Syntheses of Trehazolin Derivatives and Evaluation as Glycosidase Inhibitors

Yoshiyuki Kobayashi and Masao Shiozaki*

Exploratory Chemistry Research Laboratories, Sankyo Co., Ltd., Hiromachi 1-2-58, Shinagawa-ku, Tokyo 140, Japan

Osamu Ando

Biomedical Research Laboratories, Sankyo Co., Ltd., Hiromachi 1-2-58, Shinagawa-ku, Tokyo 140, Japan

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The trehazolin derivatives **9**–**12** were synthesized from the aminocyclitol (**7**), which is the degradation product of trehazolin (**5**). In particular, compounds **9**–**11** were pseudodisaccharides that underwent replacement of the corresponding nonreducing D-glucose moieties of isomaltose and maltose by trehalamine (**6**), and they were designed to be therapeutic drugs; however, they did not show significant activities.

Introduction

Oligosaccharides, glycolipids, and glycoproteins as glycoconjugates are distributed widely in nature, and these materials have become the subject of intense research investigation. It has been recognized that enzymes such as glycosyltransferases and glycosidases play an important role in manipulating these glycoconjugates. Explorations and evaluations of inhibitors of these enzymes are quite significant, not only for resolving the functions of the sugars in the living system but also for finding therapeutic treatment for diseases generated by disorders of these enzymes. In particular, diabetes mellitus is very prevalent among a wide range of ages, and it is necessary to find effective medicines.

It is said that α-glucosidase inhibitors such as acarbose (**1**),[1] analogues of deoxynojirimycin (**2**),[1,2] analogues of castanospermine (**3**),[3] and AO-128 (**4**),[4] which was the derivative of valiolamine, will be effective for therapies for non-insulin-dependent diabetes mellitus (NIDDM) (Figure 1). In addition, we were interested, from the biochemical viewpoint, in investigating the relationship between various oligosaccharides and glycosidases, and it was indicated that biochemical studies and chemical modification of various α-glycosidase inhibitors might have paved the way for the exploration and development of these kinds of compounds as medicines.

In 1991, trehazolin (**5**) was reported by Ando and coworkers.[5] It is a unique pseudodisaccharide isolated from culture broths of both *Micromonspola* sp. strain SANK 62390 and *Amicolatopsis* sp. strain SANK 60793. It is an α-glucosidase inhibitor, and it exhibited strong and specific inhibitory activities toward various trehalases (Figure 2). Determination of the absolute configuration of trehazolin was carried out through our total syntheses of trehazolin and its related compounds, as shown in Figure 2.[6] Judging from the similarity of trehazolin and trehalose (**8**), it could be speculated that the aglycon of trehazolin, trehalamine (**6**),[7] was a pseudocompound of D-glucose. The structural resemblance between them and the specific activity of trehazolin toward trehalases made us expect that compounds, formed by replacing the

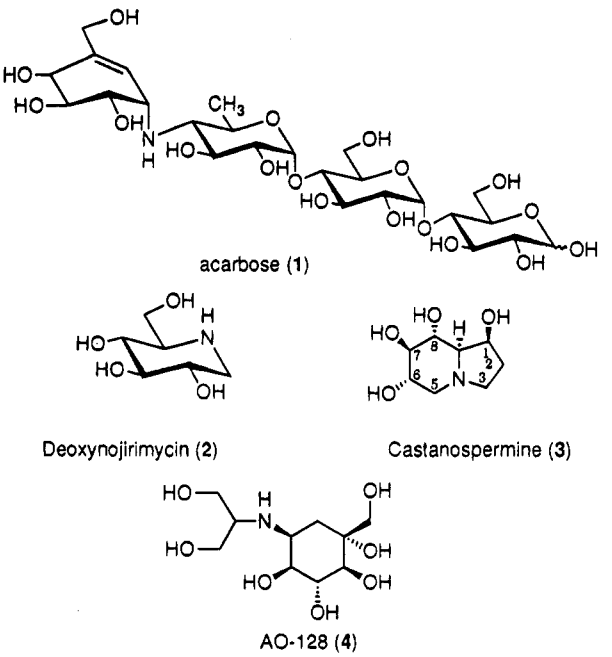

Figure 1. Structures of various α-glucosidase inhibitors.

[⊗] Abstract published in *Advance ACS Abstracts,* April 1, 1995.

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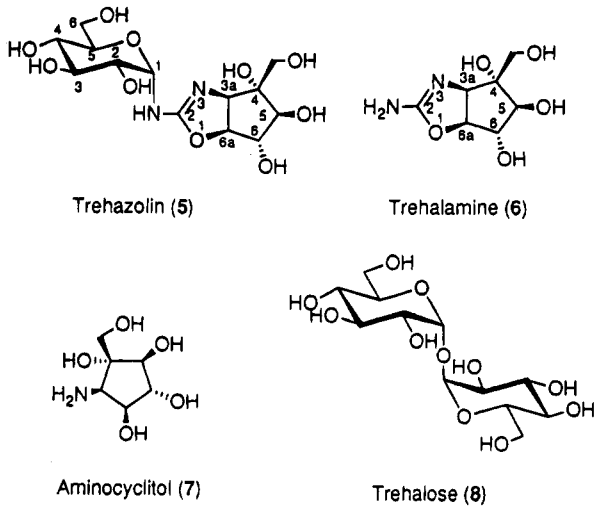

Figure 2. Structures of the compounds related to trehazolin.

nonreducing D-glucose moieties in isomaltose and maltose by **6**, would possess specific inhibitory activities toward isomaltases and maltases and also that they would have potential as drugs for NIDDM.

Therefore, we attempted syntheses of the trehazolin derivatives, in order not only to generalize a synthetic method into these trehazolin derivatives, but also to generate inhibitors toward other α-glucosidases.

Herein, we describe the syntheses of compounds **9**, **10**,[8] **11**, and **12** (Figure 3).

Synthetic Route for Trehazolin Derivatives

On the basis of our reported studies of trehazolin and its related compounds,[6,9] it was thought that the significant intermediates were thiourea derivatives II obtained from the aminocyclitol (**7**),[7] which was the degradation product of trehazolin, and the corresponding isothiocyanate compounds I derived from D-glucose and D-galactose. Subsequent treatment of these thiourea derivatives with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate[10] and triethylamine should produced the aminooxazolines III, which were the precursors of trehazoline derivatives, via the unstable carbodiimide intermediates. Finally, it was expected that cleavage of benzyl groups of III would furnish the pseudodisaccharides (Figure 4).

Synthesis of Isomaltose-Type Trehazolin Derivative 9. Compound (**9**) is the isomaltose-type trehazolin derivative, which was expected to possess specific inhibitory activity toward isomaltases (Scheme 1). Azidation of the hydroxy group[11] at the C-6 position of the D-glucose derivative **13**, which was reported by Mitsunobu *et al.*,[12] gave the corresponding azido D-glucose derivative **14**. Reduction of the azido group of compound **14** with lithium aluminum hydride produced the corresponding 6-amino sugar **15**. After treatment of **15** with carbon disulfide and triethylamine, addition of 2-chloro-1-methylpyridinium iodide[13] and Et_3N to this reaction mixture prompted β-elimination of the corresponding unstable dithiocarbamide acid triethylamine salt and afforded the isothiocyanate derivative **16**.[14]

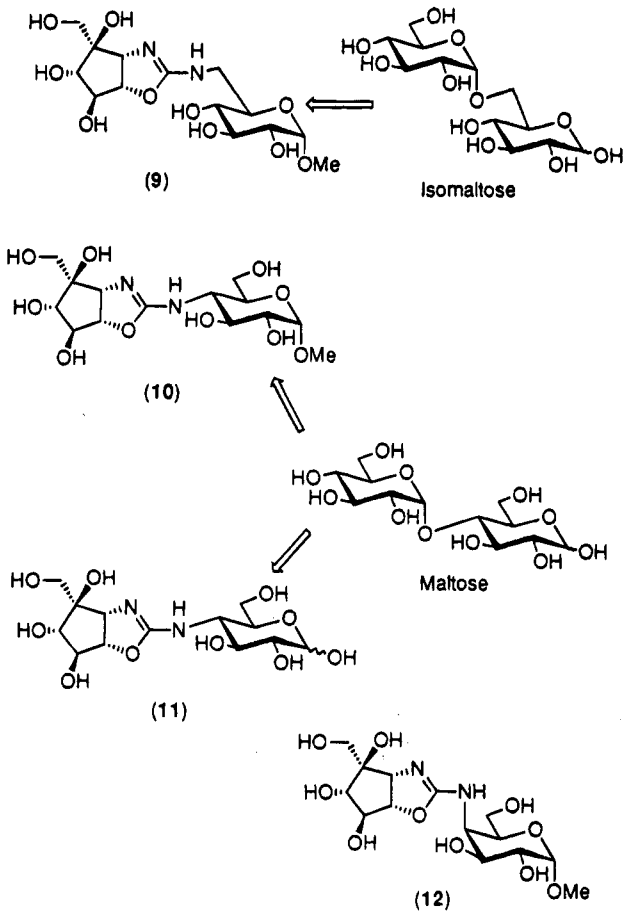

Figure 3. Structures of pseudodisaccharides related to trehazolin.

Coupling of the isothiocyanate **16** with **7** yielded the corresponding thiourea derivative **17**. Treatment of **17** with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate[10] and Et_3N produced the aminooxazoline **18**, and hydrogenolysis of **18** using $Pd(OH)_2$ on carbon as a catalyst, to cleave the three benzyl groups, furnished **9**.

Syntheses of Maltose-Type Trehazolin Derivatives 10 and 11 and α-D-Glc*p*-(1→4)-D-Gal*p*-Type Trehazolin Derivative 12. Compound **10**[8] is a maltose-type trehazolin derivative, which was expected to generate specific inhibitory activity toward maltases. The synthesis of **10** was accomplished as shown in Scheme 2.

Treatment of D-galactose derivative **19**, which was reported by Ek and Garegg *et al.*[15] with methanesulfonyl

(7) Ando, O.; Nakajima, M.; Hamano, K.; Itoi, K.; Takahashi, S.; Takamatsu, Y.; Sato, A.; Enokita, R.; Haruyama, H.; Kinoshita, T. *J. Antibiot.* **1993**, *46*, 1116–1125.

(8) The synthesis of this compound was reported by Knapp *et al.* independently: Knapp, S.; Purandare, A.; Rupitz, K.; Withers, S. G. *J. Am. Chem. Soc.* **1994**, *116*, 7461–7462.

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(15) Ek, M.; Garegg, P. J.; Hultberg, H.; Oscarson, S. *J. Carbohydr. Chem.* **1983**, *2*(3), 305–311.

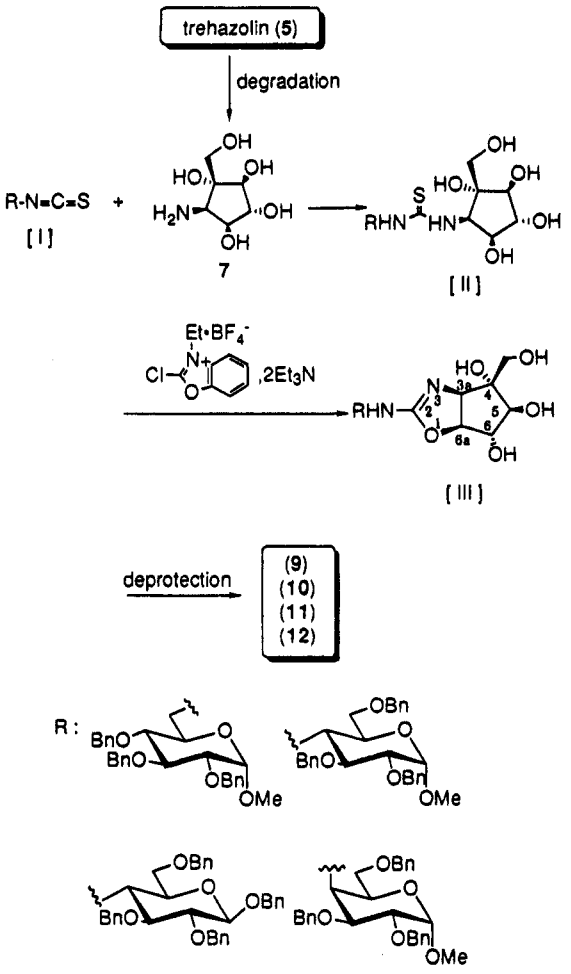


Figure 4. Synthetic route of pseudodisaccharides possessing trehalamine.

