ポリラクトサミン糖鎖の合成研究

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Synthetic Study of Polylactosamine Oligosaccharides

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CONTENTS

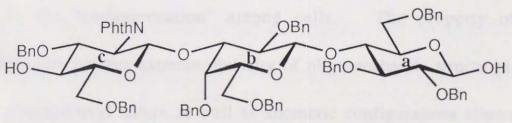
ABBREVIATIONS

Ac	acetyl
All	allyl
Bn	benzyl
BTIB	bis(trifluoroacetoxy)iodobenene
Bz	benzoyl
CAN	ceric ammonium nitrate (ammonium cerium(IV) nitrate)
Cbz	benzyloxycarbonyl (carbobenzoxy)
COD	1,5-cyclooctadiene
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCPhth	4,5-dichlorophthaloyl
DMF	dimethylformamide
Et	ethyl
Lev	levulinoyl
Me	methyl
NIS	*N*-iodosuccinimide
PEG	polyethyleneglycol
Ph	phenyl
Phth	phthaloyl
Piv	pivaloyl
Py	pyridine
TBDPS	*tert*-butyldiphenylsilyl

TCP	3,4,5,6-tetrachlorophthaloyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TMS	trimethylsilyl

Suger moieties in oligosaccharide were named a,b,c... from the reducing end.

for example;



GENERAL INTRODUCTION

Oligosaccharide structures in glycopeptides and glycolipids have gained much attention because of their variety of bioactivities.[1] Sugar chains expressed on the cell surface serve as the molecules which are used in the "communication" among cells. The property of carbohydrates enables extreme diversity of oligosaccharide structures. Their polyhydroxyl nature as well as anomeric configurations allows numerous combinations of structures to be formed. This makes oligosaccharides ideal candidates for the informative molecule. Also, this makes oligosaccharides great challenging synthetic targets. The efficient preparation of oligosaccharides, as well as their elaboration into glycopeptides and glycolipids, is central importance for the application of these compounds in biological science and medicine. Moreover oligosaccharides with strictly defined structures would be materials of great use to biochemists, especially in the study of enzyme mechanisms. In the early synthetic carbohydrate research, a great deal

of efforts has been spent to seek new glycosylation methods to suite oligosaccharide synthesis. We now have a wide range of reliable glycosylation methods and have come far being able to synthesize and supply some complex and structurally defined oligosaccharides for the evaluation of their roles in detail. Also because of the polyfunctional nature of sugar molecules, laborious protecting group manipulations are required to start synthesis of oligosaccharides. Stereocontrolled glycosylation reactions then have to be performed. However, during these manipulations, column chromatographic purification is usually required after each step to obtain pure compounds. Each of these techniques has been studied, but we also cannot say we have almighty ways. So investigation of these techniques is still important.

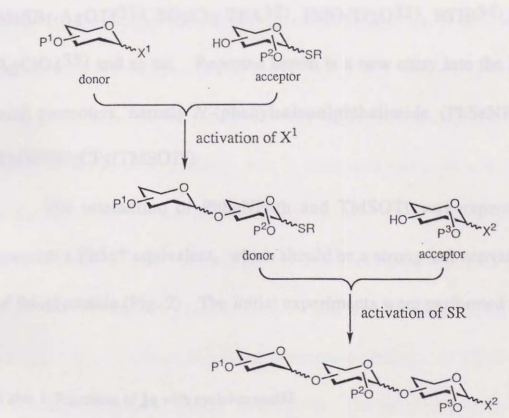
To address these problems, three topics about carbohydrate chemistry have been focused in this study and shown herein. In chapter 1, investigation of a new promoter of thioglycosides is described. It is now well known that thioalkyl groups can behave as a protecting group at the *C*-1 position of sugars and directly be activated to a glycosylation

donor. It was shown that even without neighboring participation at *C*-2, reaction proceeded in non-polar solvents to afford the β-glycoside selectively. In chapter 2, a new amino protecting group, namely 4,5-dichlorophthaloyl group (DCPhth) was designed and introduced. Also it was shown that this protecting group could be used to introduce a 1,2-*trans* glycosyl bond. Furthermore, the deprotection of the DCPhth group was proved to be easier than that of phthaloyl groups (Phth) which is used popularly. In chapter 3, a study of the polymer support synthesis of polylactosamine oligosaccharides described by avoiding step-by-step column chromatographic purification was described. Herein the glycosyl acceptor was attached onto resin at *C*-1 position. As a result simple washing of the resin becomes the only work-up procedure for purification of glycosylation products attached on the polymer.

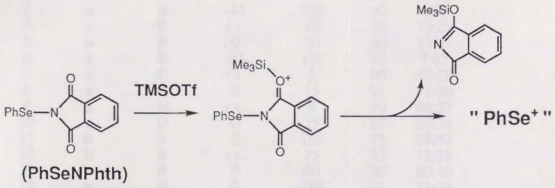
Chapter 1.

PhSeNPhth-TMSOTf as a Promoter of Thioglycosides

The use of thioglycosides as a glycosyl donor has been a subject of extensive investigations in the past decade.[2] Thioglycoside-based strategy is an especially attractive choice for complex oligosaccharide synthesis due to its orthogonal[3] nature with a variety of protecting groups and compatibility with heavy metal- or Lewis acid-catalyzed glycosylation. This feature of thioglycosides allows simplified synthesis of oligosaccharides.[4-22] This is due to the fact that thioglycosides can be activated under alkylating or oxidative conditions but are stable under the traditional glycosylation conditions such as Königs-Knorr methods,[23] so that halides can be chemoselectively activated while the thioglycosides behave as a glycosyl acceptor.(Fig. 1) In addition, it is now well-recognized that the thioglycoside is easily activated to serve as a powerful glycosylating agent once exposed to the action of certain promoters, i.e.) MeOTf[24], NIS-TfOH[25], $MeSS^{+}Me_2 \cdot TfO^{-}$[26], PhSeCl-AgOTf[27-28], $CuBr_2$-*n*-Bu_4NBr-AgOTf[29], PhHgOTf[30],



<Fig. 1> Thioglycoside as an acceptor and a donor



<Fig. 2> Activator species of thioglycoside

MeSBr-AgOTf[31], SO_2Cl_2-TFA[32], PhIO-Tf_2O[33], BTIB[34],NBS-$AgClO_4$[35] and so on. Reported herein is a new entry into the list of such promoters, namely *N*-(phenylseleno)phthalimide (PhSeNPhth)–$TMSOSO_2CF_3$(TMSOTf).

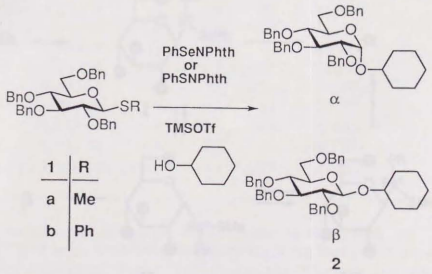
The interaction of PhSeNPhth and TMSOTf was expected to generate a $PhSe^+$ equivalent, which should be a strong soft activator[28] of thioglycoside.(Fig. 2) The initial experiments were performed by

Table 1 Reactions of **1a** with cyclohexanol[a]

entry	promoter[b]	solvent[c]	temp./°C	time/min.	yield[d]/%	α:β[e]
1	**a**	**A**	r.t.	10	83	78:22
2	**a**	**A**	0	30	95	37:62
3	**a**	**A**	-45	120	90	8:92
4	**a**	**B**	r.t.	10	90	73:27
5	**a**	**B**	0	30	90	53:47
6	**a**	**B**	-45	150	93	7:93
7	**a**	**C**	r.t.	5	90	62:38
8	**a**	**C**	0	15	91	71:29
9	**a**	**D**	r.t.	5	90	68:32
10	**a**	**D**	0	15	87	65:35
11	**b**	**A**	0	150	93	68:32
12	**b**	**B**	r.t.	25	93	72:28
13	**b**	**B**	0	60	90	60:40
14	**b**	**D**	0	180	91	71:29

[a]1.4 equiv. of cyclohexanol was used. Reactions were performed in the presence of molecular sieves AW-300. [b]**a**: PhSeNPhth(1.3 equiv.) - TMSOTf(1.0 equiv.). **b**: PhSNPhth was used in place of PhSeNPhth. [c]**A**: toluene, **B**: CH_2Cl_2, **C**: ether, **D**: acetonitrile. [d]Calculated based on **1a**. [e]Determined by HPLC.

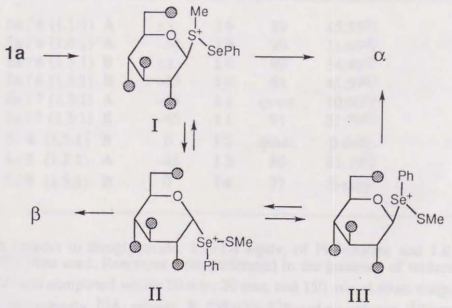
using methylthioglycoside **1a**[36] and cyclohexanol as a glycosyl donor and an acceptor (aglycon), respectively.(Fig. 3) As summarized in Table 1, the reaction proceeded smoothly to give the product **2** in a high yield. Somewhat surprisingly, both in ether and acetonitrile, a similar degree of selectivity was observed.(entry 7-10) This observation is in sharp contrast to numerous reports[37] on α– and β–directing nature of ether and acetonitrile, respectively. On the other hand, in non-participating media such as toluene or dichloromethane, the effect of the temperature is quite prominent.(entry 1–6) The selectivity (α:β = 3:1) observed at room temperature was completely reversed (α:β = 1:>10) at



<Fig. 3> Glycosylation with thioglycoside and cyclohexanol

–45°C. Since anomerically pure β–thioglycoside was used, the reaction at low temperature proceeded mainly with retention of the configuration. This result may be explained by assuming the formation of selenonium species (**II**, **III** in Fig. 4), which could be formed *via* the rearrangement (either intra– or intermolecularly) of initially formed **I**. Due to reverse anomeric effect,[38] **II** is expected to be more reactive than β–directed (and probably more abundant) **I** or **III**. Therefore, the reaction is most likely to proceed mainly *via* **I** and **III**, at room temperature and *via* **II** at lower temperature, respectively.(Fig. 4)

Several comments on additional experiments are relevant at this



<Fig. 4> Assumed reaction pathway

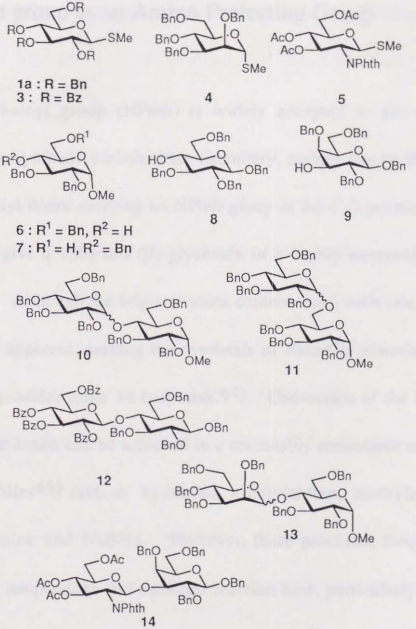
stage. First, the phenylthio (PhS) group was proved less effective than MeS as a leaving group and the reaction using **1b**[39] required longer time (24 h at room temperature) to give lower yield (67%) of the product.(α:β = 69:31) Second, as a closely related system, PhSNPhth-TMSOTf was examined.(Table 1, entries 11-14) This combination seems to be less potent than PhSeNPhth-TMSOTf and the reaction proceeded only at the temperature over 0°C. A moderate level of α-selectivity was observed in all entries.

Table 2 Synthesis of disaccharides[a)]

entry	donor/aglycon (ratio)	solvent[b)]	temp./°C	product	yield[c)]/%	α:β
1	**1a / 6** (1.1:1)	**A**	r.t.	**10**	89	45:55[d)]
2	**1a / 6** (1.4:1)	**A**	–45	**10**	99	31:69[d)]
3	**1a / 6** (1.3:1)	**B**	r.t.	**10**	99	54:46[d)]
4	**1a / 6** (1.3:1)	**B**	–45	**10**	94	41:59[d)]
5	**1a / 7** (1.3:1)	**A**	–45	**11**	quant.	10:90[d)]
6	**1a / 7** (1.3:1)	**B**	–45	**11**	91	21:79[d)]
7	**3 / 8** (1.3:1)	**B**	0	**12**	quant.	β-only
8	**4 / 6** (1.2:1)	**A**	–45	**13**	80	81:19[e)]
9	**5 / 9** (1.5:1)	**B**	0	**14**	77	β-only

[a)]With respect to thioglycoside, 1.2–1.4 equiv. of PhSeNPhth and 1.0 equiv. of TMSOTf were used. Reactions were performed in the presence of molecular sieves AW-300 and completed within 10 min, 20 min, and 150 min at room temp., 0°C, and –45°C, respectively. [b)]**A**: toluene, **B**: CH_2Cl_2. [c)]Based on aglycon. [d)]Determined by ^{1}H-NMR. [e)]Determined by separation of individual isomers.

Having established the utility of PhSeNPhth-TMSOTf as a promoter of thioglycoside, investigation of the reaction by using several combinations of thioglycoside and sugar-derived aglycon was then carried out.(Table 2, Fig. 5) A similar trend was observed as Table 1. All reactions proceeded in a high yield and synthetically useful level of β-selectivity was obtained when the reaction of **1a** was performed at -45°C.(entries 2,5,6) Although 1,2-*trans* glycosides are easily obtainable by taking advantage of a 2-*O*-acyl substituent, ether-type protection quite often simplifies and affords more flexibility on the synthetic route toward large oligosaccharides.[40] On the other hand, thiomannoside **4** afforded the α-glycoside predominantly.(entry 8) This result showed that in the case of the mannose type donor, the reaction proceeded *via* **I** or **III** by some reasons. As we expected, acyl-protected **3**[41] and 2-phthalimido **5**[42] thioglycosides gave 1,2-*trans* products selectively as we had expected.(entries 7 and 9)



<Fig. 5> Structures of donors, sugar-derived aglycon and produced diasaccharide products in Table 2

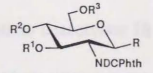
Chapter 2.

DCPhth group as an Amino Protecting Group

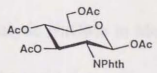
N-phthaloyl group (NPhth) is widely accepted as the amino protection in synthetic carbohydrate chemistry, mainly due to the fact that a glycosyl donor carrying an NPhth group at the *C*-2 position will predictably give a 1,2-*trans* (β)-glycoside in a highly stereoselective manner.[43] Although the origin remains controversial, such selectivity is generally apparent, making the synthesis of naturally abundant 2-amino-β-glycosides quite an easy task.[44] Conversion of the NPhth group into an amine can be achieved in a reasonably convenient manner by nucleophiles[45] such as hydrazine, *n*-butylamine, methylamine, ethylenediamine and $NaBH_4$. However, these processes frequently require high temperature and extended reaction time, particularly when applied to a large oligosaccharide carrying multiple Phth groups. As a result, the course of dephthaloylation is often difficult to monitor the reaction course, and extensive trial-and-error efforts are required to find the most favorable conditions for each specific substrate. To

address this problem, the use of Phth analogues having substituents such as electron-withdrawing groups on the aromatic ring has recently been proposed by Tsubouchi *et al.* (4-nitro-)[46] and Debenham *et al.* (tetrachloro-)[47-48] The use of 4,4',4"-tris(4,5-dichlorophthalimido) trityl group as a hydrazine-labile protecting group in nucleotide chemistry has also been reported by Sekine and Hata.[49] In connection with the synthetic studies of polylactosamine-type glycoconjugates,[50] disclosed here are the results of our efforts to develop a 4,5-dichlorophthaloyl (DCPhth) group in oligosaccharide synthesis. DCPhth has as strong 1,2-*trans*-directing nature as Phth, yet is easily removable under substantially milder conditions. Although the DCPhth group can be expected to be more stable than its tetrachloro counterpart,[47] further comparisons are necessary in use of these protecting groups in the course of complex oligosaccharide synthesis.

To test the nature of the DCPhth group (Fig. 6), tetraacetate **15** was synthesized from glucosamine hydrochloride, in an analogous manner to that described for Phth derivative **16**,[43] by using 4,5-dichlorophthalic anhydride. The anomeric position could be smoothly



	R	R^1	R^2	R^3
15	Ac	Ac	Ac	Ac
17	Br (α, β)	Ac	Ac	Ac
18	SMe	Ac	Ac	Ac
19	SMe	H	H	H
21	SMe	Bn	H	Bn



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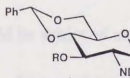
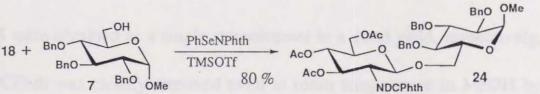
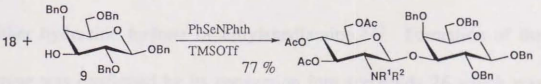


	R
20	H
22	Bn
23	Lev

15→17: HBr/AcOH, AcOH, Ac_2O, r.t., 2 d, α 30 %, β 44 %; **15→18**: *n*-Bu_3SnSMe, $SnCl_4$, $ClCH_2CH_2Cl$, 0°C~r.t., 1 n, 83 %; **18→19**: conc. HCl, MeOH, 70°C, 3.5 h, 95 %; **19→20**: $C_6H_5CH(OCH_3)_2$, Camphorsulfonic acid, CH_3CN, r.t., 1 d, 73 %; **20→22**: BnBr, NaH, DMF, 0°C~r.t., 4 h, 84 %; **22→21**: $NaCNBH_3$, HCl/ether, THF, 4A MS, r.t., 3h, 68 %; **20→23**: Lev_2O, Py., CH_2Cl_2, r.t., 1 n, 95 %; **23→20**: $H_2NNH_2 \cdot H_2O$, Py., AcOH, r.t., 5 min, quant.





Method 1: $H_2NCH_2CH_2NH_2$, MeOH, r.t., 2 h, then Ac_2O, Py., r.t., 5 h, 98 %
Method 2: $H_2NNH_2 \cdot H_2O$, MeOH r.t., 1 d, then Ac_2O, Py., r.t., 5 h, 94 %

	R^1R^2
25	DCPhth
26	Ac,H

<Fig. 6> Study of 4,5-dichlorophthaloyl group

converted into a bromide (**17**) and thioglycoside (**18**). Although attempts to deacetylate **18** by using catalytic NaOMe in MeOH at room temperature were not successful due to rapid destruction of DCPhth, triol **19** was obtained quite cleanly under acidic conditions.(HCl, MeOH, 70°C, 3.5h) Further transformation into 4,6-*O*-benzylidene (**20**), and into 3,6-di-*O*-benzyl (**21**) and 3-*O*-levulinoyl (**23**) derivatives could be achieved under standard conditions without any problems.

Glycosylation of **7** or **9** by using **18** as a glycosyl donor was performed under aforementioned conditions (PhSeNPhth-TMSOTf).(See Chapter 1.)[51] As expected, coupled products **24** and **25** were obtained as a single stereoisomer in a good yield, respectively. DCPhth was cleanly removed even at room temperature in MeOH by either hydrazine hydrate or ethylenediamine.[52] Formation of the amine was confirmed by its conversion into acetamide **26** which was isolated in a >90% yield.

Moreover it was also found that DCPhth was stable under the conditions required to remove a levulinoyl-protecting group.[53] Namely, compound **23** was quantitatively converted into **20** by brief

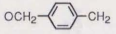
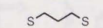
treatment with hydrazine in pyridine-acetic acid at room temperature for 5 min.

Chapter 3.

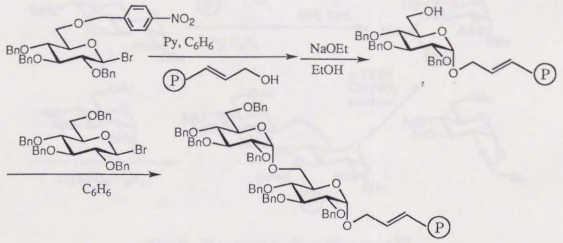
Polymer Support Synthesis of Polylactosamine Oligosaccharides

In 1963, Merrifield[54] first reported a new approach to the chemical synthesis of polypeptide; a polymer support synthesis using polystyrene resin. The use of insoluble functionalized polymer support has been extensively studied for the syntheses of polypeptides[55-60] and polynucleotides.[61-65] The main advantage of the solid-phase method is that once the growing molecules is firmly attached to a completely insoluble resin, purification can be effected at each intermediate step only by filtering and washing. Furthermore, reaction rates can be increased by using a large excess of reagent which can be easily separated after the reaction has completed. Now, polymer support syntheses of polypeptides and polynucleotides are practically used as an automatic synthesizer.

