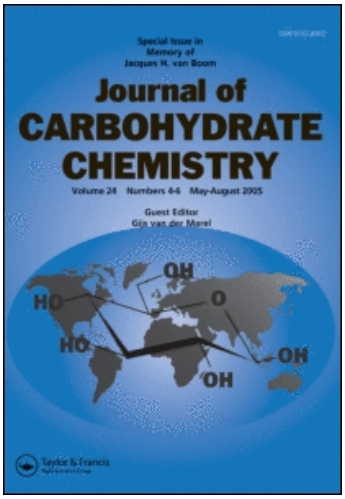

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TCP BUILDING BLOCKS FOR OLIGOSACCHARIDE SYNTHESIS: PROGRESS TOWARDS THE SYNTHESIS OF NODULATION FACTORS

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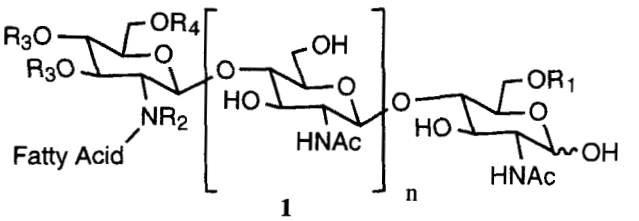
ABSTRACT

The ability of tetrachlorophthaloyl (TCP) sugars to act as glycosyl acceptors as well as the viability of TCP as a global amine protecting group in the synthesis of polyglucosamine natural products such as *N*-methyl-*N*-lipid nodulation factors have been examined. Disaccharides corresponding to the reducing end segments and the core region of the target nodulation factors were assembled from *n*-pentenyl glycosides. TCP acceptors were successfully coupled with a variety of pentenyl glycosyl donors to produce β-(1→4) oligosaccharides in good yields. Model coupling reactions to produce trisaccharides provided clear evidence for the disarming effect of an ester at O3 on a C4-OH in the glycosyl *acceptor*. Also, a unique pentenyl donor, which contained the desired *N*-methyl-*N*-lipid moiety for the non-reducing end segments of the target compounds, was synthesized and its efficacy in a coupling reaction was tested.

INTRODUCTION

The past few years have seen a burgeoning interest in the biological function of glycoconjugates such as lipopolysaccharides, glycolipids, glycopeptides, and oligosaccharides which contain polyglucosamine units.[1] Usually available only in minute amounts, these compounds are ideal candidates for chemical synthesis so that additional structure activity relationships can be established. Nodulation factors **1** comprise a family of unique oligosaccharides composed substantially of glucosamine units *N*-acylated with acetic and fatty acid residues, the latter residing at the non-reducing terminus (Scheme 1).[1a]



1

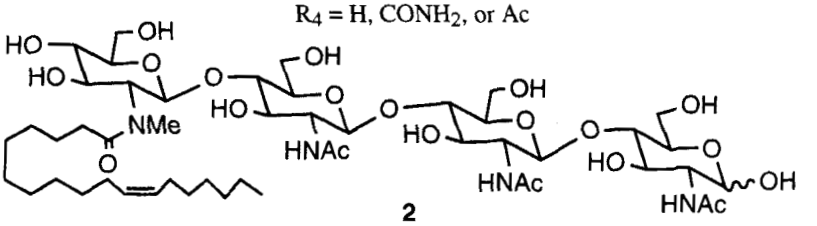
General Structure

R_1 = H, SO_3^-, $CONH_2$, or monosaccharide

R_2 = H or Me

R_3 = H, $CONH_2$, or Ac

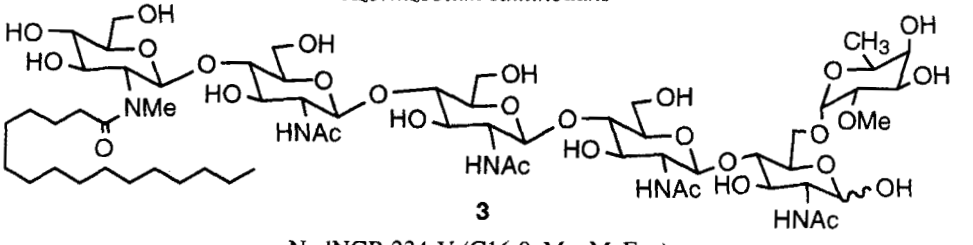
R_4 = H, $CONH_2$, or Ac



2

NodAc-IV (C18:1, Me)

Azorhizobium caulinodans



3

NodNGR 234-V (C16:0, Me, MeFuc)

Rhizobium sp. NGR 234

Scheme 1

These signal molecules are secreted by bacteria to elicit formation of leguminous root nodules in which atmospheric nitrogen is reduced to ammonia.[2] As a key part of the global nitrogen cycle, nodulation factors have become important synthetic targets.[3]

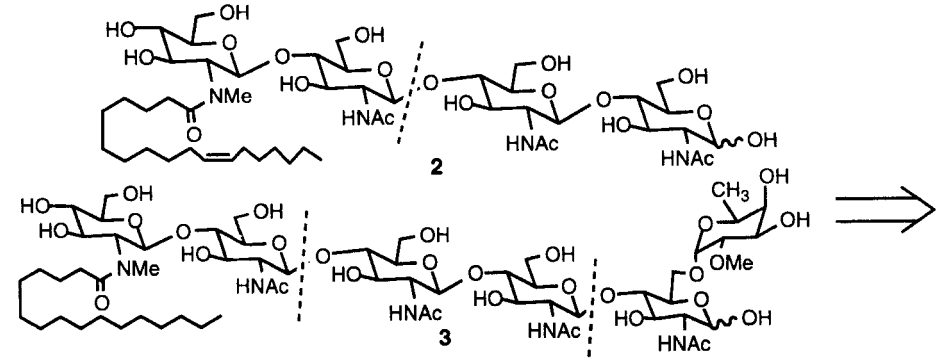
The need to differentially functionalize the glucosamine units and also achieve ready oligosaccharide assembly in the case of nodulation (nod) factors proved to be an adequate testing ground for the tetrachlorophthaloyl group (TCP) which we[4] and subsequently others[5] have reported. In our recent synthesis of NodRf-III (C18:1, MeFuc),[6] the ability to chemoselectively cleave TCP in the presence of phthalimide was exploited to install the

lipid chain on a late stage, tetrasaccharide intermediate. Although this work demonstrated the chemoselective cleavage of TCP in the presence of multiple phthalimides, we wished to investigate the TCP's ability to serve as a global nitrogen protecting group in the synthesis of nodulation factors. As an example, we pursued the construction of nod factors possessing an *N*-methyl group on the same glucosamine residue as the lipochain (i.e. **1**, R_2 = Me). Synthetic efforts toward these nod factors with secondary amide moieties have not been previously reported, and although many papers have now shown the TCP's utility as part of a glycosyl donor, no studies to date have examined its role in glycosyl acceptors and as a global amine protecting group. In this manuscript, we report our efforts toward the construction of *N*-methylated nod factors which exemplify the ability of the TCP to function in global protection.

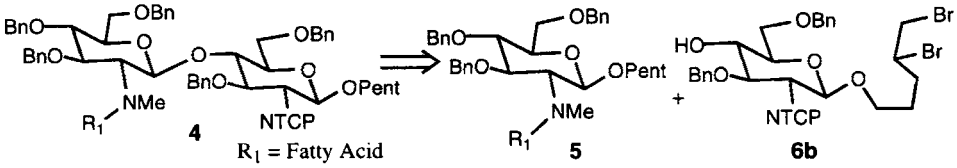
Retrosynthesis of *N*-Methyl-*N*-Lipid Nodulation Factors

In Scheme 1 is shown the general structure of a nod factor, **1**, which indicates the presence of (a) a non-reducing end glucosamine containing a primary or secondary fatty acid amide, (b) a β(1→4) linked *N*-acetyl polyglucosamide core, and (c) a reducing end *N*-acetyl glucosamide in which the C6-oxygen may be linked to H, $CONH_2$, SO_3^-, or a monosaccharide residue (generally fucose or arabinose). In our synthetic studies, we endeavored to develop a flexible plan which could lead to the construction of several possible *N*-methylated nod factors, such as the tetrasaccharide **2** from *Azorhizobium caulinodans* or the hexasaccharide **3** from *Rhizobium sp. NGR 234*.[1a] While both **2** and **3** contain a glucosamine with a secondary amide formed with a fatty acid (albeit different lipochains) at the non-reducing terminus, **2** is a linear oligosaccharide and **3** is branched, possessing a 2-*O*-methyl fucosyl residue.

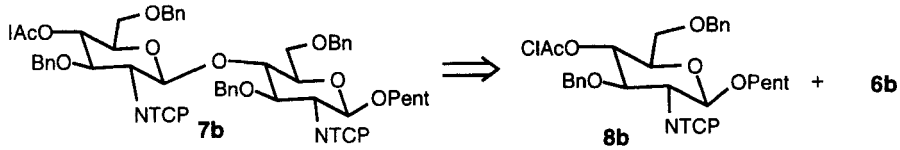
In our retrosynthetic plan, the target nod factors were scissioned into convenient disaccharide segments which would allow for the highly convergent synthesis of structurally diverse compounds using pentenyl glycosides[7] as glycosyl donors (Scheme 2). Accordingly, the non-reducing end retron **4** proceeds from monosaccharide **5**, which already contains the desired lipochain, and the dibromide **6b**. The core region (**7b**) of the larger nod factors such as **3** was envisioned as coming from a TCP protected *n*-pentenyl glycoside (NPG) **8b** and acceptor **6b**. The reducing end disaccharide would either be **9** or **10** depending on the desired target. As a retron for **2**, compound **9** could be assembled from NPG **11** and TCP acceptor **12**. Conversely for the synthesis of branched lipooligosaccharides, **10b** would proceed from fucosyl donor **13** coupled to benzyl glycoside **14b**.



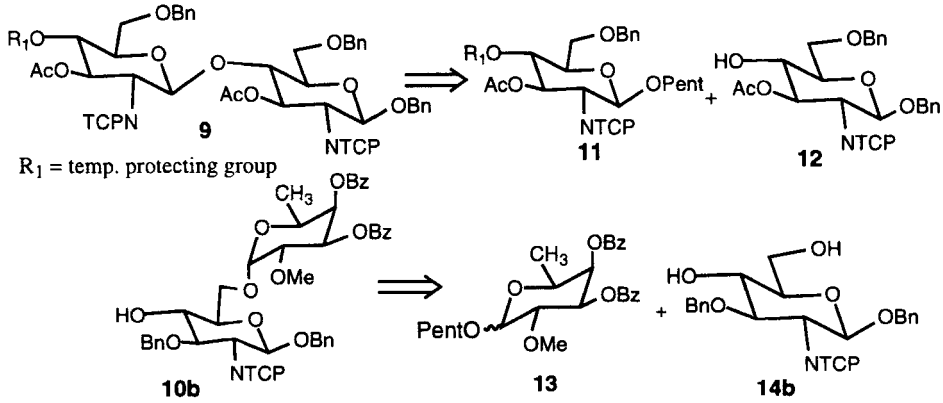
Non-Reducing End Disaccharide for **2** *and* **3**