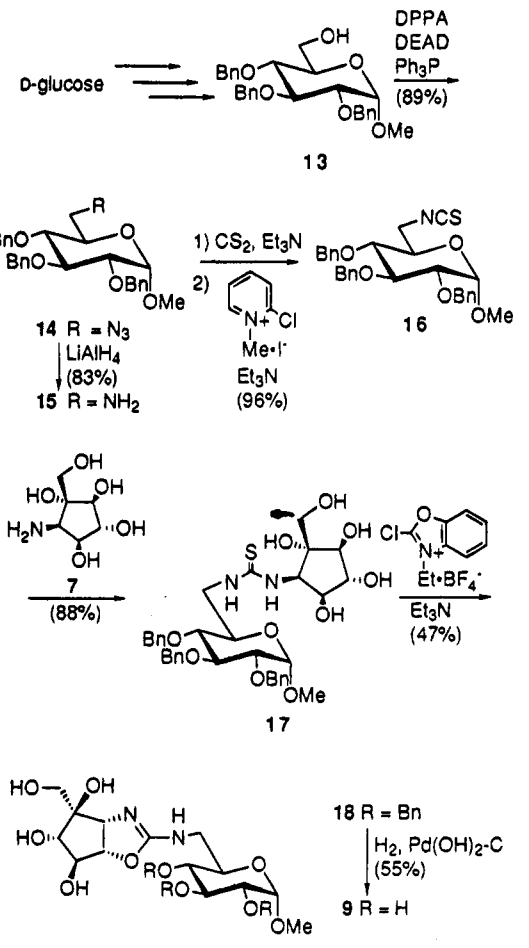
chloride in pyridine, yielded the corresponding mesylate **20**. S_N2-type azidation of **20** furnished the azido D-glucose derivative **21**. Reduction of the azido group of compound **21** with $LiAlH_4$ produced the 4-amino sugar **22**.

We attempted one-pot isothiocyanation[13] of **22**. However, in this case, the corresponding isothiocyanate derivative (**24**) was not obtained in a high yield, unfortunately. Therefore, we attempted Wittig–Horner–Emmons-type isothiocyanation.[16] Treatment of **22** with diethyl chlorophosphate and Et_3N gave the phosphoramide **23**. Reaction of **23** with sodium hydride and CS_2 yielded the expected isothiocyanate **24**[13] in a high yield.

Coupling of **24** with **7** gave the thiourea derivative **25**, and treatment of **25** with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate[10] and Et_3N afforded the aminooxazoline derivative **26**. Subsequent hydrogenolysis of **26** furnished **10**.

Compound **11** was also synthesized. It is a maltose-type pseudodisaccharide that has a reducing portion, and it is more similar structurally to maltose than **10** is. At first, the D-glucose isothiocyanate derivative **34** was synthesized from D-galactose pentaacetate **27** (Scheme 3). Glycosidation of **27** with benzyl alcohol and boron trifluoride etherate,[17] cleavage of acetyl groups, and

Scheme 1



subsequent benzylidenation of hydroxy groups at C-4 and C-6 positions gave **28**. After benzylation of the remaining hydroxy groups of **28**, regioselective benzylidene opening with boran–trimethylamine complex and aluminum trichloride in THF[15] afforded compound **29**, and mesylation of the hydroxy group at the C-4 position of **29** yielded mesylate **30**. S_N2-type azidation of **30**, and subsequent reduction of the azido group of **31** with $LiAlH_4$, furnished the 4-amino sugar **32**. After phosphorylation of the amino group of **32**, an isothiocyanate (**34**) was obtained by treatment of the corresponding phosphoramide **33** with NaH and CS_2.[16] Coupling of **34** with **7** gave the thiourea derivative **35**, and treatment of **35** with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate[10] and Et_3N produced an aminooxazoline **36**. Subsequent hydrogenolysis of **36**, to cleave the benzyl groups, furnished **11** (Scheme 4).

Compound **12** is an α-D-Glc*p*-(1→4)-D-Gal*p*-type pseudodisaccharide. The synthesis of **12** was accomplished as shown in Scheme 5. D-Glucose derivative **37**, which was reported by Ek and Garegg *et al.*,[15] was converted to the azido D-galactose derivative **39** by the same synthetic route as that for compound **10**. After reduction of the azido group of **39** with $LiAlH_4$, isothiocyanation was tried by the Mukaiyama method[14] and by Wittig–Horner–Emmons-type reaction.[16]

Unfortunately, both methods could not always produce the isothiocyanate **42** in a good yield, but we synthesized **42** by the latter method, which was a little superior in yield to the former. Coupling of **42** with **7**, treatment of thiourea (**43**) with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate[10] and Et_3N, and subsequent hydrogenoly-

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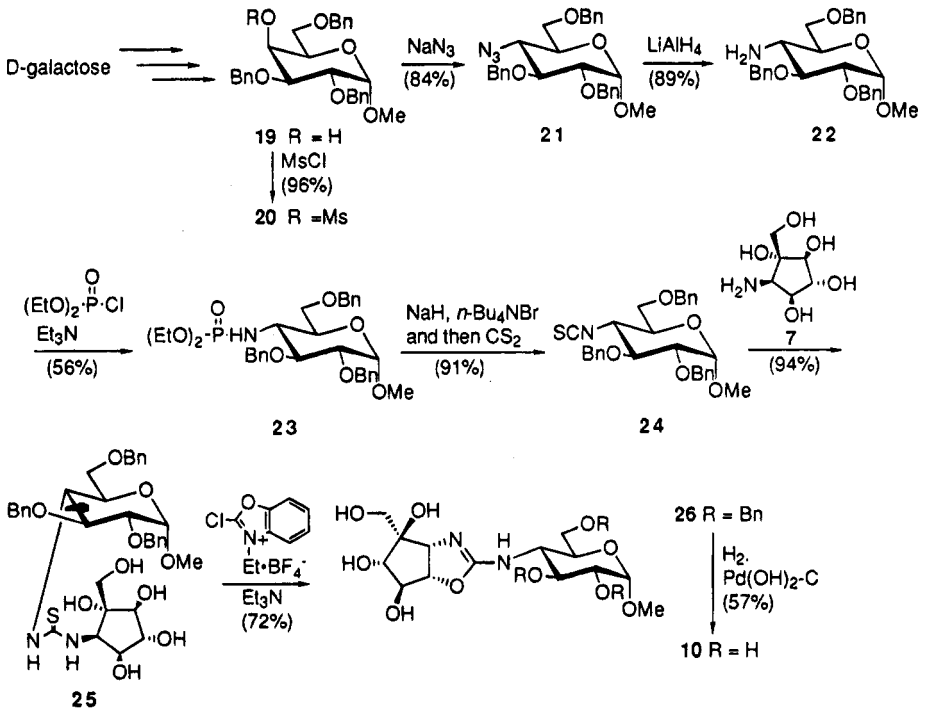
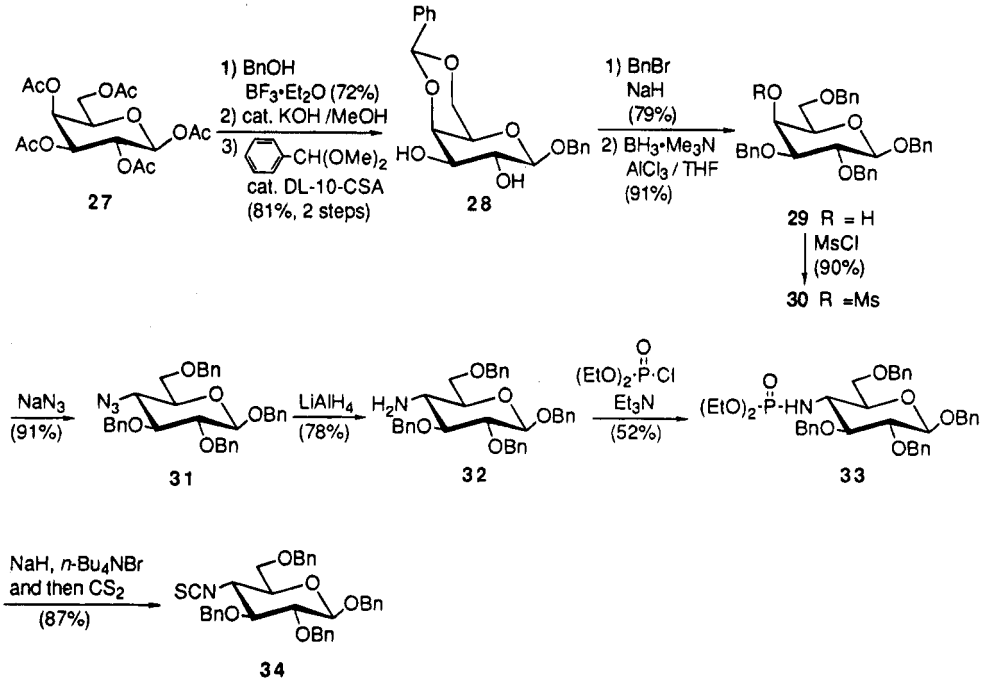
Scheme 2



Scheme 3

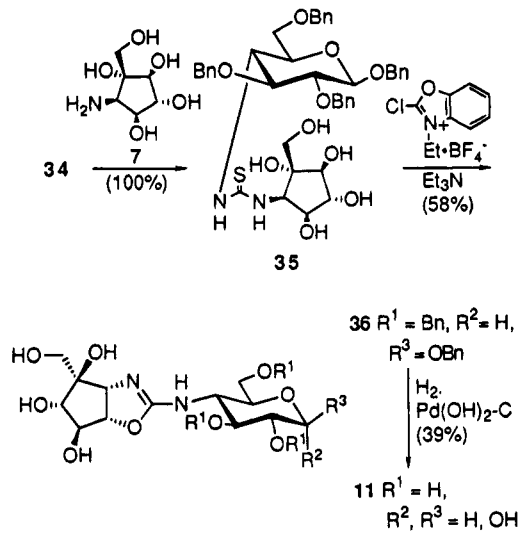


sis of aminooxazoline **44** using $Pd(OH)_2$ on carbon as a catalyst yielded **12**.

Inhibitory Activities of 9–12 toward Various α-Glucosidases. Inhibitory activities of the aforementioned synthetic pseudodisaccharides **9–12** and trehazolin toward rat intestinal α-glucosidases are listed in Table 1. Trehalase, maltase, isomaltase, and sucrase assays were carried out as previously reported,[18] using a one-step method in a microtiter plate. Enzymatic reactions were started by the addition of an enzyme solution without a preincubation of the enzyme and inhibitor. Buffers were a 20 mM citrate–40 mM phosphate buffer, at pH 5.4 for silkworm, and a buffer at pH 6.2 for other enzymes. These pseudodisaccharides were designed as intestinal maltase or isomaltase inhibitors directed to potent therapies for NIDDM; however, they possessed only weak or no inhibitory activities toward the rate enzymes. Compound **9** inhibited maltase and sucrase more potently than trehazolin, whereas **10–12** did not exhibit inhibitory activities toward maltase, isomaltase, and sucrase, compared with trehazolin. On the other hand, while none of the derivatives inhibited silkworm trehalase at a concentration of 100 μg/mL, only compound **11** possessed inhibitory activity toward porcine trehalase,

(18) Ando, O.; Nakajima, M.; Kifune, M.; Fang, H.; Tanzawa, K. *Biochim. Biophys. Acta*, in press.