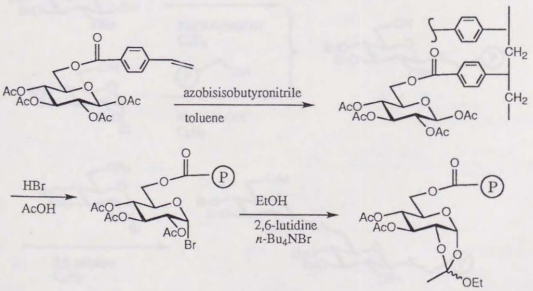
<Table 3> Past researches of chemical glycosylation on polymer[66-75]

Entry	Polymer[a]	Type[b]	Linker	Introduced compounds	Cutting way	Synthesized compound
1[66]	S	A		Glucose bromide	O_3	trisaccharide
2[67]	S	D	OCO	EtOH	not done	orthoester
3[68]	S	D	OCO	Glucosamine chloride or Glucosamine oxazoline	methanolysis	disaccharide
4[69]	S	A	SCH_2	Glucose bromide	MeI	disaccharide
5[70]	S	A		Glucose chloride (franose type)	methanolysis	pentasaccharide
6[71]	P	A		Glucosamine bromide and Galactose imidate	methanolysis or hydrazinolysis	disaccharide
7[72]	P	A		Mannose imidate and Galactose imidate	Raney Ni W-2	pentasaccharide and disaccharide
8[73]	S	D	$OSiPh_2$	Glycal *C*-6 position	TBAF, AcOH	tetrasaccharide
9[74]	S	A		Galactose sulfoxide	$Hg(OTf)_2$	trisaccharide
10[75]	S	A		Glucose imidate	DMTSB Hünig's base	pentasaccharide

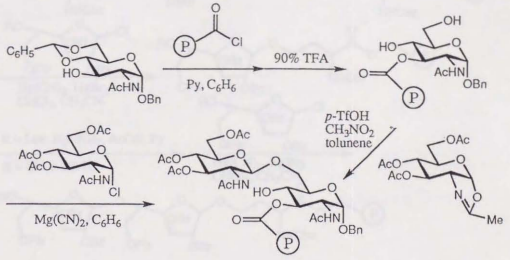
a) S: polystylene type, P: polyethylene glycol type. b) A: Attached suger on polymer is reducing end, that is, sugar on polymer is used as glycosyl acceptor, D: Attached sugar on polymer is non-reducing end, that is, sugar on polymer is used as glycosyl donor.



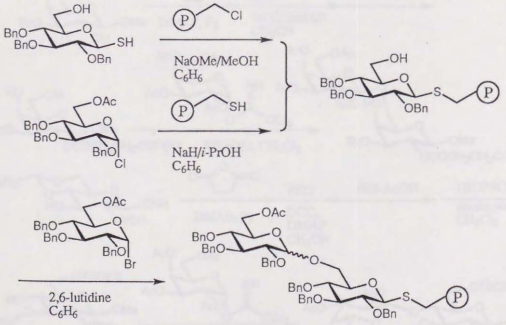
<Fig. 7> The report by Schuerch *et. al.*[66]



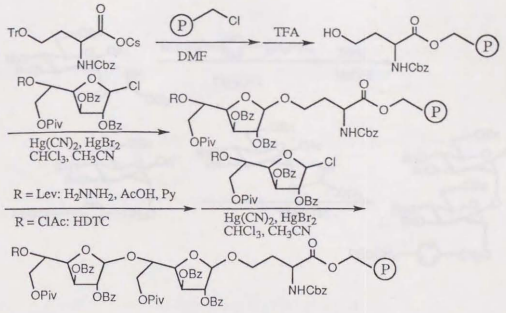
<Fig. 8> The report by Guthrie *et. al.*[67]



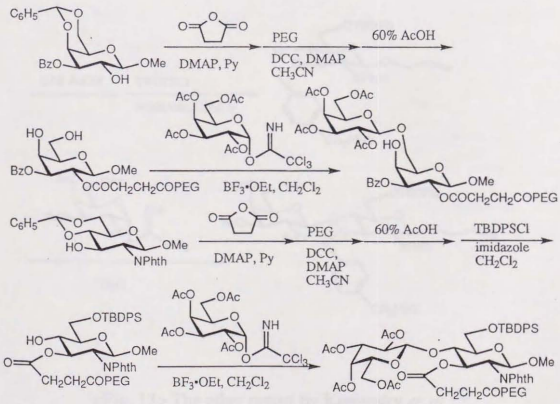
<Fig. 9> The report by Excoffier *et. al.*[68]



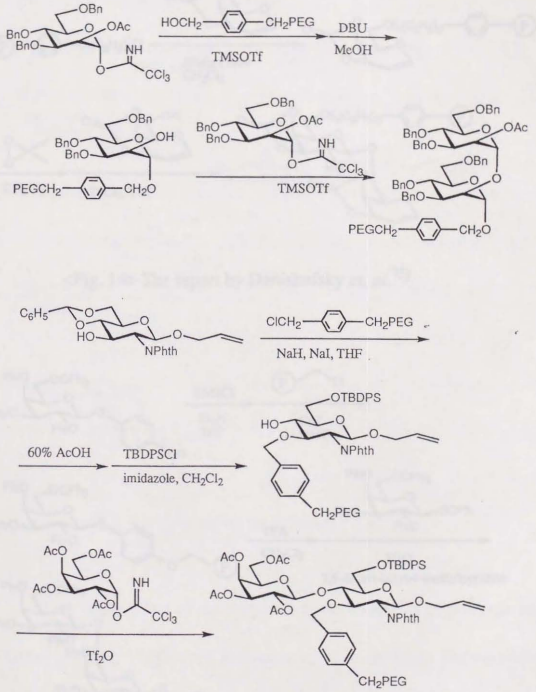
<Fig. 10> The report by Anderson *et. al.*[69]



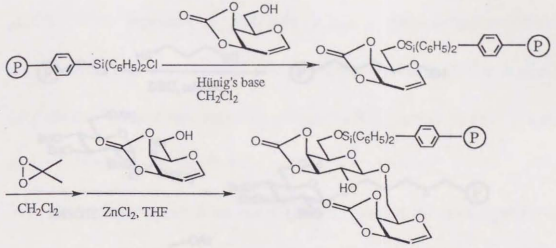
<Fig. 11> The report by van Boom *et. al.*[70]



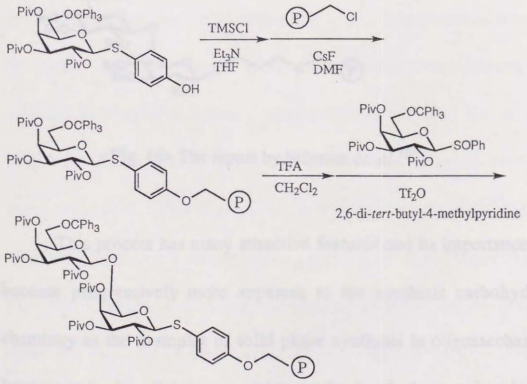
<Fig. 12> The report by Krepinsky *et. al.*[71]



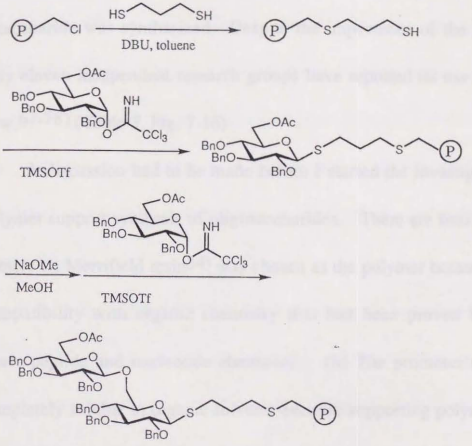
<Fig. 13> The other report by Krepinsky *et. al.*[72)]



<Fig. 14> The report by Danishefsky *et. al.*[73]



<Fig. 15> The report by Kahne *et. al.*[74]



<Fig. 16> The report by Schmidt *et. al.*[75]

This process has many attractive features and its importance has become progressively more apparent to the synthetic carbohydrate chemistry as the examples of solid phase synthesis in oligosaccharides have increased. Polymer support synthesis of oligosaccharide has gained conspicuous attention to address this issue. In 1971, Schurech *et*

al.[66] first reported a polymer support glycosylation where disaccharide was synthesized. Despite the importance of the method, only eleven independent research groups have reported its use up until now.[67-78] (Table 3, Fig. 7-16)

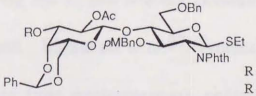
A discussion had to be made before I started the investigation of polymer support synthesis of oligosaccharides. There are four criteria, namely (i) Merrifield resin[54] was chosen as the polymer because of its compatibility with organic chemistry that had been proved by soild phase peptide and nucleotide chemistry. (ii) The promoter must be completely soluble in organic solvents because supporting polymer acts as solid in organic solvents. (iii) NPhth group was chosen as a neighboring participating group due to its strong nature to give 1,2-*trans* glycoside. This decision was also made in order to avoid any obstacle introducing a new protecting group such as DCPhth (Chapter 2). (iv) Trichloroacetimidate was selected as a leaving group to be activated by the Lewis acid chosen above (ii). Also, trichloroacetimidate is well recognized as one of the superior leaving groups in oligosaccharide synthesis.

In consideration of these criteria, I chose polylactosamine oligosaccharide as a synthetic target, because phthaloyl or dichlorophthaloyl group for the amino protecting group could be introduced β-glycosyl bond selectivitely(page 29, (iii)), and it is evident that synthesis and supply of polylactosamine oligosaccharides for biological studies have great importance, especially for the studies in the glycolipid field.

Poly-*N*-acetyllactosamine is a long chain oligosaccharide which could be subjected to various modifications and degradations generating many unique structures on cell surfaces. Poly-*N*-acetyllactosamine oligosaccharide was first recognized in the studies of *endo*-β-galactosidase [79-82] and Band-3 glycoprotein of human erythrocyte,[83-88] Recent researches have revealed that polylactosamine oligosaccharides are often found as a backbone of branched structure of the glycopetide,[85-86] in glycoprotein as a carrier of ABO determinant,[85-86] in Band-3 glycoprotein,[88] in lysosomal glycoproteins,[89] in I/i antigenic glycolipid,[90] and in mucin-type oligosaccharide.[91-92]

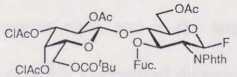
Synthetic approaches have been attempted to engage to the biological significance. Synthesis of oligosaccharide having poly-*N*-acetyllactosamine was somewhat achieved in a traditional manner. Some examples about lactosamine block are shown in Fig. 17.

Norberg *et. al.* [91-92]

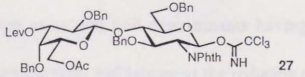


R = ClAc [92]
R = Bn [93]

Nicolaou *et. al.*[93]

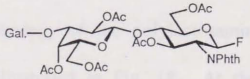


Nakano et. al.[96]

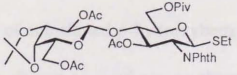


27

Matsuzaki *et. al.*[97]



Matta *et. al.* [98]

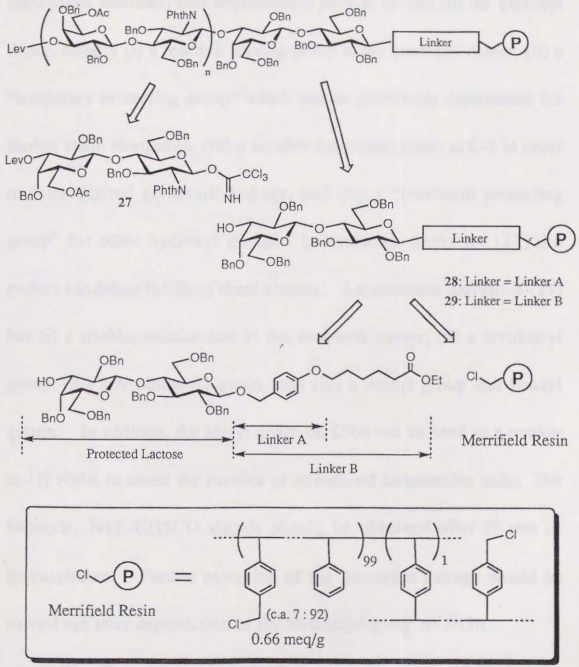


<Fig. 17> Examples of lactosamine derivatives

Norberg *et al.* reported the study of *N*-acetyllactosamine trimer (hexasaccharide)[93] and trifucosyl Le^y having three *N*-acetyllactosamine units.[94] Nicolaou *et al.*[95] reported the synthesis of trimeric Le^x. Nakano *et al.*[96] synthesized sulfated glucuronyl glycosphingolipids which are carbohydrate epitopes of neural cell-adhesion molecules having one or two *N*-acetyllactosamine units and lactose at the reducing end. Matsuzaki *et al.*[97] synthesized branched poly-*N*-acetyllactosamine type pentaantennary pentacosasaccharide which have nine lactosamine parts and is the largest synthesized oligosaccharide. Matta *et al.*[98] synthesized dimeric Le^x having two cyclic *N*-acetyllactosamine units and Le^a determinants having one or two cyclic *N*-acetyllactosamine units and lactose at the reducing end.

Our synthetic strategy of the polylactosamine molecule on polymer support is illustrated in Fig. 18. At the outset of the investigation, two types of substituted *p*-hydroxybenzyl glycosides of lactose derivatives were chosen as a primer on the polymer because poly-*N*-acetyllactosamine oligosaccharides in glycolipid have a lactose at their reducing end. Both the linker A and B would be cleaved off by

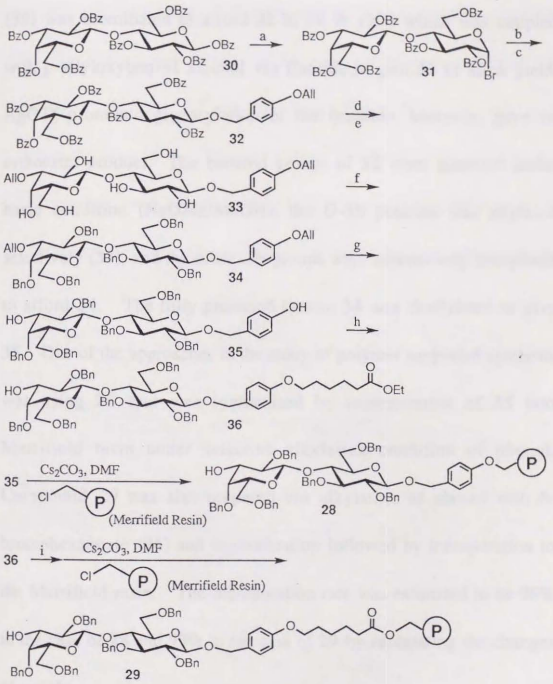
acid treatment or catalytic hydrogenation, and the linker B would alternatively be cleaved off by saponification.(Fig. 24)



<Fig.18> Synthetic strategy

LacNAc precursor (**27**) was chosen as a donor with suitable protections. In the synthetic approach to polylactosamine oligosaccharide by the solid-phase methods, four requirements have to be met for the glycosyl donor, namely (i) a reactive leaving group at the anomeric center, (ii) a "temporary protecting group" which can be selectively deprotected for further chain elongation, (iii) a suitable functional group at C-2 in order to form desired glycosidic linkage, and (iv) a "persistent protecting group" for other hydroxyl groups. Lactosamine derivative (**27**) is a perfect candidate fulfilling these criteria. Lactosamine derivative (**27**) has (i) a trichloroacetimidate at the anomeric center, (ii) a levulinoyl group, (iii) a *N*-phthaloyl group, and (iv) a acetyl group and benzyl groups. In addition, the acetyl group on C-6b can be used as a marker in ^{1}H NMR to count the number of introduced lactosamine units. For example, N+1 CH_3CO signals should be observed after N sets of glycosylation. Further extension of the glycoside linkage would be carried out after deprotection of the levulinoyl group on *O*-3b.

The first step was the introduction of acceptor lactose onto Merrifield resin through linkers.(Fig. 19) Octa-*O*-benzoyl-β-D-lactose



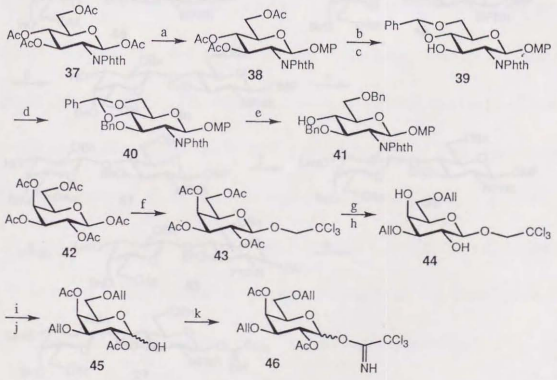
<Fig.19> Preparation of lactose unit on polymer

Reagents: a) HBr/AcOH, Ac_2O, $ClCH_2CH_2Cl$ (99%). b) ZnF_2, 2,2'-Dipyridyl, CH_3CN. c) *p*-$HOCH_2C_6H_4OAll$, AgOTf, $SnCl_2$, *s*-collidine, $ClCH_2CH_2Cl$, 4A MS (86%, 2 steps). d) NaOMe, phenolphthaleine, MeOH. e) 1) *n*-Bu_2SnO, toluene. 2) AllBr, *n*-Bu_4NBr (63%, 2 steps). f) BnBr, NaH, DMF (96%). g) 1) $Ir\{(COD)[PCH_3Ph_2]_2\}PF_6$, THF. 2) $HgCl_2$, HgO, Acetone, H_2O (88%). h) $Br(CH_2)_5COOEt$, Cs_2CO_3, DMF (92%). i) aq. NaOH, THF, EtOH

(**30**) was brominated to afford **31** in 99 % yield which was coupled with *p*-allyloxybenzyl alcohol *via* fluoride to give **32** in 86 % yield. AgOTf promoted glycosylation of the bromide, however, gave an orthoester product. The benzoyl groups of **32** were removed under basic condition (NaOMe/MeOH), the *O*-3b position was allylated selectively (**33**), and the other OH groups were successively benzylated to afford **34**. The fully protected lactose **34** was deallylated to give **35**. One of the approaches in the study of polymer supported synthesis was using **28** that was synthesized by incorporation of **35** into Merrifield resin under selective alkylation condition of phenol. Compound **29** was also prepared *via* alkylation of phenol with 6-bromohexanoate (**36**) and saponification followed by incorporation to the Merrifield resin. The incorporation rate was estimated to be 96% in the case of **28** and 99% in the case of **29** by calculating the changes of weight.