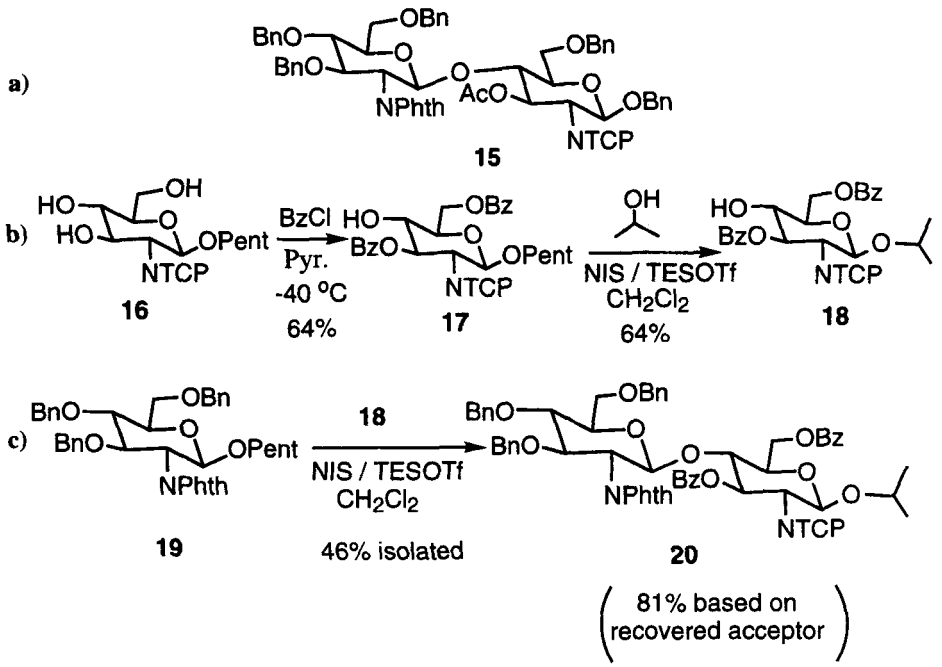
Core Region for **3**



Reducing End Disaccharides



Scheme 2



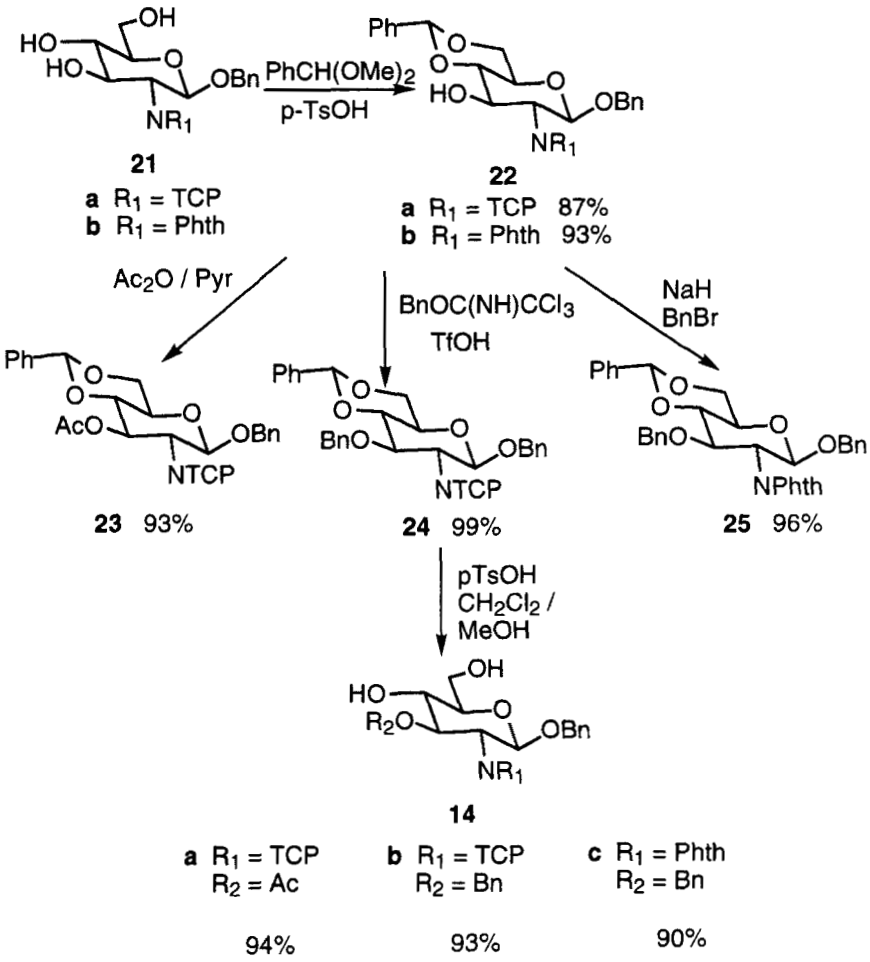
Scheme 3

RESULTS AND DISCUSSION

TCP Glycosyl Acceptors

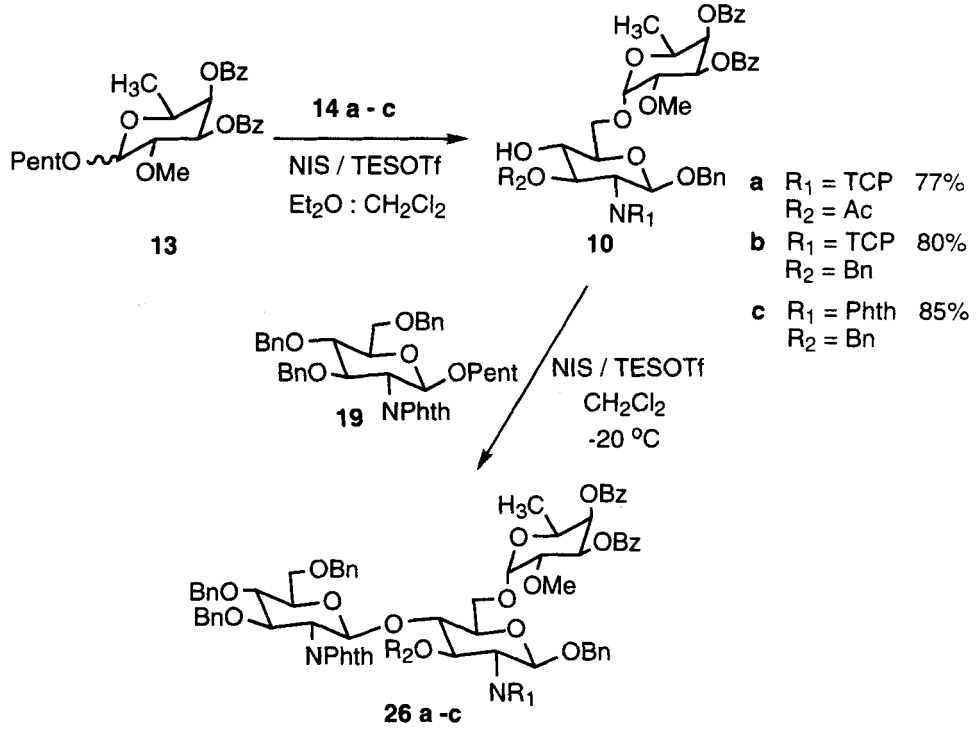
TCP protected sugars have been shown to be excellent glycosyl donors. In order to extend their applicability, we decided to first explore their role as glycosyl acceptors. Disaccharide **15** represents the only previously reported case where the TCP group was present on the acceptor molecule during the coupling event (Scheme 3a).[8]

Since facile TCP deprotection with ethylenediamine has been observed in the presence of esters,[8] dibenzoate **18** was chosen as a model compound to test whether benzoates could be utilized for hydroxyl protection in nod factor synthesis. If successful, the combination of TCP and benzoates could enable deprotection either in a stepwise manner or in one step, depending on the amount of ethylenediamine used. Thus, as depicted in Scheme 3b, pentenyl triol **16**[8] was selectively benzoylated[9] at O3 and O6 with benzoyl chloride in pyridine at -40 °C to afford NPG **17** in 64% yield. This NPG donor was then coupled to 2-propanol under standard *N*-iodosuccinimide/triethylsilyl trifluoromethanesulfonate (NIS/TESOTf) conditions to produce acceptor **18** in 64% yield.



Scheme 4

Coupling of the latter to tribenzylated phthalimide donor **19**[8] gave the desired β(1→4) disaccharide **20** in only 46% yield with recovery of a substantial amount of acceptor **18**. Coupling reactions between other donors and similar 3,6 dibenzoylated acceptors also produced modest results. The low yield for these coupling reactions may have been due to the steric hinderance caused by the benzoates on the acceptor, or a consequence of electron density withdrawal from the C4-OH either by the ester or by a combination of the ester and TCP.[10] The large steric hindrance imposed on such an acceptor by the benzoates in **18** could be alleviated by changing the benzoate at C3 to a less sterically demanding protecting group, such as an acetate. Also, the disarming effect of an



Acceptor	Product	R_1	R_2	Yield (%)
10a[d]	**26a**	TCP	Ac	37
10b[a]	**26b**	TCP	Bn	77
10c[a]	**26c**	Phth	Bn	67

a. Denotes an armed acceptor.
d. Denotes a disarmed acceptor.

Scheme 5

ester might be reversed by switching to an electron donating moiety such as a benzyl group. Thus, the ability of the TCP group to successfully function as a coupling partner in relation to the synthesis of nod factor **3** was then directly assessed by studying coupling reactions of the series of fucosylated disaccharides **10a-c** (Scheme 5) which differ from each other in the substituent at O3 and the type of phthalimide employed.

The benzyl glycoside diols used in the construction of **10a-c** were all prepared in the same general way (Scheme 4). Treatment of the triols **21a**[8] and **21b**[11] with

benzaldehyde dimethyl acetal and *p*-toluenesulfonic acid installed the benzylidene group, and the products were then differentiated at O3. Thus, the TCP sugar **22a**[8] was acetylated with acetic anhydride / pyridine to afford **23**,[8] or benzylated under acidic conditions with benzyl 2,2,2,-trichloroacetimidate to give **24** in 99% yield.[12] With regard to the latter, it is important to note that the TCP sugar can be benzylated quite successfully in acidic medium, since base-catalyzed installation leads to much lower yields.[13] Benzylation of phthalimide compound **22b** was accomplished using NaH and benzyl bromide to afford **25**.[11]
Acidolysis of the benzylidene compounds (**23, 24, 25**) with *p*-toluenesulfonic acid in CH_2Cl_2 / MeOH afforded diols **14a, 14b,** and **14c**[11] in excellent yield.

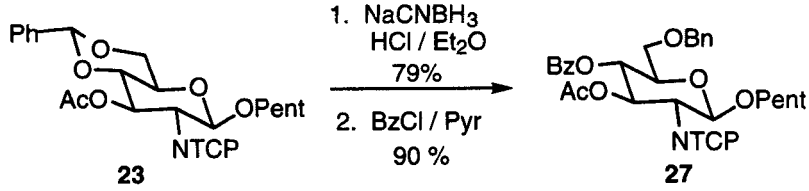
The disaccharide acceptors **10a-c** were then prepared (Scheme 5) by glycosylation of the corresponding benzyl glycosides **14a-c** with *n*-pentenyl fucoside **13**[14] in diethyl ether / dichloromethane and using NIS/TESOTf as the promoter. Notably, regioselectivity was readily achieved by relying upon the increased reactivity of the primary hydroxyl group[15] of **14a-c**, while a combination of solvent control[16] and the benzoyl esters[17] on the pentenyl fucoside ensured the stereochemistry of the desired (1→6) disaccharides (**10a**, **10b**, and **10c**[14]). The presence of the α linkage in **10a**, **10b**, and **10c** was evident by the ^{1}H NMR doublet at approximately δ 5.2 ppm ($J_{1,2} \cong 3.7$ Hz).

With the disaccharide acceptors **10a-c** in hand, the correlation between (1→4) trisaccharide formation and the electronic character of the protecting group at O3, along with TCP or phthalimide, was examined (Scheme 5). Use of the armed donor, phthalimide **19**,[8] with the 3-*O*-acetyl acceptor **10a** at low temperature (*vide infra*) was not advantageous, since trisaccharide **26a** was obtained in 37% yield. However, when the armed disaccharide acceptors **10b** and **10c**[14] were coupled to **19** under the same conditions, dramatic improvement was observed with the desired trisaccharides **26b** and **26c** being isolated in 77% and 67% yield respectively.

Of interest is the fact that the disarmed effect on the disaccharide acceptor seems to be related solely to the electron withdrawing effect of the ester at C3. Furthermore, the TCP acceptor **10b** actually affords a somewhat higher yield of the trisaccharide product than the phthalimide **10c** (77% vs. 67%). Thus, disaccharide **10b** should amply serve for construction of the reducing end of nod factor *NGR 234* (**3**).