Scheme 4



with an IC_{50} value of 0.245 μg/mL. In addition, Knapp *et al.* reported inhibition toward yeast α-glucosidase, of **10** synthesized by themselves independently,[8] and we also confirmed moderate inhibitory activities of **10** and **11** toward the same enzyme (data not shown). These results suggest that the interaction between an α-glucosidase and a glucose unit would be rather diverse among various glucosidases even though they can catalyze common substrates. Validamycins are another good example possessing similar biochemical properties related to enzyme inhibitions;[19] they inhibited porcine sucrase very potently, although yeast enzyme was poorly inhibited (as for valiolamine, IC_{50} values for porcine and yeast enzyme were 4.9×10^{-8} M and $>1.0 \times 10^{-2}$ M, respectively). In conclusion, it might be recognized that a relationship between inhibitory activities' generation and the structural resemblances of the inhibitors and the substrates did not always exist, and accurate structural analyses for the complexes consisting of the inhibitors and target enzymes were indicated to be necessary for design of the corresponding derivatives.

Conclusion

The synthetic pseudodisaccharides **9**–**12** were designed as potent inhibitors toward such α-glucosidases as intestinal maltase or isomaltase and directed to therapies for NIDDM. In particular, compounds **10** and **11** are analogous to maltose and **9** to isomaltose. Through these syntheses, the generality of the construction of the aminooxazoline framework via the carbodiimide and the utility of the aminocyclitol (**7**) as the starting material for syntheses of the various trehazolin derivatives were confirmed. In addition, the success of syntheses of these pseudodisaccharides indicated that this procedure is extensively applicable for various derivatives made through modifications at the amino group of trehalamine. On the other hand, they were expected to generate strong and enzyme-specific inhibitory activities to the corresponding α-glucosidases. However, the result was disappointing. Through the unexpected result, it was recognized that accurate structural analysis for the complex consisting of the inhibitor and target enzyme was more necessary for design of the corresponding derivatives than the structural resemblances between the inhibitors and the substrates with regard to inhibitory activities' generation.

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Experimental Section

General Method. Melting points are uncorrected. 270 MHz ^{1}H-NMR spectra were recorded using tetramethylsilane as an internal reference. Elemental analyses were performed by the Institute of Science and Technology, Inc. Analytical chromatography was performed on Merck Art 5715 silica gel 60-F_{245} plates. Flash chromatography was performed on Merck Art 9385 silica gel 60 (230–400 mesh). THF was distilled from $LiAlH_4$ and used immediately thereafter. Et_2O was dried by passage through ICN Alumina N-Super I. CH_2Cl_2 was dried by passage through ICN Alumina B-Super I. DMF and pyridine were dried by storage over 4A molecular sieves. MeCN was dried by storage over 3A molecular sieves. All other commercial reagents were used directly as received.

Methyl 6-Azido-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-glucopyranoside (14). To a solution of **13** (900 mg, 1.94 mmol) and triphenylphosphine (770 mg, 2.9 mmol) were added diethylazodicarboxylate (0.5 mL, 2.9 mmol) and diphenyl phosphorazidate (0.63 mL, 2.9 mmol) with stirring at 0 °C under N_2. After 10 min, the temperature was elevated to rt followed by stirring for 1 h. After completion of the reaction, this reaction mixture was diluted with EtOAc and washed with 1 M aqueous HCl. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (25:1) gave 843 mg (89%) of **14** as a colorless syrup: $[\alpha]^{25}_D$ +53.4° (*c* 0.82, $CHCl_3$); IR (film) ν_{max} 3032, 2919, 2100 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.45–7.20 (15H, m), 4.99 (1H, d, *J* = 10.6 Hz), 4.90 (1H, d, *J* = 11.2 Hz), 4.81 (1H, d, *J* = 11.2 Hz), 4.79 (1H, d, *J* = 12.2 Hz), 4.66 (1H, d, *J* = 12.2 Hz), 4.61 (1H, d, *J* = 3.6 Hz), 4.57 (1H, d, *J* = 10.6 Hz), 3.98 (1H, t, *J* = 9.2 Hz), 3.78 (1H, ddd, *J* = 9.2, 5.9, 2.6 Hz), 3.54 (1H, dd, *J* = 9.2, 3.6 Hz), 3.44 (1H, dd, *J* = 12.9, 2.6 Hz), 3.43 (1H, t, *J* = 9.2 Hz), 3.40 (3H, s), 3.32 (1H, dd, *J* = 12.9, 5.9 Hz); R_f = 0.3 (benzene); MS (EI) *m/z* 461 ($M^+ - N_2$), 430, 398, 370, 338. Anal. Calcd for $C_{28}H_{31}N_3O_5$: C, 68.69; H, 6.38; N, 8.58. Found: C, 68.53; H, 6.35; N, 8.67.

(Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-α-D-glucopyranosid-6-yl) Isothiocyanate (16). (a) To a suspension of $LiAlH_4$ (88 mg, 2.3 mmol) in Et_2O (10 mL) was added a solution of **14** (208 mg, 0.42 mmol) in Et_2O (6.0 mL) at 0 °C under N_2, and the mixture was stirred for 1 h, with the temperature kept at 0 °C. After completion of the reaction, the reaction mixture was diluted with Et_2O and saturated aqueous Na_2SO_4 was gradually added to the reaction mixture at 0 °C. After being stirred at 24 °C for 30 min, the mixture was extracted twice with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (15:1) gave 164 mg (83%) of an amino sugar **15** as a white gel: ^{1}H-NMR ($CDCl_3$) δ 7.45–7.23 (15H, m), 4.99 (1H, d, *J* = 11.2 Hz), 4.88 (1H, d, *J* = 11.2 Hz), 4.82 (1H, d, *J* = 11.2 Hz), 4.79 (1H, d, *J* = 12.2 Hz), 4.66 (1H, d, *J* = 12.2 Hz), 4.61 (1H, d, *J* = 11.2 Hz), 4.56 (1H, d, *J* = 3.6 Hz), 4.00 (1H, t, *J* = 9.2 Hz), 3.56 (1H, ddd, *J* = 13.9, 6.6, 2.6 Hz), 3.50 (1H, dd, *J* = 9.2, 3.6 Hz), 3.37 (3H, s), 3.34 (1H, t, *J* = 9.2 Hz), 2.98 (1H, d, *J* = 13.9, 2.6 Hz), 2.71 (1H, dd, *J* = 13.9, 6.6 Hz); R_f = 0.26 (CH_2Cl_2:MeOH = 15:1).

(b) To a solution of **15** (141 mg, 0.3 mmol) in CH_2Cl_2 (9.1 mL) were added CS_2 (0.037 mL, 0.61 mmol) and Et_3N (0.065 mL, 0.47 mmol) at 24 °C under N_2, and the mixture was stirred for 3 h. Next, to this mixture were added 2-chloro-1-methylpyridinium iodide (116 mg, 0.46 mmol) and Et_3N (0.065 mL, 0.47 mmol), with the reaction conditions maintained, and this was stirred for 2 h. After completion of the reaction, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and

Scheme 5

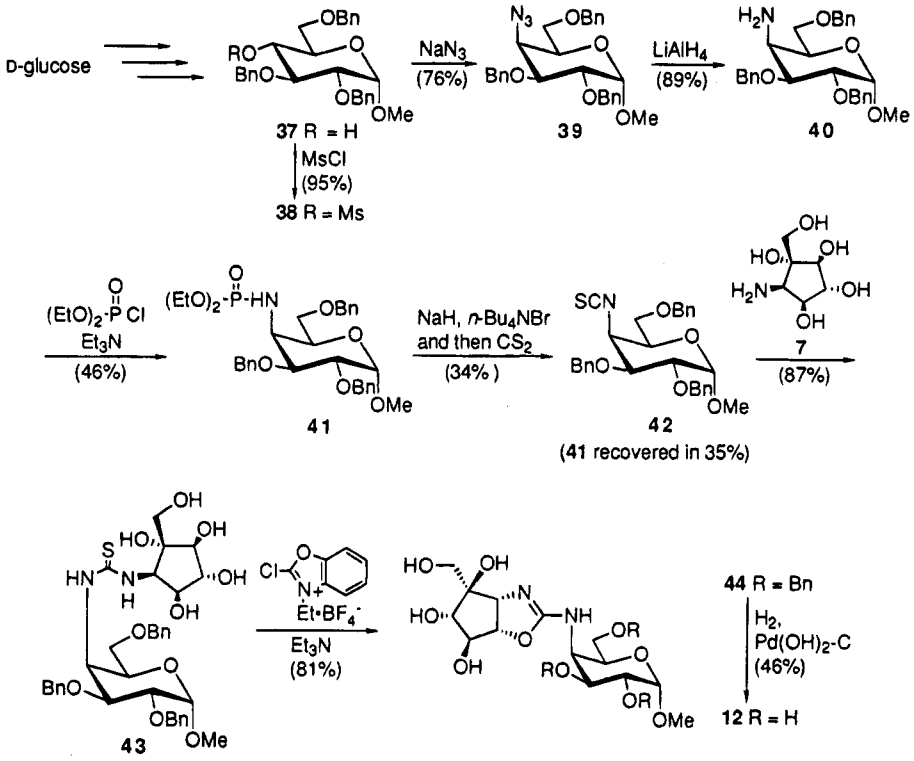

Table 1. Inhibitory Activities of the Pseudodisaccharides Possessing the Trehalamine Moiety (IC50: μg/mL)

enzyme	origin	trehazolin (5)	9	10	11	12
trehalase	silkworm	0.011	>100	>100	>100	>100
trehalase	porcine	0.006	92	>100	0.245	30
maltase	rat	76	9	>100	>100	>100
isomaltase	rat	3.9	55	>100	>100	72
sucrase	rat	76	10	>100	>100	>100

concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (5:1) gave 147 mg (96%) of **16** as a colorless syrup: $[\alpha]^{25}_D$ +86.8° (*c* 0.72, $CHCl_3$); IR (film) ν_{max} 3031, 2931, 2910, 2099 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.45–7.25 (15H, m), 5.00 (1H, d, *J* = 10.6 Hz), 4.92 (1H, d, *J* = 11.5 Hz), 4.81 (1H, d, *J* = 10.6 Hz), 4.80 (1H, d, *J* = 12.4 Hz), 4.66 (1H, d, *J* = 11.5 Hz), 4.60 (1H, d, *J* = 3.3 Hz), 4.59 (1H, d, *J* = 12.4 Hz), 3.99 (1H, t, *J* = 9.2 Hz), 3.74 (1H, ddd, *J* = 14.5, 6.2, 2.6 Hz), 3.66 (1H, dd, *J* = 14.5, 2.6 Hz), 3.544 (1H, dd, *J* = 9.2, 3.3 Hz), 3.54 (1H, dd, *J* = 14.5, 6.2 Hz), 3.392 (3H, s), 3.385 (1H, t, *J* = 9.2 Hz); R_f = 0.4 (hexane:EtOAc = 5:1); MS (EI) *m/z* 505 (M^+), 473, 440. Anal. Calcd for $C_{29}H_{31}NO_5S$: C, 68.89; H, 6.18; N, 2.77; S, 6.34. Found: C, 68.94; H, 6.19; N, 2.79; S, 6.35.