The lactosamine donor (**27**) was synthesized analogously to the method reported by Nakano *et al.*[96] as shown in Fig. 20 and 21. The anomeric position of **37** was protected by a *p*-methoxyphenyl group to

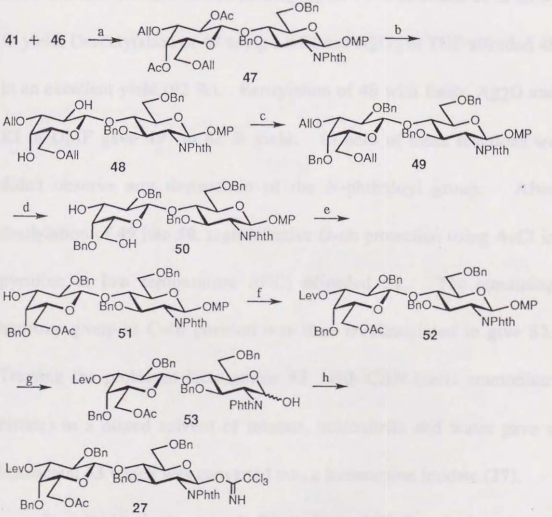
give **38**. Deacetylation of **38** followed by benzylidenation provided **39**. Hydroxy group at *O*-3 of **39** was benzylated to afford **40**. Reductive cleavage of the 4,6-benzylidene group of **40** with trifluoroacetic acid and triethyl silane[99] afforded **41** selectiviely, which was used as a glycosyl acceptor to give a key intermediate (**47**) of the lactosamine donor **27**. On the other hand, the *C*-1 position of the



<Fig 20> Preparation of glucosamine acceptor and galactosyl donor

Reagents: a) *p*-$MeOC_6H_4OH$, TMSOTf, $ClCH_2CH_2Cl$ (97%). b) NaOMe, MeOH. c) $C_6H_5CH(OMe)_2$, camphorsulfonic acid, CH_3CN (73 %, 2 steps). d) BnBr, NaH, DMF (93 %). e) CF_3COOH, Et_3SiH, CH_2Cl_2 (82 %). f) *n*-$Bu_3SnOCH_2CCl_3$, $SnCl_4$, $ClCH_2CH_2Cl$ (62%). g) NaOMe, MeOH. h) 1) (*n*-$Bu_3Sn)_2O$, toluene. 2) AllBr, *n*-Bu_4NBr (83%, 2 steps). i) Ac_2O, Py. j) Zn, AcOH (95%, 2 steps). k) Cl_3CCN, NaH, CH_2Cl_2, (91%, α/β = 6/4)

galactose moiety (**42**) was protected by a 2,2,2-trichloroethyloxy group[100] (**43**). After deacetylation of **43**, the *O*-3 and *O*-6 positions were selectively allylated by using bis(tributyltin)oxide to give **44**.



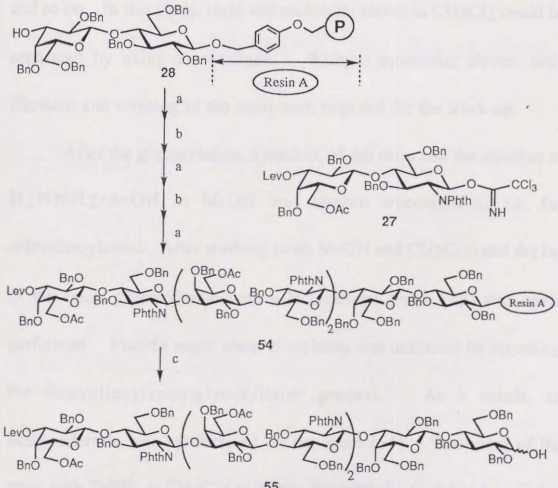
<Fig. 21> Preparation of lactosamine unit

Reagents: a) TMSOTf, MS AW-300, CH_2Cl_2 (84%). b) LiOH, H_2O_2, THF (92%). c) BnBr, Ag_2O, KI, DMF (82%). d) 1) $Ir\{(COD)[PCH_3Ph_2]_2\}PF_6$, THF. 2) $HgCl_2$, HgO, acetone, H_2O (82%) e) AcCl, Py (89%). f) Lev_2O, Py (93%) g) $Ce(NH_4)_2(NO_3)_6$, toluene, CH_3CN, H_2O (95%). h) Cl_3CCN, DBU, CH_2Cl_2 (95%)

Acetylation of **44** and the following reductive cleavage with zinc gave a hemiacetal (**45**) which was transformed into a galactose donor **46**. The compounds **41** and **46** were then coupled in the presence of TMSOTf and molecular sieves AW 300 in CH_2Cl_2 at -78°C to afford **47** in an 84 % yield. Deacetylation of **47** using LiOH and H_2O_2 in THF afforded **48** in an excellent yield (92 %). Benzylation of **48** with BnBr, Ag_2O and KI in DMF gave **49** in 82 % yield. In both of these reactions we didn't observe any destruction of the *N*-phthaloyl group. After deallylation of **49** into **50**, regioselective *O*-6b protection using AcCl in pyridine at low temperature (0°C) afforded **51**. The remaining hydroxy group at C-4b position was then levulinoylated to give **52**. Treating the protected lactosamine **52** with CAN (ceric ammonium nitrate) in a mixed solvent of toluene, acetonitrile and water gave a hemiacetal **53** which was converted into a lactosamine imidate (**27**).

In order to obtain a standard sample for HPLC analysis, solution phase glycosylation of **36** with **27** was carried out with TMSOTf in CH_2Cl_2 at -78°C for 2 h. under N_2 to give **60** in a 76 % yield.(Fig. 26) Under the same condition, glycosylation of polymer supported **28** or **29**

with **27** was then performed with stirring.(Fig. 22 and 23) After work-up, a small portion of the resin was treated with TrBF4 and the resulting resin-free products were analyzed by TLC. It was found that the glycosylation reaction was not completed under this condition and the same procedure had to be repeated again to complete the reaction.

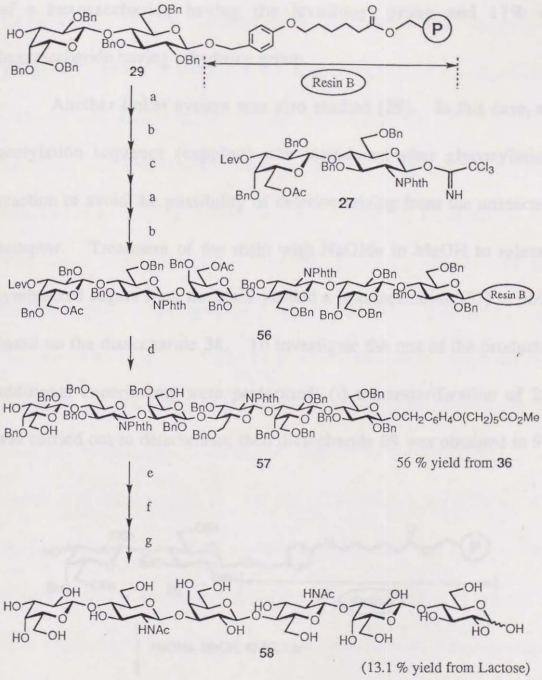


<Fig. 22> Polymer support synthesis of octasaccharide

Reagents: a) **27**, TMSOTf, CH_2Cl_2. b) NH_2NH_2•AcOH, MeOH. c) $TrBF_4$, CH_2Cl_2.

The possible reason for this would be the physical accessibility to the resin. The resin was floating on CH_2Cl_2 and attached to glass surface, so a part of the resin could not be present in the reaction mixture. This would be avoided if a suitable reaction system was used; for example, utilization of a polypropylene vessel, using a shaker instead of stirring and so on. In this study, resin and molecular sieves in CH_2Cl_2 could be separated by using a centrifuge. Without molecular sieves, only filtration and washing of the resin were required for the work-up.

After the glycosylation, a mixture of the resin and the solution of H_2NNH_2•AcOH in MeOH was shaken overnight at r.t. for delevulinoylation. After washing (with MeOH and CH_2Cl_2) and drying of the resin, glycosylation with a lactosamine donor (**28**) was again performed. Further sugar chain elongation was achieved by repeating the delevulinoylation-glycosylation process. As a result, an octasaccharide was synthesized on the resin (**54**). Treatment of the resin with $TrBF_4$ in CH_2Cl_2 to cleave the benzylic C-O bond on linker afforded **55** in 42% yield based on the disaccharide **35**, along with 13%

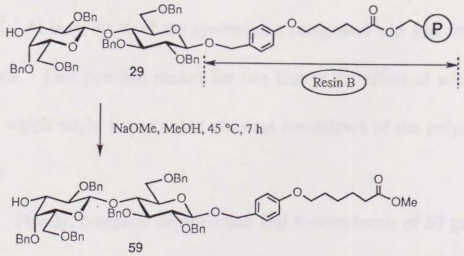


<Fig. 23> Polymer support synthesis of haxasaccharide and complete deprotection

Reagents: a) **27**, TMSOTf, CH_2Cl_2. b) Ac_2O, Py., CH_2Cl_2. c) NH_2NH_2•AcOH, MeOH. d) NaOMe, MeOH. e) $H_2NCH_2CH_2NH_2$, MeOH. f) Ac_2O, MeOH. g) H_2, Pd(OH), MeOH, H_2O (56%, 3 steps)

of a hexasaccharide having the levulinoyl group and 17% of hexasaccharide having a hydroxy group.

Another linker system was also studied (**29**). In this case, an acetylation sequence (capping) was introduced after glycosylation reaction to avoid the possibility of deletion arising from the unreacted acceptor. Treatment of the resin with NaOMe in MeOH to release synthesized sugars from the resin yielded a hexasaccharide (**57**) in 56% based on the disaccharide **36**. To investigate the rest of the products, additional experiments were performed: (i) transesterification of **29** was carried out to detachment, then disaccharide **59** was obtained in 91

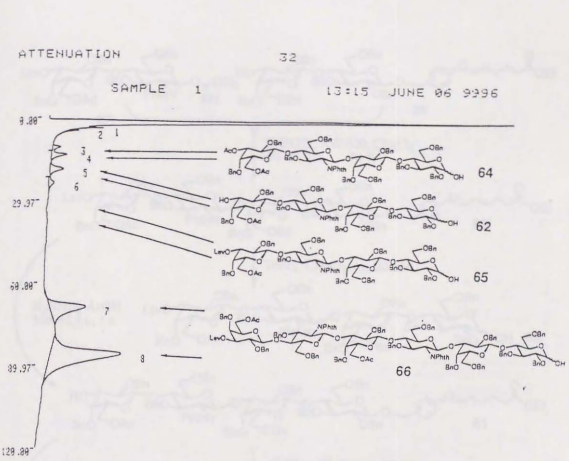


<Fig. 24> Transesterification of **29**

% yield.(Fig. 24) (ii) Compound **56** was treated with TrBF4 and analyzed by HPLC to reveal that the ratio of capped tetrasaccharide(**64**) : OH-3d tetrasaccharide(**62**) : hexasaccharide(**66**) was 1.5 : 5.6 : 92.9. Levulinoylated tetrasaccharide was not detected.(Fig. 25) These data indicate, (ii-a) capping reaction was not successful; a conversion rate was about 44% (4.4/(4.4+5.5)×100), (ii-b) deprotection of the levulinoyl group at the tetrasaccharide was completely carried out, (ii-c) the conversion of glycosylation from tetrasaccharide to hexasaccharide should be about a 94% (42/(42+17×100) yield, on the other hand, the yield of glycosylation from hexasaccharide to octasaccharide using Linker A is calculated to be 71% (42/(42+17)X100, see page 41~43) yield. At least 30 % of the synthesized compound was lost for some reasons. One possible reason for this loss is the effect of stirring of resin which might have caused physical breakdown of the polystyrene beads.

Finally, complete deprotection and *N*-acetylation of **57** gave *N*-acetyllactosaminylβ(1→3)*N*-acetyllactosaminylβ(1→3)lactose (**58**) in

56% yield based on **57**. Total yield to get **58** from lactose was 13.1 % yield.(Fig. 23)



CAL. METHOD 00

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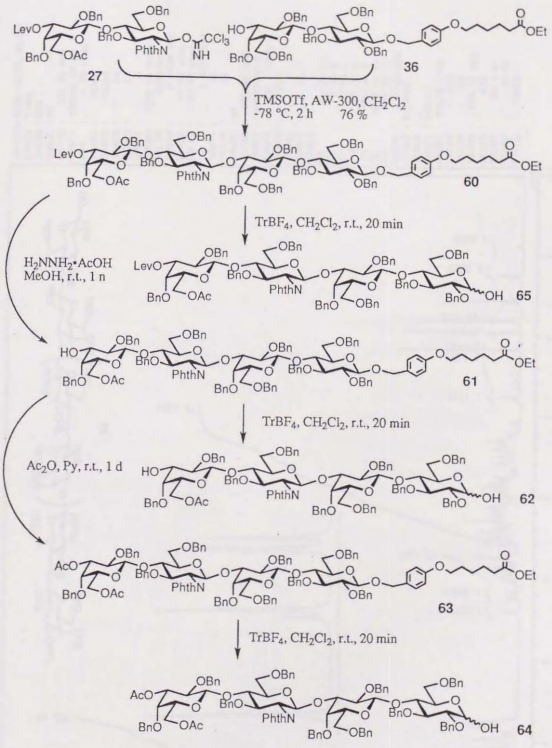
2		5.413	16103	T	0.6931
3		11.546	31072	M	1.3370
4		14.266	71552		3.0789
5		19.173	85558	M	3.6816
6		23.973	42697		1.8373
7		69.200	548932		23.6200
8		85.893	1511635		65.0465
	TOTAL		2323929		100.0000

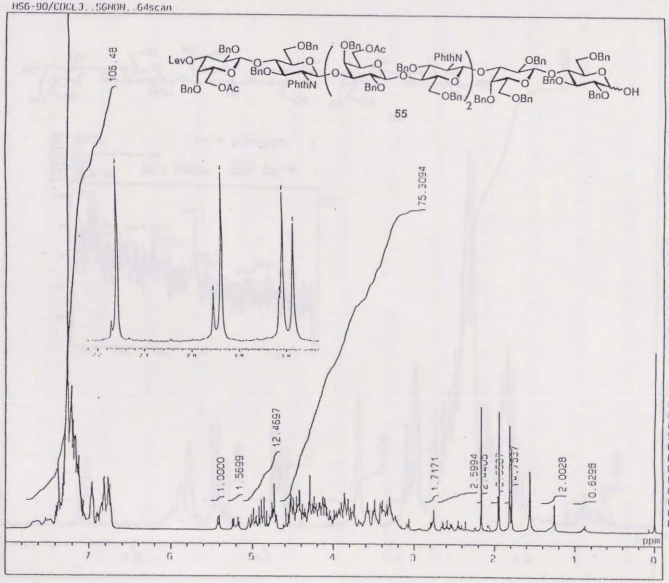
[Hibar LiChro CART®, Lichrospher®, Si 60 (5μm)
60% *n*-hexane/AcOEt, 1.8 ml/min
254 nm]

<Fig. 25> HPLC analysis of **56**



<Fig. 26> For HPLC study

HS6-90/CDCL3..SGNON..64scan



55

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FILTR : 4000 Hz
ACQTM : 2.0486 sec
DEADT : 10.00 usec
DELAY : 50.64 usec
PD : 3.0000 sec
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I2 : 0.00 %
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I4 : 100.00 %
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XS : 413.24 Hz
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MENUF : C2
SAMFL : TH5FG
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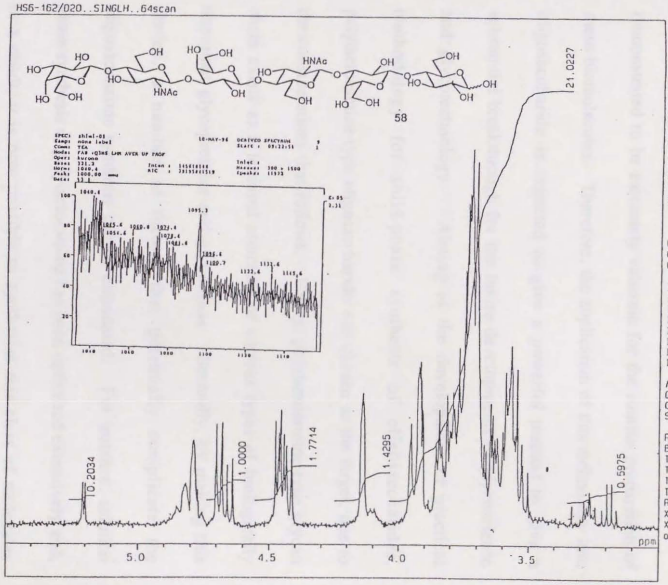

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PD : 5.0000 sec
AGAIN : 19

PW1 : 29.10 usec

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OBFRQ : 399.65 MHz
OBSET : 134362.90 Hz

IANUC : 1H
IAFRQ : 399.65 MHz
IASET : 134362.90 Hz
IATN : 200
IAPW : 50.0 usec
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IABP2 : 6
IANS : 0

AQBIT : 16
CTEMP : 23.5 c
CSPEO : 13 Hz
SLVNT : D2O

RESOL : 0.49 Hz
BF : 0.20 Hz
T1 : 0.00 %
T2 : 0.00 %
T3 : 90.00 %
T4 : 100.00 %
REFVL : 1.23 ppm
XE : 999.20 Hz
XS : 209.79 Hz
operator

CONCLUSION and FUTURE PROSPECTS

Solid phase synthetic technology has been investigated quite extensively in the fields of oligopeptide and oligonucleotide and demonstrated to be extremely valuable for the routine preparation of these biomolecules. Therefore, the application of this technology into oligosaccharide is expected to give a powerful method to give a substantial breakthrough for the future developments of glycoscience and glycotechnology. Aiming at the development of practical methodology for solid-phase synthesis of oligosaccharides, polylactosamine-type oligosaccharide was chosen as the target, due to the considerations that follows. Firstly, polylactosamine-type glycan chain exists as a terminal structure of various types of biologically important glycoproteins and glycolipids. Secondly, by making this choice, a number of factors that potentially complicate the oligosaccharide synthesis can be eliminated. For instance, solution phase synthesis of polylactosamine has been optimized extensively and, as a result, it is now possible to synthesize this class of molecules

without stereo- and regiochemical problems. Furthermore, polylactosamine oligosaccharide is well-suited for the initial development of solid phase technology because it has a repeating structure with Galβ1→4GlcNAc as the disaccharide unit. Therefore the synthesis should be possible simply by using a single type of glycosyl donor.

In order to perform the oligosaccharide synthesis on solid phase by sequential glycosylation, it is required to use the promoter that is powerful enough to activate the glycosyl donor to react with the resin-bound aglycon which should be in a sterically and entropically disfavored environment. In addition the system should be homogeneous except solid supported portion, so that the difficulty of recovering the solid supported product from the reaction mixture can be avoided. From such a point of view, I turned my attention to the use of PhSeNPhth in combination with TMSOTf as an activator of thioglycoside, which was described in Chapter 1. This system realized various types of glycosylation under quite mild conditions. Stereochemical outcomes obtained by benzyl protected glycosyl donor is

of particular note. Namely, substantial degree of β-selectivity was observed in non polar solvents such as toluene. Since there is no possibility of neighboring group participation, certain type of stereoelectronic factor should be operating to direct the reaction into 1,2-trans manner. Application of this newly developed system into solid phase synthesis should be a subject of future investigations.

In chapter 2, the potential utility of 4,5-dichlorophthaloyl group (DCPhth) is demonstrated. The preparation of polylactosamine glycan requires the removal of N-phthaloyl groups as the final step. Since complete removal of multiple Phth groups from large oligosaccharide requires quite harsh conditions and extended reaction time, some alternative to Phth group that can be removed more easily is desired for the preparation of polylactosamine glycans. Based on the consideration that introduction of electron withdrawing group should facilitate the reaction with nucleophiles, DCPhth was investigated as a candidate. As a result it was proved that DCPhth can be removed under substantially milder conditions. Namely nearly complete deprotection was achieved after 2 hours at room temperature. Compatibility of DCPhth group

with other protecting groups that are frequently used in oligosaccharide synthesis was also examined. On the other hand, DCPhth group was demonstrated to have an identical degree of 1,2-trans directing nature, when introduced at the C-2 position of the glycosyl donor. Taking together, DCPhth group should be an attractive alternative to Phth , which should find practical use in synthesis of amino sugar containing oligosaccharides, most typically polylactosamine glycans.

In Chapter 3, execution of solid phase synthesis of polylactosamine glycans is described. Starting from lactose unit (**29**, **36**) linked to Merrifield Resin *via* two types of linkers, glycan chain was planned to be extended after sequential deprotection and glycosylation with a selectively protected lactosamine donor. For that purpose, trichloroacetimidate **27** was used as the glycosyl donor, which could be activated effectively by TMSOTf. As temporary protective group of C-3b(Gal), levulinoyl (Lev) group was used and proved to be very suitable for our purpose. For instance, the hydroxy group could be liberated selectively to be a substrate for further glycosylation. The conditions were quite compatible with solid-phase chemistry and the

deprotection could be achieved without affecting other protective groups. As a result, octa- (**55**) and hexasaccharide (**57**) were synthesized from **29** and **36**, respectively. Cleavage of oligosaccharide from resin could be achieved conveniently by $TrBF_4$ in CH_2Cl_2. The hexasaccharide **57** was further converted into the completely deprotected form **58**.

