# Synthesis of Sphere-Type Monodispersed Oligosaccharide−Polypeptide Dendrimers

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ABSTRACT: A sphere-type fully substituted oligosaccharide−*β*-alanine−poly(lysine) dendrimer having a sharp molecular weight distribution was synthesized. Sphere-type poly(lysine) dendrimers were prepared using 1,4-diaminobutane as an initiator core and *N*,*N*′-bis(*tert*-butyloxycarbonyl)-L-lysine as a branching unit. *β*-Alanine was bound to the poly(lysine) dendrimer generation 3 to form *β*-alanine−poly(lysine) dendrimer generation 3, which has 16 terminal amino groups on its surface. A series of sphere-type oligosaccharide−*β*-alanine−poly(lysine) dendrimers were obtained by binding such an oligosaccharide as maltose, lactose, cellobiose, maltotriose, or a mixture of lactose and maltose to the surface of the *β*-alanine−poly(lysine) dendrimer scaffolding by reductive amination using the borane−pyridine complex. Oligosaccharide−*β*-alanine−poly(lysine) dendrimers having 32 oligosaccharide residues were obtained in high yields. NMR and MALDI−TOF mass measurements revealed that the oligosaccharide−polypeptide dendrimers have a monodispersed molecular weight distribution, the molecular weight of which was 13 418.36, 13 472.50, and 13 507.28 g/mol for cellobiose, maltose, and lactose, respectively, indicating that a complete substitution of the amino group by the oligosaccharide occurred.

## Introduction

Dendrimers represent a new class of highly branched molecules, which have received a tremendous interest over the past two decades.[1−3] The unique feature of a dendrimer depends on versatility of reactive end groups at the periphery, while the core and branching unit of the dendrimer provide a unique structural scaffold. Therefore, they exhibit great potential applications in such fields as light harvesting, molecular recognition, and biomedicine.[4,5]

Sugar-containing dendrimers are generally composed of a sugar-coated dendrimer which comprised a non-sugar dendritic scaffolding with sugar coupling to its surface and a sugar-based dendrimer which contains sugar component in both inner and outer layers.[6] Since the sugar moiety of sugar-containing polymers plays important roles in bioactivities such as celllular recognition[7] and adhesion,[8] sugar-containing dendrimers attract much interest for biomedical applications.[9−13] Aoi and co-workers synthesized spherical sugar-containing dendrimers by binding lactose and maltose derivatives to a poly(amidoamine) (PAMAM) dendrimer.[14] To prepare the spherical dendrimer, they used ammonia as a trifunctional initiator core according to Tomalia's method.[15] Roy and co-workers prepared sugar-carrying thiosialoside dendrimers using poly(lysine) dendrimer as a scaffold.[16] Ashton and co-workers synthesized lactose "64-mer" by modification of fifth-generation poly(propyleneimine) dendrimer.[17] Andre et al. prepared a wedgelike glycodendrimer containing lactose.[18]

We have been investigating the synthesis of drugs for acquired immunodeficiency syndrome (AIDS) caused by human immunodeficiency virus (HIV) using sulfated polysaccharides and sulfated oligosaccharide derivatives.[19,20] Highly anti-HIV active sulfated curdlan was examined for the phase I/II test as an AIDS drug.[21,22] However, in efforts to develop effective drugs against HIV, it has been concluded that an HIV vaccine must be the most effective drug for AIDS, and a synthetic HIV vaccine might work to exhibit an anti-HIV activity in vitro. Multiple antigenic peptide systems for HIV vaccine development were reported by a few groups.[23−25]

Previously, we reported the synthesis of a hemisphere-type multilayered oligosaccharide−poly(lysine) dendrimers using oligosaccharides and poly(lysine) scaffold.[26] The final goal of these dendrimers is the synthesis of a glycopeptide-type HIV vaccine by binding an antigen from HIV components on the dendrimer surface.

We wish to report that a sphere-type monodispersed oligosaccharide−poly(lysine) dendrimer as an antigen-carrying candidate for glycopeptide-type HIV vaccine was synthesized starting from 1,4-diaminobutane as a core initiator. Besides, since all terminal amino groups in the poly(lysine) dendrimer were substituted by *β*-alanine having highly reactive amino groups, the dendrimer contains two oligosaccharide residues bound to individual amino groups in the terminal *β*-alanine by reductive amination of the oligosaccharide. The sphere-type dendrimer is different from the hemisphere-type oligosaccharide−poly(lysine) dendrimer in shape, solubility, and the ratio of sugar to peptide.

## Experimental Section

**Materials and Measurements.** 1,4-Diaminobutane dihydrochloride, L-(+)-lysine hydrochloride, *β*-alanine, and the borane−pyridine complex were purchased from Kanto Chemical Co., Inc. *β*-D-Lactose, maltose monohydrate, cellobiose, maltotriose, *N*,*N*′-diisopropylethylamine (DIEA), and benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluoro-

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phosphate (BOP reagent, Wako Pure Chemical Industries, Ltd.) were used as received. Dimethylformamide (DMF) was distilled after drying. *N*,*N*′-Bis(*tert*-butyloxycarbonyl)-L-lysine dicyclohexylamine salt (Boc-lysine(Boc)-COOH) and Boc-*β*-alanine were prepared according to the literature.[27] A dialysis tube (cutoff molecular weight of 1000; Spectrum Laboratories, Inc.) was used for the purification of oligosaccharide−poly(lysine) dendrimers. $^1$H NMR, $^{13}$C NMR, and field gradient heteronuclear single quantum correlation (FGHSQC) $^1$H−$^{13}$C 2D-NMR spectra were recorded on a JEOL Alpha-500 NMR spectrometer. For $^1$H NMR measurement, chemical shifts ($\delta$ = 0 ppm) were referred to TMS with the residual proton of the deuterated solvent. 3-(Trimethylsilyl)-1-propanesulfonic acid sodium salt (DSS) was used as the internal standard for $^{13}$C NMR measurement. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI−TOF MS) spectra were recorded on a Bruker Biflex III instrument with a 337 nm nitrogen laser. 2,5-Dihydroxybenzoic acid (5 mg/100 $\mu$L water solution) was used as matrix. A mixture of the sample solution (1 $\mu$L, 0.5 mg/mL in 0.1 M trifluoroacetic acid) and the matrix solution was applied to the MALDI probe. The sample was allowed to dry by air evaporation and was subjected to MS analysis.