***N*-(Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-α-D-glucopyranosid-6-yl)-*N'*-[[(*1R*)-(1α,2β,3α,4β,5β)]-1-(hydroxymethyl)-1,2,3,4-tetrahydroxycyclopent-5-yl]thiourea (17).** To a solution of aminocyclitol (**7**) (32 mg, 0.18 mmol) in water (0.3 mL) and THF (0.3 mL) was added a solution of **16** (109 mg, 0.22 mmol) in THF (3.0 mL) with stirring at 24 °C. After 4 days, this reaction mixture was concentrated *in vacuo* to give a residue, which was dried under reduced pressure and chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (10:1) gave 108 mg (88%) of **17** as a white foamy glass: $[\alpha]^{25}_D$ +130.1° (*c* 0.71, $CHCl_3$); IR (KBr) ν_{max} 3336, 3064, 2924, 1547, 1496, 1454, 1071 cm^{-1}; ^{1}H-NMR ($CDCl_3/CD_3OD$ = 2/1) δ 7.45–7.25 (15H, m), 4.97 (1H, d, *J* = 10.2 Hz), 4.85 (1H, d, *J* = 10.2 Hz), 4.82 (1H, d, *J* = 10.2 Hz), 4.78 (1H, d, *J* = 11.6 Hz), 4.71 (1H, d, *J* = 10.2 Hz), 4.69 (1H, d, *J* = 4.0 Hz), 4.68 (1H, d, *J* = 11.6 Hz), 4.90–4.78 (1H, br s), 4.77–4.55 (1H, br s), 4.05–3.45 (12H, m including dd at 3.52 ppm, *J* = 9.9, 3.3 Hz), 3.38 (3H, s); R_f = 0.35 (CH_2Cl_2:MeOH = 10:1); FAB-MS positive *m/z* 685 $(M + H)^+$, negative *m/z* 683 $(M - H)^-$. Anal. Calcd for $C_{35}H_{44}N_2O_{10}S \cdot 1/2H_2O$: C, 60.59; H, 6.53; N, 4.04; S, 4.62. Found: C, 60.87; H, 6.80; N, 3.94; S, 4.39.

Methyl 2,3,4-Tri-*O*-benzyl-6-deoxy-6-[[[(3a*R*)-(3aα,4α,5β,-6α,6aα)]-4-(hydroxymethyl)-4,5,6-trihydroxy-3a,5,6,6a-tetrahydro-*4H*-cyclopentoxazol-2-yl]amino]-α-D-glucopyranoside (18). To a solution of 2-chloro-3-ethylbenzoxazolium tetrafluoroborate (59 mg, 0.22 mmol) in MeCN (4.9 mL) was added a solution of **17** (99 mg, 0.14 mmol) in MeCN (4.5 mL) at 0 °C under N_2. After being stirred for 1 h, Et_3N (0.06 mL, 0.44 mmol) was added to this mixture, with the temperature kept at 0 °C, and this was stirred for 2 h. After completion of the reaction, the reaction mixture was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (12:1) gave 44 mg (47%) of **18** as a white foamy glass: $[\alpha]^{25}_D$ +26.9° (*c* 1.10, $CHCl_3$); IR (KBr) ν_{max} 3343, 3064, 3031, 2924, 1667 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.35–7.25 (15H, m), 5.10–4.45 (5H, m), 4.94 (1H, d, *J* = 11.5 Hz), 4.89 (1H, br d, *J* = 8.3 Hz), 4.82 (1H, d, *J* = 11.5 Hz), 4.74 (1H, d, *J* = 11.5 Hz), 4.65 (1H, d, *J* = 11.5 Hz), 4.61 (1H, d, *J* = 11.5 Hz), 4.58 (1H, d, *J* = 3.1 Hz), 4.54 (1H, d, *J* = 11.5 Hz), 4.36 (1H, d, *J* = 8.3 Hz), 4.03 (1H, br s), 3.97 (1H, br s), 3.94 (1H, t, *J* = 9.2 Hz), 3.83 (1H, d, *J* = 12.3 Hz), 3.76 (1H, d, *J* = 12.3 Hz), 3.70–3.58 (1H, m), 3.47 (1H, dd, *J* = 9.2, 3.1 Hz), 3.42 (1H, br s), 3.36–3.13 (2H, m), 3.30 (3H, s); R_f = 0.58 (CH_2Cl_2:MeOH = 5:1); FAB-MS positive *m/z* 651 $(M + H)^+$, negative *m/z* 649 $(M - H)^-$; high-resolution mass (FAB) calcd for $C_{35}H_{43}N_2O_{10}$ 651.2918, found *m/z* 651.2949 $(M + H)^+$. Anal. Calcd for $C_{35}H_{42}N_2O_{10} \cdot 5/4H_2O$: C, 62.44; H, 6.66; N, 4.16. Found: C, 62.43; H, 6.50; N, 4.16.

Methyl 6-Deoxy-6-[[[(3a*R*)-(3aα,4α,5β,6α,6aα)]-4-(hydroxymethyl)-4,5,6-trihydroxy-3a,5,6,6a-tetrahydro-*4H*-cyclopentoxazol-2-yl]amino]-α-D-glucopyranoside (9). To a solution of **16** (41 mg, 0.06 mmol) in MeOH (8 mL) was added 20% $Pd(OH)_2$ on carbon (680 mg) at 24 °C, and the mixture was hydrogenolyzed at 60 °C for 30 min. After completion of the reaction, this reaction mixture was filtered and concentrated *in vacuo* to give a crude product, which was chromatographed on Amberlite CG-50 (NH_4^+ type/H^+ type = 3/2, 5 mL). Elution with 0.5 M aqueous NH_3 gave 13 mg (55%) of **9** as a

white powder: $[\alpha]^{25}_D$ +65.4° (*c* 0.87, H_2O); IR (KBr) ν_{max} 3376, 1661, 1143, 1047 cm^{-1}; ^{1}H-NMR (D_2O/external TMS) δ 4.71 (1H, dd, J = 8.8, 2.4 Hz), 4.59 (1H, d, J = 3.4 Hz), 4.14 (1H, d, J = 8.8 Hz), 3.97 (1H, d, J = 4.9, 2.4 Hz), 3.75 (1H, d, J = 4.9 Hz), 3.63 (1H, d, J = 12.2 Hz), 3.53 (1H, d, J = 12.2 Hz), 3.50–3.43 (2H, m), 3.37 (1H, dd, J = 9.8, 3.4 Hz), 3.32 (1H, dd, J = 14.7, 2.4 Hz), 3.21 (3H, s), 3.21 (1H, dd, J = 14.7, 6.3 Hz), 3.14 (1H, t, J = 9.8 Hz); FAB-MS positive *m/z* 381 (M + H)$^+$; R_f = 0.58 (MeCN:H_2O:AcOH = 13:5:2). Anal. Calcd for $C_{14}H_{24}N_2O_{10}$·1.3H_2O: C, 41.64; H, 6.64; N, 6.94. Found: C, 41.78; H, 6.38; N, 6.75.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(methanesulfonyl)-α-D-galactopyranoside (20). To a solution of **19** (208 mg, 0.45 mmol) in pyridine (6.2 mL) was added methanesulfonyl chloride (0.11 mL, 1.4 mmol) at 24 °C, and the mixture was stirred for 6 h. After completion of the reaction, MeOH (1 mL) was added to the reaction mixture followed by stirring for 30 min. Next, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (10:1) gave 234 mg (96%) of **20** as a colorless syrup: $[\alpha]^{25.5}_D$ +43.1° (*c* 0.77, $CHCl_3$); IR (film) ν_{max} 2911, 1358, 1175, 1105 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.45–7.20 (15H, m), 5.29 (1H, d, J = 2.6 Hz), 4.81 (1H, d, J = 12.2 Hz), 4.80 (1H, d, J = 11.2 Hz), 4.71 (1H, d, J = 11.2 Hz), 4.70 (1H, d, J = 4.0 Hz), 4.69 (1H, d, J = 12.2 Hz), 4.63 (1H, d, J = 11.2 Hz), 4.50 (1H, d, J = 11.2 Hz), 4.04 (1H, t, J = 7.3 Hz), 3.98 (1H, dd, J = 9.9, 2.6 Hz), 3.77 (1H, dd, J = 9.9, 4.0 Hz), 3.65 (2H, d, J = 7.3 Hz), 3.39 (3H, s), 2.96 (3H, s); MS (EI) *m/z* 542 (M$^+$), 451, 419; R_f = 0.62 (benzene:EtOAc = 8:1). Anal. Calcd for $C_{29}H_{34}O_8S$: C, 64.19; H, 6.32; S, 5.91. Found: C, 63.97; H, 6.48; S, 5.62.

Methyl 4-Azido-2,3,6-tri-*O*-benzyl-4-deoxy-α-D-glucopyranoside (21). To a solution of **20** (169 mg, 0.31 mmol) in DMF (3.4 mL) was added NaN_3 (104 mg, 1.6 mmol) at 24 °C, and the mixture was stirred at 120 °C for 2 h under a seal. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (4:1) gave 129 mg (84%) of **21** as a colorless syrup: $[\alpha]^{24}_D$ +66.4° (*c* 0.75, $CHCl_3$); IR (film) ν_{max} 2906, 2108 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.50–7.20 (15H, m), 4.96 (1H, d, J = 10.6 Hz), 4.81 (1H, d, J = 10.6 Hz), 4.78 (1H, d, J = 12.0 Hz), 4.64 (1H, d, J = 12.0 Hz), 4.63 (1H, d, J = 12.0 Hz), 4.61 (1H, d, J = 4.0 Hz), 4.50 (1H, d, J = 12.0 Hz), 3.84 (1H, t, J = 9.6 Hz), 3.71–3.59 (3H, m), 3.56 (1H, dd, J = 9.6, 4.0 Hz), 3.53 (1H, dt, J = 9.6, 2.5 Hz), 3.34 (3H, s); MS (EI) *m/z* 461 (M$^+$ − N_2), 430 (M$^+$ − N_2 − OMe), 398; R_f = 0.45 (hexane:EtOAc = 4:1). Anal. Calcd for $C_{28}H_{31}N_3O_5$: C, 68.69; H, 6.38; N, 8.58. Found: C, 68.57; H, 6.24; N, 8.59.