It was demonstrated that glycosylation on solid phase can be applied into the synthesis of up to octasaccharide. In order to apply this method into more complex structures, there still remains several issues that should be investigated systematically. 1) Although each glycosylation on solid phase proceeded in a reasonably efficient manner (ca. 90% conversion), further improvement should be required (>95%) for the preparation of larger molecules. 2) Glycan chain extension up to octasaccharide was possible starting from **29**, while conversion of ester-type linker carrying hexasaccharide **57** into octasaccharide was not successful. These results suggest that the efficiency of solid phase glycosylation is sensitive to the fine structure and/or the length of the linker. 3) All glycosylations on solid support were magnetically

EXPERIMENTAL SECTION

General methods.

Melting point (mp) data were determined with a Yanagimoto micro-melting point apparatus and were uncorrected. Optical rotation values were determined with a JASCO DIP 370 polarimeter at 20±3°C. Silica gel column chromatography was performed in columns of Merck silica gel 60 (70-230 or 230-400 mesh), while TLC was performed with silica gel 60 F_{254} (Merck). Powdered molecular sieves were purchased from Nacalai Tesque and activated at 180°C under vacuum immediately prior to use. ^{1}H- and ^{13}C- NMR spectra were measured with JEOL EX-270, JNA-A400, GX500 and JNA-A600 spectrometer. The δ_H values were expressed in ppm from the signal of internal Me_4Si (0.00 ppm) in $CDCl_3$ and CD_3OD or internal *t*-BuOH (1.23 ppm) in D_2O, while the δ_C values were expressed in ppm from the signal of $CDCl_3$ (77.0 ppm) in $CDCl_3$, internal Me_4Si (0.00 ppm) in $CDCl_3$ or internal *t*-BuOH (31.3 ppm) in D_2O. FABMS were measured with JEOL JMS-HX110 spectrometer.

Cyclohexyl O-*2,3,4,6-tetra*-O-*benzyl*-α *and* β-*D*-*glucopyranose*. (**2**) (A typical experimental procedure in case of entry 3 in Table 1.) To a stirred mixture of **1a** (60.0 mg, 0.105 mmol), cyclohexanol (0.0150 ml, 0.144 mmol), PhSeNPhth (40.0 mg, 0.132 mmol) and AW-300 molecular sieves (100 mg) in dry toluene (1 ml) was added dropwise TMSOTf (0.0200 ml, 0.103 mmol) at -45 °C and the mixture was stirred for 2.5 h at same temperature. The reaction mixture was quenched with $NaHCO_3$ in water-THF, added extra $NaHCO_3$, allowed to room temperature and filtered through Celite. The aqueous layer was extracted with AcOEt. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (100 mg) was chromatographed on LX-20 gel. Elution with toluene gave **2** (58.8 mg, 90 %); **2**α ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.3-7.1 (20 H, m, Arom *H*), 5.00 (1 H, d, *J* = 10.9 Hz, $C_6H_5CH_2$), 4.95 (1 H, d, *J* = 3.6 Hz, *H*-1), 4.70 (1 H, d, *J* = 13.5 Hz, $C_6H_5CH_2$), 4.61 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 2.2-1.1 (10 H, m, cyclohexane-CH_2); ^{13}C-NMR

(67.5 MHz, $CDCl_3$) δ: 139.01, 138.33, 138.28, 138.02, 128.34, 128.07, 127.96, 127.89, 127.84, 127.76, 127.66, 127.60, 127.48, 94.70, 82.09, 80.02, 77.92, 75.60, 75.29, 75.10, 73.41, 72.90, 70.08, 68.64, 33.32, 31.43, 25.61, 24.42, 24.14: **2β** ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.4-7.2 (20 H, m, Arom *H*), 4.99 (1 H, d, *J* = 10.9 Hz, $C_6H_5CH_2$), 4.92 (1 H, d, *J* = 10.9 Hz, $C_6H_5CH_2$), 4.81 (1 H, d, *J* = 11.5 Hz, $C_6H_5CH_2$), 4.77 (1 H, d, *J* = 11.5 Hz, $C_6H_5CH_2$), 4.71 (1 H, d, *J* = 11.2 Hz, $C_6H_5CH_2$), 4.57 (1 H, d, *J* = 8.9 Hz, *H*-1), 2.2-1.3 (10 H, m, cyclohexane-CH_2); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 138.74, 138.61, 138.38, 138.20, 128.59, 128.35, 128.21, 128.01, 127.89, 127.73, 127.69, 127.62, 127.55, 101.99, 84.89, 82.34, 78.09, 77.99, 77.79, 77.23, 75.67, 74.99, 74.84, 73.44, 69.25, 33.84, 32.06, 25.68, 24.12, 23.99; HPLC analysis: **2β**; Rf = 14 min, **2α**; Rf = 16 min (Senshu Pak, 10×250, SSC, Silica 4251N, No. 4010, Elution with *n*-hexane/AcOEt (9/1), 2.7 ml/min., UV detecter 254 nm)

Methyl O-*(2,3,4,6-tetra*-O-*benzyl-α and β-D-glucopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-α-D-glucopyranoside.* (**10**) (A typical experimental

procedure in case of entry 2 in Table 2.) To a stirred mixture of **1a** (61.5 mg, 0.108 mmol), **6** (37.9 mg, 0.0816 mmol), PhSeNPhth (42.7 mg, 0.141 mmol) and AW-300 molecular sieves (100 mg) in dry toluene (1 ml) was added dropwise TMSOTf (0.0200 ml, 0.103 mmol) at -45 °C and the mixture was stirred for 1 h at the same temperature. The reaction mixture was quenched with $NaHCO_3$ in water-THF, added extra $NaHCO_3$, diluted with AcOEt, allowed to room temperature and filtered through Celite. The aqueous layer was extracted with AcOEt. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (137 mg) was chromatographed on Bio beads (S-X2). Elution with toluene gave **10** (80.4 mg, 90 %, α/β = 31/69 by ^{1}H-NMR); mixture of **10**α and **10**β: ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 5.69 (1 H, d, J = 3.6 Hz, *H*-1bα), 4.75 (1 H, d, J = 7.8 Hz, *H*-1bβ), 3.37 (1 H, s, α-OC*H3*), 3.36 (1 H, s, β-OC*H3*); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 139.55, 138.94, 138.74, 138.54, 138.45, 138.37, 138.29, 138.15, 137.95, 137.81, 128.99, 128.37, 128.28, 128.18, 128.05, 127.96, 127.85, 127.71, 127.57, 127.51, 127.48, 127.31, 127.24, 127.21, 127.03, 126.70, 125.25,

102.43, 98.38, 97.72, 96.60, 84.82, 82.79, 81.98, 80.38, 80.18, 79.44, 78.80, 78.01, 77.61, 77.20, 75.53, 75.47, 75.33, 75.13, 74.86, 74.72, 74.36, 73.57, 73.41, 73.30, 73.17, 73.10, 72.35, 70.94, 69.94, 69.51, 68.97, 68.16, 67.82, 60.33, 55.24, 55.10, 21.40, 20.97.

*Methyl (2,3,4,6-tetra-*O*-benzyl-α and β-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside.* (**11**) (A typical experimental procedure in case of entry 5 in Table 2.) To a stirred mixture of **1a** (60.0 mg, 0.105 mmol), **7** (40.0 mg, 0.0861 mmol), PhSeNPhth (40.0 mg, 0.132 mmol) and AW-300 molecular sieves (100 mg) in dry toluene (1 ml) was added dropwise TMSOTf (0.0200 ml, 0.103 mmol) at -45 °C and the mixture was stirred for 30 min at same temperature. The reaction mixture was quenched with $NaHCO_3$ in water-THF, added extra $NaHCO_3$, diluted with AcOEt, allowed to room temperature and filtered through Celite. The aqueous layer was extracted with AcOEt. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (140 mg) was chromatographed on Bio beads (S-X2). Elution with toluene gave **11** (

84.6 mg, quant., α/β = 10/90 by ^{1}H-NMR); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.60 (1 H, d, *J* = 3.6 Hz, *H*-1bα), 4.34 (1 H, d, *J* = 7.6 Hz, *H*-1bβ), 3.35 (1 H, s, α-OC*H*$_3$), 3.32 (1 H, s, β-OC*H*$_3$).

Benzyl O-*(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside*. (**12**) To a stirred mixture of **3**[41] (61.0 mg, 0.0973 mmol), **8** (41.9 mg, 0.0775 mmol), PhSeNPhth (41.4 mg, 0.137 mmol) and AW-300 molecular sieves (100 mg) in dry CH_2Cl_2 (1 ml) was added dropwise TMSOTf (0.0200 ml, 0.103 mmol) at 0 °C and the mixture was stirred for 20 min at the same temperature. The reaction mixture was quenched with $NaHCO_3$ in water-THF, added extra $NaHCO_3$, diluted with AcOEt, allowed to room temperature and filtered through Celite. The aqueous layer was extracted with AcOEt. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (149 mg) was chromatographed on silica gel (230-400 mesh, 10 g). Elution with toluene/AcOEt (20/1) gave **12** (87.0 mg, quant.); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 5.67 (1 H, t, *J* = 9.6 Hz, *H*-3b), 5.58 (1 H, t, *J* = 9.6 Hz, *H*-

4b), 5.48 (1 H, t, J = 9.6, 7.9 Hz, *H*-2b), 4.95 (1 H, d, J = 7.9 Hz, *H*-1b), 4.23 (1 H, dd, J = 12.2, 5.0 Hz, *H*-6b), 4.05 (1 H, t, J = 9.2 Hz, *H*-4a), 3.46 (1 H, dd, J = 8.9, 7.9 Hz, *H*-2a); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 166.00, 165.71, 165.05, 164.83, 138.98, 138.38, 138.11, 137.38, 133.35, 133.17, 132.97, 129.74, 129.69, 129.56, 129.02, 128.81, 128.68, 128.48, 128.34, 128.27, 128.19, 128.05, 127.80, 127.69, 127.48, 127.37, 127.19, 102.43, 100.38, 82.53, 81.69, 77.27, 75.20, 74.88, 74.31, 73.48, 73.08, 72.24, 71.92, 71.02, 69.67, 67.76, 63.00.

Methyl O-*(2,3,4,6-tetra*-O-*benzyl-α and β-D-mannopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-α-D-glucopyranoside*. (**13**) To a stirred mixture of **4** (62.1 mg, 0.109 mmol), **8** (41.0 mg, 0.0883 mmol), PhSeNPhth (41.3 mg, 0.137 mmol) and AW-300 molecular sieves (100 mg) in dry toluene (1 ml) was added dropwise TMSOTf (0.0200 ml, 0.103 mmol) at -45 °C and the mixture was stirred for 2.5 h at the same temperature. The reaction mixture was quenched with $NaHCO_3$ in water-THF, added extra $NaHCO_3$, diluted with AcOEt, allowed to room temperature and filtered through Celite. The aqueous layer was extracted with AcOEt.

The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (143 mg) was chromatographed on silica gel (230-400 mesh, 3 g). Elution with toluene/AcOEt (20/1, 5/1) gave **13**α (56.5 mg, 65 %) and **13**β (13.2 mg, 15 %). **13**α; $[\alpha]_D$ +23.1° (c 0.3, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.3-7.1 (35 H, m, Arom *H*), 5.29 (1 H, d, *J* = 2.0 Hz, *H*-1b), 5.08 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.84 (1 H, d, *J* = 10.9 Hz, $C_6H_5CH_2$), 3.39 (3 H, s, OCH_3); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 138.77, 138.61, 138.52, 138.40, 138.31, 137.82, 128.39, 128.32, 128.28, 128.17, 128.08, 127.98, 127.90, 127.65, 127.54, 127.47, 127.31, 127.06, 126.75, 126.65, 100.45 ($J_{C\text{-}H}$ = 170 Hz, *C*-1b), 97.63 ($J_{C\text{-}H}$ = 165 Hz, *C*-1a), 81.49, 79.93, 79.70, 77.70, 77.29, 77.11, 76.70, 76.23, 74.92, 74.79, 73.30, 73.21, 73.10, 72.94, 72.20, 71.99, 69.76, 69.33. **13**β; ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.4-7.2 (35 H, m, Arom *H*), 5.15 (1 H, d, *J* = 11.2 Hz, $C_6H_5CH_2$), 4.82 (1 H, s, *H*-1b), 3.38 (3 H, s, OCH_3); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 139.62, 138.81, 138.51, 138.29, 129.74, 129.00, 128.50, 128.36, 128.27, 128.14, 128.10, 127.98, 127.93, 127.80, 127.71, 127.60, 127.48, 127.28, 127.17,

126.97, 100.85 ($J_{C\text{-}H}$ = 158 Hz, *C*-1b), 98.37 ($J_{C\text{-}H}$ = 168 Hz, *C*-1a), 97.84, 82.57, 80.32, 79.10, 77.22, 76.17, 75.20, 74.99, 74.79, 74.07, 73.62, 73.53, 73.44, 71.63, 69.67, 69.53, 68.68, 55.26.

Benzyl O-*(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-2,3,6-tri-*O*-benzyl-β-D-galactopyranoside.* (**14**) To a stirred mixture of **5** (51.0 mg, 0.110 mmol), **8** (40.0 mg, 0.0740 mmol), PhSeNPhth (40.0 mg, 0.132 mmol) and AW-300 molecular sieves (100 mg) in dry CH_2Cl_2 (1 ml) was added dropwise TMSOTf (0.0200 ml, 0.103 mmol) at 0 °C and the mixture was stirred for 1.5 h at same temperature. The reaction mixture was quenched with $NaHCO_3$ in water-THF, added extra $NaHCO_3$, diluted with AcOEt, allowed to room temperature and filtered through Celite. The aqueous layer was extracted with AcOEt. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (126 mg) was chromatographed on Bio beads. Elution with toluene gave **14** (54.3 mg, 77 %); ^{1}H-NMR (270 MHz, C_6D_6) δ: 7.6-6.9 (24 H, m, Arom *H*), 5.86 (1 H, d, *J* = 8.6 Hz, *H*-1b), 4.36 (1 H, d, *J*

= 7.6 Hz, *H*-1a), 1.72 (3 H, s, COC*H*3), 1.64 (3 H, s, COC*H*3), 1.48 (3 H, s, COC*H*3); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 170.55, 169.99, 169.60, 169.52, 167.71, 167.40, 138.76, 138.69, 138.51, 138.26, 137.92, 137.14, 134.00, 131.02, 130.84, 128.75, 128.45, 128.36, 128.30, 128.23, 128.10, 127.92, 127.75, 127.71, 127.62, 127.48, 127.42, 127.30, 127.12, 126.81, 123.40, 102.50 (*C*-1a), 99.03 (*C*-1b), 81.55, 78.26, 77.20, 75.81, 75.47, 74.84, 74.65, 73.73, 73.42, 73.35, 71.61, 71.47, 70.66, 70.48, 69.20, 69.09, 69.02, 68.86, 68.11, 61.94, 55.04, 38.69, 30.32, 28.88, 23.70, 22.93, 20.60, 20.38, 14.02, 10.93.

3,4,6-Tri-O-acetyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranosyl acetate. (**15**) To a stirred mixture of D-glucosamine hydrochloride (6.48 g, 30.0 mmol) in MeOH (100 ml) was added NaOMe (1M in MeOH; 30 ml, 30 mmol) at room temperature. The mixture was stirred for 10 min, and the insoluble materials were removed by filtration. To the filtrate were successively added triethylamine (4.6 ml, 33 mmol) and 4,5-dichlorophthalic anhydride (6.8 g, 31 mmol). The mixture was stirred for 20 min at 50°C and then concentrated *in vacuo*. The residue was dissolved in pyridine-Ac_2O (1:1, 100 ml) and stirred at room temperature overnight. The resulting mixture was concentrated *in vacuo*, and the residue was crystallized from AcOEt/Et_2O/hexane to afford 5.3 g (32%) of compound **15**; mp 179-180°C; $[\alpha]_D$ +75.4° (c 1.0, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.95 and 7.93 (2 H, s, Arom *H*), 6.48 (1 H, d, *J* = 8.9 Hz, *H*-1), 5.82 (1 H, dd, *J* = 10.6, 9.2 Hz, *H*-3), 5.22 (1 H, dd, *J* = 10.2, 9.2 Hz, *H*-4), 4.43 (1 H, dd, *J* = 10.6, 8.9 Hz, *H*-2), 4.37 (1 H, dd, *J* = 12.5, 4.3 Hz, *H*-6), 4.15 (dd, *J* = 12.5, 2.3 Hz, *H*-6), 4.02 (1 H, ddd, *J* = 10.2, 4.3, 2.3 Hz, *H*-5), 2.12, 2.05, 2.01, and 1.89 (3 H×4, s, $COCH_3$); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 89.45 (*C*-1), 72.58, 70.42,

67.98, 61.39, 53.82, 20.63 (2×$COCH_3$), 20.51 ($COCH_3$), 20.31 ($COCH_3$). *Anal.* Calcd. for $C_{22}H_{21}NO_{11}Cl_2$: C, 48.37; H, 3.87; N, 2.56. Found: C, 48.38; H, 3.93; N, 2.52.

3,4,6-Tri-O-acetyl-2-deoxy-2-(4,5-dichlorophthalimido)-D-glucopyranosyl bromide. (**17**) 30% HBr/AcOH (3.0 ml, 17 mmol) was added to a solution of compound **15** (3.00 g, 5.49 mmol) in a mixture of AcOH (8 ml) and Ac_2O (4 ml). The resulting mixture was stirred at room temperature for 2 days and then quenched with ice. The mixture was extracted with $CHCl_3$, and the organic layer was successively washed with aq. $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was crystallized from ether to afford 798 mg of **17**β. The mother liquor was concentrated and purified by silica gel column chromatography (toluene/AcOEt = 14/1) to afford **17**α (947 mg, 30%) and an additional amount of **17**β (total yield of 1.37 g, 44%). **17**β; mp 89°C; $[\alpha]_D$ +95.8° (c 1.4, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.97 (2 H, b, Arom *H*), 6.36 (1 H, d, *J* = 9.6 Hz, *H*-1), 5.70 (1 H, dd, *J* = 10.2, 9.2 Hz, *H*-3), 5.26 (1 H, dd, *J* = 10.2, 9.2 Hz, *H*-4), 4.59 (1 H, dd, *J* = 10.2, 9.6 Hz, *H*-2), 4.32 (1 H, dd, *J* = 12.5, 4.6 Hz, *H*-6), 4.20 (1 H, dd, *J* = 12.5, 2.3 Hz, *H*-6), 3.95 (1 H, ddd, *J* = 10.2, 4.6, 2.3 Hz, *H*-5), 2.13, 2.05, and 1.88 (3 H×3, s,

COC*H*3). *Anal.* Calcd. for $C_{20}H_{18}NO_9BrCl_2$: C, 42.35; H, 3.20; N, 2.47. Found: C, 42.64; H, 3.29; N, 2.30. **17**α; ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 6.60 (1 H, dd, *J* = 11.4, 8.9 Hz, *H*-3), 6.54 (1 H, d, *J* = 5.2 Hz, *H*-1), 5.15 (1 H, dd, *J* = 11.4, 8.9 Hz, *H*-4), 4.65 (1 H, dd, *J* = 11.4, 5.2 Hz, *H*-2), 2.11, 2.07, and 1.89 (3 H×3, s, COC*H*3).

*Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(4,5-dichlorophthalimido)-1-thio-β-D-glucopyranoside.* (**18**) To a stirred solution of compound **15** (15.0 g, 27.5 mmol) and *n*-Bu_3SnSMe (18.0 g, 53.4 mmol) in dichloroethane (150 ml) was added $SnCl_4$ (11.5 ml, 98.2 mmol) at 0°C. The mixture was gradually warmed to ambient temperature, stirred overnight and diluted with AcOEt. An aq. KF solution and aq. $NaHCO_3$ solution were added, and the mixture was stirred for 2h. The precipitate was filtered off, and the filtrate was extracted with AcOEt. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was crystallized from ether to afford compound **18** (11.9 g, 83%); mp 179-180°C; $[\alpha]_D$ +54.7° (c 1.2, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.95 and 7.94 (2 H, s, Arom *H*), 5.79 (1 H, dd, *J* = 10.2, 9.3 Hz, *H*-3), 5.34 (1 H, d, *J* = 10.2 Hz, *H*-1), 5.18 (1 H, dd, *J* = 10.2, 9.3 Hz, *H*-4), 4.38 (1 H, t, *J* = 10.2 Hz, *H*-2), 4.32 (1 H, dd, *J* = 12.2, 4.6 Hz, *H*-6), 4.19 (1 H, dd, *J* = 12.2, 2.3 Hz, *H*-

6), 3.90 (1 H, ddd, J = 10.2, 4.6, 2.3 Hz, H-5), 2.16, 2.11, 2.04 and 1.88 (3 H×4, s, 3×COCH_3 and SCH_3); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 80.27 (*C*-1), 75.90, 71.32, 68.48, 62.01, 53.29, 20.61 (COCH_3), 20.47 (CO*C*H_3), 20.38 (CO*C*H_3), 11.27 (S*C*H_3). *Anal.* Calcd. for $C_{21}H_{21}NO_9Cl_2S$: C, 47.20; H, 3.96; N, 2.62. Found: C, 47.44; H, 3.98; N, 2.62.

Methyl 2-deoxy-2-(4,5-dichlorophthalimido)-1-thio-β-D-glucopyranoside. (**19**) A solution of compound **18** (306 mg, 0.573 mmol) in MeOH (5 ml) containing 0.60 ml of *conc.* HCl was stirred for 3.5 h at 70°C. The mixture was concentrated *in vacuo*, and the residue was subjected to silica gel column chromatography (hexane/AcOEt = 1/4) to afford 222 mg (95%) of compound **19**; mp 147-149°C; [α]D +24.7° (c 1.0, MeOH); ^{1}H-NMR (CD_3OD) δ: 8.07 and 8.05 (1 H×2, s, Arom *H*), 5.16 (1 H, d, J = 10.2 Hz, H-1), 4.25 (1 H, dd, J = 10.2, 8.3 Hz, H-3), 4.08 (1 H, t, J = 10.2 Hz, H-2), 3.92 (1 H, dd, J = 11.9, 1.7 Hz, H-6), 3.73 (1 H, dd, J = 11.9, 5.3 Hz, H-6), 2.14 (3 H, s, SCH_3). *Anal.* Calcd. for $C_{15}H_{15}NO_6Cl_2S$: C, 44.13; H, 3.70; N, 3.43. Found: C, 43.97; H, 4.01; N, 3.23.

Methyl 4,6-O-benzylidene-2-deoxy-2-(4,5-dichlorophthalimido)-1-thio-β-D-glucopyranoside. (**20**) A solution of compound **19** (1.96 g, 4.80 mmol) and benzaldehyde dimethylacetal (2.0 ml, 13 mmol) in acetonitrile (20 ml) containing camphorsulfonic acid (0.20 g, 0.80 mmol) was stirred for 24 h at room temperature. The mixture was diluted with AcOEt and quenched with ice-aq. $NaHCO_3$. The aqueous layer was back-extracted with AcOEt, and the combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (toluene/AcOEt = 19/1) to afford 1.74 g (73%) of compound **20**; $[\alpha]_D$ +8.9° (c 1.2, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.94 and 7.92 (1 H×2, s, Arom *H*), 7.5-7.3 (5 H, m, Arom *H*), 5.56 (1 H, s, benzylidene C*H*), 5.25 (1 H, d, *J* = 10.6 Hz, *H*-1), 4.65 (1 H, ddd, *J* = 9.9, 8.9, 3.3 Hz, *H*-3), 4.41 (1 H, dd, *J* = 9.9, 4.3 Hz, *H*-6), 4.31 (1 H, dd, *J* = 10.6, 9.9 Hz, *H*-2), 3.80 (1 H, t, *J* = 9.9 Hz, *H*-6), 3.70 (1 H, ddd, *J* = 9.9, 8.9, 4.3 Hz, *H*-5), 3.58 (1 H, t, *J* = 8.9 Hz, *H*-4), 2.70 (1 H, d, *J* = 3.3 Hz, O*H*), 2.16 (3 H, s, SC*H*$_3$). *Anal.* Calcd. for $C_{22}H_{19}NO_6Cl_2S$: C, 54.24; H, 3.86; N, 2.82. Found: C, 53.99; H, 3.98; N, 2.60.

Methyl 3-O-benzyl-4,6-O-benzylidene-2-deoxy-2-(4,5-

dichlorophthalimido)-1-thio-β-D-glucopyranoside. (**22**) To a stirred solution of compound **20** (70 mg, 0.14 mmol) and BnBr (0.12 ml, 1.0 mmol) in DMF (3 ml) was added NaH (oil free; 15 mg, 0.63 mmol) at 0°C. The mixture was gradually warmed to room temperature and stirred for 4h. After being diluted with AcOEt, the mixture was quenched with MeOH and washed with water. The aqueous layer was back-extracted with AcOEt, and the combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (toluene/AcOEt = 20/1) to afford 69 mg (84%) of compound **22**; mp 118-120°C (from ether); $[\alpha]_D$ +48.6° (c 0.3, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.89 and 7.68 (1 H×2, s, Arom *H*), 7.6-6.8 (10 H, m, Arom *H*), 5.63 (1 H, s, benzylidene C*H*), 5.18 (1 H, d, *J* = 10.6 Hz, *H*-1), 4.27 (1 H, t, *J* = 10.6 Hz, *H*-2), 3.80 (1 H, dd, *J* = 9.4, 8.6 Hz, *H*-4), 2.13 (3 H, s, SC*H*$_3$). *Anal.* Calcd. for $C_{29}H_{25}NO_6Cl_2S$: C, 59.39; H, 4.30; N, 2.39. Found: C, 59.36; H, 4.29; N, 2.37.

*Methyl 3,6-di-*O*-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-1-thio-β-D-glucopyranoside.* (**21**) Compound **22** (635 mg, 1.08 mmol), $NaCNBH_3$ (570 mg, 9.07 mmol) and 4A molecular sieves (0.15 g) were mixed in THF (15 ml) containing *ca.* 1 mg of methyl orange as an

indicator. A saturated HCl solution in ether was added dropwise until the mixture became acidic. After being stirred at room temperature for 3 h, the mixture was diluted with AcOEt and washed with an ice-cooled $NaHCO_3$ solution. The aqueous layer was back-extracted with AcOEt, and the combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (toluene/AcOEt = 20/1) to afford 429 mg (68%) of compound **21**; $[\alpha]_D$ +33.2° (c 1.1, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.85 and 7.69 (1 H×2, s, Arom *H*), 7.4-6.9 (10 H, m, Arom *H*), 5.10 (1 H, d, *J* = 8.6 Hz, *H*-1), 4.18-4.28 (2 H, m, *H*-2 and *H*-3), 3.02 (1 H, d, *J* = 2.6 Hz, O*H*), 2.08 (3 H, s, SC*H*3). *Anal.* Calcd. for $C_{29}H_{27}NO_6Cl_2S$: C, 59.19; H, 4.62; N, 2.38. Found: C, 59.68; H, 4.72; N, 2.36.

Methyl 4,6-O-benzylidene-2-deoxy-2-(4,5dichlorophthalimido)-3-O-levulinoyl-1-thio-β-D-glucopyranoside. (**23**) To a solution of compound **20** (100 mg, 0.201 mmol) in CH_2Cl_2-pyridine (2:1; 1.5 ml) was added levulinic anhydride (500 mg, 2.0 mmol). The solution was stirred at room temperature overnight, diluted with AcOEt, and washed with ice-cooled aq. $NaHCO_3$. The aqueous layer was back-extracted with AcOEt, and the combined organic layers were washed with brine,

dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (toluene/AcOEt = 10/1) to afford 114 mg (95%) of compound **23**; $[\alpha]_D$ -6.8° (c 1.0, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.98 and 7.68 (1 H×2, s, Arom *H*), 7.5-7.3 (10 H, m, Arom *H*), 5.95 (1 H, dd, *J* = 9.6, 9.2 Hz, *H*-3), 5.54 (1 H, s, benzylidene C*H*), 5.39 (1 H, d, *J* = 10.6 Hz, *H*-1), 4.39 (1 H, dd, *J* = 10.6, 9.2 Hz, *H*-2), 2.69-2.32 (4 H, m, $COCH_2CH_2CO$), 2.17 and 1.89 (3 H×2, s, CH_3CO and SCH_3). *Anal.* Calcd. for $C_{27}H_{25}NO_8Cl_2S$: C, 54.55; H, 4.23; N, 2.36. Found: C, 54.38; H, 4.25; N, 2.30.

Removal of the levulinoyl group. To a mixture of hydrazine hydrate (48.5 μl), pyridine (1.6 ml) and acetic acid (0.4 ml) was added compound **23** (52 mg, 0.0875 mmol). The solution was stirred at room temperature for 5 min, diluted with AcOEt, successively washed with aq. $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/AcOEt = 3/1) to afford compound **20** (45 mg, quantitative).

Methyl O-*[3,4,6-tri*-O-*acetyl 2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranosyl]-(1→6)-2,3,4-tri*-O-*benzyl-α-D-glucopyranoside.* (**24**) A mixture of compounds **18** (84.2 mg, 0.158 mmol) and **6** (55.5 mg, 0.12 mmol), *N*-(phenylseleno)phthalimide (62.5 mg, 0.207 mmol), and

AW-300 molecular sieves (0.13 g) in dichloroethane (1 ml) was stirred at -40°C. TMSOTf (30 µl, 0.16 mmol) was added, and stirring was continued for 20 min. The mixture was quenched with aq. $NaHCO_3$, diluted with AcOEt and filtered through Celite. The filtrate was washed with water, and the aqueous layer was back-extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified in a column of Bio Beads S-X2 (Bio Rad) in toluene to afford 91.3 mg (80%) of compound **24**; $[\alpha]_D$ +39.1° (c 1.0, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 5.69 (1 H, dd, *J* = 10.2, 9.2 Hz, *H*-3b), 5.42 (1 H, d, *J* = 8.6 Hz, *H*-1b), 4.46 (1 H, d, *J* = 3.6 Hz, *H*-1a), 3.85 (1 H, dd, *J* = 9.6, 9.2 Hz, *H*-3a), 3.44 (1 H, dd, *J* = 9.6, 3.6 Hz, *H*-2a), 3.32 (1 H, t, *J* = 9.2 Hz, *H*-4a), 3.26 (3 H, s, OCH_3), 2.08 (3 H, s, $COCH_3$), 2.03 (3 H, s, $COCH_3$), 1.84 (3 H, s, $COCH_3$); ^{13}C-NMR (67.5 MHz, CDCl3) δ: 98.06 (*C*-1a), 97.79 (*C*-1b), 81.83, 79.59, 77.54, 75.76, 74.77, 73.37, 71.90, 70.68, 69.00, 68.64, 68.56, 61.98, 55.08, 20.67 ($COCH_3$), 20.54 ($COCH_3$), 20.33 ($COCH_3$). *Anal.* Calcd. for $C_{48}H_{49}NO_{15}Cl_2$: C, 60.64; H, 5.19; N, 1.47. Found: C, 60.65; H, 5.13; N, 1.48.

Benzyl O-*[3,4,6-tri*-O-*acetyl 2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranosyl]-(1→3)-2,4,6-tri*-O-*benzyl-β-D-galactopyranoside.* (**25**)

Compounds **18** (70.0 mg, 0.131 mmol) and **8** (50.0 mg, 0.0925 mmol) were reacted in a similar manner to that described for the preparation of compound **24** to afford 73.6 mg (77%) of compound **25**; mp 147-149°C; $[\alpha]_D$ +3.2° (c 1.3, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 5.72 (1 H, dd, *J* = 10.6, 9.2 Hz, *H*-3b), 5.62 (1 H, d, *J* = 8.3 Hz, *H*-1b), 5.13 (1 H, dd, *J* = 10.2, 9.2 Hz, *H*-4b), 4.35 (1 H, d, *J* = 7.3 Hz, *H*-1a), 4.31 (1 H, dd, *J* = 10.6, 8.3 Hz, *H*-2b), 2.03, 1.98, and 1.82 (3 H×3, s, $COCH_3$); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 102.32 (*C*-1a), 99.25 (*C*-1b), 82.57, 78.08, 75.76, 74.61, 73.51, 73.46, 73.28, 71.59, 70.59, 70.50, 69.29, 68.69, 61.91, 55.40, 20.58 ($COCH_3$), 20.36 ($COCH_3$). *Anal.* Calcd. for $C_{54}H_{59}NO_{15}Cl_2$: C, 63.16; H, 5.20; N, 1.36. Found: C, 63.31; H, 5.15; N, 1.12.

Benzyl O-(2-acetamido-3,4,6-tri-O-acetyl 2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-O-benzyl-β-D-galactopyranoside. (**26**)

Method A. To a solution of compound **25** (100 mg, 0.097 mmol) in MeOH (1 ml) was added ethylenediamine (0.57 ml), the mixture then being stirred for 2h at room temperature. The volatiles were removed by evaporation, and the residue was treated with Ac_2O (1 ml) and Py (1 ml). The solution was stirred at room temperature for 5h and concentrated *in vacuo*. The residue was diluted with AcOEt,

successively washed with aq. $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (toluene/AcOEt = 2/1) to afford 93.0 mg (98%) of compound **26**; mp 112°C; $[\alpha]_D$ -40.2° (c 1.3, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.81 (1 H, d, *J* = 8.6 Hz, *H*-1b), 4.43 (1 H, d, *J* = 7.6 Hz, *H*-1a), 2.02, 2.01, 1.98, and 1.54 (3 H×4, s, $COCH_3$); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 102.41 (*C*-1a), 101.73 (*C*-1b), 80.88, 79.55, 75.40, 74.50, 74.36, 73.68, 73.48, 72.80, 71.72, 70.68, 68.97, 68.47, 62.03, 54.20, 22.81 ($COCH_3$), 20.65 ($COCH_3$), 20.60 ($COCH_3$). *Anal.* Calcd. for $C_{48}H_{55}NO_{14}Cl_2$: C, 66.27; H, 6.37; N, 1.61. Found: C, 66.47; H, 6.32; N, 1.67.

Method B. A solution of compound **25** (36.0 mg, 0.0351 mmol) and $H_2NNH_2 \cdot H_2O$ (0.15 ml) in MeOH (1 ml) was stirred for 1 d at room temperature. The volatiles were removed by evaporation, and the residue was treated with Ac_2O and Py as described in **Method A** to afford 28.6 mg (94 %) of compound **26**.

O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-(1→4)-2,4,6-tri-O-benzoyl-β-D-glucopyranosyl benzoate. (**30**) To a stirred solution of β-D-lactose (55.0 g, 140 mmol) in Py (500 ml) was added benzoyl chloride (240 ml, 2.07 mol) at room temperature and the reaction mixture was stirred for 1 d at 90 °C. The reaction mixture was concentrated *in vacuo* and co-evaporated with toluene. The residue was dissolved in AcOEt, washed with water and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue (300 g) was chromatographed on silica gel (70-230 mesh, 1500 g). Elution with toluene/AcOEt (15/1) gave **30**. (170.7 g, 95 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 8.2-7.21 (40 H, m, Arom-*H*), 6.14 (1 H, d, *J* = 8.2, *H*-1a), 5.95 (1 H, dd, *J* = 9.9, 8.9 Hz, *H*-3a), 5.79 (1 H, dd, *J* = 9.9, 8.2 Hz, *H*-2a), 5.74 (1 H, dd, *J* = 10.2, 7.9 H, *H*-2b), 5.37 (1 H, dd, *J* = 10.2, 3.6 Hz, *H*-3b), 4.89 (1 H, d, *J* = 7.9 Hz, *H*-1b), 4.39 (1 h, dd, *J* = 9.2, 8.9 Hz, *H*-4a); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 165.75, 165.53, 165.41, 165.23, 165.19, 164.78, 164.51, 133.73, 133.53, 133.37, 133.26,

132.88, 130.12, 129.97, 129.81, 129.74, 129.67, 129.54, 129.49, 129.40, 129.02, 128.82, 128.77, 128.59, 128.53, 128.45, 128.39, 128.28, 128.23, 125.28, 101.04, 92.58, 77.22, 75.51, 73.80, 72.81, 71.74, 71.38, 70.68, 69.79, 67.46, 62.09, 60.97.

2,3,4,6-tetra-O-*benzoyl-β-D-galactopyranosyl)-(1→4)-2,4,6-tri*-O-*benzoyl-β-D-glucopyranosyl bromide*. (**31**) To a stirred solution of **30** (23.3 g, 19.8 mmol) in dichloroethane (20 ml) and Ac_2O (5 ml) was added 33% HBr/AcOH (23.0 ml, 392 mmol) at 0 °C under N_2 and the mixture was stirred for 3 h at room temperature. The reaction mixture was poured into ice and stirred for 1 h. The aqueous layer was extracted twice with AcOEt and the combined organic layers were washed with ice-cooled water, cold *sat*. $NaHCO_3$, cold brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was triturated with *n*-hexane to afford **31**. (22.2 g, 99 %); $[\alpha]_D$ +99.6° (c 1.1, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 8.1-7.2 (35 H, m, Arom *H*), 6.75 (1 H, d, *J* = 4.0 Hz, *H*-1a), 6.15 (1 H, dd, *J* = 9.9, 9.2 Hz, *H*-3a), 5.40 (1 H, dd, *J* = 10.2, 3.3 Hz, *H*-3b), 5.26 (1 H, dd, *J* = 9.9, 4.0 Hz, *H*-2a), 4.95 (1 H, d,

J = 7.9 Hz, H-1b), 4.35 (1 H, dd, J = 9.9, 9.2 Hz, H-4a); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 165.70, 165.53, 165.44, 165.37, 165.19, 165.09, 164.74, 133.73, 133.51, 133.48, 133.42, 133.30, 130.15, 130.05, 129.96, 129.74, 129.63, 129.43, 129.31, 129.25, 128.77, 128.59, 128.54, 128.45, 128.37, 128.30, 128.23, 101.04, 86.70, 74.83, 73.32, 71.84, 71.38, 71.29, 70.50, 69.79, 67.40, 61.46, 60.99; *Anal.* Calcd. for $C_{61}H_{49}O_{17}Br$: C, 64.61; H, 4.36. Found: C, 64.76; H, 4.35.

p-*Allyloxybenzyl* O-*(2,3,4,6-tetra*-O-*benzoyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzoyl-β-D-glucopyranoside.*

(**32**) A stirred solution of ZnF_2 (5.20 g, 50.3 mmol) and 2,2'-dipyridyl (1.30 g, 8.32 mmol) in acetonitrile (200 ml) was heated for reflux and ca. 100 ml of acetonitrile was removed from the reaction flask. The reaction mixture was cooled down to room temperature and **31** (14.4 g, 12.7 mmol) was added and the mixture was stirred overnight at 90°C. After cooled, the reaction mixture was diluted with AcOEt and water. The aqueous layer was extracted three times with AcOEt. The combined organic layers were washed with *sat.* $NaHCO_3$

and brine, dried with $MgSO_4$, and concentrated *in vacuo*. To this crude fluoride(14.1 g) in dichloroethane (100 ml) were added *p*-$HOCH_2C_6H_4OAll$ (5.40 g, 32.9 mol), *s*-collidine (2.00 g, 16.5 mmol) and 4A molecular sieves (2 g) successively under N_2 with exclusion of light. To this mixture AgOTf (4.96 g, 17.8 mmol) and $SnCl_2$(3.36 g, 17.8 mmol) were added at room temperature and stirred overnight at 55°C. The reaction mixture was allowed to cool down to room temperature, diluted with dichloromethane and *sat*. $NaHCO_3$ and filtered through Celite. The aqueous layer was extracted three times with AcOEt. The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue (19.9 g) was chromatographed on silica gel (230-400 mesh, 600 g). Elution with toluene/AcOEt (15/1) gave **32** (14.8 g, 86 %); mp 105-107 °C; $[\alpha]_D$ +38.8° (c 1.2, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 8.0-7.1 (35 H, m, Arom *H*), 7.04 (2 H, d, *J* = 8.6 Hz, Arom *H*), 6.68 (2 H, d, *J* = 8.6 Hz, Arom *H*), 6.1-6.0 (1 H, m, CH_2=C*H*), 5.73 (1 H, dd, *J* = 9.6, 9.2 Hz, *H*-3a), 5.72 (1 H, d, *J* = 3.3 Hz, *H*-4b), 5.71 (1 H, dd, *J* = 10.2, 7.2 Hz, *H*-2b), 5.51 (1 H, dd, *J* = 9.6, 7.9 Hz, *H*-2a), 5.37 (1 H, dd, *J* =