**Synthesis of Poly(lysine) Dendrimer Generation 1 (LDG1).** To a suspension of 1,4-diaminobutane dihydrochloride (0.81 g, 5 mmol) in DMF (100 mL) were added Boc-lysine(Boc)-COOH dicyclohexylamine salt (5.3 g, 10 mmol) and DIEA (2.9 mL, 17 mmol) under a nitrogen atmosphere. After the suspension was stirred and cooled to 0 °C in an ice bath, BOP reagent (4.4 g, 10 mmol) was added. The reaction was performed at 0 °C for 30 min and then at room temperature for 24 h. The solvent was removed under reduced pressure, and the obtained syrup was dissolved in 200 mL of ethyl acetate, followed by washing successively with 30% NaCl solution, 5% aqueous citric acid solution, 5% $NaHCO_3$ solution, and water. After the solution was dried over anhydrous $Na_2SO_4$, it was concentrated. A syrup was purified by column chromatography over silica gel using chloroform and methanol (15:1) as an eluent. A white crystal (2.85 g) was obtained by recrystallization from a methanol and ethyl acetate mixture in 76.4% yield.

**Deprotection of Poly(lysine) Dendrimer Generation (G) 1.** Poly(lysine) dendrimer generation 1 was stirred in a mixed solution of trifluoroacetic acid (TFA) and dichloromethane (1:1) at room temperature for 30 min. After the solvent was evaporated under reduced pressure, diethyl ether was added to cause precipitation. The precipitate was collected by centrifugation and washed with anhydrous diethyl ether three times. The deprotected poly(lysine) dendrimer G1 was dried in vacuo.

**Synthesis of Poly(lysine) Dendrimer Generation 2 (LDG2).** Deprotected poly(lysine) dendrimer generation 1 (1.6 g, 2 mmol), Boc-lysine(Boc)-COOH dicyclohexylamine salt (4.31 g, 8.2 mmol), and DIEA (2.32 mL, 6.8 mmol) were dissolved in DMF (30 mL) in a three-necked flask under nitrogen. The solution was cooled to 0 °C under stirring. After BOP (3.63 g, 8.2 mmol) was added, the reaction was performed at 0 °C for 30 min and then at room temperature for 24 h. Thereafter, cold water was added until precipitates appeared. The precipitate was collected by filtration, followed by washing successively with water and 1,4-dioxane. Reprecipitation of the methanol solution by addition of ethyl acetate gave white powdery poly(lysine) dendrimer generation 2, after drying. Yield: 88.5%.

**Deprotection of Poly(lysine) Dendrimer Generation 2.** Poly(lysine) dendrimer generation 2 was deprotected in the same way as that of poly(lysine) dendrimer generation 1.

**Synthesis of Poly(lysine) Dendrimer Generation 3 (LDG3).** Poly(lysine) dendrimer G3 was synthesized by adding Boc-lysine(Boc)-COOH to a deprotected LDG2 solution in a method similar to that of poly(lysine) dendrimer G2 in 90.7% yield.

**Synthesis of *β*-Alanine—Poly(lysine) Dendrimer Generation 3 (ALDG3).** Instead of lysine, *β*-alanine was connected to the dendrimer generation 3. Boc-*β*-alanine was coupled to each amino group of deprotected poly(lysine) dendrimer G3 in the similar method described above. Boc-*β*-alanine-poly(lysine) dendrimer G3 was obtained in 74.8% yield.

**Synthesis of Sphere-Type Oligosaccharide—*β*-Alanine—Poly(lysine) Dendrimer Generation 3.** Deprotected *β*-alanine−poly(lysine) dendrimer G3 (0.2 g, 0.04 mmol) and maltose monohydrate (4.73 g, 13.15 mmol) were dissolved in 10 mL of 0.1 M borate buffer. After the borane−pyridine complex (1.33 mL, 13.15 mmol) was added, the solution was heated under stirring at 50 °C in an oil bath for 7 days. The product was purified by dialysis against deionized water for 3 days. White powdery maltose−*β*-alanine−poly(lysine) dendrimer G3 (M2ALDG3) was obtained by freeze-drying from water. Yield 81.5%.

Sphere-type lactose−poly(lysine) dendrimer generation 3 (L2ALDG3), cellobiose−*β*-alanine−poly(lysine) dendrimer generation 3 (C2ALDG3), maltotriose−*β*-alanine−poly(lysine) dendrimer generation 3 (M3ALDG3), and lactose/maltose−*β*-alanine−poly(lysine) dendrimer generation 3 (L/MALDG3) were synthesized in a similar way.

## Results and Discussion

**Synthesis of Sphere-Type Poly(lysine) Dendrimers.** To distinguish the dendrimer obtained in this study from the hemisphere-type poly(lysine) dendrimers consisting of a monodendron previously reported,[26] it is designated as a sphere-type dendrimer consisting of a didendron. Sphere-type poly(lysine) dendrimers were prepared by the synthetic route as illustrated in Scheme 1.