Methyl 2,3,6-Tri-*O*-benzyl-4-deoxy-4-(diethylphosphoramido)-α-D-glucopyranoside (23). To a suspension of $LiAlH_4$ (136 mg, 3.6 mmol) in Et_2O (21 mL) was added a solution of **21** (424 mg, 0.87 mmol) in Et_2O (6.0 mL) at 0 °C under N_2, and the mixture was stirred for 2.5 h with the temperature kept at 0 °C. After completion of the reaction, the reaction mixture was diluted with Et_2O, and saturated aqueous Na_2SO_4 was gradually added to the reaction mixture at 0 °C. After being stirred at 24 °C for 30 min, the mixture was extracted twice with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (20:1) gave 357 mg (89%) of an amino sugar **22** as a colorless syrup; ^{1}H-NMR ($CDCl_3$) δ 7.45–7.20 (15H, m), 5.05 (1H, d, J = 11.3 Hz), 4.77 (1H, d, J = 11.3 Hz), 4.68 (1H, d, J = 11.3 Hz), 4.67 (1H, d, J = 3.7 Hz), 4.66 (1H, d, J = 11.3 Hz), 4.63 (1H, d, J = 11.3 Hz), 4.48 (1H, d, J = 11.3 Hz), 3.69–3.53 (5H, m), 3.38 (3H, s), 2.91 (1H, t, J = 9.3 Hz), 1.38 (2H, br s). To a solution of **22** (310 mg, 0.67 mmol) in CH_2Cl_2 (16 mL) were added diethyl chlorophosphate (0.29 mL, 2.0 mmol) and Et_3N (0.28 mL, 2.1 mmol) at 24 °C under N_2, and the mixture was stirred at 40 °C for 17 h. After completion of the reaction, the reaction mixture was concentrated *in vacuo* to give a crude product, which was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–MeCN (1:1) gave 223 mg (56%) of **23** as white crystals: $[\alpha]^{25}_D$ +17.4° (*c* 0.7, $CHCl_3$); mp 134–135 °C (recrystallized from hexane–EtOAc); IR (KBr) ν_{max} 3180, 2909, 1227, 1064, 1048 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.45–7.20 (15H, m), 5.00 (1H, d, J = 10.9 Hz), 4.78 (1H, d, J = 10.9 Hz), 4.74 (1H, d, J = 11.7 Hz), 4.63 (1H, d, J = 3.3 Hz), 4.62 (1H, d, J = 12.4 Hz), 4.61 (1H, d, J = 11.7 Hz), 4.53 (1H, d, J = 12.4 Hz), 4.00–3.77 (5H, m), 3.76–3.63 (3H, m), 3.55 (1H, dd, J = 9.2, 3.3 Hz), 3.39 (3H, s), 3.20 (1H, dq, J = 13.7, 9.2 Hz), 2.35 (1H, t, J = 9.2 Hz), 1.15 (3H, t, J = 6.2 Hz), 1.13 (3H, t, J = 6.2 Hz); MS (EI) *m/z* 599 (M$^+$), 568, 554; R_f = 0.54 (benzene:MeCN = 1:1); high-resolution mass (EI) calcd for $C_{32}H_{42}O_8NP$ 599.2649, found 599.2639.

(Methyl 2,3,6-tri-*O*-benzyl-4-deoxy-α-D-glucopyranosid-4-yl) Isothiocyanate (24). To a suspension of NaH (25 mg, 1.1 mmol) and tetra-*n*-butylammonium bromide (13 mg, 0.04 mmol) in benzene (10 mL) was added a solution of **23** (200 mg, 0.33 mmol) in benzene (4 mL) at 24 °C under N_2, and the mixture was stirred at 70 °C. After 3 h, CS_2 (1.0 mL) was added to this reaction mixture, with the temperature kept at 70 °C, and this was stirred for 1 h. After completion of the reaction, the reaction mixture was diluted with benzene and washed with 1 M hydrochloric acid. The aqueous layer was extracted twice with benzene. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (4:1) gave 154 mg (91%) of **24** as a pale yellow syrup: $[\alpha]^{25}_D$ −7.0° (*c* 0.7, $CHCl_3$); IR (film) ν_{max} 2906, 2067 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.45–7.25 (15H, m), 4.93 (1H, d, J = 10.2 Hz), 4.85 (1H, d, J = 10.2 Hz), 4.79 (1H, d, J = 11.9 Hz), 4.63 (2H, d, J = 11.9 Hz), 4.60 (1H, d, J = 3.7 Hz), 4.53 (1H, d, J = 11.9 Hz), 3.90–3.87 (2H, m), 3.79 (1H, dt, J = 10.6, 2.6 Hz), 3.67 (2H, d, J = 2.6 Hz), 3.49 (1H, ddd, J = 7.3, 3.6, 1.8 Hz), 3.38 (3H, s); MS (EI) *m/z* 505 (M$^+$), 473, 414; R_f = 0.69 (benzene:EtOAc = 2:1). Anal. Calcd for $C_{29}H_{31}O_5SN$: C, 68.89; H, 6.18; N, 2.77; S, 6.34. Found: C, 69.11; H, 6.12; N, 2.78; S, 6.47.

***N*-(Methyl 2,3,6-tri-*O*-benzyl-4-deoxy-α-D-glucopyranosid-4-yl)-*N'*-[(*1R*)-(1α,2β,3α,4β,5β)]-1-(hydroxymethyl)-1,2,3,4-tetrahydroxycyclopent-5-yl]thiourea (25).** To a solution of aminocyclitol (**7**) (35 mg, 0.2 mmol) in water (0.6 mL) was added a solution of **24** (66 mg, 0.13 mmol) in THF (3.3 mL) with stirring at 24 °C. After 6 days, this reaction mixture was concentrated *in vacuo* to give a residue, which was dried under reduced pressure and chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (10:1) gave 83 mg (94%) of **25** as a white foamy glass: $[\alpha]^{24}_D$ +76.5° (*c* 0.54, MeOH); IR (KBr) ν_{max} 3323, 2929, 1537, 1497, 1043 cm^{-1}; ^{1}H-NMR (CD_3OD) δ 7.45–7.25 (15H, m), 4.85–4.45 (9H, m), 4.10–3.45 (12H, m), 3.40 (3H, s); R_f = 0.47 (CH_2Cl_2:MeOH = 10:1); FAB-MS positive *m/z* 685 (M + H)$^+$, negative *m/z* 683 (M − H)$^-$; high-resolution mass (FAB) calcd for $C_{35}H_{45}O_{10}N_2S$ 685.2796, found 685.2796 (M + H)$^+$. Anal. Calcd for $C_{35}H_{44}N_2O_{10}S$: C, 61.39; H, 6.48; N, 4.09; S, 4.68. Found: C, 61.13; H, 6.62; N, 4.01; S, 4.58.

Methyl 2,3,6-Tri-*O*-benzyl-4-deoxy-4-[[[(3a*R*)-(3aα,4α,5β,6α,6aα)]-4-(hydroxymethyl)-4,5,6-trihydroxy-3a,5,6,6a-tetrahydro-4*H*-cyclopentoxazol-2-yl]amino]-α-D-glucopyranoside (26). To a solution of 2-chloro-3-ethylbenzoxazolium tetrafluoroborate (59 mg, 0.22 mmol) in MeCN (3.6 mL) was added a solution of thiourea **25** (73 mg, 0.11 mmol) in MeCN (3.0 mL) at 0 °C under N_2. After being stirred for 1 h, Et_3N (0.06 mL, 0.43 mmol) was added to this mixture, with the temperature kept at 0 °C, and this was stirred for 2 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH

(8:1) gave 50 mg (72%) of **26** as a pale yellow foamy glass: $[\alpha]^{25}_D$ +27.2° (*c* 0.54, $CHCl_3$); IR (KBr) ν_{max} 3343, 2926, 1697, 1661, 1047 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.45–7.20 (15H, m), 4.87 (1H, d, J = 11.2 Hz), 4.714 (1H, d, J = 11.8 Hz), 4.708 (1H, d, J = 7.9 Hz), 4.64 (1H, d, J = 11.8 Hz), 4.58 (1H, d, J = 11.2 Hz), 4.56 (1H, d, J = 3.7 Hz), 4.48 (2H, s), 4.21 (1H, d, J = 7.9 Hz), 5.00–3.88 (5H, br s), 3.95 (1H, br s), 3.90 (1H, br s), 3.84–3.69 (4H, m), 3.63–3.45 (4H, m), 3.32 (3H, s); R_f = 0.38 (CH_2Cl_2:MeOH = 8:1); FAB-MS positive *m/z* 651 $(M + H)^+$, negative *m/z* 649 $(M - H)^-$; high-resolution mass (FAB) calcd for $C_{35}H_{43}N_2O_{10}$ 651.2918, found *m/z* 651.2921 $(M + H)^+$. Anal. Calcd for $C_{35}H_{42}N_2O_{10}\cdot H_2O$: C, 62.85; H, 6.63; N, 4.19. Found: C, 62.63; H, 6.68; N, 4.19.

Methyl 4-Deoxy-4-[[[(3a*R*)-(3aα,4α,5β,6α,6aα)]-4-(hydroxymethyl)-4,5,6-trihydroxy-3a,5,6,6a-tetrahydro-4*H*-cyclopentoxazol-2-yl]amino]-α-D-glucopyranoside (10). To a solution of **26** (46 mg, 0.07 mmol) in MeOH (9.5 mL) was added 20% $Pd(OH)_2$ on carbon (700 mg) at 24 °C, and the mixture was hydrogenolyzed at 60 °C for 1 h. After completion of the reaction, this reaction mixture was filtered and concentrated *in vacuo* to give a crude product, which was chromatographed on Amberlite CG-50 (NH_4^+ type/H^+ type = 3/2, 6 mL). Elution with 0.5 M aqueous NH_3 gave 15 mg (57%) of **10** as a white powder: $[\alpha]^{25}_D$ +107.8° (*c* 0.99, H_2O); IR (KBr) ν_{max} 3376, 1660, 1047 cm^{-1}; ^1H-NMR (D_2O/external TMS) δ 4.74 (1H, dd, J = 8.3, 1.5 Hz), 4.64 (1H, d, J = 3.9 Hz), 4.13 (1H, d, J = 8.3 Hz), 3.98 (1H, dd, J = 3.4, 1.5 Hz), 3.75 (1H, d, J = 3.4 Hz), 3.64 (1H, d, J = 12.2 Hz), 3.60–3.40 (6H, m), 3.21 (3H, s), 3.16 (1H, t, J = 10.0 Hz); FAB-MS positive *m/z* 381 $(M + H)^+$ negative *m/z* 379 $(M - H)^-$; high-resolution mass (FAB) calcd for $C_{14}H_{25}N_2O_{10}$ 381.1509, found 381.1502 $(M + H)^+$; R_f = 0.41 (MeCN:H_2O:AcOH = 13:5:2). Anal. Calcd for $C_{14}H_{24}N_2O_{10}\cdot H_2O$: C, 42.20; H, 6.57; N, 7.03. Found: C, 42.18; H, 6.75; N, 7.08.

Benzyl 4,6-*O*-Benzylidene-β-D-galactopyranoside (28). (a) To a solution of **27** (3.0 g, 7.7 mmol) in CH_2Cl_2 (60 mL) were added benzyl alcohol (4.0 mL) and $BF_3\cdot Et_2O$ (9.5 mL, 77 mmol) at 0 °C, and the mixture was stirred for 3.5 h, with the temperature kept at 0 °C. After completion of the reaction, the reaction mixture was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with CH_2Cl_2. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (2:1) gave 2.41 g (72%) of benzyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside as a colorless syrup: $[\alpha]^{24}_D$ −44.5° (*c* 0.56, $CHCl_3$); IR (film) ν_{max} 1748, 1370, 1221, 1055 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.45–7.20 (5H, m), 5.39 (1H, dd, J = 3.6, 1.3 Hz), 5.28 (1H, dd, J = 10.6, 7.9 Hz), 4.99 (1H, dd, J = 10.6, 3.6 Hz), 4.92 (1H, d, J = 12.7 Hz), 4.64 (1H, d, J = 12.7 Hz), 4.52 (1H, d, J = 7.9 Hz), 4.22 (1H, dd, J = 11.2, 6.6 Hz), 4.15 (1H, dd, J = 11.2, 6.6 Hz), 3.89 (1H, dt, J = 6.6, 1.3 Hz), 2.16 (3H, s), 2.07 (3H, s), 2.04 (3H, s), 1.98 (3H, s); MS (EI) *m/z* 378, 347, 331; R_f = 0.20 (hexane:EtOAc = 2:1). Anal. Calcd for $C_{21}H_{26}O_{10}$: C, 57.53; H, 5.98. Found: C, 57.25; H, 6.21.