10.2, 3.3 Hz, *H*-3b), 5.29 (1 H, dd, *J* = 10.6, 1.3 Hz, CH_2=CH), 4.86 (1 H, d, *J* = 7.9 Hz, *H*-1b), 4.76 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.68 (1 H, d, *J* = 7.9 Hz, *H*-1a), 4.53 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.26 (1 H, dd, *J* = 9.6, 9.2 Hz, *H*-4a), 3.88 (1 H, t, *J* = 6.6 Hz, *H*-5b), 3.68 (1 H, d, *J* = 11.2, 6.6 Hz, *H*-6b); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 165.82, 165.52, 165.34, 165.17, 165.10, 164.71, 158.35, 133.48, 133.35, 133.21, 133.12, 129.94, 129.83, 129.69, 129.60, 129.47, 129.38, 129.31, 128.99, 128.90, 128.79, 128.73, 128.64, 128.52, 128.23, 128.19, 125.25, 117.66, 114.52, 100.95, 98.71, 76.01, 72.96, 72.89, 71.74, 71.65, 71.34, 70.17, 69.85, 68.68, 67.46, 62.39, 61.03; *Anal.* Calcd. for $C_{71}H_{66}O_{19}$: C, 69.56; H, 4.89. Found: C, 70.06; H, 4.97.

p-*Allyloxybenzyl* O-*(3*-O-*allyl*-β-*D*-*galactopyranosyl*)-*(1*→*4)*-β-*D*-*glucopyranoside*. (**33**) To a stirred solution of **32** (7.10 g, 5.83 mmol) and phenolphthalein in MeOH (200 ml) was added NaOMe (ca. 70 mg) and the mixture was stirred overnight at room temperature. The reaction mixture was neutrized with Amberlyst-50 and concentrated *in vacuo*. To this heptaol in toluene (100 ml) were added *n*-Bu_2SnO

(1.40 g, 5.62 mol) and refluxed, then removed H_2O. After cooled down to room temperature, allyl bromide (2.7 ml, 31.2 mmol) and *n*-Bu_4NBr (180 mg, 0.558 mmol) were added and stirred overnight at 90°C. The reaction mixture was allowed cooled down to room temperature and diluted with chloroform and 20% aq. KF. The aqueous layer was extracted three times with $CHCl_3$. The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue (9.9 g) was chromatographed on silica gel (230-400 mesh, 500 g). Elution with AcOEt/EtOH/H_2O (45/2/1) gave **33** (1.94 g, 63 %); $[\alpha]_D$ -12.0° (c 1.1, CH_3OH); ^{1}H-NMR (270 MHz, CD_3OD) δ: 7.32 (2 H, d, *J* = 8.6 Hz, Arom *H*), 6.90 (2 H, d, *J* = 8.6 Hz, Arom *H*), 6.1-5.9 (2 H, m, CH_2=C*H*), 5.4-5.1 (4 H, m, C*H*$_2$=CH), 4.83 (1 H, d, *J* = 11.2 Hz, $C_6H_5CH_2$), 4.59 (1 H, d, *J* = 11.2 Hz, $C_6H_5CH_2$), 4.52 (2 H, dt, *J* = 5.3, 1.3 Hz, CH_2=CHC*H*$_2$), 4.38 (1 H, d, *J* = 7.9 Hz, *H*-1b), 4.37 (1 H, d, *J* = 7.6 Hz, *H*-1a), 4.22 (1 H, ddt, *J* = 12.5, 5.6, 1.3 Hz, CH_2=CHC*H*$_2$), 4.13 (1 H, ddt, *J* = 12.5, 5.6, 1.3 Hz, CH_2=CHC*H*$_2$O), 3.62 (1 H, dd, *J* = 9.6, 7.9 Hz, *H*-2b); ^{13}C-NMR (67.5 MHz, CD_3OD) δ: 159.76, 136.38, 134.86, 130.89, 117.50, 117.44, 115.52, 105.01,

102.73, 81.97, 80.73, 76.89, 76.44, 76.33, 74.68, 71.77, 71.57, 69.74, 66.97, 62.50, 61.90; *Anal.* Calcd. for $C_{25}H_{36}O_{12}$: C, 56.86; H, 7.10. Found: C, 56.81; H, 6.87.

p-*Allyloxybenzyl* O-*(3-O-allyl-2,4,6-tri*-O-*benzyl-β–D-galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β-D-glucopyranoside.*

(**34**) To a stirred mixture of **33** (300 mg, 0.568 mmol) and BnBr (0.900 ml, 7.57 mmol) in DMF (18 ml) was added NaH (360 mg, 5.00 mmol) at 0 °C under N_2 and the mixture was stirred overnight at room temperature. The reaction mixture was diluted with ether and quenched with MeOH and water. The aqueous layer was extracted three times with ether and the combined organic layers were dried with $MgSO_4$, and concentrated *in vacuo*. The residue (900 mg) was chromatographed on silica gel (70-230 mesh, 27 g). Elution with toluene/AcOEt (15/1) gave **34**. (580 mg, 96 %); $[\alpha]_D$ -9.6° (c 1.7, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.4-7.1 (32 H, m, Arom *H*), 6.86 (2 H, d, *J* = 8.6 Hz, Arom *H*), 6.2-5.8 (2 H, m, CH_2=C*H*), 5.4-5.1 (4 H, m, C*H*$_2$=CH), 4.46 (1 H, d, *J* = 7.6 Hz, *H*-1), 4.42 (1 H, d, *J* = 7.6

Hz, *H*-1), 4.32 (1 H, d, *J* = 11.7 Hz, $C_6H_5CH_2$), 4.23 (1 H, d, *J* = 11.7 Hz, $C_6H_5CH_2$); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 158.24, 139.14, 139.08, 138.87, 138.67, 138.45, 138.08, 134.97, 133.26, 129.78, 129.54, 128.41, 128.32, 128.19, 128.10, 128.00, 127.91, 127.84, 127.80, 127.71, 127.62, 127.48, 127.44, 127.37, 127.28, 127.01, 117.61, 116.35, 114.57, 109.81, 102.75, 102.23, 97.22, 83.02, 82.36, 81.76, 79.89, 76.82, 75.33, 75.20, 74.93, 74.57, 73.50, 73.37, 73.05, 72.94, 71.45, 70.66, 68.79, 68.38, 68.09, 66.97; *Anal.* Calcd. for $C_{67}H_{72}O_{12}$: C, 75.26; H, 6.80. Found: C, 75.26; H, 6.79.

p-*Hydoroxybenzyl* O-*(2,4,6-tri*-O-*benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β-D-glucopyranoside.*

(**35**) Ir{(COD)[PCH_3Ph_2]2}PF_6 (18 mg) in fresh distilled THF (5 ml) was treated under H_2 for 10 min at room temperature and this mixture was added to a stirred solution of **34** (700 mg, 0.655 mmol) in fresh distilled THF (5 ml) and stirred for 30 min at room temperature. The reaction mixture was concentrated *in vacuo*. To a solution of this residue in acetone/H_2O was added $HgCl_2$ (380 mg, 1.40 mmol) and

HgO (55.0 mg, 0.254 mmol) at room temperature and stirred for 6 h at room temperature. The reaction mixture was diluted with $CHCl_3$, filtered through Celite, wash twice with 10% aq. KI, dried with $MgSO_4$, and concentrated *in vacuo*. The residue (1.02 g) was chromatographed on silica gel (70-230 mesh, 30 g). Elution with toluene/AcOEt (5/1) gave **35**. (571 mg, 88 %); $[\alpha]_D$ -15.9° (c 0.65, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.3-7.1 (32 H, m, Arom *H*), 6.73 (2 H, d, *J* = 8.6 Hz, Arom *H*), 5.16 (1 H, b, O*H*), 5.00 (1 H, d, *J* = 10.6 Hz, $C_6H_5CH_2$), 4.87 (1 H, d, *J* = 10.9 Hz, $C_6H_5CH_2$), 4.84 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.80 (1 H, d, *J* = 11.5 Hz, $C_6H_5CH_2$), 4.75 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.71 (1 H, d, *J* = 10.9 Hz, $C_6H_5CH_2$), 4.67 (1 H, d, *J* = 11.5 Hz, $C_6H_5CH_2$), 4.60 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.59 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.56 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.46 (1 H, d, *J* = 7.3 Hz, *H*-1), 4.45 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.42 (1 H, d, *J* = 10.6 Hz, $C_6H_5CH_2$), 4.41 (1 H, d, *J* = 7.3 Hz, *H*-1), 4.38 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.27 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 3.97 (1 H, dd, *J* = 9.3, 8.9 Hz, *H*-4a), 3.83 (1 H, d, *J* = 2.0 Hz, *H*-4b), 3.55 (1 H, t, *J* = 8.9 Hz, *H*-3a), 2.19 (1 H, d, *J*

= 5.6 Hz, O*H*); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 155.47, 139.03, 138.65, 138.54, 138.40, 138.17, 137.95, 129.79, 129.38, 128.43, 128.36, 128.30, 128.23, 128.09, 127.98, 127.92, 127.75, 127.69, 127.60, 127.53, 127.15, 115.20, 102.64, 102.14, 82.82, 81.71, 80.58, 76.70, 75.92, 75.33, 75.08, 74.97, 74.05, 73.35, 73.17, 70.69, 68.29, 67.94; *Anal.* Calcd. for $C_{61}H_{64}O_{12}$•1/2H_2O: C, 73.40; H, 6.56. Found: C, 73.43; H, 6.66.

O-4-(5-Ethoxycarbonylpentaoxy)benzyl O-(2,4,6-tri-O-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside.

(**36**) To a stirred mixture of **35** (128 mg, 0.129 mmol) and Cs_2CO_3 (51.0 mg, 0.156 mmol) in DMF (2 ml) was added Ethyl 6-bromohexanoate (0.0270 ml, 0.152 mmol) and the mixture was stirred over night at room temperature. The reaction mixture was diluted with ether, washed with cold-water and cold-brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (142 mg) was chromatographed on silica gel (70-230 mesh, 7 g). Elution with toluene/AcOEt (6/1) gave **36**. (134 mg, 92 %); $[\alpha]_D$ -12.5° (c 1.1,

$CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 7.4-7.1 (32 H, m, Arom *H*), 6.83 (2 H, d, *J* = 8.6 Hz, Arom *H*), 4.99 (1 H, d, *J* = 10.6 Hz, $C_6H_5CH_2$), 4.88 (1 H, d, *J* = 10.6 Hz, $C_6H_5CH_2$), 4.87 (1 H, d, *J* = 11.6 Hz, $C_6H_5CH_2$), 4.80 (1 H, d, *J* = 11.2 Hz, $C_6H_5CH_2$), 4.72 (1 H, d, *J* = 10.6 Hz, $C_6H_5CH_2$), 4.72 (1 H, d, *J* = 11.2 Hz, $C_6H_5CH_2$), 4.67 (1 H, d, *J* = 11.6 Hz, $C_6H_5CH_2$), 4.60 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.58 (1 H, d, *J* = 11.6 Hz, $C_6H_5CH_2$), 4.46 (1 H, d, *J* = 7.6 Hz, *H*-1a or *H*-1b), 4.45 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.42 (1 H, d, *J* = 7.3 Hz, *H*-1a or *H*-1b), 4.38 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.28 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.13 (2 H, q, *J* = 7.3 Hz, $COOCH_2CH_3$), 3.84 (1 H, d, *J* = 2.1 Hz, *H*-4b), 2.33 (2 H, t, *J* = 7.6 Hz, CH_2COO), 1.9-1.4 (8 H, m, $OC_4H_8CH_2COO$), 1.25 (3 H, t, *J* = 7.3 Hz, $COOCH_2CH_3$); ^{13}C-NMR ($CDCl_3$) δ: 173.57, 158.67, 139.05, 138.67, 138.62, 138.40, 138.24, 137.97, 129.67, 129.58, 129.34, 128.45, 128.37, 128.30, 128.23, 128.18, 128.09, 128.03, 128.00, 127.92, 127.85, 127.67, 127.64, 127.53, 127.49, 127.44, 127.08, 114.27, 102.61, 102.10, 82.84, 81.69, 80.56, 76.66, 75.87, 75.29, 75.10, 75.02, 74.88, 74.04, 73.30, 73.14, 73.10, 70.62, 68.25, 67.89, 67.57, 60.18, 34.18, 28.90, 25.59, 24.66,

14.20; *Anal.* Calcd. for $C_{69}H_{78}O_{14}$•3/2H_2O: C, 71.54; H, 7.05. Found: C, 71.56; H, 6.94.

*1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose.* (**37**) Data; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.9-7.8 (2 H, m, Arom *H*), 7.8-7.7 (2 H, m, Arom *H*), 6.52 (1 H, d, *J* = 8.9 Hz, *H*-1), 5.89 (1 H, dd, *J* = 10.6, 9.2 Hz, *H*-3), 5.22 (1 H, dd, *J* = 10.2, 9.2 Hz, *H*-4), 4.48 (1 H, dd, *J* = 10.6, 8.9 Hz, *H*-2), 4.37 (1 H, dd, *J* = 12.5, 4.6 Hz, *H*-6), 4.15 (1 H, dd, *J* = 12.5, 2.0 Hz, *H*-6), 4.03 (1 H, ddd, *J* = 10.2, 4.6, 2.0 Hz, *H*-5), 2.12, 2.04, 2.00 and 1.87 (1 H×4, s, COC*H*$_3$).

*p-Methoxyphenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside.* (**38**) To a stirred solution of **37** (40.0 g, 83.8 mmol) and 4-methoxyphenol (13.0 g, 105 mmol) in dichloroethane (200 ml) was added dropwise TMSOTf (1.00 ml, 5.17 mmol) in dichloroethane (10 ml) at room temperature under N_2 and the mixture was stirred for 1 d at room temperature. The reaction mixture was diluted with CH_2Cl_2 and *sat.* $NaHCO_3$. The aqueous layer was extracted twice with

$CHCl_3$ and the combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was crystallized from ether to afford **38**. (44.0g, 97 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.8-7.7 (2 H, m, Arom *H*), 7.8-7.7 (2 H, m, Arom *H*), 6.9-6.7 (5 H, m, Arom *H*), 5.85 (1 H, d, *J* = 8.6 Hz, *H*-1), 5.85 (1 H, dd, *J* = 10.9, 8.9 Hz, *H*-3), 5.24 (1 H, dd, *J* = 10.2, 8.9 Hz, *H*-4), 4.57 (1 H, dd, *J* = 10.9, 8.6 Hz, *H*-2), 4.35 (1 H, dd, *J* = 12.2, 5.0 Hz, *H*-6), 4.18 (1 H, dd, *J* = 12.2, 2.3 Hz, *H*-6), 3.96 (1 H, ddd, *J* = 10.2, 5.0, 2.3 Hz, *H*-5), 3.73 (3 H, s, OC*H*$_3$), 2.11, 2.05 and 1.89 (1 H×3, s, COC*H*$_3$).

p-*Methoxyphenyl 4,6*-O-*benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside*. (**39**) To a stirred solution of **38** (66.4 g, 138 mmol) and phenolphthalein in MeOH (1500 ml) was added 28% NaOMe in MeOH (3.00 ml, 15.6 mmol) dropwise and the mixture was stirred overnight at room temperature under basic condition. The reaction mixture was neutralized with Amberlyst-50 and concentrated *in vacuo*. To this triol in acetonitrile (500 ml) were added camphorsulfonic acid (3.77 g, 14.9 mmol) and successively added dropwise benzaldehyde

dimethyl acetal (45.0 ml, 300 mol) and the mixture was stirred for 2 d at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was dissolved in AcOEt. The organic layer was treated with Amberlyst-50, filtered, washed with *sat.* $NaHCO_3$ and brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue was crystallized from MeOH to afford **39**. (45.1 g, 73 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.9-7.7 (4 H, m, Arom *H*), 7.5-7.4 (5 H, m, Arom *H*), 6.9-6.7 (5 H, m, Arom *H*), 5.81 (1 H, d, *J* = 8.3 Hz, *H*-1), 5.60 (3 H, s, C_6H_5CH), 4.71 (1 H, m, *H*-3), 4.51 (1 H, dd, *J* = 10.6, 8.3 Hz, *H*-2), 4.41 (1 H, dd, *J* = 10.2, 4.3 Hz, *H*-6), 3.72 (3 H, s, OCH_3), 2.50 (1 H, b, O*H*).

p-*Methoxyphenyl 4,6-O-benzylidene-3-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside.* (**40**) To a stirred mixture of **39** (30.0 g, 59.6 mmol) and BnBr (32.0 ml, 269 mmol) in DMF (300 ml) was added NaH (60% oil suspension, 9.00 g, 225 mmol) at 0 °C and the mixture was stirred overnight at room temperature. The reaction mixture was diluted with ether and quenched with MeOH and water. The aqueous layer was extracted three times with ether and the

combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue (50 g) was chromatographed on silica gel (70-230 mesh, 1500 g). Elution with toluene/AcOEt (15/1) gave **40**. (33.1 g, 94 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.7 (4 H, b, Arom *H*), 7.6-7.4 (5 H, m, Arom *H*), 7.0-6.7 (9 H, m, Arom *H*), 5.7 (1 H, d, *J* = 7.9 Hz, *H*-1), 5.65 (3 H, s, C_6H_5CH), 4.82 (1 H, d, *J* = 12.5 Hz, $C_6H_5CH_2$), 4.53 (1 H, d, *J* = 12.5 Hz, $C_6H_5CH_2$), 3.71 (3 H, s, OCH_3).

p-*Methoxyphenyl 3,6-di*-O-*benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside*. (**41**) To a stirred mixture of **40** (8.60 g, 14.5 mmol), triethylsilane (12.0 ml, 75.1 mmol) and AW-300 molecular sieves (7 g) in dry CH_2Cl_2 (70 ml) was added trifluoroacetic acid (5.60 ml, 72.7 mmol) in dry CH_2Cl_2 (10 ml) at 0 °C under N_2 and the mixture was stirred for 6 h at 0°C to room temperature. The reaction mixture was diluted with AcOEt, quenched with *sat.* $NaHCO_3$ and filtered through Celite. The aqueous layer was extracted with AcOEt and the combined organic layer was dried with $MgSO_4$, and

concentrated *in vacuo*. The residue (9.0 g) was chromatographed on silica gel (70-230 mesh, 450 g). Elution with toluene/AcOEt (7/1) gave **41**. (7.15 g, 83 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.81 (4 H, b, Arom *H*), 7.4-7.3 (5 H, m, Arom *H*), 7.1-7.0 (5 H, m, Arom *H*), 6.8-6.7 (4 H, m, Arom *H*), 5.66 (1 H, d, *J* = 8.3 Hz, *H*-1), 4.77 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.63 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.59 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.57 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.40 (1 H, dd, *J* = 10.6, 8.3 Hz, *H*-2), 4.31 (1 H, dd, *J* = 10.9, 8.3 Hz, *H*-3), 3.70 (3 H, s, OCH_3), 2.91 (1 H, d, 2.3 Hz, O*H*).