Using BOP reagent as a condensation catalyst, Boc-lysine(Boc)-COOH was reacted with 1,4-diaminobutane acting as a bifunctional core in DMF. Although 1,4-diaminobutane dihydrochloride was not soluble in DMF at room temperature, high solubility of the resulting product in DMF might have caused the reaction to proceed smoothly, providing a poly(lysine) dendrimer generation 1 (LDG1) in a high 76.4% yield. The result is summarized in Table 1.

Proceeding the reaction of amino groups in one generation younger dendrimer with Boc-lysine(Boc)-COOH, poly(lysine) dendrimers 2 (LDG2) and 3 (LDG3) were produced in high yields of 88.5% and 90.7%, respectively. The high yield might be due both to considerable solubility of LDG2 and LDG3 in DMF and to high reactivity of amino groups in the dendrimer. In addition, their large molecular weights facilitated these dendrimers to separate from unreacted compounds and to purify by precipitation.

To enhance reactivity of all amino groups of the poly(lysine) dendrimer and to prepare a thoroughly oligosaccharide-bound dendrimer, Boc-*β*-alanine was condensed with the amino groups of LDG3 to provide *β*-alanine−poly(lysine) dendrimer generation 3 (ALDG3).

The removal of Boc groups from the poly(lysine) dendrimers was easily carried out with a mixed solution of trifluoroacetic acid and methylene chloride, producing the dendrimers with free amino groups.

$^1$H NMR spectra of four poly(lysine) dendrimers are shown in Figure 1. In the spectrum of LDG1, the α proton of lysine residues appears at 3.80 ppm as a single peak. On the other hand, for LDG2 and LDG3, the outermost α protons (α2 and α4 in Figure 1, B and C, respectively) and inner α protons (Figure 1B: α; Figure 1C: α, α2) of lysine residues appear separately at 3.80 and 4.15 ppm, respectively. This indicates that since the α proton bound to Boc-protected amino groups exhibits a higher magnetic field shift, the α proton in the outermost lysine residue appears at higher magnetic fields than that of inner lysines in LDG2 and LDG3.