(b) To a solution of this benzyl glycoside (2.41 g, 5.5 mmol) in MeOH (60 mL) was added KOH (30 mg, 0.45 mmol), at rt, and the mixture was stirred for 2.5 h. After completion of the reaction, the reaction mixture was concentrated *in vacuo* and dried under reduced pressure to give the tetrol. To a solution of the crude tetrol in DMF (72 mL) were added benzaldehyde dimethyl acetal (4.1 mL, 27.5 mmol) and DL-10-camphorsulfonic acid (640 mg, 2.7 mmol) at 24 °C, and this was stirred at 80 °C for 16 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with EtOAc gave 1.56 g (81%) of **28** as white crystals: $[\alpha]^{24}_D$ −62° (*c* 0.65, $CHCl_3$); mp 213–215 °C (recrystallized from hexane–EtOAc); IR (KBr) ν_{max} 3402, 1170, 1089, 1078, 1054 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.60–7.20 (10H, m), 5.57 (1H, s), 5.01 (1H, d, J = 11.9 Hz), 4.64 (1H, d, J = 11.9 Hz), 4.45–4.32 (2H, m), 4.22 (1H, d, J = 4.0 Hz), 4.11 (1H, dd, J = 12.6, 1.7 Hz), 3.83 (1H, ddd, J = 9.3, 7.4, 1.7 Hz), 3.68 (1H, dt, J = 9.3, 4.0 Hz), 3.53–3.44 (2H, m), 2.52 (2H, s); MS (EI) *m/z* 341 $(M^+ - H_2O)$; R_f = 0.55 (EtOAc). Anal. Calcd for $C_{20}H_{23}O_6\cdot 1/3H_2O$: C, 65.74; H, 6.53. Found: C, 65.67; H, 6.57.

Benzyl 2,3,6-Tri-*O*-benzyl-β-D-galactopyranoside (29). (a) To a solution of **28** (152 mg, 0.42 mmol) was added 55% NaH (0.056 g, 1.3 mmol, oil dispersion) at 0 °C, and the mixture was stirred at 24 °C. After 30 min, BnBr (0.16 mL, 1.3 mmol) was added to the reaction mixture at 0 °C, and this was stirred at 24 °C for 1 h. After completion of the reaction, EtOH (1 mL) was added to the mixture at 0 °C, and this was stirred at 24 °C for 30 min. The reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (2:1) gave 0.18 g (79%) of the corresponding dibenzyl ether as white crystals: $[\alpha]^{25}_D$ −0.4° (*c* 0.5, $CHCl_3$); mp 168–170 °C (recrystallized from hexane–EtOAc); IR (KBr) ν_{max} 1453, 1368, 1120, 1101, 1062 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.70–7.20 (20H, m), 5.51 (1H, s), 5.01 (1H, d, J = 12.5 Hz), 4.94 (1H, d, J = 11.2 Hz), 4.80 (1H, d, J = 11.2 Hz), 4.79 (1H, d, J = 12.5 Hz), 4.73 (1H, d, J = 12.5 Hz), 4.67 (1H, d, J = 12.5 Hz), 4.51 (1H, d, J = 7.3 Hz), 4.34 (1H, br d, J = 12.5 Hz), 4.11 (1H, d, J = 3.3 Hz), 4.03 (1H, br d, J = 12.5 Hz), 3.92 (1H, dd, J = 9.4, 7.3 Hz), 3.56 (1H, dd, J = 9.4, 3.3 Hz), 3.32 (1H, br s); MS (EI) *m/z* 538 (M^+), 447, 430; R_f = 0.57 (hexane:EtOAc = 2:1). Anal. Calcd for $C_{34}H_{34}O_6\cdot 1/4H_2O$: C, 75.18; H, 6.40. Found: C, 75.06; H, 6.51. (b) To a solution of the dibenzyl ether (1.12 g, 2.1 mmol) in THF (60 mL) were added $BH_3\cdot NMe_3$ (960 mg, 13 mmol), $AlCl_3$ (1.7 g, 13 mmol), and MS-4A powder (3.5 g) at 0 °C under N_2, and the mixture was stirred at 24 °C for 18 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (8:1) gave 1.02 g (91%) of **29** as a colorless syrup: $[\alpha]^{25}_D$ −24.4° (*c* 0.54, $CHCl_3$); IR (film) ν_{max} 3479, 2870, 1455, 1098, 1074 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.50–7.20 (20H, m), 4.97 (1H, d, J = 11.9 Hz), 4.92 (1H, d, J = 10.6 Hz), 4.73 (1H, d, J = 10.6 Hz), 4.66 (1H, d, J = 11.9 Hz), 4.71 (2H, s), 4.61 (2H, s), 4.47 (1H, d, J = 8.0 Hz), 4.25 (1H, br s), 3.83 (1H, dd, J = 10.2, 5.9 Hz), 3.76 (1H, dd, J = 10.2, 5.9 Hz), 3.72 (1H, dd, J = 9.2, 8.0 Hz), 3.56 (1H, br t, J = 5.9 Hz), 3.49 (1H, dd, J = 9.2, 3.3 Hz), 2.53 (1H, br s); MS (EI) *m/z* 389, 371, 341; R_f = 0.57 (benzene:EtOAc = 8:1). Anal. Calcd for $C_{34}H_{36}O_6\cdot 1/4H_2O$: C, 74.90; H, 6.75. Found: C, 74.61; H, 6.75.

Benzyl 2,3-Di-*O*-benzyl-4-*O*-(methanesulfonyl)-β-D-galactopyranoside (30). To a solution of **29** (1.02 g, 1.9 mmol) in pyridine (30 mL) was added methanesulfonyl chloride (0.44 mL, 5.7 mmol) at 0 °C, and the mixture was stirred at 24 °C for 15 h. After completion of the reaction, MeOH (1 mL) was added to the mixture at 0 °C, and this was stirred at 24 °C for 30 min. The reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (15:1) gave 1.05 g (90%) of **30** as a pale yellow syrup: $[\alpha]^{25}_D$ +11.6° (*c* 0.51, $CHCl_3$); IR (film) ν_{max} 2873, 1357, 1106, 1075, 928 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.50–7.20 (20H, m), 5.29 (1H, d, J = 2.6 Hz), 4.94 (1H, d, J = 11.9 Hz), 4.91 (1H, d, J = 10.6 Hz), 4.86 (1H, d, J = 10.6 Hz), 4.75 (1H, d, J = 10.6 Hz), 4.67 (1H, d, J = 11.5 Hz), 4.65 (1H, d, J = 11.9 Hz), 4.63 (1H, d, J = 10.6 Hz), 4.51 (1H, d, J = 11.5 Hz), 4.49 (1H, d, J = 7.3 Hz), 3.78–3.68 (3H, m), 3.66 (1H, dd, J = 9.9, 7.3 Hz), 3.56 (1H, dd, J = 9.9, 2.6 Hz), 3.00 (3H, s); MS (EI) *m/z* 527, 419, 391; R_f = 0.87 (benzene:EtOAc = 8:1). Anal. Calcd for $C_{35}H_{38}O_8S$: C, 67.94; H, 6.19. Found: C, 67.65; H, 6.13.

Benzyl 4-Azido-2,3,6-tri-*O*-benzyl-4-deoxy-β-D-glucopyranoside (31). To a solution of **30** (1.05 g, 1.7 mmol) in DMF (30 mL) was added NaN_3 (560 mg, 8.6 mmol) at 24 °C, and

the mixture was stirred at 100 °C for 20 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (5:1) gave 870 mg (91%) of **31** as a colorless syrup: $[\alpha]^{25}_D$ +50.2° (*c* 0.53, $CHCl_3$); IR (film) ν_{max} 2869, 2110, 1497, 1361, 1091, 1073 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.40–7.20 (20H, m), 4.97 (1H, d, J = 10.5 Hz), 4.96 (1H, d, J = 12.2 Hz), 4.91 (1H, d, J = 10.9 Hz), 4.77 (1H, d, J = 10.9 Hz), 4.71 (1H, d, J = 10.5 Hz), 4.67 (1H, d, J = 12.5 Hz), 4.65 (1H, d, J = 12.2 Hz), 4.57 (1H, d, J = 12.5 Hz), 4.46 (1H, d, J = 7.3 Hz), 3.78 (1H, dd, J = 10.2, 2.2 Hz), 3.70 (1H, dd, J = 10.2, 4.4 Hz), 3.63 (1H, t, J = 9.9 Hz), 3.58–3.45 (2H, m), 3.26 (1H, ddd, J = 9.9, 4.4, 2.2 Hz); MS (EI) *m/z* 537 ($M^+ - N_2$), 474, 464; R_f = 0.55 (hexane:EtOAc = 5:1). Anal. Calcd for $C_{34}H_{35}O_5N_3$: C, 72.19; H, 6.24; N, 7.43. Found: C, 72.16; H, 6.18; N, 7.40.

Benzyl 4-Amino-2,3,6-tri-*O*-benzyl-4-deoxy-β-D-glucopyranoside (32). To a suspension of $LiAlH_4$ (240 mg, 6.3 mmol) in Et_2O (44 mL) was added a solution of **31** (870 mg, 1.5 mmol) in Et_2O (22 mL) at 0 °C under N_2, and the mixture was stirred for 2 h with the temperature kept at 0 °C. After completion of the reaction, the reaction mixture was diluted with Et_2O, and saturated aqueous Na_2SO_4 was gradually added to the reaction mixture at 0 °C. After being stirred at 24 °C for 30 min, the mixture was extracted twice with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (1:1) gave 650 mg (78%) of **32** as a white foamy glass: $[\alpha]^{25}_D$ −43.8° (*c* 0.61, $CHCl_3$); IR (KBr) ν_{max} 2870, 1095, 1073, 752 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.50–7.20 (20H, m), 4.99 (1H, d, J = 10.6 Hz), 4.98 (1H, d, J = 10.6 Hz), 4.97 (1H, d, J = 12.2 Hz), 4.72 (1H, d, J = 10.6 Hz), 4.67 (1H, d, J = 12.2 Hz), 4.65 (1H, d, J = 12.5 Hz), 4.63 (1H, d, J = 10.6 Hz), 4.55 (1H, d, J = 12.5 Hz), 4.53 (1H, d, J = 7.9 Hz), 3.77 (1H, dd, J = 10.6, 3.3 Hz), 3.69 (1H, dd, J = 10.6, 4.4 Hz), 3.54 (1H, dd, J = 9.2, 7.9 Hz), 3.36–3.24 (2H, m), 2.94 (1H, t, J = 9.2 Hz), 1.48 (2H, br s); MS (EI) *m/z* 540 (M^+ + H), 433, 403, 388; R_f = 0.53 (CH_2Cl_2:MeOH = 10:1). Anal. Calcd for $C_{34}H_{37}O_5N$: C, 75.67; H, 6.91; N, 2.60. Found: C, 75.57; H, 6.87; N, 2.65.