TCP-TCP Oligosaccharides

In keeping with the objective of using TCP as a global amine protecting group, TCP-TCP disaccharides (e.g. **9**) corresponding to synthons for the reducing end of linear nod factor **2** as well as the core region of the branched target **3** were of interest. To this end, Garegg reductive cleavage[18] of **23**[8] followed by treatment with benzoyl chloride in pyridine produced a differentially protected pentenyl donor **27** in near quantitative yield



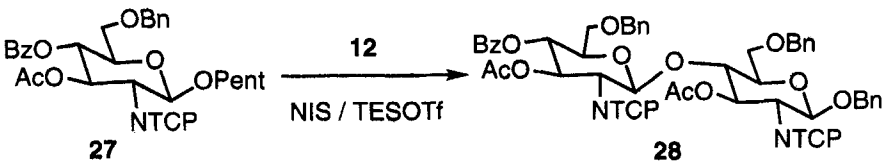
Scheme 6

(Scheme 6). It is important to note that this protocol allows for a variety of easily removed protecting groups to be installed at O4, so as to facilitate the eventual assembly of the desired benzyl glycoside **9**.

NPG **7** and benzyl glycoside **12**[8] were coupled using NIS/TESOTf in CH_2Cl_2 at room temperature to afford **28** in a modest yield of 40%. Although this result displayed the possibility of using TCP global protection, the coupling yield was not encouraging for the synthesis of polyglucosamine units. Thus, we studied the effects of varying solvent, temperature, and TESOTf concentration on the yields. As noted in Scheme 7, entries (i) and (ii), the coupling produced almost identical results at room temperature when carried out in either dichloromethane or acetonitrile. The yield increased from 40% to 52% when the temperature was lowered to -20 °C in CH_2Cl_2 (entry iii).[19] However, a dramatic increase (67%) was realized when glycosylation at -20 °C was carried out with the aid of an additional amount of TESOTf (entry iv). Only β products were obtained as judged by the ^{1}H NMR coupling constants of the disaccharides ($J_{1,2} \cong 8.5$ Hz).

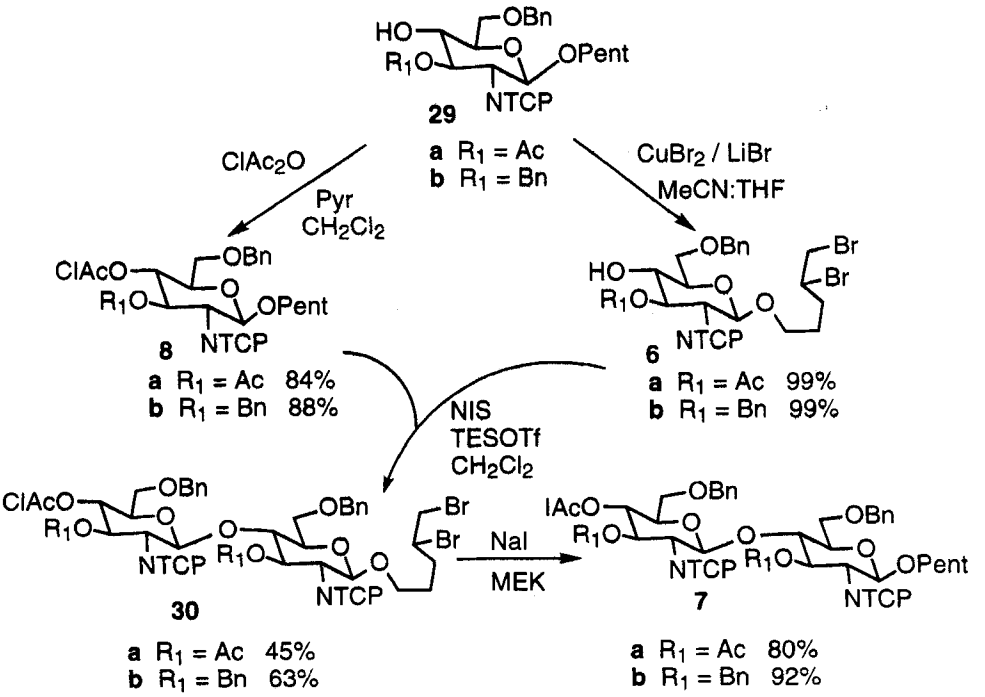
Thus, standard activation conditions for pentenyl glycosylation have been extended successfully to low temperature reactions.[20] More importantly, the acceptable yield of **28** indicates that such TCP-TCP disaccharides can be used for the efficient construction of **2**.

Monosaccharide precursors for our approach to the core disaccharide segment of NodNGR 234 (**7b**) were assembled from common TCP intermediate **29**[8] (Scheme 8). Thus, chloroacetylation of **29a** and **29b** at O4 with chloroacetic anhydride / pyridine / CH_2Cl_2 afforded the desired pentenyl donors **8a** and **8b**.[8] Sidetracking of the same pentenyl glycosides was accomplished by dibromination with $CuBr_2$ / LiBr[21,22] in acetonitrile:THF (3:1) to give the desired acceptors **6a** and **6b** in quantitative yield. Coupling of the 3-*O*-acetyl derivatives **6a** and **8a** afforded dibromide **30a** 45% yield.[23] In contrast, the 3-*O*-benzyl derivatives **8b**[8] and **6b** showed a significant yield increase (63%) for the glycosidation reaction. These results are in keeping with the above studies on disarming effects at O3 (*vide supra*).



Entry	Solvent	Temp. (°C)	TESOTf (eq.)	Yield (%)
i	CH_2Cl_2	25	0.4	40
ii	MeCN	25	0.4	39
iii	CH_2Cl_2	-20	0.4	52
iv	CH_2Cl_2	-20	0.7	67

Scheme 7



Scheme 8

Debromination of **30a** and **30b** with NaI simultaneously converted chloroacetate to iodoacetate,[24] a result which should greatly facilitate deprotection[25] as a prelude to final assembly of a late stage hexasaccharide intermediate.

N-Methyl-*N*-Lipid Pentenyl Donor Assembly

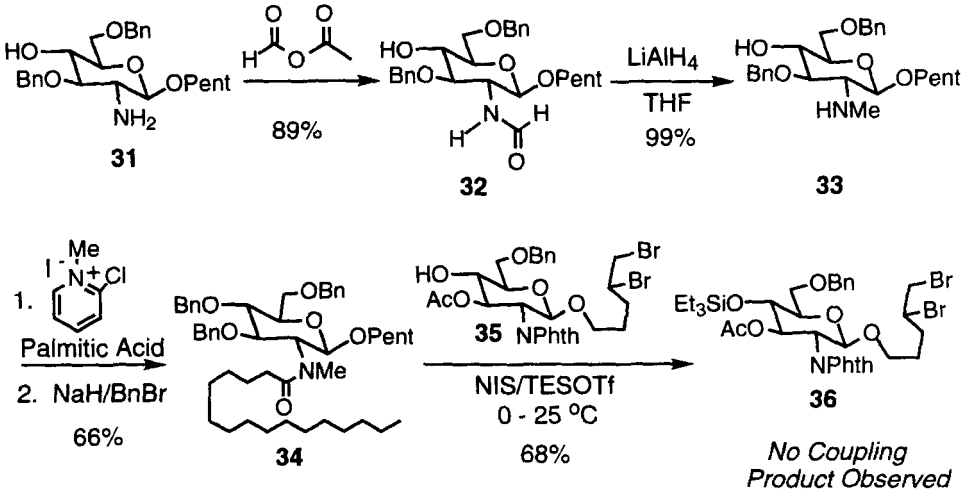
It was now of interest to see whether a pentenyl glycoside which contained the preinstalled *N*-methyl group and lipochain could be used as a glycosyl donor to produce the non-reducing end disaccharide **4**. Success with such a glycosyl donor would obviate the need to monomethylate an amine on a late stage intermediate.

Pentenyl glucosamine **31**[8] was treated with the mixed anhydride formed from acetic anhydride and formic acid to afford the formamide **32** in 89% yield (Scheme 9),[26] which upon reduction with lithium aluminum hydride (LAH) afforded quantitative recovery of the methyl amine **33**. The amine was further acylated with palmitic acid by activation with 2-chloro-1-methylpyridinium iodide[27] and benzylated at the 4 OH with NaH and benzyl bromide to afford pentenyl donor **34** in a 66% yield for two steps. Unfortunately, attempted glycosylation of dibromide **35**[14] in a model reaction with **34** and NIS/TESOTf at $0 \rightarrow 25$ °C did not produce the desired coupling product, but instead afforded silylated acceptor **36** in 68% yield.

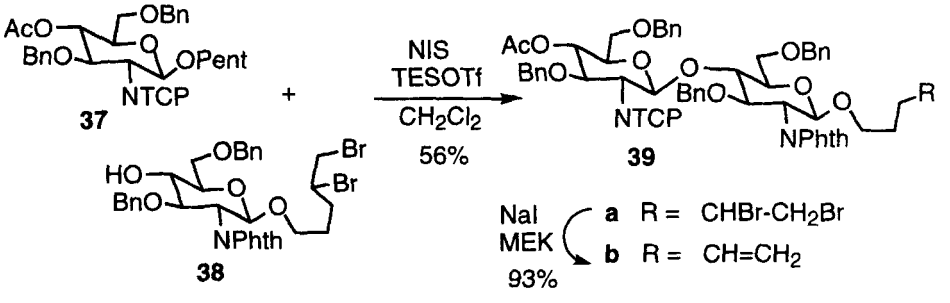
Since this reaction produced only silylated acceptor, different promoters[28] as well as glycosylation methods are currently being investigated for the assembly of compound **4**. As an alternative, TCP pentenyl glycoside **37**[8] and dibromide **38**[8] were coupled and subsequently debrominated with NaI[24] in methyl ethyl ketone to afford pentenyl glycoside **39b** (Scheme 10). Chemoselective cleavage of the TCP group to produce the free amine can easily be accomplished.[8] Different methods to install the *N*-methyl-*N*-lipo moiety on such an intermediate are currently being examined.

CONCLUSION

The tetrachlorophthaloyl (TCP) group for amine protection has been applied to the assembly of oligosaccharides and glycopeptides. In this manuscript, we have examined the ability of TCP sugars to act as glycosyl acceptors, as well as potential use of the TCP as a global amine protecting group in the synthesis of polyglucosamine natural products such as nodulation factors. TCP acceptors readily undergo couplings at low temperature with both phthalimido and TCP pentenyl donors to produce oligosaccharides in good yields, provided that the disarming effect of an ester is not present in the acceptor. Thus, progress towards the *N*-methyl-*N*-lipid nodulation factors has included the assembly of oligosaccharide segments corresponding to the core region of **3** and the reducing end



Scheme 9



Scheme 10

segments of **2** and **3**. Further progress in the construction of the secondary amide on a suitable glycosyl donor as well as optimization of the final coupling reactions will be reported in due course.

EXPERIMENTAL

General Procedures. All reactions were conducted under a dry argon atmosphere. THF was distilled from sodium benzophenone ketyl. Dichloromethane and acetonitrile were distilled from calcium hydride. Cyclohexane was stored over 4Å

molecular sieves. Solutions of compounds in organic solvents were dried over sodium sulfate prior to rotary evaporation. TLC plates were Kieselgel 60 F254 (Merck Art. 5554). Carbohydrate compounds were visualized on the TLC plate by charring with H_2SO_4/EtOH/H_2O (1:10:10). Flash column chromatography was done with silica gel 60 (230-400 mesh, Merck). Optical rotations were determined at the sodium D line with a Perkin-Elmer 241 polarimeter. Mass spectra were recorded on a JEOL JMS-SX102A mass spectrometer operating at 3k resolution for low resolution fast atom bombardment (FAB) mass spectra or a Hewlett-Packard 5988A mass spectrometer using chemical ionization with ammonia as the reagent gas. FAB mass spectra were conducted using a *m*-nitrobenzyl alcohol matrix with xenon as the fast atom. Accurate mass measurements were made using FAB at 10k resolution. All FAB data for chlorinated compounds represents the monoisotopic mass (^{35}Cl) of the molecule. ^1H and ^{13}C NMR spectra were recorded on a Varian XL-300, Inova-400 or GE QE-300 spectrometer. Abbreviations for NMR data are as follows: s= singlet, bs= broad singlet, d= doublet, bd= broad doublet, m= multiplet, dd= doublet of doublets, t= triplet. Coupling constants are reported in Hertz and chemical shifts are in ppm on the delta scale. ^1H and ^{13}C chemical shifts are reported relative to internal tetramethylsilane (0.00 ppm). Elemental analyses were conducted by Atlantic Microlab, Inc., P.O. Box 2288, Norcross, GA 30091.