2,2,2-Trichloroethyl 2,3,4,6-tetra-O-*acetyl-β-D-galactopyranoside.* (**43**) To a stirred solution of **42** (80.0 g, 205 mmol) and *n*-$Bu_3SnOCH_2CCl_3$ (115 g, 263 mmol) in dichloroethane (900 ml) was added $SnCl_4$ (28.0 ml, 239 mmol) in dichloroethane (100 ml) dropwise at 0 °C under N_2 and stirred for 1 d at room temperature. To the reaction mixture was added KI (210 g) in water (300 ml) and stirred overnight at room temperature, filtered through Celite, washed with *sat*. $NaHCO_3$, filtered through Celite again, dried with $MgSO_4$ and

concentrated *in vacuo*. The residue was precipitated with *i*-Pr_2O to afford **43**. (60.9 g, 62 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 5.42 (1 H, d, *J* = 3.3 Hz, *H*-4), 5.33 (1 H, dd, *J* = 10.6, 7.9 Hz, *H*-2), 5.07 (1 H, dd, *J* = 10.6, 3.3 Hz, *H*-3), 4.83 (1 H, d, *J* = 7.9 Hz, *H*-1), 4.41 (1 H, d, *J* = 12.2 Hz, CCl_3CH_2), 4.17 (1 H, d, *J* = 12.2 Hz, CCl_3CH_2), 2.16, 2.10 and 2.09 (3 H×3, s, $COCH_3$).

2,2,2-Trichloroethyl 3,6-di-O-allyl-β-D-galactopyranoside. (**44**) To a stirred solution of **43** (46.6 g, 97.1 mmol) and phenolphthalein in MeOH (500 ml) was added 28% NaOMe in MeOH (7.00 ml, 36.3 mmol) and the mixture was stirred overnight at room temperature. The reaction mixture was neutralized with Amberlyst-50 and concentrated *in vacuo*. To this tetraol in toluene (1500 ml) were added (*n*-$Bu_3Sn)_2O$ (90.0 g, 151 mol) and the mixture was refluxed with azeotropic removal of H_2O by the additional of toluene (500 ml). After cooled down to room temperature, AllBr (146 ml, 1.69 mol) and *n*-Bu_4NBr (4.5 g, 14.0 mmol) were added and the mixture was stirred 1 d at 110°C. The reaction mixture was cooled down to room

temperature and to this were added KF (200 g) and water (500 ml). The mixture was stirred overnight at room temperature and filtered through Celite. The filter-cake was washed with *sat.*$NaHCO_3$ and the filtrate was filtered through Celite again. The filtrate was dried with $MgSO_4$ and concentrated *in vacuo*. The residue (80 g) was chromatographed on silica gel (70-230 mesh, 1800 g). Elution with toluene/AcOEt (2/1) gave **44** (31.7 g, 83 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.0-5.8 (2 H, m, CH_2=C*H*), 5.35 (1 H, dd, *J* = 8.3, 1.7 Hz, C*H*$_2$=CH), 5.29 (1 H, dd, *J* = 8.6, 1.7 Hz, C*H*$_2$=CH), 5.25 (1 H, dd, *J* = 4.6, 1.7 Hz, C*H*$_2$=CH), 5.21 (1 H, dd, *J* = 4.6, 1.7 Hz, C*H*$_2$=CH), 4.57 (1 H, d, *J* = 7.6 Hz, *H*-1), 4.46 (1 H, d, *J* = 11.6 Hz, CCl_3C*H*$_2$), 4.20 (1 H, d, *J* = 11.6 Hz, CCl_3C*H*$_2$), 3.88 (1 H, ddd, *J* = 9.6, 7.6, 2.3 Hz, *H*-2), 3.43 (1 H, dd, *J* = 9.6, 3.3 Hz, *H*-3).

*2,4-Di-*O*-acetyl-3,6-di-*O*-allyl-D-galactopyranoside.* (**45**) To a stirred solution of **44** (25.8 g, 65.9 mmol) in pyridine (50 ml, 621 mmol) and CH_2Cl_2 (25 ml) was added dropwise acetic anhydride (50 ml, 529 mmol) at room temperature and the mixture was stirred overnight at

room temperature. The reaction mixture was concentrated *in vacuo* and the residue was co-evaporated with toluene. The residue was dissolved in acetic acid (200 ml, 3.49 mol). To this reaction mixture was added Zn (70 g, 1.07 mol) in several portions and the mixture was stirred overnight at room temperature. The reaction mixture was filtered through Celite and concentrated *in vacuo*. The residue (24 g) was chromatographed on silica gel (70-230 mesh, 730 g). Elution with toluene/AcOEt (5/1, 2/1) gave **45** (21.5 g, 95 %); **45**α: ^{1}H-NMR (270 MHz, $CDCl_3$) δ 5.9-5.8 (2 H, m, CH_2=C*H*), 5.50 (1 H, d, *J* = 3.0 Hz, *H*-1), 5.08 (1 H, dd, *J* = 10.2, 3.3 Hz, *H*-2), 4.34 (1 H, dd, *J* = 6.3, 5.3 Hz, *H*-5), 2.14 and 2.13 (3 H×2, s, C*H*$_3$).; **45**β: ^{1}H-NMR (270 MHz, $CDCl_3$) δ 5.9-5.8 (2 H, m, CH_2=C*H*), 4.95 (1 H, dd, *J* = 9.9, 7.9 Hz, *H*-2), 3.77 (1 H, dd, *J* = 6.9, 5.9 Hz, *H*-5), 2.15 and 2.14 (3 H×2, s, COC*H*$_3$).

2,4-Di-O-acetyl-3,6-di-O-allyl-D-galactopyranosyl 2,2,2-trichloroacetoimidate. (**46**) To a stirred solution of **45** (4.14 g, 12.0 mmol) and Cl_3CCN (8.40 ml, 83.8 mmol) in dry CH_2Cl_2 (50 ml) was

added NaH (60% oil suspension, 45.0 mg, 1.12 mmol) at 0 °C and the mixture was stirred for 15 min at room temperature. The reaction mixture was directly chromatographed on silica gel (70-230 mesh, 230 g). Elution with *n*-hexane/AcOEt (2/1) gave **46**α (3.32 g, 57 %) and **46**β (2.00 g, 34 %); **46**α: ^{1}H-NMR (270 MHz, $CDCl_3$) δ 8.59 (1 H, s, $CCl_3C(N=H)$), 6.56 (1 H, d, *J* = 3.6 Hz, *H*-1), 5.9-5.8 (2 H, m, $CH_2=CH$), 5.63 (1 H, dd, *J* = 3.3, 1.1 Hz, *H*-4), 4.28 (1 H, ddd, *J* = 6.6, 5.9, 1.1 Hz, *H*-5), 3.98 (1 H, dd, *J* = 10.2, 3.3 Hz, *H*-3), 3.53 (1 H, dd, *J* = 9.6, 5.9 Hz, *H*-6), 3.45 (1 H, dd, *J* = 9.6, 6.6 Hz, *H*-6), 2.16 and 2.04 (3 H×2, s, $COCH_3$); *Anal.* Calcd. for $C_{18}H_{24}Cl_3NO_8$: C, 44.24; H, 4.95; N, 2.87. Found: C, 43.90; H, 4.88; N, 2.72.; **46**β : ^{1}H-NMR (270 MHz, $CDCl_3$) δ 8.66 (1 H, s, $CCl_3C(N=H)$), 5.9-5.7 (2 H, m, $CH_2=CH$), 5.77 (1 H, d, *J* = 8.3 Hz, *H*-1), 5.55 (1 H, dd, *J* = 3.3, 1.1 Hz, *H*-4), 5.38 (1 H, dd, *J* = 10.2, 8.3 Hz, *H*-2), 3.62 (1 H, dd, *J* = 10.2, 3.3 Hz, *H*-3), 3.61 (1 H, dd, *J* = 9.9, 5.9 Hz, *H*-6), 3.52 (1 H, dd, *J* = 9.9, 6.6 Hz, *H*-6), 2.18 and 2.04 (3 H×2, s, $COCH_3$); *Anal.* Calcd. for $C_{18}H_{24}Cl_3NO_8$: C, 44.24; H, 4.95; N, 2.87. Found: C, 43.93; H, 4.94; N, 2.87.

p-*Methoxyphenyl* O-*(2,4-di-O-acetyl-3,6-di-O-allyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside.* (**47**) To a stirred mixture of **41** (3.23 g, 5.42 mmol), TMSOTf (0.16 ml, 0.828 mmol) and AW-300 molecular sieves (8.5 g) in dry CH_2Cl_2 (85 ml) was added dropwise **46** (4.55 g, 9.30 mmol) in dry CH_2Cl_2 (35 ml) over 1.5 h at -78 °C and the mixture was stirred for 20 min. at -78 °C. The reaction mixture was quenched with $NaHCO_3$ in water-THF, added extra $NaHCO_3$, allowed to room temperature and filtered through Celite. The aqueous layer was extracted with $CHCl_3$. The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue (8.2 g) was chromatographed on silica gel (230-400 mesh, 250 g). Elution with toluene/AcOEt (7/1) gave **47** (4.20 g, 84 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.67 (4 H, b, Arom *H*), 7.4-6.7 (14 H, m, Arom *H*), 5.9-5.7 (2 H, m, CH_2=C*H*), 5.62 (1 H, d, *J* = 7.9 Hz, *H*-1a), 5.41 (1 H, d, *J* = 3.0 Hz, *H*-4b), 4.87 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.77 (1 H, d, *J* =

11.9 Hz, $C_6H_5CH_2$), 4.56 (1 H, d, J = 8.3 Hz, H-1b), 3.69 (3 H, s, OCH_3), 2.07 and 2.06 (3 H×2, s, $COCH_3$).

p-*Methoxyphenyl* O-*(3,6-di*-O-*allyl-β-D-galactopyranosyl)-(1→4)-3,6-di*-O-*benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside*. (**48**) To a stirred mixture of **47** (3.51 g, 3.81 mmol), 31% H_2O_2 in H_2O (32.0 ml, 291 mmol) in THF (87 ml) was added LiOH (400 mg, 17.0 mmol) at -0 °C and the mixture was stirred overnight at room temperature. The reaction mixture was diluted with AcOEt and H_2O, added a drop of AcOH and stirred for 1 h. The aqueous layer was extracted with AcOEt. The combined organic layers were washed with *sat.*$NaHCO_3$, aq. $Na_2S_2O_3$ and brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (3.2 g) was chromatographed on silica gel (70-230 mesh, 100 g). Elution with toluene/AcOEt (2/1) gave **48** (2.90 g, 92 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.66 (4 H, b, Arom H), 7.4-6.7 (14 H, m, Arom H), 6.0-5.7 (2 H, m, CH_2=CH), 5.58 (1 H, d, J = 7.9 Hz, H-1a), 5.4-5.1 (4 H, m, CH_2=CH), 4.88 (1 H, d, J = 12.5 Hz, $C_6H_5CH_2$), 4.73

(1 H, d, J = 12.2 Hz, $C_6H_5CH_2$), 4.61 (1 H, d, J = 12.2 Hz, $C_6H_5CH_2$), 4.58 (1 H, d, J = 7.6 Hz, *H*-1b), 3.70 (3 H, s, OCH_3).

p-*Methoxyphenyl* O-*(3,6-di*-O-*allyl*-*2,4-di*-O-*benzyl*-*β*-*D*-*galactopyranosyl)*-*(1→4)*-*3,6-di*-O-*benzyl*-*2*-*deoxy*-*2*-*phthalimido*-*β*-*D*-*glucopyranoside*. (**49**) To a stirred mixture of **48** (707 mg, 0.843 mmol), Ag_2O (2.35 g, 10.1 mmol) and KI (842 mg, 5.07 mmol) in DMF (7 ml) was added BnBr (1.30 ml, 10.9 mmol) at -0 °C and the mixture was stirred 4.5 h at room temperature. The reaction mixture was diluted with ether and H_2O. The aqueous layer was extracted three times with ether. The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue (1.6 g) was chromatographed on silica gel (70-230 mesh, 90 g). Elution with *n*-hexane/AcOEt (5/2) gave **49** (705 mg, 82 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.68 (4 H, b, Arom *H*), 7.4-6.7 (24 H, m, Arom *H*), 6.0-5.7 (2H, m, CH_2=C*H*), 5.62 (1 H, d, J = 7.9 Hz, *H*-1a), 5.4-5.1 (4 H, m, CH_2=CH), 4.93 (1 H, d, J = 11.5 Hz, $C_6H_5CH_2$), 4.84 (1 H, d, J = 11.5 Hz, $C_6H_5CH_2$), 4.45 (1 H, d, J = 7.9 Hz, *H*-1b), 3.70 (3 H, s, OCH_3).

p-*Methoxyphenyl* O-*(2,4-di-O-benzyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside*. (**50**) $Ir\{(COD)[PCH_3Ph_2]_2\}PF_6$ (20 mg) in fresh distilled THF (10 ml) was treated under H_2 for 10 min at room temperature and this mixture was added to a stirred solution of **49** (909 mg, 0.893 mmol) in fresh distilled THF (35 ml) and the mixture was stirred for 30 min at room temperature. The reaction mixture was concentrated *in vacuo*. To a solution of this residue in acetone/H_2O was added $HgCl_2$ (645 mg, 2.24 mmol) and HgO (77.0 mg, 0.356 mmol) at room temperature and the mixture was stirred for 2 h at room temperature. The reaction mixture was diluted with $CHCl_3$, added aq. KI, filtered through Celite. The aqueous layer was extracted three times with $CHCl_3$. The combined organic layers were washed with *sat*. $NaHCO_3$ and brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (1.2 g) was chromatographed on silica gel (70-230 mesh, 60 g). Elution with toluene/AcOEt (2/1) gave **50**. (690 mg, 82 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.69 (4 H, b, Arom *H*), 7.4-6.7 (24 H, m, Arom *H*), 5.64 (1

H, d, J = 7.9 Hz, H-1a), 4.93 (1 H, d, J = 12.2 Hz, $C_6H_5CH_2$), 4.92 (1 H, d, J = 11.2 Hz, $C_6H_5CH_2$), 4.80 (1 H, d, J = 11.6 Hz, $C_6H_5CH_2$), 4.72 (1 H, d, J = 11.6 Hz, $C_6H_5CH_2$), 4.58 (1 H, d, J = 11.9 Hz, $C_6H_5CH_2$), 4.58 (1 H, d, J = 11.6 Hz, $C_6H_5CH_2$), 4.46 (1 H, d, J = 7.3 Hz, H-1b), 4.11 (1 H, dd, J = 10.9, 6.9 Hz, H-4a), 3.70 (3 H, s, OCH_3).

p-Methoxyphenyl O-(6-O-acetyl-2,4-di-O-benzyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside. (**51**) To a stirred mixture of **50** (690 mg, 0.736 mmol) in pyridine (9 ml, 112 mmol) was added AcCl (0.110 ml, 1.56 mmol) at 0 °C and the mixture was stirred 3 h at 0 °C. The reaction mixture was quenched with MeOH, stirred for 1 h at room temperature and diluted with AcOEt and H_2O. The organic layer was extracted three times with AcOEt. The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue (707 mg) was chromatographed on silica gel (70-230 mesh, 35 g). Elution with toluene/AcOEt (4/1) gave **51** (643 mg, 89 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.68 (4 H, b, Arom H), 7.4-6.7 (24 H, m, Arom H), 5.62 (1

H, d, J = 8.3 Hz, *H*-1a), 4.91 (1 H, d, J = 11.6 Hz, $C_6H_5CH_2$), 4.86 (1 H, d, J = 11.2 Hz, $C_6H_5CH_2$), 4.79 (1 H, d, J = 11.5 Hz, $C_6H_5CH_2$), 4.70 (1 H, d, J = 11.2 Hz, $C_6H_5CH_2$), 4.60 (1 H, d, J = 11.8 Hz, $C_6H_5CH_2$), 4.60 (1 H, d, J = 11.8 Hz, $C_6H_5CH_2$), 4.50 (1 H, d, J = 12.9 Hz, $C_6H_5CH_2$), 4.46 (1 H, d, J = 7.3 Hz, *H*-1b), 3.98 (1 H, dd, J = 11.2, 6.6 Hz, *H*-6b), 3.70 (3 H, s, OCH_3), 2.00 (3 H, s, $COCH_3$).

p-*Methoxyphenyl* O-*(6*-O-*acetyl-2,4-di*-O-*benzyl-3*-O-*levulinoly-β-D-galactopyranosyl)-(1→4)-3,6-di*-O-*benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside*. (**52**) To a stirred solution of **51** (377 mg, 0.385 mmol) and DMAP (cat.) in pyridine (5 ml, 62.1 mmol) was added Lev_2O (300 mg, 1.23 mmol) at 0 °C and the mixture was stirred overnight at room temperature. The reaction mixture was concentrated *in vacuo* and co-evaporated with toluene. The residue (700 mg) was chromatographed on silica gel (70-230 mesh, 70 g). Elution with *n*-hexane/AcOEt (3/2) gave **52** (381 mg, 93 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.68 (4 H, b, Arom *H*), 7.3-6.7 (24 H, m, Arom *H*), 5.61 (1 H, d, J = 7.9 Hz, *H*-1a), 4.85 (1 H, d, J = 11.6 Hz,

$C_6H_5CH_2$), 4.82 (1 H, d, J = 11.6 Hz, $C_6H_5CH_2$), 4.74 (1 H, d, J = 11.6 Hz, $C_6H_5CH_2$), 4.68 (1 H, d, J = 11.6 Hz, $C_6H_5CH_2$), 4.51 (1 H, d, J = 7.0 Hz, *H*-1b), 3.70 (3 H, s, OCH_3), 3.50 (1 H, t, J = 7.0 Hz, *H*-5b), 2.8-2.4 (4 H, m, $CH_3COCH_2CH_2$-), 2.36 and 1.99 (3 H×2, s, $COCH_3$).

O-*(6-O-Acetyl-2,4-di-O-benzyl-3-O-levulinoly-β-D-galactopyranosyl)-(1→4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranose.*

(**53**) To a solution of **52** (1.43 g, 1.34 mmol) in toluene (27 ml), acetonitrile (36 ml) and H_2O (27 ml) was added CAN (3.30 g, 6.02 mmol) at 0 °C and the mixture was stirred for 1.5 h at 0 °C. The reaction mixture was diluted with AcOH and H_2O. The aqueous layer was extracted three times with AcOH. The combined organic layers were washed with *sat.* $NaHCO_3$ and brine, dried with $MgSO_4$ and concentrated *in vacuo*. The residue (1.7 g) was chromatographed on silica gel (70-230 mesh, 90 g). Elution with toluene/AcOEt (2/1) gave **53** (1.20 g, 95 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.69 (4 H, m, Arom *H*), 7.4-7.2 (15 H, m, Arom *H*), 7.1-7.0 (2 H, m, Arom *H*), 6.9-6.8 (3

H, m, Arom *H*), 5.29 (1 H, t, *J* = 8.6 Hz, *H*-1a), 4.86 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.81 (1 H, dd, *J* = 10.2, 3.3 Hz, *H*-3b), 4.77 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.73 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.68 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.58 (1 H, d, *J* = 12.2 Hz, $C_6H_5CH_2$), 4.50 (1 H, d, *J* = 11.5 Hz, $C_6H_5CH_2$), 4.47 (1 H, d, *J* = 11.9 Hz, $C_6H_5CH_2$), 4.44 (1 H, d, *J* = 7.6 Hz, *H*-1b), 2.86 (1 H, d, *J* = 8.6 Hz, O*H*), 2.8-2.4 (4 H, m, $CH_3COCH_2CH_2$-), 2.16 and 1.97 (3 H×2, s, $COCH_3$).