Benzyl 2,3,6-Tri-*O*-benzyl-4-deoxy-4-(diethylphosphoramido)-β-D-glucopyranoside (33). To a solution of **32** (650 mg, 1.2 mmol) in CH_2Cl_2 (30 mL) were added diethyl chlorophosphate (0.52 mL, 3.6 mmol) and Et_3N (0.5 mL, 3.6 mmol) at 24 °C under N_2, and the mixture was stirred at 40 °C for 24 h, while the nitrogen atmosphere was maintained. After completion of the reaction, the reaction mixture was evaporated *in vacuo*. The residue was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (1:2) gave 411 mg (52%) of **33** as white crystals: $[\alpha]^{25}_D$ −14.8° (*c* 0.58, $CHCl_3$); mp 159–161 °C (recrystallized from hexane–EtOAc); IR (KBr) ν_{max} 3155, 2918, 1224, 1127, 1063 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.45–7.20 (20H, m), 4.97 (1H, d, J = 11.7 Hz), 4.96 (1H, d, J = 11.7 Hz), 4.95 (1H, d, J = 11.7 Hz), 4.76 (1H, d, J = 11.7 Hz), 4.68 (2H, d, J = 11.7 Hz), 4.62 (2H, s), 4.52 (1H, d, J = 7.2 Hz), 4.04–3.80 (5H, m), 3.73 (1H, dd, J = 10.6, 5.7 Hz), 3.60–3.40 (3H, m), 3.30–3.07 (1H, m), 2.46 (1H, t, J = 8.4 Hz), 1.17 (3H, t, J = 7.5 Hz), 1.16 (3H, t, J = 7.5 Hz); MS (EI) *m/z* 676 (M^+ + H), 658, 584; R_f = 0.67 (hexane:EtOAc = 1:2). Anal. Calcd for $C_{38}H_{46}O_8NP$: C, 67.54; H, 6.86; N, 2.07; P, 4.58. Found: C, 67.54; H, 6.98; N, 2.10; P, 4.58.

(Benzyl 2,3,6-tri-*O*-benzyl-4-deoxy-β-D-glucopyranosid-4-yl) Isothiocyanate (34). To a suspension of NaH (69 mg, 1.66 mmol) and tetra-*n*-butylammonium bromide (21 mg, 0.06 mmol) in benzene (19 mL) was added a solution of **33** (373 mg, 0.57 mmol) in benzene (7.5 mL) at 24 °C under N_2, and the mixture was stirred at 70 °C. After 3 h, CS_2 (1.9 mL) was added to this reaction mixture, with the temperature kept at 70 °C, and this was stirred for 1.5 h. After completion of the reaction, the reaction mixture was diluted with benzene and washed with 1 M hydrochloric acid. The aqueous layer was extracted twice with benzene. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (6:1) gave 288 mg (87%) of **34** as a pale yellow syrup: $[\alpha]^{25}_D$ −35.6° (*c* 0.52, $CHCl_3$); IR (film) ν_{max} 2869, 2068, 1123, 1091, 1073 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.50–7.20 (20H, m), 4.95 (2H, d, J = 10.2 Hz), 4.88 (1H, d, J = 10.2 Hz), 4.81 (1H, d, J = 10.2 Hz), 4.71 (1H, d, J = 10.2 Hz), 4.68 (1H, d, J = 10.2 Hz), 4.66 (1H, d, J = 10.2 Hz), 4.59 (1H, d, J = 10.2 Hz), 4.49 (1H, d, J = 7.9 Hz), 3.92 (1H, t, J = 9.3 Hz), 3.80 (1H, dd, J = 10.5, 1.9 Hz), 3.71 (1H, dd, J = 10.5, 4.3 Hz), 3.59 (1H, t, J = 9.3 Hz), 3.49 (1H, ddd, J = 9.3, 4.8, 1.9 Hz), 3.48 (1H, dd, J = 9.3, 7.9 Hz); MS (EI) *m/z* 581 (M^+), 490, 475, 430; R_f = 0.49 (hexane:EtOAc = 6:1). Anal. Calcd for $C_{35}H_{35}O_5NS$: C, 72.26; H, 6.06; N, 2.41; S, 5.51. Found: C, 72.33; H, 5.92; N, 2.23; S, 5.19.

***N*-(Benzyl 2,3,6-tri-*O*-benzyl-4-deoxy-β-D-glucopyranosid-4-yl)-*N'*-[[(*1R*)-(1α,2β,3α,4β,5β)]-1-(hydroxymethyl)-1,2,3,4-tetrahydroxycyclopent-5-yl]thiourea (35).** To a solution of aminocyclitol (**7**) (34 mg, 0.06 mmol) in water (0.75 mL) was added a solution of **34** (74 mg, 0.13 mmol) in THF (4.0 mL) with stirring at 24 °C. After 3 days, this reaction mixture was concentrated *in vacuo* to give a residue, which was dried under reduced pressure and chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (12:1) gave 97 mg (100%) of **35** as a white foamy glass: $[\alpha]^{24}_D$ + 42.4° (*c* 0.58, $CHCl_3$); IR (KBr) ν_{max} 3312, 2869, 1546, 1497, 1073 cm^{-1}; ^1H-NMR (CD_3OD) δ 7.45–7.10 (20H, m), 5.15–4.40 (11H, m), 4.20–3.40 (12H, m); R_f = 0.3 (CH_2Cl_2:MeOH = 15:1); FAB-MS positive *m/z* 761 (M + H)$^+$, negative *m/z* 759 (M − H)$^-$. Anal. Calcd for $C_{41}H_{48}N_2O_{10}S{\cdot}H_2O$: C, 63.22; H, 6.47; N, 3.60; S, 4.12. Found: C, 63.48; H, 6.49; N, 3.58; S, 4.21.

Benzyl 2,3,6-Tri-*O*-benzyl-4-deoxy-4-[[[(3a*R*)-(3aα,4α,5β,6α,6aα)]-4-(hydroxymethyl)-4,5,6-trihydroxy-3a,5,6,6a-tetrahydro-*4H*-cyclopentoxazol-2-yl]amino]-β-D-glucopyranoside (36). To a solution of 2-chloro-3-ethylbenzoxazolium tetrafluoroborate (53 mg, 0.19 mmol) in MeCN (3.2 mL) was added a solution of thiourea **35** (65 mg, 0.08 mmol) in MeCN (3.0 mL) at 0 °C under N_2. After being stirred for 40 min, Et_3N (0.05 mL, 0.36 mmol) was added to this mixture, with the temperature kept at 0 °C, and this was stirred for 50 min. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (10:1) gave 35 mg (58%) of **36** as a pale yellow foamy glass: $[\alpha]^{25}_D$ −0.26° (*c* 1.14, $CHCl_3$); IR (KBr) ν_{max} 3351, 2924, 1664, 1072 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.40–7.15 (20H, m), 4.93 (1H, d, J = 11.2 Hz), 4.91 (1H, d, J = 11.2 Hz), 4.77 (1H, d, J = 11.2 Hz), 4.71 (1H, d, J = 8.4 Hz), 4.67 (1H, d, J = 11.2 Hz), 4.62 (1H, d, J = 11.2 Hz), 4.59 (1H, d, J = 11.2 Hz), 4.55 (2H, s), 4.45 (1H, d, J = 7.4 Hz), 4.19 (1H, d, J = 8.4 Hz), 3.98 (1H, br s), 3.90–3.10 (14H, m); R_f = 0.37 (CH_2Cl_2:MeOH = 10:1); FAB-MS positive *m/z* 727 (M + H)$^+$, negative *m/z* 725 (M − H)$^-$; high-resolution mass (FAB) calcd for $C_{41}H_{47}N_2O_{10}$ 727.3231, found *m/z* 727.3205 (M + H)$^+$.

4-Deoxy-4-[[[(3a*R*)-(3aα,4α,5β,6α,6aα)]-4-(hydroxymethyl)-4,5,6-trihydroxy-3a,5,6,6a-tetrahydro-*4H*-cyclopentoxazol-2-yl]amino]-α-D-glucopyranose (11). To a solution of **36** (27 mg, 0.04 mmol) in MeOH (5.4 mL) was added 20% $Pd(OH)_2$ on carbon (540 mg) at 24 °C, and the mixture was hydrogenolyzed at 60 °C for 1 h. After completion of the reaction, this reaction mixture was filtered and concentrated *in vacuo* to give a crude product, which was chromatographed on Amberlite CG-50 (NH_4^+ type/H^+ type = 3/2, 5 mL). Elution with 0.5 M aqueous NH_3 gave 5.4 mg (39%) of **11** as a white powder: $[\alpha]^{24}_D$ +53.1° (*c* 0.36, H_2O); IR (KBr) ν_{max} 3357, 1660, 1059 cm^{-1}; ^1H-NMR (D_2O/external TMS) δ 5.07 (1/3H, d, J = 3.9 Hz), 4.76 (1H, br d, J = 7.8 Hz), 4.43 (2/3H, d, J = 7.8 Hz), 4.15 (1H, d, J = 7.8 Hz), 4.00 (1H, dd, J = 3.4, 2.0 Hz), 3.77 (1H, d, J = 3.4 Hz), 3.70–3.05 (8H, m); FAB-MS positive

m/z 367 $(M + H)^+$ negative *m/z* 365 $(M - H)^-$; high-resolution mass (FAB) calcd for $C_{13}H_{22}N_2O_{10}$ 367.1353, found 367.1354 $(M + H)^+$; $R_f = 0.59$ (MeCN:H_2O:AcOH = 13:5:2).

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(methanesulfonyl)-α-D-glucopyranoside (38). To a solution of **37** (567 mg, 1.2 mmol) in pyridine (17 mL) was added methanesulfonyl chloride (0.3 mL, 3.9 mmol) at 24 °C, and the mixture was stirred for 5 h. After completion of the reaction, MeOH (2 mL) was added to the reaction mixture, and this was stirred for 30 min. Next, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (2:1) gave 625 mg (95%) of **38** as a colorless syrup: $[\alpha]^{24.5}_D$ +30° (*c* 0.61, $CHCl_3$); IR (film) ν_{max} 2910, 1357, 1178, 1100 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.45–7.20 (15H, m), 5.07 (1H, d, *J* = 11.6 Hz), 4.74 (1H, d, *J* = 11.6 Hz), 4.68 (1H, t, *J* = 9.2 Hz), 4.61 (1H, d, *J* = 3.3 Hz), 4.608 (2H, d, *J* = 11.6 Hz), 4.605 (1H, d, *J* = 11.6 Hz), 4.53 (1H, d, *J* = 11.6 Hz), 4.01 (1H, t, *J* = 9.2 Hz), 3.88 (1H, ddd, *J* = 9.2, 4.6, 2.2 Hz), 3.76 (1H, dd, *J* = 11.2, 2.2 Hz), 3.67 (1H, dd, *J* = 11.2, 4.6 Hz), 3.61 (1H, dd, *J* = 9.2, 3.3 Hz), 3.40 (3H, s), 2.80 (3H, s); MS (EI) *m/z* 542 (M^+), 451, 419; $R_f = 0.86$ (benzene:EtOAc = 2:1). Anal. Calcd for $C_{29}H_{34}O_8S$: C, 64.19; H, 6.32; S, 5.91. Found: C, 64.59; H, 6.57; S, 5.99.

Methyl 4-Azido-2,3,6-tri-*O*-benzyl-4-deoxy-α-D-galactopyranoside (39). To a solution of **38** (516 mg, 0.95 mmol) in DMF (10 mL) was added NaN_3 (310 mg, 4.8 mmol) at rt, and the mixture was stirred at 100 °C for 24 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (4:1) gave 354 mg (76%) of **38** as a colorless syrup: $[\alpha]^{25}_D$ +6.0° (*c* 0.75, $CHCl_3$); IR (film) ν_{max} 2913, 2106 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.50–7.20 (15H, m), 4.83 (1H, d, *J* = 11.9 Hz), 4.82 (1H, d, *J* = 11.9 Hz), 4.74 (1H, d, *J* = 11.9 Hz), 4.65 (1H, d, *J* = 11.9 Hz), 4.581 (1H, d, *J* = 3.8 Hz), 4.575 (1H, d, *J* = 11.9 Hz), 4.51 (1H, d, *J* = 11.9 Hz), 4.03 (1H, dd, *J* = 9.2, 3.8 Hz), 3.99 (1H, d, *J* = 3.8 Hz), 3.93 (1H, br t, *J* = 6.6 Hz), 3.83 (1H, dd, *J* = 9.2, 3.8 Hz), 3.58 (1H, d, *J* = 9.5, 6.6 Hz), 3.53 (1H, d, *J* = 9.5, 6.6 Hz), 3.34 (3H, s); MS (EI) *m/z* 461 ($M^+ - N_2$), 430 ($M^+ - N_2$ – OMe); $R_f = 0.35$ (hexane:EtOAc = 4:1). Anal. Calcd for $C_{28}H_{31}N_3O_5$: C, 68.69; H, 6.38; N, 8.58. Found: C, 68.55; H, 6.57; N, 8.57.

