjected to flash chromatography (4:1 light petroleum–EtOAc) to give **34** as a mixture (α/β 3:2) of anomers (128 mg, 61%); $[\alpha]_D^{22}$ +60.1° (*c* 1, $CHCl_3$); R_f 0.46 (1:1 light petroleum–EtOAc); ^{13}C NMR: δ 169.2, 169.1 (C=O Ac), 167.6 (C=O Pht), 139.0–123.4 (C_{arom}), 107.1 ($J_{C,F}$ 243 Hz, C-1Aα), 106.2 ($J_{C,F}$ 211 Hz, C-1Aβ), 100.6 (C-1Bα), 100.5 (C-1Bβ), 80.4, 80.3, 76.9, 75.8, 74.9, 73.4, 73.3, 73.1, 72.7, 72.6, 71.8 (α,β: C-2B, C-3A, C-3B, C-4A, C-4B, C-5A, C5-B), 74.6, 74.4, 73.5, 73.4, 71.7 (Ph-CH_2), 68.1, 67.3 (C-6Aβ, C-6Bβ), 68.0, 67.1 (C-6Aα, C-6Bα), 55.7 ($J_{C,F}$ 21.5 Hz, C-2Aβ), 55.0 ($J_{C,F}$ 26.6 Hz, C-2Aα), 21.0 (CH_3 Ac); ^1H, α anomer: δ 5.62 (dd, $J_{F,1}$ 53.9, $J_{1,2}$ 2.6 Hz, H-1A), 5.36 (dd, $J_{1,2}$ 8.0, $J_{2,3}$ 10.1 Hz, H-2B), 4.09 (dd, $J_{2,3}$ 10.1, $J_{3,4}$ 8.5 Hz, H-3A), 4.05 (dd, $J_{4,5}$ 9.3 Hz, H-4A); β anomer: 5.83 (dd, $J_{F,1}$ 53.6, $J_{1,2}$ 7.4 Hz, H-1A), 5.34 (dd, $J_{1,2}$ 8.0, $J_{2,3}$ 10.1 Hz, H-2B). Anal. Calcd for $C_{57}H_{56}FNO_{12}$: C, 70.87; H, 5.84; N, 1.45. Found: C, 70.39; H, 6.04 N, 1.45.

1-(2,3,4,6-Tetra-O-pivaloyl-β-D-glucopyranosyl)-4,5-dibenzoyl-1,2,3-triazole (**36**). —A solution of 2,3,4,6-tetra-*O*-pivaloyl-β-D-glucopyranosyl azide **5** (ref 11) (541 mg, 1 mmol) and dibenzoyl acetylene[20] (250 mg, 1.1 mmol) in dry toluene (40 mL) was heated for 20 h under reflux. The cooled mixture was evaporated to dryness. Flash chromatography (4:1 light petroleum–EtOAc) gave amorphous **36** (433 mg, 56%); $[\alpha]_D^{22}$ −45.2° (*c* 1.0, $CHCl_3$); R_f 0.28 (4:1 light petroleum–EtOAc); ^{13}C NMR: δ 185.8, 184.5 (triazole C=O), 177.6, 177.1, 176.1, 175.6 (Piv-C=O), 147.1, 138.4, 136.2, 135.9 (triazole C=C, Ph-C_{ipso}), 134.4, 133.6, 130.5, 129.1, 128.8, 128.4 (Ph-C_{arom}), 85.7 (C-1), 75.8, 72.3, 69.9, 66.8 (C-2, C-3, C-4, C-5), 61.1 (C-6), 38.74, 38.71, 38.62, 38.59 [Piv-*C*$(CH_3)_3$], 27.1, 26.9, 26.8 [Piv-C(C(*C*$H_3)_3$]; ^1H NMR: δ 8.22, 7.71 (d, 1 H, $J_{ortho,meta}$ 7.7 Hz, Ph_{ortho}-H), 7.59–7.53 (m, 2 H, Ph_{para}-H), 7.44–7.38 (dd, 1 H, $J_{meta,para}$ 7.7 Hz, Ph_{meta}-H), 6.03 (dd, 1 H, $J_{1,2}$ 9.3, $J_{2,3}$ 9.4 Hz, H-2), 5.94 (d, 1 H, H-1), 5.48 (dd, 1 H, $J_{3,4}$ 9.6 Hz, H-3), 5.19 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 3.89 (d, 1 H, $J_{6a,6b}$ 12.2 Hz, H-6a), 3.84 (dd, 1 H, $J_{5,6b}$ 5.1 Hz, H-5), 3.78 (dd, 1 H, H-6b), 1.12, 1.11, 1.02, 1.00 [s, 9 H, Piv-C$(CH_3)_3$]. Anal. Calcd for $C_{42}H_{53}N_3O_{11}$: C, 65.02; H, 6.89; N, 5.42. Found: C, 65.45; H, 6.50; N, 5.23.