**Scheme 1. Synthesis of Sphere-Type Poly(lysine) Dendrimers**

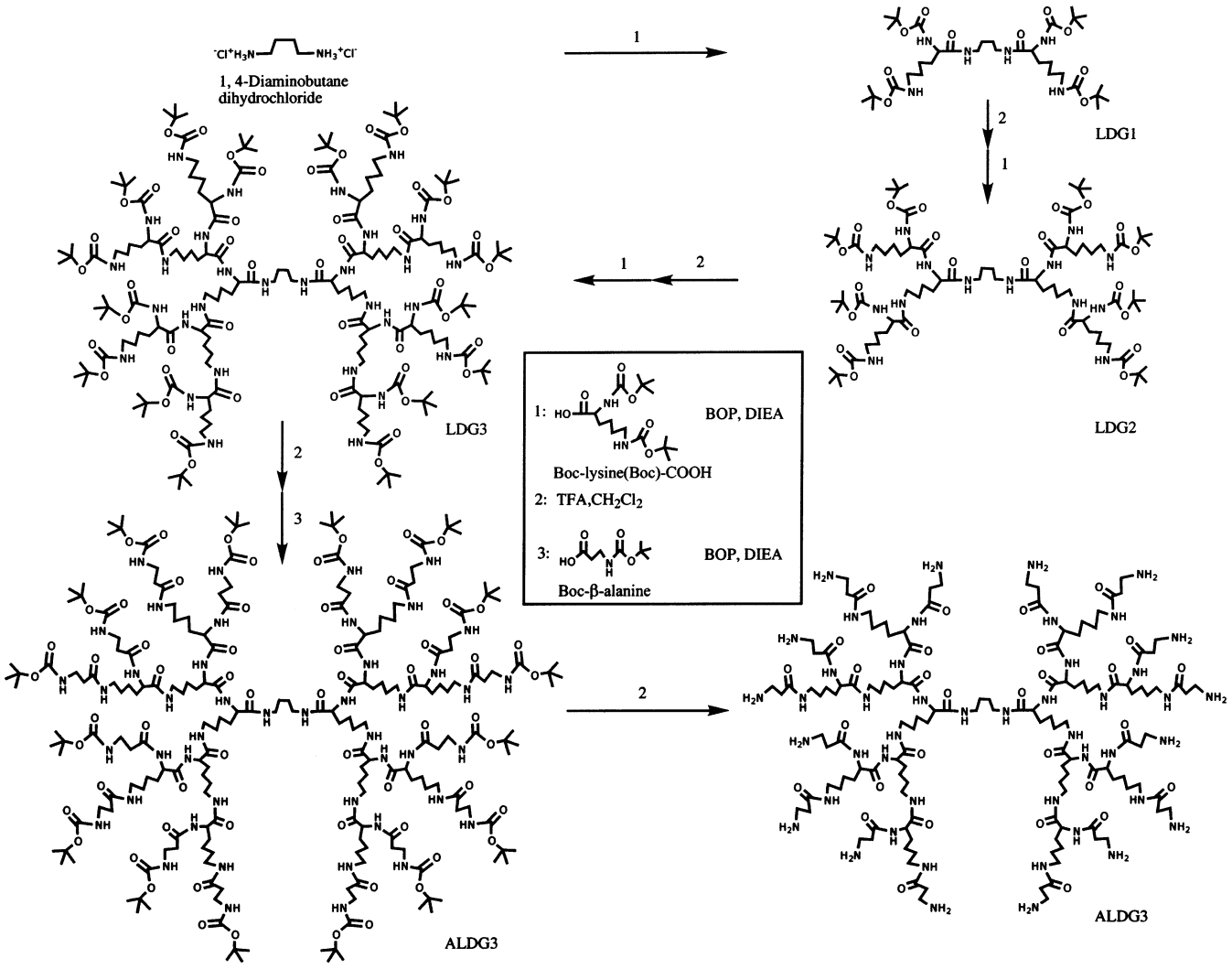



**Table 1. Synthesis of Sphere-Type Poly(lysine) Dendrimer of Generation 1 through 3**[a]

| | starting material | | | branching unit | | | BOP reagent[b] | | DIEA[c] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| dendrimer | type | g | (mmol) | type | g | (mmol) | g | (mmol) | mL | (mmol) | yield,[d] g (%) |
| LDG1 | DAB[e] | 0.81 | (5) | Di-Boc-lysine[f] | 5.26 | (10) | 4.43 | (10) | 2.9 | (17) | 2.85 (76.4) |
| LDG2 | LDG1[g] | 1.60 | (2) | Di-Boc-lysine | 4.26 | (8.2) | 3.58 | (8.2) | 2.4 | (13) | 2.94 (88.5) |
| LDG3 | LDG2 | 1.78 | (1) | Di-Boc-lysine | 4.26 | (8.2) | 3.58 | (8.2) | 2.4 | (13) | 3.16 (90.7) |
| ALDG3 | LDG3 | 1.22 | (0.33) | Boc-$\beta$-alanine | 2.08 | (5.6) | 2.48 | (5.6) | 1.2 | (9.2) | 2.94 (85.7) |

[a] The reaction was conducted in DMF at room temperature for 24 h. [b] Benzotriazol-1-yl-oxytris(dimethylamino)phosphonium hexafluorophosphate. [c] Diisopropylethylamine. [d] Based on the starting one generation younger dendrimer. [e] 1,4-Diaminobutane dihydrochloride. [f] *N,N′*-Bis(*tert*-butyloxycarbon-yl)-L-lysine dicyclohexylamine salt. [g] Deprotected sphere-type poly(lysine) dendrimer generation 1.

The same phenomenon was observed in $\epsilon$ proton absorptions in the range from 2.8 to 3.1 ppm.

In the spectrum of ALDG3 (Figure 1D), three new peaks due to $\beta$-alanine appear, that is, $\alpha'$-$CH_2$ at 2.18 and 2.27 ppm and $\beta'$-$CH_2$ at 3.09 ppm. The reason that the $\alpha'$-$CH_2$ absorption consists of two peaks is assumed to be the two different binding positions of $\beta$-alanine, i.e., the $\alpha$-NH and $\epsilon$-NH groups of lysine residues. Dendrimers of all generations were obtained as designed.

Results of the synthesis of sphere-type poly(lysine) dendrimers are summarized in Table 1. When 1,4-diaminobutane was reacted with Boc-lysine(Boc)-COOH in the ratio of 1:2, LDG1 was obtained in 76.4% yield. In the synthesis of LDG2 and LDG3, higher yields were attained when the same 1:2 ratio of $-NH_2$ to $-COOH$ was used. $\beta$-Alanine was bound to all amino groups of poly(lysine) dendrimer to give ALDG3 in 85.7% yield.

**Synthesis of Sphere-Type Oligosaccharide−$\beta$-Alanine−Poly(lysine) Dendrimer Generation 3.** A few kinds of oligosaccharides were connected to the $\beta$-alanine−poly(lysine) dendrimer generation 3 (ALDG3) by reductive amination between the sugar reducing end and the terminal amino group of the dendrimer, as shown in Scheme 2.

As the $^1$H NMR spectrum of maltose-connected ALDG3 (M2ALDG3) is shown in Figure 2, the H1′ absorption of the reduced maltose residue appears at 2.72 ppm. Composition of M2ALDG3 was determined from the NMR spectrum using integration ratio of an absorption due to $\beta$-$CH_2$ of lysine residues at 1.72 ppm to the H1 absorption of the maltose residue. It was revealed that