General Procedures Pentenyl Glycoside Couplings. *Procedure A:* To pentenyl donor (1.3 equiv) and acceptor (1 equiv) (both dried by azeotroping together with toluene) in CH_2Cl_2 (0.125 - 0.150 M soln.) was added *N*-iodosuccinimide (1.7 equiv) and triethylsilyl triflate (0.4 equiv, unless otherwise noted in text) at room temperature (unless otherwise noted in text). After stirring for 35 min, the reaction was quenched with 10% $Na_2S_2O_3$ and sat aq $NaHCO_3$ (1:1). The mixture was stirred for an additional 5 min before separating the layers and extracting the aq phase with CH_2Cl_2. The organic phase was then washed with brine, and the concentrated CH_2Cl_2 solution was purified via flash chromatography to afford the title compound.

Procedure B: To the pentenyl donor (1.0 equiv) and acceptor (1.0 equiv) (both dried by azeotroping together with toluene) in Et_2O : CH_2Cl_2 (3:1, 0.100 M soln.) was added N-iodosuccinimide (1.5 equiv) and triethylsilyl triflate (0.3 equiv) at room temperature. After stirring for 25 min, the reaction was quenched and worked up as in Procedure A to afford the title compound.

Pent-4-enyl 3,6-Di-*O*-benzoyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (17). To **16**[8] (5.000 g, 9.706 mmol) in pyridine (39 mL) at -40 °C was added benzoyl chloride (2.60 mL, 22.32 mmol). The reaction was stirred 4 h before diluting with $CHCl_3$ (150 mL). The solution was washed with 5% aq HCl (3×100 mL), back extracting with $CHCl_3$ (1×90 mL), and then washed with sat aq $NaHCO_3$ (1×150 mL) solution, back

extracting with $CHCl_3$ (1 × 90 mL). The concentrated solution was purified *via* flash chromatography eluting with 3:97 EtOAc/ CH_2Cl_2 affording **17** as a white foam (4.512 g, 64%); R_f 0.50 (5:95 EtOAc/ CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-8.11 (m, 10H, Ph), 5.80-5.86 (m, 1H), 5.58-5.70 (m, 1H, $OCH_2CH_2CH_2C\underline{H}=CH_2$), 5.45 (d, J = 8.4 Hz, 1H, H-1), 4.78-4.86 (m, 3H), 4.64-4.69 (m, 1H), 4.45 (dd, J = 8.4, 10.8 Hz, 1H), 3.82-3.91 (m, 3H), 3.48-3.56 (m, 1H), 3.43 (bs, 1H, OH), 1.90-1.97 (m, 2H, $OCH_2CH_2C\underline{H}_2CH=CH_2$), 1.53-1.64 (m, 2H, $OCH_2C\underline{H}_2CH_2CH=CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.11 (C=O Bz), 166.70 (C=O Bz), 163.28 (bs, C=O TCP), 162.66 (bs, C=O TCP), 140.33, 137.54, 133.63, 133.12, 129.89, 129.68, 129.54, 128.51, 128.42, 128.28, 126.83, 114.77 ($OCH_2CH_2CH_2CH=\underline{C}H_2$), 97.65 (C-1), 74.22, 74.02, 70.50, 69.04, 63.73, 55.27 (C-2), 29.77 ($OCH_2CH_2\underline{C}H_2CH=CH_2$), 28.39 ($OCH_2\underline{C}H_2CH_2CH=CH_2$).

Isopropyl 3,6-Di-*O*-benzoyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (18). Compound **17** was coupled with 2-propanol (2 equiv) using procedure A to afford **18** as a white foam (0.186 g, 64%); R_f 0.28 (20:80 EtOAc/ petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-8.11 (m, 10H, Ph), 5.81 (dd, J = 8.4, 10.8 Hz, 1H), 5.53 (d, J = 8.4 Hz, 1H, H-1), 4.65-4.80 (m, 2H), 4.44 (dd, J = 8.4, 10.8 Hz, 1H), 3.87-3.99 (m, 3H), 3.40 (d, J = 3.9 Hz, 1H, 4-OH), 1.18 (d, J = 6.2 Hz, 3H, CH_3), 1.60 (d, J = 6.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.22 (C=O Bz), 166.82 (C=O Bz), 140.44, 133.71, 133.20, 129.95, 129.79, 129.72, 129.65, 128.58, 128.50, 128.36, 126.85, 96.40 (C-1), 74.40, 74.27, 72.32, 70.61, 63.82, 55.39 (C-2), 23.23 (-$CH\underline{C}H_3$), 21.87 (-$CH\underline{C}H_3$); HRMS (FAB) *m/e* calcd for $C_{31}H_{26}NO_9Cl_4$ MH^+: 698.0332, Found 698.0323.

Isopropyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzoyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (20). Glycosylation of **18** with **19**[8] was carried out employing procedure A to give **20** as a white foam (79.0 mg, 46%, 81% based on recovered acceptor); R_f 0.45 (4:96 EtOAc/CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78-7.91 (m, 29H, Phth, Bz, Ph), 5.99 (dd, J = 8.4, 10.3 Hz, 1H), 5.41-5.44 (m, 2H), 3.69-4.70 (m, 15H), 3.15-3.28 (m, 2H), 2.94 (bd, J = 9.7 Hz, 1H), 1.02 (d, J = 5.8 Hz, 3H, CH_3), 0.90 (d, J = 6.17 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.38 (C=O Bz), 165.25 (C=O Bz), 138.18, 137.78, 137.67, 133.52, 132.87, 129.65, 129.17, 128.92, 128.62, 128.33, 128.28, 128.15, 127.92, 127.73, 127.67, 127.42, 127.28, 123.50 (bs), 97.85 (C-1A), 96.26 (C-1B), 78.88, 78.47, 75.76, 74.75, 74.66, 73.12, 73.08, 72.22, 72.18, 67.48, 62.33, 56.29, 56.05, 23.08 (-$CH\underline{C}H_3$), 21.78 (-$CH\underline{C}H_3$); HRMS (FAB) *m/e* calcd for $C_{66}H_{55}N_2O_{15}Cl_4$ $(M-H)^+$: 1255.2352, Found 1255.2334.

Benzyl 3-*O*-Benzyl-4,6-benzylidene-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (24). To **22a**[8] (10.24 g, 16.38 mmol) in CH_2Cl_2 (85 mL) and cyclohexane (50 mL) was added benzyl 2,2,2-trichloroacetimidate (6.09 mL, 32.76 mmol, 2 equiv) and triflic acid (38 μL, 0.426 mmol). The reaction mixture was stirred for 3 h and an additional amount of benzyl 2,2,2-trichloroacetimidate (6.09 mL, 32.76 mmol, 2 equiv) and triflic acid (38 μL, 0.426 mmol). After stirring for an additional 12 h, the reaction was quenched with pyridine (1.5 mL) and diluted with CH_2Cl_2 (300 mL). The reaction mixture was washed with 5% aqueous HCl (80 mL), back extracting the aqueous phase with CH_2Cl_2 (1 × 50 mL) and then with saturated aqueous $NaHCO_3$ (100 mL), back extracting the aqueous phase again with CH_2Cl_2 (1 × 50 mL). The organic phase was concentrated, and the residue was purified by flash chromotography (96:4 → 90:10 petroleum ether / ethyl acetate → 1:1 ethyl acetate / CH_2Cl_2) to give compound **24** as a white powder (11.59 g, 99%). R_F 0.67 (85:15 petroleum ether / ethyl acetate); $[\alpha]^{21}_D$ +9.72° (*c* 1.06, $CHCl_3$); ^{1}H NMR (400 MHz) δ 6.89-7.55 (m, 15H, Ph), 5.45 (s, 1H, C<u>H</u>Ph), 5.00 (d, *J* = 8.5 Hz, 1H, H-1), 4.58-4.63 (m, 3H), 4.11-4.33 (m, 5H), 3.54-3.88 (m, 3H); ^{13}C NMR (100 MHz) δ 163.20 (C=O TCP), 138.22, 129.78, 129.07, 128.98, 128.88, 127.31, 127.07, 126.69, 126.24, 125.99, 101.29 (<u>C</u>HPh), 97.70 (C-1), 82.48, 74.75, 74.29, 71.56, 68.45, 66.08, 56.30 (C-2); FAB (MS) *m/e* 714.96 M^-.

Benzyl 3-*O*-Acetyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (14a) To **23**[8] (14.21 g, 21.29 mmol) in CH_2Cl_2 / MeOH (1.5:1, 320 mL) was added *p*-toluenesulfonic acid (808.4 mg, 0.2 equiv), and the solution was refluxed at 45 °C for 4.5 h. The reaction was quenched with Et_3N (592 μL), the solvent evaporated, and the residue was purified *via* flash chromatography eluting with 1:1 → 3:2 EtOAc / CH_2Cl_2 to give **14a** as a white foam (11.53 g, 94%). R_F 0.45 (3:2 EtOAc / CH_2Cl_2); $[\alpha]^{21}_D$ -29.3° (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.07-7.26 (m, 5H, Ph), 5.56 (dt, *J* = 8.9, 10.6 Hz, 1H), 5.36 (d, *J* = 8.4 Hz, 1H, H-1), 4.83 (d, *J* = 12.2 Hz, 1H), 4.52 (d, *J* = 12.3, 1H), 4.23 (dt, *J* = 8.4, 10.5 Hz, 1H), 3.79-4.13 (m, 3H), 3.56-3.62 (m, 1H), 2.96 (bs, 1H, OH), 2.18 (bs, 1H, OH), 1.96 (s, 3H, OAc); ^{13}C NMR (75 MHz) δ 171.48 (C=O Ac), 163.7 (bs, C=O TCP), 163.3 (bs, C=O TCP), 136.85, 129.68, 128.14, 128.13, 127.91, 127.70, 126.74, 97.36 (C-1), 75.36, 73.27, 72.03, 69.53, 61.94, 60.36, 55.43 (C-2), 20.67 (CH_3 OAc); MS (FAB) *m/e* 578.95 M^-.

Anal. Calcd for $C_{23}H_{19}NO_8Cl_4 \cdot H_2O$: C, 46.26; H, 3.54. Found: C, 46.15; H, 3.38.

Benzyl 3-*O*-Benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (14b) Compound **24** was treated as above in the preparation of **14a** to give **14b** as a white foam (6.77 g, 93%). R_F 0.49 (65:35 CH_2Cl_2 / ethyl acetate); $[\alpha]^{21}_D$ +6.61° (*c* 1.27, $CHCl_3$); ^{1}H

NMR (400 MHz) δ 6.87-7.21 (m, 10H, Ph), 5.30 (d, *J* = 8.2 Hz, 1H, H-1), 5.04 (d, *J* = 13 Hz, 1H), 4.94 (d, *J* = 12.3 Hz, 1H), 4.60 (m, 2H), 4.06-4.36 (m, 5H), 3.69 (m, 1H), 3.52 (bs, 2H, OH); ^{13}C NMR (100 MHz) δ 162.85 (C=O TCP), 162.46 (C=O TCP), 139.34, 137.00, 129.22, 128.11, 128.05, 127.91, 127.87, 127.64, 127.00, 126.77, 126.50, 97.43 (C-1), 79.66, 75.41, 75.19, 71.71, 71.64, 61.88, 56.29 (C-2); HRMS (FAB) *m/e* calcd for $C_{28}H_{24}NO_7Cl_4$ MH^+: 628.0282, Found 628.0263.