O-*(6-O-Acetyl-2,4-di-O-benzyl-3-O-levulinoly-β-D-galactopyranosyl)-(1→4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl 2,2,2-trichloroacetoimidate.* (**27**) To a stirred solution of **53** (239 mg, 0.254 mmol) and Cl_3CCN (0.180 ml, 1.80 mmol) in dry CH_2Cl_2 (2 ml) was added DBU (7 µl, 0.050 mmol) at 0 °C and the mixture was stirred for 30 min. at room temperature. The reaction mixture was directly chromatographed on silica gel (70-230 mesh, 25 g). Elution with toluene/AcOEt (5/1) gave **27** (261 mg, 95 %); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 8.53 (1 H, s, N*H*), 7.76 (4 H, m, Arom H), 7.7-7.2 (15 H, m, Arom H), 7.0-6.9 (2 H, m, Arom H), 6.9-6.8 (3 H, m, Arom H),

6.39 (1 H, d, J = 8.3 Hz, H-1a), 4.86 (1 H, d, J = 12.2 Hz, $C_6H_5CH_2$), 4.82 (1 H, dd, J = 9.9, 3.3 Hz, H-3b), 4.80 (1 H, d, J = 11.9 Hz, $C_6H_5CH_2$), 4.73 (1 H, d, J = 11.6 Hz, $C_6H_5CH_2$), 4.67 (1 H, d, J = 12.2 Hz, $C_6H_5CH_2$), 4.63 (1 H, d, J = 12.5 Hz, $C_6H_5CH_2$), 4.50 (1 H, d, J = 11.9 Hz, $C_6H_5CH_2$), 4.22 (1 H, dd, J = 9.6, 8.2 Hz, H-4a), 3.46 (1 H, t, J = 6.6 Hz, H-5b), 3.0-2.2 (4 H, m, $CH_3COCH_2CH_2$-), 2.16 and 1.99 (3 H×2, s, $COCH_3$).

Linker A type. (i) *35 on Resin A* (**28**); To a stirred solution of **35** (190 mg, 0.192 mmol) in DMF (7 ml) were added Merrifield resin (960 mg, 1% cross-linked, 100-200 mesh, PEPTIDE INSTITUTE. INC., 0.66 meq/g) and Cs_2CO_3 (116 mg, 0.356 mmol) at room temperature and the mixture was shaked for 2 d at 50 °C. The resin was filtered, washed with DMF, MeOH, H_2O, MeOH and CH_2Cl_2 successively, and dried to afford to **28** (1.098 g, 96 % calculated by increased weight, 0.132 mmol/g).

(ii) *Synthesis of tetrasaccharide on Resin A*; To a stirred mixture of the resin **28** (60.0 mg) and 0.2 M TMSOTf in dry CH_2Cl_2 (18.0 µl, 3.6

μmol) was added dropwise 50 μM solution of **27** in dry CH_2Cl_2 (150 μl, 7.5 μmol) at -78°C and the mixture was stirred for 30 min at -78°C. To this was added dropwise additional 50 μM **27** in dry CH_2Cl_2 (150 μl, 7.5 μmol) and the whole was stirred for additional 1.5 h at -78°C. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried. The same procedure was repeated to give presumed tetrasaccharide on the resin (66.7 mg).

(iii) *Deprotection of levulinoyl group of presumed tetrasaccharide on Resin A*; To a mixture of this resin (57.7 mg) in CH_2Cl_2 (0.7 ml) were added H_2NNH_2•AcOH (16 mg, 174 μmol) in MeOH (0.6 ml) and the mixture was shaked overnight at room temperature. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried to give presumed tetrasaccharide with hydroxy group on Resin A (56.4 mg).

(iv) *Synthesis of hexasaccharide on Resin A*; To a stirred mixture of this resin (50.0 mg) and 0.2 M TMSOTf in dry CH_2Cl_2 (4.5 μl, 0.9 μmol) was added dropwise 50 μM solution of **27** in dry CH_2Cl_2 (50 μl, 2.5 μmol) at -78°C and the mixture was stirred for 30 min at - 78°C.

To this was added dropwise additional 50 μM solution of **27** in dry CH_2Cl_2 (50 μl, 2.5 μmol) and the whole was stirred for 1.5 h at -78°C. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried. The same procedure was repeated to give presumed hexasaccharide on the Resin A. (57.0 mg)

(v) *Deprotection of levulinoyl group of presumed hexasaccharide on Resin A*; To a mixture of the hexasaccharide (31.8 mg) of resin A on in CH_2Cl_2 (0.7 ml) was added H_2NNH_2•AcOH (16 mg, 174 μmol) in MeOH (0.6 ml) and the mixture was shaked overnight at room temperature. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried to give presumed hexasaccharide with hydroxy group on Resin A (28.0 mg).

(vi) *Synthesis of octasaccharide on Resin A* (**54**); To a stirred mixture of this resin (25.0 mg) and 0.2 M TMSOTf in dry CH_2Cl_2 (3.0 μl, 0.6 μmol) was added dropwise 50 μM solution of **27** in dry CH_2Cl_2 (30 μl, 1.5 μmol) at -78°C and the mixture was stirred for 30 min at - 78°C. To this was added dropwise additional 50 μM solution of **27** in dry CH_2Cl_2 (30 μl, 1.5 μmol) and the whole was stirred for 1.5 h at -78°C.

The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried. The same procedure was repeated to give presumed octasaccharide on the Resin A. (28.0 mg)

(vii) *Detachment octasaccharide from Resin A*; (O-*(6*-O-*Acetyl-2,4-di*-O-*benzyl-3*-O-*levulinoly-β-D-galactopyranosyl)-(1→4)*-O-*(3,6-di*-O-*benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)*-O-*(6*-O-*acetyl-2,4-di*-O-*benzyl-β-D-galactopyranosyl)-(1→4)*-O-*(3,6-di*-O-*benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)*-O-*(6*-O-*acetyl-2,4-di*-O-*benzyl-β-D-galactopyranosyl)-(1→4)*-O-*(3,6-di*-O-*benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-α and β-D-glucopyranose*. (**55**) To a stirred mixture of **54** (18.5 mg) in CH_2Cl_2 (0.5 ml) was added $TrBF_4$ (8 mg, 24 μmol) and the mixture was shaked for 3 min at room temperature. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and the filtrate was washed with *sat.* $NaHCO_3$. Second treatment of resin with $TrBF_4$ (8 mg, 24 μmol) in CH_2Cl_2 (0.5 ml) was carried out for 10 min at room temperature. The resin was filtered, washed with CH_2Cl_2, MeOH and

CH_2Cl_2 again and the filtrate was washed with *sat.* $NaHCO_3$. Third treatment of resin with $TrBF_4$ (8 mg, 24 μmol) in CH_2Cl_2 (0.5 ml) was carried out for 20 min at room temperature. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and the filtrate was washed with *sat.* $NaHCO_3$. The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residure was chromatographed on Bio-beads S-X2. Elution with toluene gave octasaccharide (3.9 mg, 42 % yield from **35**), hexasaccharide having levulinoyl group (0.9 mg, 13 % yield from **35**) and haxasaccharide having hydroxy group (1.1 mg, 17 % yield from **35**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.41 (1 H, d, J = 8.4 HZ, *H*-1), 5.23 (1 H, d, J = 8.0 Hz, *H*-1), 5.16 (1 H, d, J = 7.2 Hz, *H*-1), 2.16, 1.94, 1.81 and 1.79 (3 H×4, s, $COCH_3$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 170.36, 138.79, 138.29, 138.06, 137.95, 133.41, 131.02, 128.42, 128.37, 128.30, 128.21, 128.11, 128.06, 127.99, 127.93, 127.88, 127.73, 127.61, 127.45, 127.38, 127.07, 126.91, 126.33, 126.25, 122.94, 103.13, 102.44, 99.82, 91.33, 81.74, 78.28, 77.20, 75.60, 75.17, 74.81, 74.52, 74.04, 73.58, 73.17, 73.02, 71.65, 70.07, 68.49, 62.73, 61.81, 56.27,

37.71, 29.76, 27.87, 20.74, 20.64; FABMS: Calcd. 3548.4, Found: (positive); m/z 3571.9 $[M+Na]^+$

Linker B type. (i) ***36*** *on Resin B*; To a stirred solution of **36** (82 mg, 0.0725 mmol) in THF (5 ml) and EtOH (1 ml) was added dropwise 1.0 M NaOH (0.165 ml, 0.165 mmol) and the mixture was stirred overnight at 45 °C. The reaction mixture was diluted with AcOEt and acidified with 1N aq. HCl. The aqueous layer was extracted three times with AcOEt. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated *in vacuo*. To a stirred solution of the residue (80 mg) in DMF (10 ml) were added Merrifield resin (662 mg, 1% cross-linked, 100-200 mesh, PEPTIDE INSTITUTE.INC., 0.66 meq/g) and Cs_2CO_3 (45 mg, 0.138 mmol) at room temperature and the mixture was shaked overnight at 50 °C. The resin was filtered, washed with DMF, MeOH, H_2O, MeOH and CH_2Cl_2 successively and dried to afford to **29** (736 mg, 99 % calculated by increased weight, 0.0944 mmol/g).

(ii) *Synthesis of tetrasaccharide on Resin B*; To a stirred mixture of the disaccharide with hydroxy group on Resin B (700 mg) and 0.2 M TMSOTf in dry CH_2Cl_2 (70 µl, 14 µmol) was added dropwise 130 µM solution of **27** in dry CH_2Cl_2 (350 µl, 45.5 µmol) at -78°C and the mixture was stirred for 30 min at - 78°C. To this was added dropwise additional 130 µM **27** in dry CH_2Cl_2 (350 µl, 45.5 µmol) and the whole was stirred for 1.5 h at -78°C. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried. The same procedure was repeated to give presumed tetrasaccharide on Resin B (758 mg).

(iii) *Capping of unreacted hydroxy groups in disaccharide on Resin B and deprotection of levulinoyl group of presumed tetrasaccharide on Resin B*; To a mixture of the resin (753 mg) in CH_2Cl_2 (7 ml) were added Ac_2O (3 ml) and pyridine (2 ml) and the mixture was shaked overnight at room temperature. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried. To a mixture of this resin B in CH_2Cl_2 (7 ml) was added H_2NNH_2•AcOH (270 mg, 2.94 mmol) in MeOH (7 ml) and the whole was shaked overnight at room

temperature. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried to give presumed tetrasaccharide with hydroxy group on Resin B (760 mg).

(iii) *Synthesis of hexasaccharide on Resin B*; To a stirred mixture of the tetrasaccharide having hydroxy group on Resin B (728 mg) and 0.2 M TMSOTf in dry CH_2Cl_2 (70 µl, 14 µmol) was added dropwise 130 µM solution of **27** in dry CH_2Cl_2 (350 µl, 45.5 µmol) at -78°C and the mixture was stirred for 30 min at - 78°C. To this was added dropwise additional 130 µM solution of **27** in dry CH_2Cl_2 (350 µl, 45.5 µmol) and the whole was stirred for 1.5 h at -78°C. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried. The same procedure was repeated to give presumed hexasaccharide on the resin (755 mg).

(iv) *Capping of unreacted hydroxy groups in tetrasaccharide on Resin B* (**56**); To a mixture of the resin (764 mg) in CH_2Cl_2 (7 ml) were added Ac_2O (3 ml) and pyridine (2 ml) and shaked overnight at room temperature. The resin was filtered, washed with CH_2Cl_2, MeOH and CH_2Cl_2 again and dried. (755 mg)

(v) Detachment hexasaccharide from **56**; (p-*(5-Methoxycarbonylpentaoxy)benzyl* O-*(2,4-Di*-O-*benzyl-β-D-galactopyranosyl)-(1→4)*-O-*(3,6-di*-O-*benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)*-O-*(2,4-Di*-O-*benzyl-β-D-galactopyranosyl)-(1→4)*-O-*(3,6-di*-O-*benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)*-O-*(2,4,6-tri*-O-*benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β-D-glucopyranose.* (**57**))

To a stirred mixture of **56** (164 mg) in MeOH (3 ml) was added NaOMe (7 mg, 130 μmol) and the mixture was shaked for 7 h at 45 °C. The reaction mixture was neutralized with AcOH and concentrated *in vacuo*. The residure (20 mg) was chromatographed on PTLC. Elution with *n*-hexane/AcOEt (3/4) gave hexasaccharide **57** (12.7 mg, 56 % from **36**); $[\alpha]_D$ -3.30° (c 1.15, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 7.7-6.8 (82 H, m, Arom *H*), 5.40 (1 H, d, *J* = 8.6 Hz, *H*-1c or *H*-1e), 5.21 (1 H, d, *J* = 7.6 Hz, *H*-1c or *H*-1e), 4.98 (1 H, d, *J* = 11.6 Hz, $C_6H_5CH_2$), 4.95 (1 H, d, *J* = 11.6 Hz, $C_6H_5CH_2$), 3.66 (3 H, s, $COOCH_3$), 2.34 (2 H, t, CH_2COOCH_3), 1.8-1.4 (8 H, m, $OC_4H_8CH_2COOCH_3$); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ:;174.07,

168.21, 168.03, 167.98, 167.80, 167.73, 167.69, 167.58, 167.51, 167.40, 163.45, 158.63, 139.30, 138.96, 138.72, 138.60, 138.51, 138.35, 138.26, 138.15, 137.84, 133.50, 131.11, 131.02, 129.51, 129.42, 128.59, 128.43, 128.32, 128.19, 128.16, 127.98, 127.89, 127.75, 127.60, 127.57, 127.51, 127.40, 127.13, 127.08, 126.99, 126.63, 126.22, 123,02, 114,23, 103.22, 102.93, 102.32, 102.05, 99.93, 99.55, 91.86, 82.88, 82.18, 81.83, 81.53, 80.32, 78.78, 78.64, 78.37, 77.93, 77.20, 75.94, 75.49, 75.29, 75.20, 75.02, 74.88, 74.81, 74.63, 74.54, 74.31, 73.89, 73.17, 73.12, 73.01, 72.89, 70.55, 68.36, 67.57, 62.09, 61.96, 56.28, 51.48, 33.95, 29.65, 28.90, 25.63, 24.64; FABMS: Calcd. 2744.2, Found: (negative); m/z 2742.6 $[M-H]^-$

O-β-D-galactopyranosyl-(1→4)-O-*(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)*-O-*β-D-galactopyranosyl-(1→4)*-O-*(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)*-O-*β-D-galactopyranosyl-(1→4)-α and β-D-glucopyranose*. (**58**) To a stirred solution of **57** (12 mg, 0.00450 mmol) in EtOH (1 ml) was added $H_2NCH_2CH_2NH_2$ (0.0700 ml, 1.05 mmol) at room temperature and the

mixture was stirred for 3 d at 90 °C. The reaction mixture was concentrated *in vacuo*. The residue was dissolved in MeOH (1 ml) and to this was added Ac_2O (0.5 ml) dropwise at room temperature and the mixture was stirred for 1 d at room temperature. The reaction mixture was concentrated *in vacuo*. To the residue in MeOH (0.7 ml) was added $Pd(OH)_2$ (3.6 mg) and the mixture was stirred for 7 h at room temperature under H_2. To this was added H_2O (0.3 ml) and the whole was stirred for further 3 h at room temperature. The reaction mixture was filtered through Celite and the filtration was concentrated *in vacuo*, solved with H_2O, washed with ether. The aqueous layer was concentrated *in vacuo* afford to **58**. (2.6 mg, 56 %); $[\alpha]_D$ +21.1° (c 0.700, H_2O); ^{1}H-NMR (400 MHz, D_2O) δ: 5.21 (1 H, d, J = 3.9 Hz, *H*-1a), 4.69 (2 H, d, J = 8.3 Hz, *H*-1 and *H*-1), 4.65 (1 H, d, J = 7.8 Hz, *H*-1), 4.46 (1 H, d, J = 7.8 Hz, *H*-1), 4.45 (1 H, d, J = 7.8 Hz, *H*-1), 4.42 (1 H, d, J = 7.8 Hz, *H*-1); ^{13}C-NMR (125 MHz, D_2O) δ: 176.57, 104.58, 104.47, 97.44, 93.52, 83.77, 79.95, 79.83, 77.06, 76.59, 76.51, 76.26, 76.05, 75.48, 74.20, 73.87, 73.10, 72.82, 72.67, 71.83, 71.68, 70.26, 70.05, 62.75, 62.67, 61.78, 61.55, 56.89, 23.88; FABMS: Calcd.

1072.3, Found: (positive); m/z 1095.3 $[M+Na]^+$, (negative); m/z 1071.0 $[M-H]^-$

p-*(5-Methoxycarbonylpentaoxy)benzyl* O-*(2,4,6-tri*-O-*benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl-β-D-glucopyranoside.*

(**59**) To a mixture of **29** (0.0830 mmol/g calcd. from **36**, 98 mg, 0.00813 mmol) in CH_2Cl_2 (2 ml) was added NaOMe (7 mg, 0.130 mmol) in MeOH (2 ml) and the mixture was shaked for 7 h at 45 °C. The reaction mixture was filtered and the resin was washed with MeOH. The combined organic layers were neutralized with AcOH and concentrated *in vacuo*. The residue was chromatographed by PTLC afford to **59**. (8.3 mg, 91 %); ^{1}H-NMR ($CDCl_3$) δ: 7.4-7.1 (32 H, m, Arom *H*), 6.83 (2 H, d, *J* = 8.6 Hz, Arom *H*), 4.99 (1 H, d, *J* = 10.6 Hz, $C_6H_5CH_2$), 4.89 (1 H, d, *J* = 10.9 Hz, $C_6H_5CH_2$), 4.87 (1 H, d, *J* = 11.6 Hz, $C_6H_5CH_2$), 4.81 (1 H, d, *J* = 11.5 Hz, $C_6H_5CH_2$), 4.73 (1 H, d, *J* = 10.6 Hz, $C_6H_5CH_2$), 4.72 (1 H, d, *J* = 10.9 Hz, $C_6H_5CH_2$), 4.72 (1 H, d, *J* = 11.5 Hz, $C_6H_5CH_2$), 4.67 (1 H, d, *J* = 11.6 Hz, $C_6H_5CH_2$), 4.61 (1 H, d, *J* = 11.6 Hz, $C_6H_5CH_2$), 4.58 (1 H, d, *J* = 12.2 Hz,

$C_6H_5CH_2$), 4.58 (1 H, d, J = 11.6 Hz, $C_6H_5CH_2$), 4.46 (1 H, d, J = 7.6 Hz, *H*-1a or *H*-1b), 4.45 (1 H, d, J = 12.2 Hz, $C_6H_5CH_2$), 4.42 (1 H, d, J = 7.3 Hz, *H*-1a or *H*-1b), 4.38 (1 H, d, J = 11.9 Hz, $C_6H_5CH_2$), 4.28 (1 H, d, J = 11.9 Hz, $C_6H_5CH_2$), 3.94 (1 H, t, J = 6.4 Hz, *H*-4a), 3.84 (1 H, d, J = 2.0 Hz, *H*-4b), 3.67 (3 H, s, $COOCH_3$), 2.35 (2 H, t, J = 7.4 Hz, CH_2COO), 1.8-1.4 (8 H, m, $OC_4H_8CH_2COO$).

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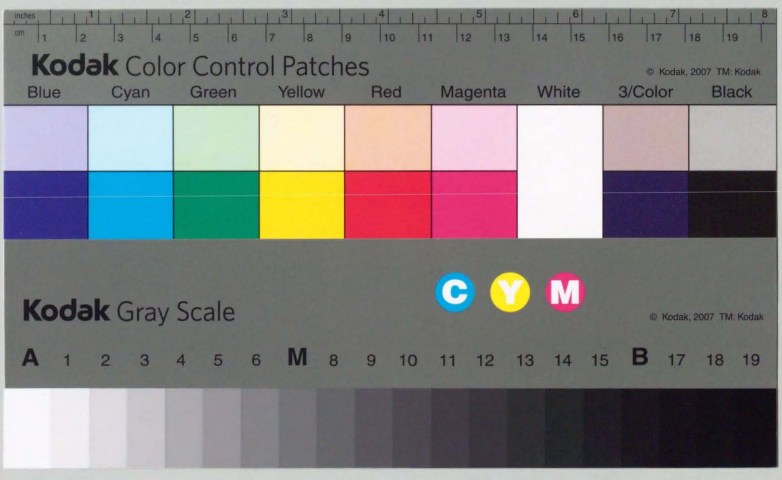
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