1'-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-4,5-di-O-benzoyl-1,2,3-triazole (**37**).—A solution of 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl azide **6** (ref 10) (3.8 g, 10 mmol) and dibenzoyl acetylene (2.5 g, 10.7 mmol) in dry toluene (60 mL) was kept at 90°C for 5 days. The cooled mixture was evaporated to dryness. Crystallization of the resulting residue from MeOH gave **37** (4.5 g, 76%); mp

> 250°C; $[\alpha]_D^{22}$ −30.1° (*c* 1.0, $CHCl_3$); R_f 0.33 (2:1 light petroleum–EtOAc); ^{13}C NMR: δ 185.6, 184.3 (triazole C=O), 169.92, 169.89, 168.7 (Ac-C=O), 147.0, 138.9, 136.2, 135.9 (triazole C=C, Ph-C_{ipso}), 134.3, 133.6, 130.7, 129.1, 128.7, 128.4 (Ph-C_{arom}), 86.6 (C-1), 74.0, 70.8, 67.7, 66.5 (C-2, C-3, C-4, C-5), 60.8 (C-6), 20.5, 20.4, 20.3 (Ac-CH_3); ^1H NMR: δ 8.33, 7.75 (m_c, 2 H, Ph$_{ortho}$-H), 7.60–7.55 (m, 2 H, Ph$_{para}$-H), 7.48–7.39 (m, 4 H, Ph$_{meta}$-H), 5.95–5.89 (m, 2 H, H-1, H-2), 5.37 (d, 1 H, $J_{3,4}$ 2.9 Hz, H-4), 5.19–5.13 (m, 1 H, H-3), 4.02 (dd, 1 H, $J_{5,6a}$ 5.7, $J_{5,6b}$ 7.1 Hz, H-5), 3.67 (dd, 1 H, $J_{6a,6b}$ 11.6 Hz, H-6a), 3.47 (dd, 1 H, H-6b), 2.18, 1.99, 1.98, 1.82 (s, 3 H, Ac-CH_3). Anal. Calcd for $C_{42}H_{53}N_3O_{11}$: C, 59.31; H, 4.81; N, 6.92. Found: C, 59.33; H, 4.79; N, 7.09.

Benzyl O-*(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-*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* (**40**).—To a solution of benzyl-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[22] (**39**) (339 mg, 349 μmol), and the glycosyl fluoride **32** (462 mg, 612 μmol) in dry CH_2Cl_2 (50 mL) was added 4 Å molecular sieves. The mixture was stirred under dry Ar for 1 h at 5°C. Within 5 min a solution of $BF_3 \cdot OEt_2$ (0.62 mL, 5 mmol) in CH_2Cl_2 (20 mL) was added dropwise at 0°C. After 1 h at 0°C the mixture was stirred for 2 h at room temperature, then filtered through Celite and washed with satd $NaHCO_3$. After drying with $MgSO_4$ and evaporation of the solvent the product was purified by flash chromatography (3:1 light petroleum–EtOAc) to give **40** (527 mg, 88%); $[\alpha]_D^{22}$ −14.4° (*c* 1, $CHCl_3$); R_f 0.23 (2:1 light petroleum–EtOAc); ^{13}C NMR: δ 170.2, 170.1, 170.0, 169.1 (Ac-C=O), 139.4, 139.1, 138.7, 138.5, 138.4, 138.3, 137.8, 137.6 (Bzl-C_{ipso}), 134.8 (H_2C=*C*H-CH_2), 133.7 (Pht-C-4/5), 131.7 (Pht-C-1/2), 128.3–126.5 (Bzl-C_{arom}), 123.1 (Pht-C-3/6), 116.2 (H_2C = CH-CH_2), 102.4 (C-1A, C-1B), 100.4 (C-1D), 99.7 (C-1C), 83.0 (C-3A), 81.7 (C-2A), 82.0 (C-3B), 78.9 (C-2B), 77.8, 76.7 (C-4C, C-4B), 76.8 (C-3C), 76.0 (C-4A), 75.4, 75.1, 75.0, 74.1, 73.8, 73.0, 70.8 (Ph-CH_2), 73.1 (C-5B), 74.9 (C-5A), 74.6 (C-5C), 73.4 (Ph-CH_2, H_2C=CH-*C*H_2), 71.1 (C-3D), 70.5

TABLE II

Assignment of ^1H NMR signals of the neo-lacto tetrasaccharide **40** (400 MHz)

Unit	Position	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,4}$)	H-4 ($J_{4,5}$)	H-5 ($J_{5,6}$)	H-6a	H-6b
Glc	A	4.32	3.37	3.36 (8.5)	3.86 (9.1)	2.95	3.52	3.34
Gal	B	4.26	3.47 (9.8)	3.57 (2.8)	4.01	not assigned	not assigned	not assigned
GlcNPht	C	5.39 (7.9)	4.24	4.30	3.98	3.57	3.77	3.73
Ga	D	4.60 (8.0)	5.11 (10.4)	4.85 (2.8)	5.29	3.70 (7.0)	4.06	4.06

(C-5D), 69.5 (C-2D), 68.3, 67.8 (C-6A, C-6B), 68.0 (C-6C), 66.9 (C-4D), 60.9 (C-6D), 56.4 (C-2C), 20.72, 20.61, 20.54, 20.51 (Ac-CH_3); ^{1}H NMR: see Table II. Anal. Calcd for $C_{99}H_{105}NO_{26}$: C, 68.94; H, 6.14; N, 0.81. Found: C, 68.82; H, 6.03; N, 0.84.

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