Benzyl (3,4-Di-*O*-benzoyl-2-*O*-methyl-α-L-fucopyranosyl)-(1→6)-3-*O*-acetyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (10a). Compounds **13**[14] and **14a** were coupled using procedure B to afford **10a** as a white foam (105.2 mg, 0.111 mmol) and recovered **14a** (18.8 mg, 0.032 mmol). The total yield of **10a** was 77% based on recovered alcohol **14a**. R_F 0.37 (1:1 petroleum ether / ethyl acetate); $[\alpha]^{21}_D$ -46.8° (*c* 1.14, $CHCl_3$); ^{1}H NMR (300 MHz) δ 8.04 - 8.11 (m, 2H, Bz), 7.82 - 7.90 (m, 2H, Ph), 7.47 - 7.67 (m, 4H, Ph), 7.32 - 7.37 (m, 3H, Ph), 7.05 - 7.18 (m, 4H, Ph), 5.53 - 5.74 (m, 3H), 5.35 (d, *J* = 8.4 Hz, 1H), 5.19 (d, *J* = 3.7 Hz, 1H), 4.87 (d, *J* = 12.1 Hz, 1H), 4.51 (d, *J* = 12.3 Hz, 1H), 4.48 (m, 1H), 4.27 (dt, *J* = 9.0, 10.5 Hz, 1H), 3.91 - 4.15 (m, 5H), 3.71 (m, 1H), 3.52 (m, 1H), 3.48 (s, 3H), 3.42 (m, 1H), 2.78 (m, 1H), 1.93 (s, 3H, Ac CH_3), 1.23 (d, *J* = 6.4 Hz, 3H, CHC$\underline{H}_3$ Fuc); ^{13}C NMR (75 MHz) δ 171.35 (C=O Ac), 165.86 (C=O Bz), 165.55 (C=O Bz), 136.98, 133.33, 133.05, 129.79, 129.62, 128.57, 128.31, 128.26, 127.94, 127.75, 127.01, 97.97 (C-1), 97.25 (C-1), 76.44, 73.93, 73.10, 72.16, 71.58, 71.04, 70.22, 68.36, 65.34, 59.87, 55.72 (C-2A), 20.80 ($\underline{C}H_3$ Ac), 16.12 (CH$\underline{C}H_3$ Fuc); MS (FAB) *m/e* 948.1 $(M+H)^+$, 954.1 $(M+Li)^+$.

Anal. Calcd for $C_{44}H_{39}NCl_4O_{14} \cdot H_2O$: C, 54.73; H, 4.28; Found: C, 54.95; H, 4.44.

Benzyl (3,4-Di-*O*-benzoyl-2-*O*-methyl-α-L-fucopyranosyl)-(1→6)-3-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (10b). Compounds **13**[14] and **14b** were coupled employing procedure B to afford **10b** as a white foam (1.154 g, 1.16 mmol) and recovered **14b** (163 mg, 0.26 mmol). The total yield of **10b** was 80% based on recovered alcohol **14b**. R_F 0.32 (1:1 petroleum ether / ethyl acetate); $[\alpha]^{21}_D$ -113° (*c* 1.13, $CHCl_3$); ^{1}H NMR (400 MHz) δ 8.03 - 8.05 (m, 2H, Bz), 7.84 - 7.86 (m, 2H, Ph), 7.44 - 7.58 (m, 4H, Ph), 7.23 - 7.31 (m, 2H, Ph), 7.01 - 7.05 (m, 6H, Ph), 6.85 - 6.88 (t, *J* = 7.5 Hz, 2H, Ph), 6.71 (m, 1H), 5.68 (m, 2H), 5.19 (d, *J* = 3.4 Hz, 1H, H-1B), 5.08 (d, *J* = 8.3 Hz, 1H, H-1A), 4.82 (d, *J* = 12.7 Hz, 1H), 4.77 (d, *J* = 12.2 Hz, 1H), 4.40 - 4.46 (m, 3H), 4.05 - 4.11 (m, 3H), 3.98 - 4.03 (m, 1H), 3.84 - 3.93 (m, 2H), 3.61 - 3.67 (m, 1H), 3.48 (s, 3H), 1.21 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz) δ 165.84 (C=O Bz), 165.47 (C=O Bz), 162.95 (C=O TCP), 162.37, 139.38, 138.82, 137.07, 133.32, 133.01, 129.81, 129.73, 129.65, 129.41, 129.22, 128.57, 128.29, 128.20,

128.17, 127.88, 127.67, 127.17, 126.83, 126.66, 97.95 (C-1), 97.18 (C-1), 78.92, 76.30, 74.90, 73.58, 72.15, 71.16, 71.00, 68.68, 65.26, 59.70, 56.26 (C-2A), 27.96, 16.14 ($CH\underline{C}H_3$ Fuc); HRMS (FAB) *m/e* calcd for $C_{49}H_{43}NO_{13}Cl_4$ M^+: 995.1459, Found 995.1483.

Benzyl (3,4,6-Tri-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-[(3,4-di-*O*-benzoyl-2-*O*-methyl-α-L-fucopyranosyl)-(1→6)]-3-*O*-acetyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (26a). Pentenyl glycoside **19**[8] and disaccharide acceptor **10a** were coupled using procedure A to afford **26a** as a white foam (36.3 mg, 37%). R_F 0.31 (70:30 petroleum ether / ethyl acetate); ^1H NMR (300 MHz) δ 7.89-8.11 (m, 2H, Bz), 7.45-7.71 (m, 9H, Ph), 7.13-7.40 (m, 16H, Ph), 6.81-6.97 (m, 7H, Ph), 5.53-5.69 (m, 1H), 5.35 (d, *J*=8.6 Hz, 1H), 5.24 (m, 1H), 4.22-4.80 (m, 13H), 4.02-4.12 (m, 4H), 3.87-3.92 (m, 1H), 3.77-3.82 (m, 1H), 4.65 (m, 2H), 3.52 (s, 3H, OMe), 3.33-3.48 (m, 2H), 1.86 (s, 3H, OAc), 1.13 (d, *J* = 6.4 Hz, 3H, $-CHC\underline{H}_3$).

Anal. Calcd for $C_{79}H_{70}N_2Cl_4O_{20}$: C, 62.87; H, 4.69; N, 1.86; Found: C, 62.71; H, 4.75; N, 1.84.

Benzyl (3,4,6-Tri-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-[(3,4-di-*O*-benzoyl-2-*O*-methyl-α-L-fucopyranosyl)-(1→6)]-3-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (26b). The pentenyl glycoside **19**[8] and disaccharide acceptor **10b** were coupled using procedure A to give **26b** as a white foam (194.5 mg, 77%). R_F 0.64 (65:35 petroleum ether / ethyl acetate); $[\alpha]^{21}_D$ -40.6° (*c* 1.61, $CHCl_3$); ^1H NMR (400 MHz) δ 8.03-8.05 (m, 2H, Bz), 7.84-7.89 (m, 2H, Ph), 7.44-7.76 (m, 9H, Ph), 7.14-7.38 (m, 12H, Ph), 6.79-7.08 (m, 13H, Ph), 6.65 (m, 1H), 5.68 (d, *J* = 3.2 Hz, 1H), 5.62 (dd, *J* = 3.3, 10.3 Hz, 1H), 5.43 (d, *J* = 8.2 Hz, 1H), 5.21 (d, *J* = 3.3 Hz, 1H, H-1 Fuc), 4.97 (d, *J* = 8.4 Hz, 1H), 4.85 (d, *J* = 13.1 Hz, 1H), 4.78 (dd, *J* = 3.7, 11.0 Hz, 2H), 4.68 (m, 4H), 4.58 (d, *J* = 12.1 Hz, 1H), 4.32-4.45 (m, 5H), 4.11-4.23 (m, 3H), 3.87-4.04 (m, 4H), 3.75-3.83 (m, 3H), 3.55 (s, 3H, OMe), 3.46 (dd, *J* = 4.1, 11.1 Hz, 1H), 3.28 (m, 1H), 1.15 (d, *J* = 6.5 Hz, 3H, $-CHC\underline{H}_3$); ^{13}C NMR (100 MHz) δ 168.46 (bs, C=O Phth), 167.42 (bs, C=O Phth), 165.74 (C=O Bz), 165.19 (C=O Bz), 162.63 (C=O TCP), 162.07 (C=O TCP), 139.07, 139.04, 138.18, 138.01, 133.88, 133.09, 132.65, 131.55, 129.88, 129.69, 129.61, 129.44, 129.13, 129.00, 128.35, 128.16, 128.13, 128.07, 128.00, 127.85, 127.72, 127.45, 127.41, 127.37, 127.17, 127.11, 126.50, 126.26, 123.55, 122.91, 96.68 (C-1), 96.67 (C-1), 96.62 (C-1), 79.40, 78.95, 76.88, 76.15, 75.42, 74.79, 74.64, 74.49, 73.91, 73.17, 70.59, 68.15, 65.13, 64.51, 59.08, 58.61, 56.44, 57.30, 15.95 ($-CH\underline{C}H_3$); HRMS (FAB) *m/e* calcd for $C_{84}H_{73}N_2O_{19}Cl_4$ $(M-H)^+$: 1555.3558, Found 1555.3591.

Benzyl (3,4,6-Tri-*O*-benzyl-2-deoxy-phthalimido-β-D-glucopyranosyl)-(1→4)-[(3,4-di-*O*-benzoyl-2-*O*-methyl-α-L-fucopyranosyl)-(1→6)]-3-*O*-benzyl-2-deoxy-2-phth-

alimido-β-D-glucopyranoside (26c). The pentenyl glycoside **19**[8] and disaccharide acceptor **10c**[14] were coupled using procedure A to afford **26c** as a white foam (97.3 mg, 67%). R_F 0.34 (65:35 petroleum ether / ethyl acetate); $[\alpha]^{21}_D$ -35.6° (*c* 1.61, $CHCl_3$); ^1H NMR (400 MHz) δ 8.03-8.05 (m, 2H, Bz), 7.83-7.87 (m, 2H, Bz), 7.42-7.76 (m, 13H, Ph), 7.13-7.33 (m, 12H, Ph), 6.86-7.04 (m, 12H, Ph), 6.73 (m, 2H, Ph), 5.67 (d, *J* = 3.1 Hz, 1H), 5.62 (dd, *J* = 3.4, 10.2 Hz, 1H), 5.44 (d, *J* = 8.4 Hz, 1H), 5.21 (d, *J* = 3.4 Hz, 1H, H-1 Fuc), 4.98 (d, *J* = 8.5 Hz, 1H), 4.63-4.86 (m, 7H), 4.54 (dd, *J* = 5.1, 12.8 Hz, 2H), 4.36-4.42 (m, 4H), 4.16-4.25 (m, 3H), 4.10 (dd, *J* = 8.4, 10.5 Hz, 1H), 3.88-3.96 (m, 3H), 3.72-3.82 (m, 3H), 3.53 (s, 3H, OMe), 3.48 (dd, *J* = 4.3, 11.1 Hz, 1H), 3.34 (m, 1H), 1.14 (d, *J* = 6.5 Hz, 3H, -CHC$\underline{H}_3$); ^{13}C NMR (100 MHz) δ 168.62 (bs, C=O Phth), 167.60 (bs, C=O Phth), 165.89 (C=O Bz), 165.28 (C=O Bz), 138.76, 138.53, 138.44, 138.44, 138.20, 137.15, 133.95, 133.78, 133.44, 133.18, 132.75, 131.72, 131.42, 130.10, 129.92, 129.80, 129.63, 128.50, 128.28, 128.25, 128.20, 128.01, 127.93, 127.86, 127.73, 127.69, 127.60, 127.50, 127.41, 127.38, 127.27, 127.24, 126.75, 123.69, 123.06, 96.89 (C-1), 96.80 (C-1), 96.75 (C-1), 79.65, 79.17, 76.34, 76.17, 75.58, 74.87, 74.64, 74.60, 74.17, 73.94, 73.59, 73.34, 72.42, 70.70, 70.01, 68.33, 65.41, 64.69, 59.15, 56.64, 55.71, 16.05 (-CH$\underline{C}H_3$); HRMS (FAB) *m/e* calcd for $C_{84}H_{77}N_2O_{19}$ $(M-H)^+$: 1417.5121, Found 1417.5165.