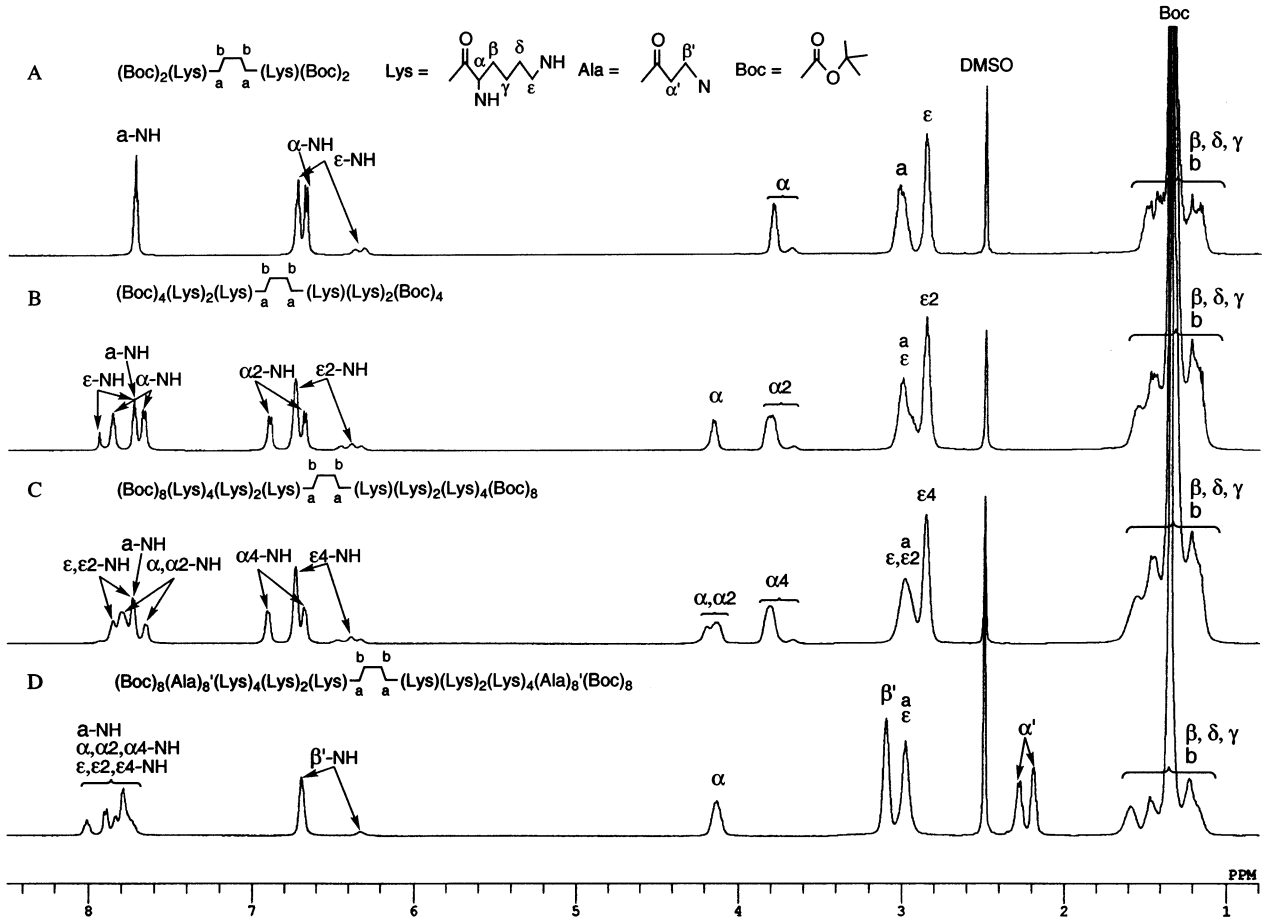
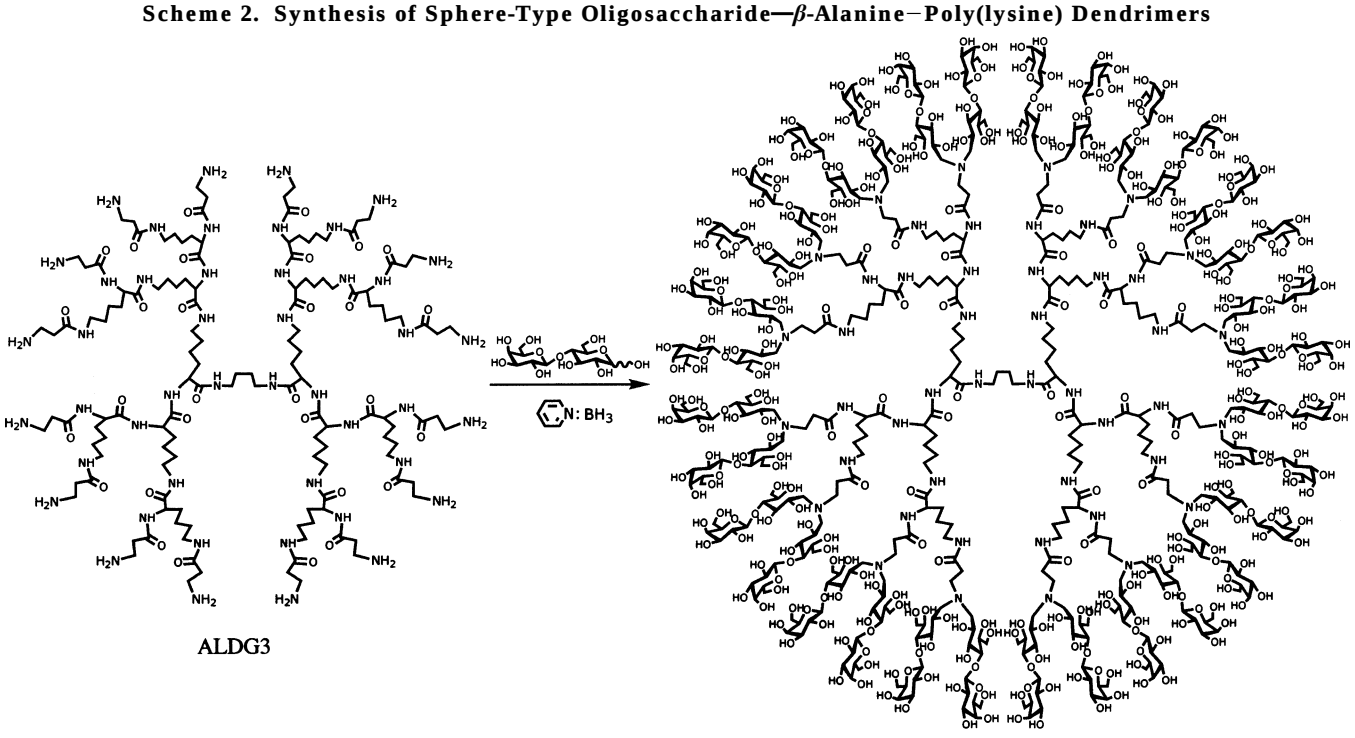



**Figure 1.** $^1$H NMR spectra of Boc-protected sphere-type poly(lysine) dendrimers in DMSO-$d_6$ (A, LDG1; B, LDG2; C, LDG3; D, ALDG3).

**Scheme 2. Synthesis of Sphere-Type Oligosaccharide—*β*-Alanine−Poly(lysine) Dendrimers**




all 16 amino groups were substituted individually by two maltose residues, giving 32 maltose residues connected to a dendrimer. As shown in Figure 3, the $^1$H−$^{13}$C 2D-NMR spectrum of M2ALDG3 expresses that the dendrimer has a clear structure of maltose-containing *β*-alanine−poly(lysine) dendrimer.