Methyl 2,3,6-Tri-*O*-benzyl-4-deoxy-4-(diethylphosphoramido)-α-D-galactopyranoside (41). (a) To a suspension of $LiAlH_4$ (35 mg, 0.92 mmol) in Et_2O (5.4 mL) was added a solution of **39** (108 mg, 0.22 mmol) in Et_2O (3.0 mL) at 0 °C under N_2, and the mixture was stirred for 2.5 h, with the temperature kept at 0 °C. After completion of the reaction, the reaction mixture was diluted with Et_2O, and saturated aqueous Na_2SO_4 was gradually added to the reaction mixture at 0 °C. After being stirred at 24 °C for 30 min, the mixture was extracted twice with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (15:1) gave 357 mg (89%) of amino sugar **40** as a colorless syrup: ^{1}H-NMR ($CDCl_3$) δ 7.45–7.20 (15H, m), 4.82 (1H, d, *J* = 11.9 Hz), 4.74 (1H, d, *J* = 11.9 Hz), 4.67 (1H, d, *J* = 11.9 Hz), 4.66 (1H, d, *J* = 11.9 Hz), 4.656 (1H, d, *J* = 2.6 Hz), 4.60 (1H, d, *J* = 11.9 Hz), 4.51 (1H, d, *J* = 11.9 Hz), 4.00 (1H, dt, *J* = 5.9, 1.4 Hz), 3.85 (1H, dd, *J* = 7.6, 3.1 Hz), 3.76 (1H, dd, *J* = 7.6, 2.6 Hz), 3.63 (2H, d, *J* = 5.9 Hz), 3.39 (3H, s), 3.30 (1H, dd, *J* = 3.1, 1.4 Hz), 1.37 (2H, br s).

(b) To a solution of **40** (254 mg, 0.55 mmol) in CH_2Cl_2 (13 mL) were added diethyl chlorophosphate (0.24 mL, 1.7 mmol) and Et_3N (0.23 mL, 1.7 mmol) at 24 °C under N_2, and the mixture was stirred at 40 °C for 18 h. After completion of the reaction, the reaction mixture was evaporated under reduced pressure to give a crude product, which was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (1:1) gave 150 mg (46%) of **41** as a pale yellow syrup: $[\alpha]^{25}_D$ +40.7° (*c* 1.02, $CHCl_3$); IR (film) ν_{max} 2907, 1496, 1454, 1235, 1042 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.50–7.20 (15H, m), 4.89 (1H, d, *J* = 12.0 Hz), 4.84 (1H, d, *J* = 12.5 Hz), 4.71 (1H, d, *J* = 12.5 Hz), 4.63 (1H, d, *J* = 3.7 Hz), 4.62 (1H, d, *J* = 12.0 Hz), 4.55 (2H, s), 4.10–3.80 (7H, m), 3.65 (1H, dd, *J* = 9.7, 4.6 Hz), 3.61 (1H, d, *J* = 7.1 Hz), 3.53 (1H, dd, *J* = 9.7, 3.6 Hz), 3.40 (3H, s), 2.63 (1H, t, *J* = 10.6 Hz), 1.19 (3H, t, *J* = 7.1 Hz), 1.13 (3H, t, *J* = 7.1 Hz); MS (EI) *m/z* 599 (M^+), 568, 554; (FAB) positive *m/z* 600 $(M + H)^+$; $R_f = 0.87$ (benzene:MeCN = 1:1); high-resolution mass (FAB) calcd for $C_{32}H_{43}O_8NP$ 600.2726, found 600.2724 $(M + H)^+$.

(Methyl 2,3,6-tri-*O*-benzyl-4-deoxy-α-D-galactopyranosid-4-yl) Isothiocyanate (42). To a suspension of NaH (57 mg, 2.38 mmol) and tetra-*n*-butylammonium bromide (28 mg, 0.08 mmol) in benzene (23 mL) was added a solution of **41** (456 mg, 0.76 mmol) in benzene (7.5 mL) at 24 °C under N_2, and the mixture was stirred at 70 °C. After 2 h, CS_2 (2.5 mL) was added to this reaction mixture, with the temperature kept at 70 °C, and this was stirred for 2 h. After completion of the reaction, the reaction mixture was diluted with benzene and washed with 1 M hydrochloric acid. The aqueous layer was extracted twice with benzene. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (4:1) gave 130 mg (34%) of **42** as a pale yellow syrup: $[\alpha]^{24}_D$ +71.0° (*c* 0.5, $CHCl_3$); IR (film) ν_{max} 2914, 2079 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.45–7.20 (15H, m), 4.85 (1H, d, *J* = 11.9 Hz), 4.73 (2H, s), 4.66 (1H, d, *J* = 11.9 Hz), 4.59 (1H, d, *J* = 4.0 Hz), 4.54 (2H, s), 4.27 (1H, dd, *J* = 4.0, 1.7 Hz), 3.96 (1H, dd, *J* = 9.9, 4.0 Hz), 3.91 (1H, ddd, *J* = 7.3, 5.8, 1.7 Hz), 3.75 (1H, dd, *J* = 9.9, 4.0 Hz), 3.574 (1H, d, *J* = 5.8 Hz), 3.57 (1H, d, *J* = 7.3 Hz), 3.35 (3H, s); MS (EI) *m/z* 505 (M^+), 473, 414; $R_f = 0.67$ (benzene:EtOAc = 2:1). Anal. Calcd for $C_{29}H_{31}O_5SN$: C, 68.89; H, 6.18; N, 2.77; S, 6.34. Found: C, 68.80; H, 6.02; N, 2.78; S, 6.38.

***N*-(Methyl 2,3,6-tri-*O*-benzyl-4-deoxy-α-D-galactopyranosid-4-yl)-*N'*-[[(*1R*)-(1α,2β,3α,4β,5β)]-1-(hydroxymethyl)-1,2,3,4-tetrahydroxycyclopent-5-yl]thiourea (43).** To a solution of **7** (34 mg, 0.19 mmol) in water (0.7 mL) was added a solution of **42** (68 mg, 0.13 mmol) in THF (3.4 mL) with stirring at 24 °C. After 7 days, this reaction mixture was concentrated *in vacuo* to give a residue, which was dried *in vacuo* and chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (10:1) gave 80 mg (87%) of **43** as a white foamy glass: $[\alpha]^{26}_D$ +113.6° (*c* 0.56, $CHCl_3$); IR (KBr) ν_{max} 3328, 2927, 1538, 1497, 1102, 1040 cm^{-1}; ^{1}H-NMR (CD_3OD) δ 7.50–7.20 (15H, m), 5.37 (1H, br s), 4.95–4.50 (8H, m), 4.20–4.10 (1H, m), 4.09–3.45 (11H, m), 3.38 (3H, s); $R_f = 0.48$ (CH_2Cl_2:MeOH = 10:1); FAB-MS positive *m/z* 685 $(M + H)^+$, negative *m/z* 683 $(M - H)^-$. Anal. Calcd for $C_{35}H_{44}N_2O_{10}S \cdot 1/2H_2O$: C, 60.59; H, 6.39; N, 4.03; S, 4.62. Found: C, 60.79; H, 6.54; N, 4.01; S, 4.47.

Methyl 2,3,6-Tri-*O*-benzyl-4-deoxy-4[[[(3a*R*)-(3a*R*)-(3aα,4α,5β,6α,6aα)]-4-(hydroxymethyl)-3a,5,6,6a-4,5,6-trihydroxytetrahydro-4*H*-cyclopentoxazol-2-yl]amino]-α-D-galactopyranoside (44). To a solution of 2-chloro-3-ethylbenzoxazolium tetrafluoroborate (56 mg, 0.21 mmol) in MeCN (3.5 mL) was added a solution of **43** (69 mg, 0.1 mmol) in MeCN (3.0 mL) at 0 °C under N_2. After being stirred for 1 h, Et_3N (0.06 mL, 0.43 mmol) was added to this mixture, with the temperature kept at 0 °C, and this was stirred for 2 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (8:1) gave 53 mg (81%) of **44** as a white foamy glass: $[\alpha]^{25}_D$ +24.5° (*c* 0.51, $CHCl_3$); IR (KBr) ν_{max} 3341, 2924, 1698, 1664, 1047 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.45–7.15 (15H, m), 4.81 (1H, d, *J* = 7.9 Hz), 4.75 (1H, d, *J* = 11.9 Hz), 4.68 (2H, s), 4.60 (1H, d, *J* = 3.3 Hz), 4.57 (1H, d, *J* = 11.9 Hz),

4.48 (2H, s), 4.32 (1H, d, J = 7.9 Hz), 4.18 (1H, br d, J = 2.6 Hz), 4.10–3.40 (14H, m including dd at 3.72 ppm (J = 9.2, 3.3 Hz), d at 3.51 ppm (J = 5.9 Hz)), 3.28 (3H, s); R_f = 0.44 (CH_2Cl_2:MeOH = 8:1); FAB-MS positive m/z 651 $(M + H)^+$, negative m/z 649 $(M - H)^-$. Anal. Calcd for $C_{35}H_{42}N_2O_{10}\cdot 3/2H_2O$: C, 62.00; H, 6.69; N, 4.13. Found: C, 61.83; H, 6.78; N, 4.16.

Methyl 4-Deoxy-4-[[[(3a*R*)-(3aα,4α,5β,6α,6aα)]-4-(hydroxymethyl)-4,5,6-trihydroxy-3a,5,6,6a-tetrahydro-4*H*-cyclopentoxazol-2-yl]amino]-α-D-galactopyranoside (12). To a solution of **44** (47 mg, 0.07 mmol) in MeOH (9.3 mL), was added 20% $Pd(OH)_2$ on carbon (700 mg) at 24 °C, and the mixture was hydrogenolyzed at 60 °C for 30 min. After completion of the reaction, this reaction mixture was filtered and concentrated *in vacuo* to give a crude product, which was chromatographed on Amberlite CG-50 (NH_4^+ type/H^+ type = 3/2, 5 mL). Elution with 0.5 M aqueous NH_3 gave 13 mg (46%) of **12** as a white powder: $[\alpha]^{25}_D$ +107.1° (*c* 0.89, H_2O); IR (KBr) ν_{max} 3366, 1660, 1039 cm^{-1}; ^{1}H-NMR (D_2O/external TMS) δ 4.68 (1H, dd, J = 8.8, 2.9 Hz), 4.65 (1H, d, J = 4.4 Hz), 4.10 (1H, d, J = 8.8 Hz), 3.99 (1H, dd, J = 6.6, 2.9 Hz), 3.85–3.80 (2H, m), 3.76 (1H, dd, J = 10.7, 4.4 Hz), 3.73 (1H, d, J = 6.6 Hz), 3.58 (1H, d, J = 12.2 Hz), 3.52 (1H, dd, J = 10.7, 4.4 Hz), 3.49 (1H, d, J = 12.2 Hz), 3.46 (2H, d, J = 6.4 Hz), 3.22 (3H, s); FAB-MS positive m/z 381 $(M + H)^+$ negative m/z 379 $(M - H)^-$; high-resolution mass (FAB) calcd for $C_{14}H_{25}N_2O_{10}$ 381.1510, found 381.1507 $(M + H)^+$; R_f = 0.38 (MeCN:H_2O:AcOH = 13:5:2).

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