Pent-4-enyl 3-*O*-Acetyl-4-*O*-benzoyl-6-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (27). Pent-4-enyl 3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside[14] (840 mg, 1.3 mmol) was dissolved in pyridine (6 mL) at 0 °C and benzoyl chloride (302 μL) was added dropwise. The reaction was stirred at 0 °C for 1 h, and then at room temperature for 19 h. The pyridine was then removed under high vacuum, and the residue was taken up in diethyl ether (100 mL). The organic layer was washed with H_2O (2 × 50 mL), sat aq $NaHCO_3$ (2 × 50 mL), and H_2O (1 × 50 mL). The concentrated solution was purified via flash chromatography eluting with 93:7 petroleum ether / ethyl acetate to give **27** (881.7 mg, 90%) as an off-white amorphous solid. R_F 0.51 (90:10 petroleum ether / ethyl acetate); ^1H NMR (300 MHz) δ 7.94 - 7.97 (m, 2H, Bz), 7.40 - 7.61 (m, 4H, Ph), 7.18 - 7.26 (m, 4H, Ph), 5.86 (dt, *J* = 9.0, 10.6 Hz, 1H), 5.72 (m, 1H), 5.43 (m, 3H), 4.84 - 4.89 (m, 2H), 4.57 (dt, *J* = 12.1, 15.5 Hz, 2H), 4.37 (dt, *J* = 8.5, 10.7 Hz, 1H), 3.84 - 3.98 (m, 2H), 3.49 - 3.68 (m, 3H), 1.97 (m, 2H, $OCH_2CH_2C\underline{H}_2CH{=}CH_2$), 1.80 (s, 3H, Ac), 1.55 - 1.65 (m, 2H, $OCH_2C\underline{H}_2CH_2CH{=}CH_2$); ^{13}C NMR (75 MHz) δ 170.67 (C=O Ac), 165.11 (C=O Bz), 140.57, 137.66, 137.58, 133.48, 129.98, 129.78, 128.93, 128.48, 128.24, 128.12, 128.04, 128.00, 127.85, 127.80, 127.65, 127.58, 126.94, 114.84 ($OCH_2CH_2CH{=}\underline{C}H_2$), 97.69 (C-1), 73.61, 71.03, 70.05, 69.20, 68.97, 55.60, 29.84 ($OCH_2CH_2\underline{C}H_2CH{=}CH_2$), 28.45 ($OCH_2\underline{C}H_2CH_2CH{=}CH_2$), 20.45 (Ac).

Anal. Calcd for $C_{35}H_{31}NCl_4O_9$: C, 55.94; H, 4.16; Found: C, 55.70; H, 4.26.

Benzyl (3-*O*-Acetyl-6-*O*-benzyl-4-*O*-benzoyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranosyl)-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (28). Pentenyl glycoside **27** and benzyl glycoside acceptor **12**[8] were coupled using procedure A to afford **28** (110.3 mg, 67%) as a yellow foam. R_F 0.59 (4:1 petroleum ether / ethyl acetate); $[\alpha]^{21}_D$ +14.5° (*c* 1.09, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.91 - 8.00 (m, 2H, Bz), 7.31 - 7.61 (m, 8H, Ph), 7.03 - 7.29 (m, 10H, Ph), 5.78 (t, *J* = 9.3 Hz, 1H), 5.62 - 5.69 (m, 1H), 5.57 (d, *J* = 8.3 Hz, 1H), 5.47 (t, *J* = 9.5 Hz, 1H), 5.26 (d, *J* = 8.4 Hz, 1H, H-1), 4.78 (m, 1H), 4.13 - 4.52 (m, 9H), 3.51 - 3.74 (m, 5H), 1.91 (s, 3H, Ac), 1.76 (s, 3H, Ac); ^{13}C NMR (75 MHz) δ 170.63 (C=O Ac), 170.46 (C=O Ac), 164.94 (C=O Bz), 163.78 (C=O TCP), 162.94 (C=O TCP), 140.35, 137.80, 137.29, 136.91, 133.87, 133.51, 133.40, 130.12, 130.00, 129.93, 129.79, 129.73, 128.96, 128.48, 128.42, 128.42, 128.18, 128.14, 127.80, 127.56, 127.48, 126.93, 126.68, 97.25 (C-1), 97.01 (C-1), 74.41, 73.60, 73.40, 73.22, 73.17, 71.67, 71.54, 70.79, 70.75, 69.58, 68.40, 67.83, 55.99, 55.87, 20.66 (Ac), 20.36 (Ac); HRMS (FAB) *m/e* calcd for $C_{60}H_{45}N_2O_{16}Cl_8$ $(M-H)^+$: 1333.0237, Found 1333.0254.

Pent-4-enyl 3-*O*-Acetyl-6-*O*-benzyl-4-*O*-chloroacetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (8a) To pent-4-enyl 3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside **30a**[8] (0.500g g, 0.7724 mmol) in CH_2Cl_2 (5.5 mL) was added chloroacetic anhydride (0.225 g, 1.313 mmol) and pyridine (94 μL, 1.159 mmol). The reaction was stirred 11 h before diluting with CH_2Cl_2 (90 mL). The solution was washed with 5% aq HCl (1×30 mL), back extracting with CH_2Cl_2 (1×15 mL), and then washed with sat aq $NaHCO_3$ (1×90 mL) solution, back extracting with CH_2Cl_2 (1×15 mL). The concentrated solution was purified *via* flash chromatography eluting with 12:88 EtOAc/ petroleum ether affording a white foam (0.469 g, 84%); R_f 0.38 (15:85 EtOAc/petroleum ether); $[\alpha]_D^{20}$ 24.6° (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.38 (m, 5H, Ph), 5.63-5.72 (m, 2H), 5.33 (d, *J* = 8.4 Hz, 1H, H-1), 5.27 (t, *J* = 9.1 Hz, 1H), 4.83-4.87 (m, 2H), 4.54 (dd, *J* = 11.9, 48.8 Hz, 2H), 4.31 (d, *J* = 8.4, 10.6 Hz, 1H), 3.76-3.85 (m, 3H), 3.62-3.65 (m, 2H), 3.45-3.50 (m, 1H), 1.90-1.95 (m, 2H, $OCH_2CH_2\underline{C}H_2CH{=}CH_2$), 1.90 (s, 3H, OAc), 1.56-1.61 (m, 2H, $OCH_2\underline{C}H_2CH_2CH{=}CH_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.60 (C=O Ac), 166.07 (C=O ClAc), 163.50 (C=O TCP), 140.52, 137.56, 137.38, 129.92, 128.38, 127.95, 127.85, 126.87, 114.82 ($OCH_2CH_2CH_2CH{=}\underline{C}H_2$), 97.65 (C-1), 73.61, 72.56, 71.42, 70.73, 69.15, 68.66, 55.39 (C-2), 40.35 ($ClCH_2$-), 29.77 ($OCH_2CH_2\underline{C}H_2CH{=}CH_2$), 28.37 ($OCH_2\underline{C}H_2CH_2CH{=}CH_2$), 20.46 ($CH_3$ OAc); MS (FAB) *m/e* 723.02 M^-.

Anal. Calcd for $C_{30}H_{28}Cl_5NO_9$: C, 49.78; H, 3.90; found: C, 49.84; H, 3.89.

4,5-Dibromopentanyl 3-*O*-Acetyl-6-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (6a). Pentenyl glycoside **30a**[8] (353.0 mg, 0.545 mmol) (dried by azeotroping with toluene) was dissolved in MeCN:THF (3:1, 3 mL). $CuBr_2$ (608.6 mg , 2.73 mmol, 5 equiv) and LiBr (473.3 mg, 5.45 mmol, 10 equiv) were weighed into a round bottom flask previously flushed with argon and dissolved in MeCN:THF (3:1, 12 mL). The sugar solution was then cannulated dropwise into the flask containing the $CuBr_2$ and LiBr with two solvent rinses of the origin flask (2 × 1 mL). The mixture was stirred at room temperature for 18 h before being diluted with EtOAc (60 mL) and washed with H_2O (2 × 20 mL) and brine (2 × 20 mL). The concentrated solution was purified through a short silica column (80:20 → 70:30 petroleum ether / ethyl acetate) to afford **6a** as a yellow foam (435.5 mg, 99%); R_F 0.69 (65:35 petroleum ether / ethyl acetate); $[\alpha]^{21}_D$ -4.4° (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz) δ 7.30-7.39 (m, 5H, Ph), 5.53 (dt, *J* = 8.9, 10.6 Hz, 1H), 5.33 (d, *J* = 8.4 Hz, 1H, H-1), 4.65 (dd, *J* = 11.9, 31.1 Hz, 2H), 4.19-4.24 (m, 1H), 4.02-4.05 (m, 1H), 3.66-3.88 (m, 6H), 3.44-3.50 (m, 2H), 2.94 (d, *J* = 3.4 Hz, 1H), 2.05-2.09 (m, 1H), 1.97 (s, 3H, OAc), 1.60-1.77 (m, 3H, $OCH_2C\underline{H}_2C\underline{H}HCHBrCH_2Br$); ^{13}C NMR (125 MHz) δ 171.36 (C=O Ac), 140.50, 137.47, 129.91, 128.47, 127.99, 127.73, 126.99, 97.65 (C-1), 97.62 (C-1), 74.01, 73.75, 73.53, 71.11, 69.90, 68.62, 68.59, 55.32 (C-2), 52.21, 36.21, 36.11, 32.76, 32,72, 26.98, 26.86, 20.70 (CH_3 OAc); MS (FAB) *m/e* 806.7 M^-.

Anal. Calcd for $C_{28}H_{27}NO_8Br_2Cl_4$: C, 41.67; H, 3.37. Found: C, 41.75; H, 3.41.

4,5 Dibromopentanyl 3,6-Di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (6b). Pentenyl glycoside **30b**[8] (800 mg, 1.15 mmol) was treated as above in the preparation compound **6a** to afford the dibromide **6b** as a foam (973.7 mg, 99%). R_F 0.51 (70:30 petroleum ether / ethyl acetate); ^{1}H NMR (400 MHz) δ 7.30-7.40 (m, 5H, Ph), 6.75-7.07 (m, 5H, Ph), 5.09 (d, *J* = 8.2 Hz, 1H, H-1), 4.85 (d, *J* = 13 Hz, 1H), 4.61 (dd, *J* = 12.0, 27.3 Hz, 2H), 4.42 (d, *J* = 13 Hz, 1H), 3.96-4.14 (m, 3H), 3.76-3.86 (m, 6H), 3.36-3.45 (m, 2H), 3.04 (bs, 1H, 4-OH), 1.97-2.04 (m, 1H), 1.51-1.72 (m, 3H, $OCH_2C\underline{H}_2C\underline{H}HCHBrCH_2Br$); ^{13}C NMR (100 MHz) δ 163.38 (C=O TCP), 162.46 (C=O TCP), 139.68, 138.63, 137.42, 128.56, 128.04, 128.00, 127.95, 127.84, 126,92, 97.89 (C-1), 79.37, 75.00, 74.72, 73.83, 70.61, 68.37, 68.30, 55.95, 55.94, 52.29, 36.25, 36.17, 32.78, 32.72, 26.97, 26.85; HRMS (FAB) *m/e* calcd for $C_{33}H_{32}NO_7Cl_4$ MH^+: 851.9300, Found 851.9319.

4,5-Dibromopentanyl (3-*O*-Acetyl-6-*O*-benzyl-4-*O*-chloroacetyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranosyl)-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (30a). Compounds **8a** and **6a** were coupled

using procedure A to afford **31a** as a white foam (0.290 g, 45%); R_f 0.25 (15:85 EtOAc/petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08-7.39 (m, 10H, Ph), 5.60-5.70 (m, 2H), 5.51 (d, *J*=8.4 Hz, 1H), 5.20-5.34 (m, 2H), 3.36-4.64 (m, 20H), 1.92 (s, 3H, OAc), 1.93-2.08 (m, 1H), 1.85 (s, 3H, OAc), 1.54-1.76 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.60 (C=O Ac), 170.45 (C=O Ac), 165.92 (C=O ClAc), 163.41 (bs, C=O TCP), 162.76 (bs, C=O TCP), 140.42, 137.68, 137.14, 129.70, 128.41, 128.21, 128.03, 127.90, 127.70, 127.54, 126.84, 126.63, 97.67, 96.97, 74.47, 74.38, 73.47, 73.22, 72.22, 71.89, 70.92, 70.44, 68.51, 68.18, 67.79, 55.77, 55.73, 52.17, 52.11, 40.32 ($ClCH_2$-), 36.13, 36.07, 32.68, 26.91, 26.82, 20.63 (CH_3 OAc), 20.41 (CH_3 OAc); MS (FAB) *m/e* 1444.0 M^-.