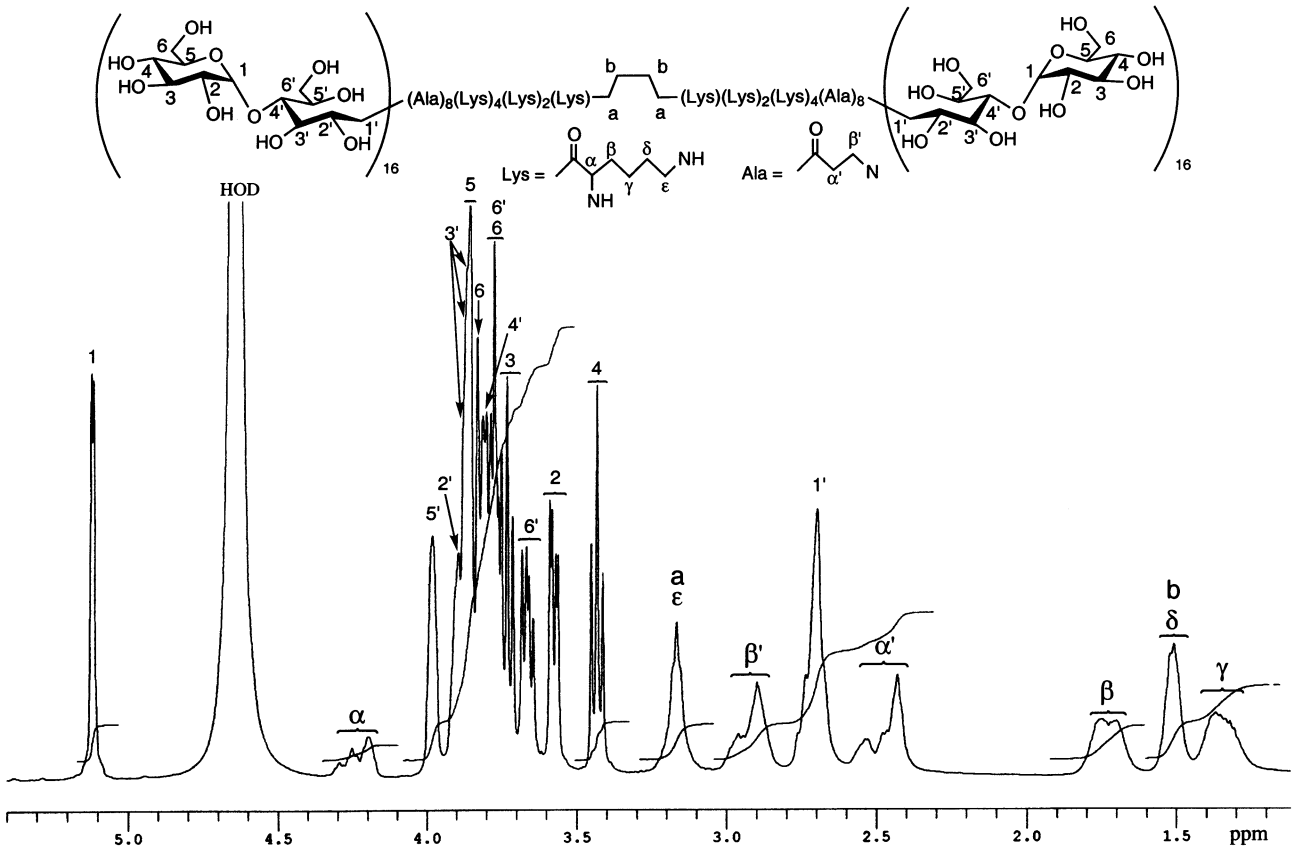



**Figure 2.** $^1$H NMR spectrum of sphere-type maltose−$\beta$-alanine−poly(lysine) dendrimer generation 3 (M2ALDG3) in $D_2O$ at 40 °C.

**Table 2. Molecular Formula, Calculated Mass, Mass Determined by MALDI−TOF Mass Spectrometry, and Number of Sugar Residues Contained within the Sphere-Type Monodispersed Oligosaccharide−Polypeptide Dendrimers**

| | | molecular mass (g/mol) | | no. of sugar residues |
|---|---|---|---|---|
| dendrimer | mol formula[a] | calcd | found | calcd |
| M2ALDG4 | $C_{520}H_{964}N_{46}O_{350}$ | 13453.87 | 13472.50 | 32 |
| L2ALDG4 | $C_{520}H_{964}N_{46}O_{350}$ | 13453.87 | 13507.28 | 32 |
| C2ALDG4 | $C_{520}H_{964}N_{46}O_{350}$ | 13453.87 | 13418.36 | 32 |
| L/MALDG4 | $C_{520}H_{964}N_{46}O_{350}$ | 13453.87 | 13384.36 | 32 |
| M3ALDG4 | $C_{712}H_{1284}N_{46}O_{510}$ | 18638.05 | | 32 |

[a] Based on 32 sugars substitution.

Combining the data obtained from Figure 2 with Figure 3, it was suggested that the dendrimer is composed of the following sphere-type structure, i.e., [(maltose)$_{16}$-($\beta$-Ala)$_8$(Lys)$_4$(Lys)$_2$(Lys)-CONH-CH$_2$-CH$_2$-]$_2$.