Pent-4-enyl (3-*O*-Acetyl-6-*O*-benzyl-4-*O*-iodoacetyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranosyl)-(1→4)-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (7a). To **30a** (0.287 g, 0.1986 mmol) in methyl ethyl ketone (12 mL) was added NaI (0.595 g, 3.973 mmol). The reaction was stirred 12 h at 75 °C and was then concentrated *in vacuo*. The syrup was dissolved in EtOAc (80 mL) and washed with 10% aq $Na_2S_2O_3$ (15 mL) back extracting the aqueous phase with EtOAc (2×15 mL). The concentrated EtOAc solution was purified *via* flash chromatography eluting with a gradient of 15→20% EtOAc/petroleum ether affording **7a** as a white foam (0.218 g, 80%); R_f 0.25 (15:85 EtOAc/petroleum ether); $[\alpha]_D^{20}$ 45.8° (*c* 3.19, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14-7.36 (m, 10H, Ph), 5.59-5.67 (m, 3H), 5.52 (d, *J* = 8.4 Hz, 1H), 5.21-5.25 (m, 2H), 4.83-4.84 (m, 2H), 4.45-4.83 (m, 4H), 4.10-4.21 (m, 3H), 3.37-3.74 (m, 10H), 1.91 (s, 3H, OAc), 1.86-1.95 (m, 2H, $OCH_2CH_2C\underline{H}_2CH=CH_2$), 1.87 (s, 3H, OAc), 1.48-1.62 (m, 2H, $OCH_2C\underline{H}_2CH_2CH=CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.59 (C=O Ac), 170.48 (C=O Ac), 167.26 (C=O IAc), 163.16 (bs, C=O TCP), 162.77 (bs, C=O TCP), 140.48, 140.33, 137.74, 137.59, 137.35, 129.64, 128.34, 128.17, 128.01, 127.90, 127.74, 127.66, 127.47, 126.89, 126.65, 114.77 ($OCH_2CH_2CH_2CH=\underline{C}H_2$), 97.62, 96.94, 74.46, 74.35, 73.40, 73.13, 72.53, 71.92, 70.54, 70.07, 68.88, 68.16, 67.74, 55.90, 55.77, 29.76 ($OCH_2CH_2\underline{C}H_2CH=CH_2$), 28.37 ($OCH_2\underline{C}H_2CH_2CH=CH_2$), 20.68 ($CH_3$ OAc), 20.61 (CH_3 OAc); MS (FAB) *m/e* 1376.09 M^-.

Anal. Calcd for $C_{53}H_{45}N_2O_{16}Cl_8I$: C, 46.25; H, 3.30; found: C, 46.16; H, 3.35.

Pentenyl (3,6-Di-*O*-benzyl-4-*O*-iodoacetyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranosyl)-(1→4)-4,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (7b). Pentenyl glycoside **8b**[8] and dibromide acceptor **6b** were coupled using procedure A to afford **30b** (455.0 mg, 63%) as a yellow foam. R_F 0.49 (85:15 petroleum

ether / ethyl acetate); FAB(MS) 1540.1 M^-. Compound **30b** (450.0 mg, 0.292 mmol) was immediately treated as above in the preparation of **7a** to give **7b** as a pale yellow amorphous powder (371.1 mg, 92%); R_F 0.44 (85:15 petroleum ether / ethyl acetate); $[\alpha]^{21}_D$ +43.1° (*c* 0.98, $CHCl_3$); ^1H NMR (400 MHz) δ 7.17-7.35 (m, 10H, Ph), 6.67-7.03 (m, 10H, Ph), 5.59 (m, 1H, $OCH_2CH_2CH_2C\underline{H}=CH_2$), 5.38 (d, *J* = 8.2 Hz, 1H), 5.19 (t, *J* = 9.3 Hz, 1H), 4.70-4.90 (m, 5H), 4.30-4.55 (m, 7H), 4.09-4.24 (m, 3H), 4.02 (t, *J* = 9.5 Hz, 2H), 3.53-3.62 (m, 3H), 3.21-3.43 (m, 3H), 1.82 (m, 2H, $OCH_2CH_2C\underline{H}_2CH=CH_2$), 1.43 (m, 2H, $OCH_2C\underline{H}_2CH_2CH=CH_2$); ^{13}C NMR (100 MHz) δ 167.33 (C=O IAc), 163.79 (C=O TCP), 162.57 (C=O TCP), 139.50, 139.05, 138.29, 137.94, 137.77, 137.69, 128.42, 128.21, 127.91, 127.92, 127.82, 127.73, 127.70, 127.47, 127.19, 126.99, 126.87, 126.45, 114.68 ($OCH_2CH_2CH_2CH=\underline{C}H_2$), 97.70 (C-1A), 97.13 (C-1B), 78.59, 77.81, 76.86, 75.31, 75.26, 74.57, 74.02, 73.53, 73.06, 72.87, 69.04, 68.50, 68.06, 56.94, 56.27, 29.78 ($OCH_2CH_2\underline{C}H_2CH=CH_2$), 28.38 ($OCH_2\underline{C}H_2CH_2CH=CH_2$); HRMS (FAB) *m/e* calcd for $C_{63}H_{54}N_2O_{14}Cl_8I$ MH^+: 1469.0128, Found 1469.0101.

Pent-4-enyl 3,6-Di-*O*-benzyl-2-deoxy-2-formamido-β-D-glucopyranoside (32). To acetic anhydride (0.362 mL, 3.841 mmol) was added formic acid (0.186 mL, 4.727 mmol) at 25 °C. The reaction mixture was heated to 55 °C for 2.2 h and then allowed to cool to 25 °C before addition of pent-4-enyl 2-amino-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside **31** (0.525 g, 1.231 mmol) in THF (2.1 mL). The reaction stirred 70 min before being quenched with MeOH (1 mL) and then concentrated *in vacuo*. The residue was diluted with CH_2Cl_2 (100 mL) and washed with sat aq $NaHCO_3$ (25 mL) back extracting the aqueous portion with CH_2Cl_2 (2×15 mL). The reaction mixture was concentrated, and the residue was purified by flash chromatography eluting with 4:96 $MeOH/CH_2Cl_2$. Compound **32** was recovered as an amorphous solid (0.499 g, 89%); R_f 0.25 (5:95 $MeOH/CH_2Cl_2$); ^1H NMR (400 MHz, $CDCl_3$) δ Rotomeric Mixture (25 °C), 8.00-8.04 (m, 1H, H-C(=O)NH), 7.22-7.38 (m, 10H, Ph), 6.47 (d, *J* = 8.2 Hz, 1H, H-C(=O)NH), 5.72-5.84 (m, 1H, $OCH_2CH_2CH_2C\underline{H}=CH_2$), 4.94-5.07 (m, 2H, $OCH_2CH_2CH_2CH=C\underline{H}_2$), 4.52-4.83 (m, 4H), 4.07 (d, *J* = 8.2 Hz, 1H, H-1), 3.60-3.88 (m, 5H), 3.34-3.50 (m, 3H), 3.21 (dd, J=9.6, 18.2 Hz, 1H), 2.04-2.12 (m, 2H, $OCH_2CH_2C\underline{H}_2CH=CH_2$), 1.68-1.70 (m, 2H, $OCH_2C\underline{H}_2CH_2CH=CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ Rotomeric Mixture (25 °C), 166.33(C=O Formyl), 161.54 (C=O Formyl), 138.13, 137.74, 137.69, 137.62, 137.58, 128.28, 128.27, 128.18, 128.15, 127.92, 127.76, 127.67, 127.60, 127.51, 127.45, 127.41, 114.84 ($OCH_2CH_2CH_2CH=CH_2$), 114.67 ($OCH_2CH_2CH_2CH=\underline{C}H_2$), 100.78 (C-1), 99.90 (C-1), 81.55, 80.70, 74.35, 74.25, 74.06, 73.35, 71.62, 69.97, 69.70, 68.94, 68.52, 57.88, 54.66, 29.70

($OCH_2CH_2\underline{C}H_2CH=CH_2$), 28.44 ($OCH_2\underline{C}H_2CH_2CH=CH_2$), 28.38 ($OCH_2\underline{C}H_2CH_2CH=CH_2$); MS (FAB) *m/e* 456.2 MH^+.

Pent-4-enyl 2-Amino-3,6-di-*O*-benzyl-2-deoxy-2-*N*-methyl-β-D-glucopyranoside (33). To pent-4-enyl 3,6-di-*O*-benzyl-2-deoxy-2-formamido-β-D-glucopyranoside **32** (61.0 mg, 0.1339 mmol) in THF (1.6 mL) was added LAH in THF (0.60 mL, 0.60 mmol). The reaction was heated to reflux for 3.5 h and then cooled to 25 °C before quenching with Na_2SO_4 sat aq (0.5 mL). The slurry was filtered through celite and the solution was concentrated *in vacuo*. and the residue was purified by flash chromatography eluting with 5:95 $MeOH/CH_2Cl_2$. Compound **33** was recovered as a film (59.0 mg, 100%); R_f 0.25 (5:95 $MeOH/CH_2Cl_2$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.39 (m, 10H, Ph), 5.72-5.86 (m, 1H, $OCH_2CH_2CH_2C\underline{H}=CH_2$), 4.90-5.04 (m, 3H, $OCH_2CH_2CH_2CH=C\underline{H}_2$, C<u>H</u>HPh), 4.73 (d, J=11.6 Hz, 1H, CH<u>H</u>Ph), 4.58 (dd, J=11.2, 19.9 Hz, 2H, $C\underline{H}_2Ph$), 4.23 (d, J=7.9 Hz, 1H, H-1), 3.84-3.92 (m, 1H), 3.70-3.78 (m, 4H), 3.40-3.52 (m, 2H), 3.34 (dd, J=8.9, 9.5 Hz, 1H, H-3), 2.49 (s, 3H, NMe), 2.44 (dd, J=7.9, 10.0 Hz, 1H, H-2), 2.08-2.16 (m, 2H, $OCH_2CH_2C\underline{H}_2CH=CH_2$), 1.68-1.75 (m, 2H, $OCH_2C\underline{H}_2CH_2CH=CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.43, 138.03, 137.56, 128.55, 128.43, 127.86, 127.85, 127.82, 127.72, 114.78 ($OCH_2CH_2CH_2CH=\underline{C}H_2$), 104.42 (C-1), 83.09, 74.03, 73.72, 73.50, 73.40, 71.06, 69.10, 63.97, 36.27 (NMe), 30.20 ($OCH_2CH_2\underline{C}H_2CH=CH_2$), 28.85 ($OCH_2\underline{C}H_2CH_2CH=CH_2$); HRMS(FAB) *m/e* calcd for $C_{26}H_{36}NO_5$ (MH^+): 442.2593, Found 442.2609.