MALDI−TOF mass spectrometric measurements revealed that the M2ALDG3 dendrimer has a monodisperse molecular weight distribution. As shown in Figure 4, M2ALDG3 exhibited a sharp single peak at the molecular weight of 13 472.50 g/mol. Similarly, lactose-bound dendrimer L2ALDG3 and cellobiose-bound dendrimer C2ALDG3 also showed single peaks at 13 507.28 and 13 418.36 g/mol, respectively. As the data are summarized in Table 2, the calculated molecular weight for $C_{520}H_{964}N_{46}O_{350}$ which corresponds to the dendrimer having the above chemical structure is 13 453.87 g/mol based on the atomic weights of the predominant isotopes ($^1$H: 1.0078; $^{12}$C: 12.0000; $^{14}$N: 14.0030; $^{16}$O: 15.9949). Although the mass value was either 18.63 g/mol (M2ALDG3) to 53.41 g/mol (L2ALDG3) higher or 35.51 g/mol (C2ALDG3) lower than the calculated value, it is assumed that such mass differences might be attributed to errors usually occurring from salt, solvent, matrix, desorption/ionization efficiency, and the detector response.[28,29] Accordingly, it was concluded that these dendrimers were composed of sphere-type $\beta$-alanine−poly(lysine) dendrimer generation 3 and 32 sugar residues in which the terminal amino groups were completely substituted by the oligosaccharide.

In the previous paper, we reported the synthesis of hemisphere-type oligosaccharide−poly(lysine) dendrimer generation 3 without $\beta$-alanine moiety according to a similar reductive amination.[26] Since the eight amino groups included in the dendrimer had different reactivity, the number of oligosaccharide residues connected to the dendrimer ranged from 13 to 16.

No significant difference in reactivity was observed among maltose, lactose, cellobiose, and maltotriose when a strong reducing agent borane−pyridine complex was used. When a mixture of lactose and maltose was used in the 1:1 ratio, a fully mixed sugar-substituted $\beta$-alanine−poly(lysine) dendrimer containing the ratio of lactose to maltose residues of 1:1.1 was obtained.

The results of synthesis of sphere-type oligosaccharide−$\beta$-alanine−poly(lysine) dendrimers are summarized in Table 3. To accomplish a complete substitution by oligosaccharides to the amino group of $\beta$-alanine moiety, i.e., approximately 32 oligosaccharide residues, optimum reaction conditions were chosen in reference to the literature.[30,31] Although the degree of substitution obtained from $^1$H NMR measurement is slightly higher than the calculated maximum value, it is assumed that the NMR sample might include a small amount of unreacted oligosaccharide because of difficulty in its

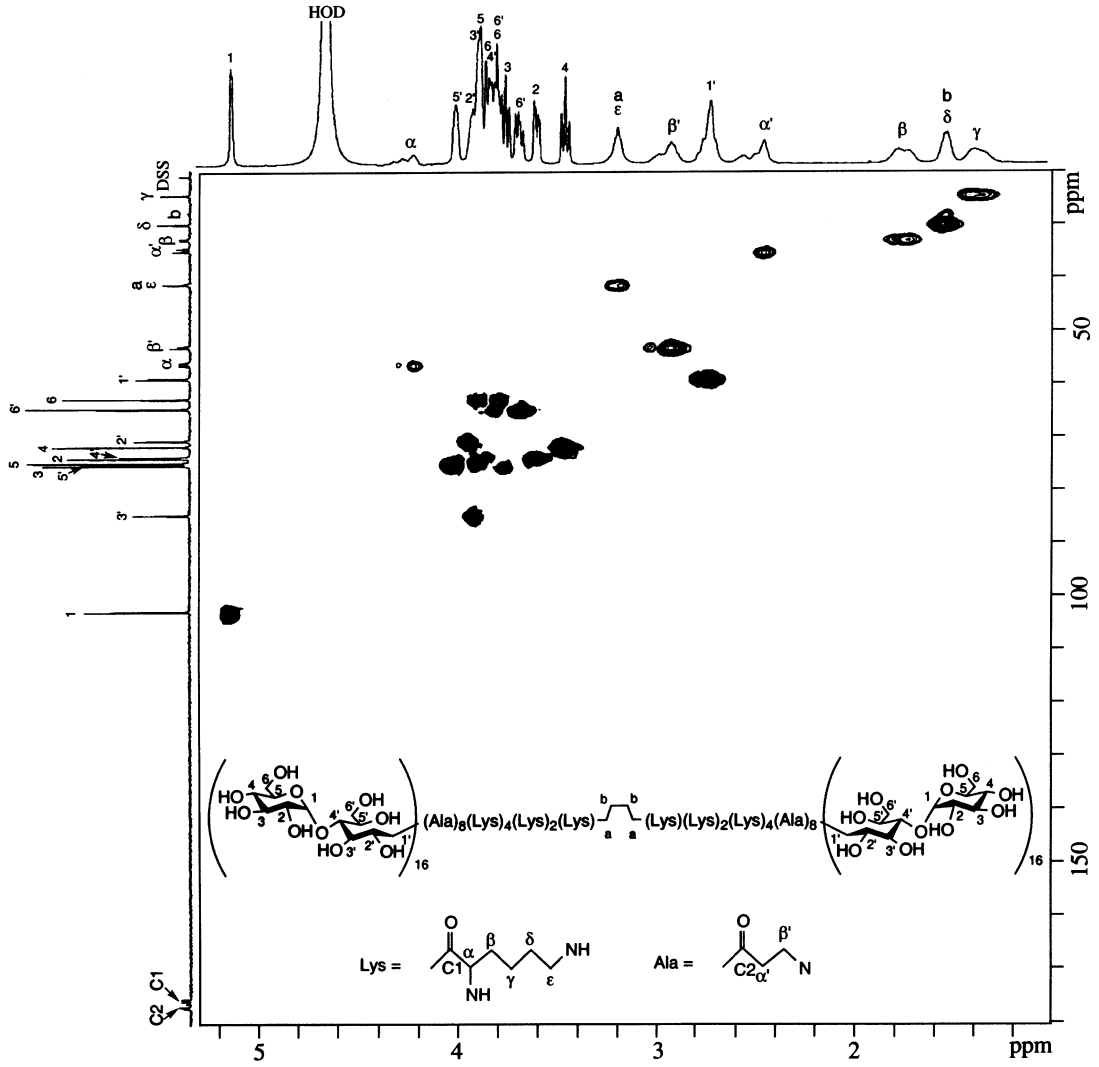



**Figure 3.** $^{1}H-^{13}C$ 2D-NMR spectrum of sphere-type maltose−$\beta$-alanine−poly(lysine) dendrimer generation 3 (M2ALDG3) in $D_2O$ at 40 °C.