Pent-4-enyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-hexadecanamido-2-*N*-methyl-β-D-glucopyranoside (34) Pent-4-enyl 2-amino-3,6-di-*O*-benzyl-2-deoxy-2-*N*-methyl-β-D-glucopyranoside **33** (103.0 mg, 0.2333 mmol) in CH_3CN (2 mL) and DMF (2 mL) was added to palmitic acid (179.0 mg, 0.698 mmol) pretreated with both triethylamine (0.33 mL, 2.33 mmol) for 15 min and then 2-chloro-*N*-methylpyridinium iodide (179.0 mg, 0.701 mmol) in CH_3CN (2 mL) and DMF (1 mL) for 15 min at 40 °C. The reaction stirred 3 h at 45 °C and was then concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (100 mL) and washed with sat aq $NaHCO_3$ (25 mL) back extracting the aqueous portion with CH_2Cl_2 (2×15 mL). The reaction mixture was concentrated, and the residue was purified by flash chromatography eluting with a gradient of 5% MeOH/ CH_2Cl_2. To this residue in DMF (2 mL) was added Bu_4NI (8.6 mg, 0.0233 mmol), benzyl bromide (55.0 μL, 0.4664 mmol) and NaH (60% activity, 23.0 mg, 0.583 mmol). The reaction stirred 2 h before being quenched with AcOH (4 drops) and concentrated *in vacuo*. The residue was purified by flash chromatography eluting with 5:95 $EtOAc/CH_2Cl_2$ affording **34** (0.118 g, 66%); R_f 0.77 (5:95 $EtOAc/CH_2Cl_2$); ^1H NMR (400 MHz, $CDCl_3$) δ Rotomeric Mixture

(25 °C), 7.18-7.34 (m, 15H, Ph), 5.73-5.81 (m, 1H, $OCH_2CH_2CH_2C\underline{H}=CH_2$), 5.31 (bs, 1H), 4.43-5.02 (m, 9H), 3.41-3.93 (m, 7H), 3.04 (s, 1H), 2.76 (s, 2H), 2.38-2.48 (m, 1H), 2.10-2.18 (m, 4H), 1.52-1.70 (m, 4H), 1.18-1.34 (m, 24H, Fatty CH_2), 0.84-0.92 (m, 3H, H-16'); ^{13}C NMR (100 MHz, $CDCl_3$) δ Rotomeric Mixture (25 °C), 174.80 (C=O NAcyl), 173.51 (C=O NAcyl), 138.18, 137.99, 137.83, 137.78, 137.71, 137.51, 128.37, 128.29, 128.24, 128.20, 128.04, 127.76, 127.73, 127.63, 127.50, 127.41, 114.97 ($OCH_2CH_2CH_2CH=\underline{C}H_2$), 114.67 ($OCH_2CH_2CH_2CH=\underline{C}H_2$), 99.55 (C-1), 99.18 (C-1), 79.88, 79.71, 78.81, 75.00, 74.90, 74.68, 74.47, 73.50, 73.30, 70.11, 69.09, 68.83, 68.49, 62.32, 41.04, 34.87, 33.34, 31.84, 30.01, 29.89, 29.62, 29.59, 29.45, 29.27, 28.82, 28.60, 27.85, 25.13, 24.74, 22.60, 14.05 (C-16'); MS (FAB) *m/e* 770.57 MH^+.

4,5-Dibromopentanyl (4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (39a). Pentenyl glycoside **37**[8] and dibromide acceptor **38**[8] were coupled using procedure A to give **39a** as a white foam (0.667 g, 56%); R_f 0.17 (20:80 EtOAc/ petroleum ether); $[\alpha]_D^{20}$ 53.4° (*c* 1.06, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.74-7.71 (m, 4H, Phth), 6.67-7.36 (m, 20H, Ph), 5.4 (d, J=8.3 Hz, 1H), 5.12 (t, J=9.1 Hz, 1H), 4.96 (d, J=8.3 Hz, 1H), 4.67 (dd, J=12.6, 37.9 Hz, 2H), 3.21-4.51 (m, 22H), 1.98 (s, 3H), 1.86-1.94 (m, 1H), 1.42-1.62 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.33 (C=O Ac), 167.70 (bs, C=O Phth), 163.47 (C=O TCP), 162.18 (C=O TCP), 139.45, 139.32, 138.17, 138.02, 137.85, 137.76, 133.60, 131.41, 129.28, 129.00, 128.17, 128.03, 127.72, 127.68, 127.60, 127.55, 127.37, 127.32, 127.23, 127.04, 126.72, 126.30, 123.11, 98.00 (C-1B), 97.91 (C-1B), 96.68 (C-1A), 77.67, 77.09, 76.26, 74.55, 74.46, 73.72, 73.35, 73.07, 72.91, 72.52, 69.04, 68.07, 67.93, 56.80, 55.28, 52.31, 52.26, 36.04, 32.62, 32.57, 26.75, 26.68, 20.74 (CH_3 OAc); MS (FAB) *m/e* 1368.2 M^-.

Anal. Calcd for $C_{63}H_{58}Br_2N_2O_{14}Cl4$: C, 55.28; H, 4.27; N, 2.05; found: C, 55.39; H, 4.32; N, 2.04.

Pent-4-enyl (4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (39b). Dibromide **39a** was treated as above in the preparation of **7a** to afford **39b** as a white foam (0.531 g, 93%); R_f 0.17 (20:80 EtOAc/ petroleum ether); $[\alpha]_D^{20}$ 33.0° (*c* 1.11, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.60-7.72 (m, 4H, Phth), 6.68-7.34 (m, 20H, Ph), 5.43-5.56 (m, 1H), 5.41 (d, J=8.2 Hz, 1H), 5.11 (t, J=8.8 Hz, 1H), 4.91 (d, J=8.2 Hz, 1H), 4.82 (d, J=12.3 Hz, 1H), 4.59-4.76 (m, 3H), 4.00-4.51 (m, 11H), 3.22-3.68 (m, 8H), 1.97 (s, 3H), 1.73-1.79 (m, 2H, $OCH_2CH_2C\underline{H}_2CH=CH_2$), 1.36-1.46 (m, 2H,

$OCH_2C\underline{H}_2CH_2CH{=}CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.30 (C=O Ac), 167.59 (bs, C=O Phth), 163.43 (C=O TCP), 162.16 (C=O TCP), 139.29, 138.19, 138.00, 137.87, 137.74, 137.47, 133.53, 131.38, 129.24, 128.96, 128.14, 127.97, 127.64, 127.57, 127.52, 127.29, 127.16, 127.01, 126.70, 126.29, 122.95, 114.41 ($OCH_2CH_2CH_2$-$CH{=}\underline{C}H_2$), 97.92 (C-1B), 96.66 (C-1A), 77.60, 77.09, 76.29, 74.51, 74.41, 73.64, 73.32, 73.03, 72.84, 72.49, 68.99, 68.28, 68.05, 56.78, 55.32, 29.54 (OCH_2CH_2-$\underline{C}H_2CH{=}CH_2$), 28.20 ($OCH_2\underline{C}H_2CH_2CH{=}CH_2$), 20.69 ($CH_3$ OAc); MS (FAB) *m/e* 1208.2 M^-.

Anal. Calcd for $C_{63}H_{58}N_2O_{14}Cl_4$: C, 62.59; H, 4.84; N, 2.32; found: C, 62.67; H, 4.84; N, 2.31.

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REFERENCES AND NOTES

1. See for example: (a) P. Lerouge, *Glycobiology*, **4**, 127 (1994). (b) C. H. R. Raetz, *Ann. Rev. Biochem.*, **59**, 129 (1990). (c) C. H. R. Raetz, *J. Bacteriology*, **175**, 5745 (1993).
2. (a) J. Denarie and J. Cullimore, *Cell*, **74**, 951 (1993). (b) J. P. Nap and T. Bisseling, *Science*, **250**, 948 (1990). (c) S. R. Long, *Cell*, **56**, 203 (1989).
3. For related synthetic efforts see: (a) K. C. Nicolaou, N. J. Bockovich, D. R. Carcanague, C. W. Hummel and L. F. Even, *J. Am. Chem. Soc.*, **114**, 8701 (1992). (b) L. X. Wang, C. Li, Q. W. Wang and Y. Z. Hui, *J. Chem. Soc., Perkin Trans. 1*, 621 (1994). (c) D. Tailler, J. C. Jacquinet and J. M. Beau, *J. Chem. Soc., Chem. Commun.*, 1827 (1994). (d) S. Ikeshita, A. Sakamoto, Y. Nakahara, Y. Nakahar and T. Ogawa, *Tetrahedron Lett.*, **35**, 3123 (1994). (e) S. Ikeshita, Y. Nakahar, and T. Ogawa, *Glycoconjugate J.*, **11**, 257 (1994).
4. (a) J. S. Debenham, R. Madsen, C. Roberts and B. Fraser-Reid, *J. Am. Chem. Soc.*, **117**, 3302 (1995). (b) J. S. Debenham and B. Fraser-Reid, *J. Org. Chem.*, **61**, 432 (1996).
5. (a) J. C. Castro-Palomino and R. R. Schmidt, *Tetrahedron Lett.*, **36**, 5343 (1995). (b) P. Stangier and O. Hindsgaul, *Synlett*, **179** (1996). (c) B. A. Roe, C. G. Boojamra, J. L. Griggs, and C. R. Bertozzi, *J. Org. Chem.*, **61**, 6442 (1996).
6. J. S. Debenham, R. Rodebaugh and B. Fraser-Reid, *J. Org. Chem.*, **61**, 6478 (1996).
7. a) B. Fraser-Reid, U. E. Udodong, Z. Wu, H. Ottosson, J. R. Merritt, C. S. Rao, C. Roberts, R. Madsen, *Synlett*, 927 (1992). b) R. Madsen, B. Fraser-Reid. In *Modern Methods in Carbohydrate Synthesis*, S. H. Khan, R. A. O'Neill, Eds, Harwood Academic Publishers: Amsterdam, 155 (1996).
8. J. S. Debenham, S. D. Debenham and B. Fraser-Reid, *Bioorg. Med. Chem.*, **4**, 1909 (1996).
9. (a) M. Imoto, H. Yoshimura, M. Yamamoto, T. Shimamoto, N. Skakguchi, S. Jusumoto and T. Shiba, *Bull Chem. Soc. Jpn.*, **60**, 2197 (1987). (b) R. I. El-

Sokkary, B. A. Silwanis, M. A. Nashed, H. Paulsen, *Carbohydr. Res.*, **203**, 319 (1990).
10. Low yield in the coupling reaction may have also been due to the poor solubility of the acceptor. However, improvements in the yield were not realized with other solvent systems such as $CHCl_3$ and DMF / CH_2Cl_2.
11. T. Ogawa and S. Nakabayashi,*Carbohydr. Res.*,**97**, 81 (1981).
12. H. P. Wessel, T. Iverson and D. R. Bundle, *J. Chem. Soc., Perkin Trans. 1*, 2247 (1985).
13. J. S. Debenham, Ph.D. Dissertation, Duke University, 1997.
14. J. S. Debenham, R. Rodebaugh and B. Fraser-Reid, *J. Org. Chem.*, **62**, 4591, (1997).
15. H. Paulsen, *Angew. Chem. Int. Eng. Ed.*, **21**, 155 (1982).
16. R. Rodebaugh, Ph.D. Dissertation, Duke University, 1997.
17. H. M. Zuurmond, S. van der Lann, G. A. van der Marel and J. H. van Boom, *Carbohydr. Res.*, **215**, c1 (1991).
18. (a) P. J. Garegg and H. Hultberg, *Carbohydr. Res.*, **93**, c10 (1981). (b) P. J. Garegg, H. Hultberg and S. Wallen, *Carbohydr. Res.*, **108**, 97 (1982).
19. Further lowering of the reaction temperature was not advantageous.
20. See also refs. 6 and 14 for additional examples of low temperature coupling reactions involving pentenyl glycosides.
21. For studies on halogenation of olefins with copper (II) halides see: W. C. Baird, J. H. Surridge and M. Buza, *J. Org. Chem.*, **36**, 3324 (1971).
22. Additional studies and mechanistic rationale of this dibromination reaction will be published in due course.
23. Note: Yield has not been optimized.
24. J. R. Merritt, J. S. Debenham and B. Fraser-Reid, *J. Carbohydr. Chem.*, **15**, 65 (1996).
25. C.A.A. van Boeckel and T. Beetz, *Tetrahedron Lett.*, **24**, 3775 (1983).
26. S. Krishnamurthy, *Tetrahedron Lett.*, **23**, 3315 (1982).
27. J. K. Sutherland and P. A. Widdowson, *J. Chem. Soc.*, 4650 (1964). See also ref 3a.
28. R. Madsen and B. Fraser-Reid. Unpublished results.