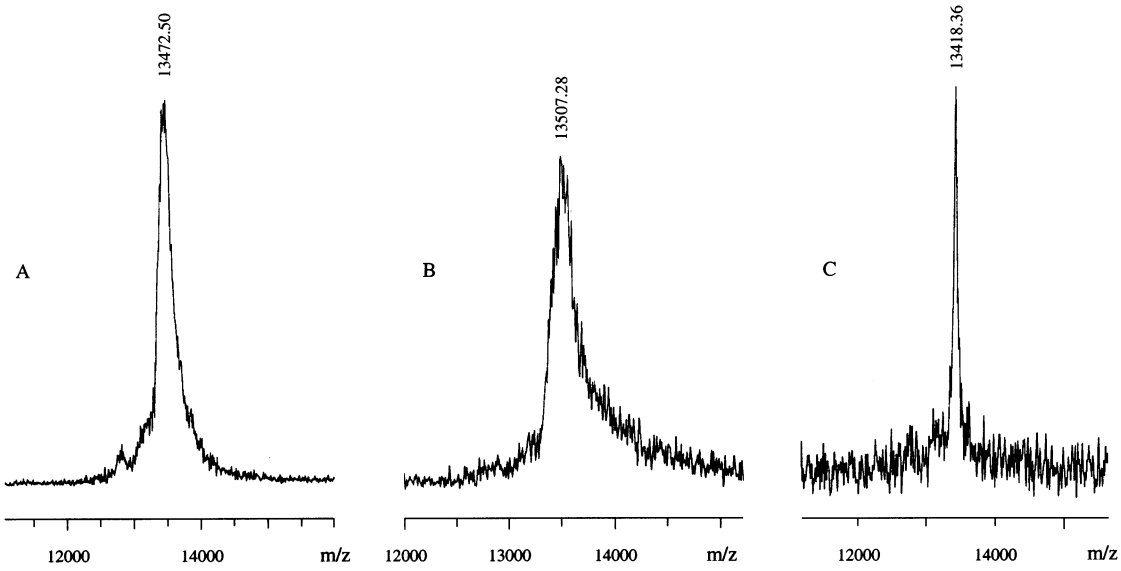



**Figure 4.** MALDI−TOF MS spectra of (A) sphere-type maltose−$\beta$-alanine− poly(lysine) dendrimer generation 3 (M2ALDG3), (B) sphere-type lactose−$\beta$-alanine−poly(lysine) dendrimer generation 3 (L2ALDG3), and (C) sphere-type cellobiose−$\beta$-alanine−poly(lysine) dendrimer generation 3 (C2ALDG3).

complete removal. Reaction between the carbonyl group of the reducing sugar and the amino group in $\beta$-alanine might be a rate-determining step. Previously, it was found that high degrees of substitution were attained by increasing the molar ratio of oligosaccharides to amino groups.[26] In this study, a high ratio of 10:1 was

**Table 3. Synthesis of Sphere-Type Monodispersed Oligosaccharide−Polypeptide Dendrimers[a]**

| | starting dendrimer | | | oligosaccharide | | | $BH_3$−pyridine | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| dendrimer | kind | g | (mmol) | type | g | (mmol) | mL | (mmol) | DS[b] | yield, g (%) |
| L2ALDG3 | ALDG3[c] | 0.2 | (0.04) | lactose | 4.5 | 13.2 | 1.3 | (13.2) | 32.6 | 0.42 (76.1) |
| M2ALDG3 | ALDG3 | 0.2 | (0.04) | maltose[d] | 4.7 | 13.2 | 1.3 | (13.2) | 32.9 | 0.45 (81.5) |
| C2ALDG3 | ALDG3 | 0.2 | (0.04) | cellobiose | 4.5 | 13.2 | 1.3 | (13.2) | 32.6 | 0.41 (75.0) |
| M3ALDG | ALDG3 | 0.2 | (0.04) | maltotriose | 6.6 | 13.2 | 1.3 | (13.2) | 35.5 | 0.62 (79.3) |
| L/MALDG3 | ALDG3 | 0.2 | (0.04) | lactose, maltose[e] | 2.2/2.3 | 6.6/6.6 | 1.3 | (13.2) | 14.8/16.1 | 0.41 (75.0) |

[a] The solvent was borate buffer (pH 9.0, 10 mL, 0.05 M). The temperature was 50 °C. The time was 7 days. [b] The degree of substitution was estimated from $^1$H NMR measurement using the integration ratio of peaks for $\beta$-$CH_2$ of lysine residue and H1 of oligosaccharide residue. [c] Deprotected sphere-type $\beta$-alanine−poly(lysine) dendrimer generation 3. [d] Maltose monohydrate. [e] Lactose and maltose monohydrate were used in a 1:1 ratio.

chosen. In addition, such optimum conditions as high temperature, high pH (=9.0), and long reaction time might have produced fully oligosaccharide-substituted dendrimers in high yields.

Coupling of an antigen peptide sequence from HIV to these oligosaccharide−$\beta$-alanine−poly(lysine) dendrimers is now in progress in our laboratory.

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