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Introduction of monosaccharides having functional groups onto a carbosilane dendrimer: A broadly applicable one-pot reaction in liquid ammonia involving Birch reduction and subsequent SN2 reaction☆

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Abstract

Benzylthioalkyl glycosides of D-glucuronic acid, *N*-acetyl-D-glucosamine, and *N*-acetylneuraminic acid (common monosaccharide constituents of natural oligosaccharide chains) have been prepared as sulfide precursors for the carbohydrate coating of dendric carbosilane cores and used in a generally applicable one-pot reaction (Birch reduction in liquid ammonia and subsequent SN2 reaction) to generate a thioether linkage between the monosaccharide moieties and a carbosilane dendrimer. The dendrimers were uniformly functionalized with the monosaccharides in good yields.

Keywords: Carbosilane dendrimers; Glycodendrimers; Birch reduction; Sulfides; SN2 reaction

1. Introduction

The sugar clustering effect is well-known as a phenomenon, originally reported by Lee [1], that can enhance the weak individual interactions between carbohydrates and proteins. For example, Lee synthesized cluster glycosides from aminotris(hydroxymethyl)methane as the core for investigation of such interactions [2]. Recently a number of glycodendrimers intended for similar purposes have been synthesized and investigated [3]. We have also reported a novel class of glycodendrimers using carbosilane dendrimers as the core structures [4,5]. For the construction of carbosilane dendrimers uniformly functionalized with carbohydrate moieties, as shown in Fig. 1, a successful one-pot coupling procedure between the carbohydrate moieties and carbosilane dendrimers was developed. The method utilizes Birch reduction [Na in liquid ammonia (liquid NH_3)] of benzyl-thioether-functionalized carbohydrate precursors and the subsequent SN2 replacement of ω-bromo groups in dendric carbosilane scaffolds [4,5]. In our previous study, this procedure was used exclu-

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sively to attach bioactive oligosaccharides having only hydroxyl groups (neutral sugars) such as β-cyclodextrin and a globotriaosyl moiety. We have since directed our attention toward the feasibility of a one-pot reaction for other saccharides having such functional groups as carboxyl or acetamido groups.

In this study, we demonstrate the broad applicability of a one-pot reaction for constructing carbosilane dendrimers uniformly coated with D-glucuronic acid, *N*-acetyl-D-glucosamine, or *N*-acetylneuraminic acid (Fig. 1).

2. Results and discussion

To construct a carbosilane dendrimer functionalized with monosaccharides having a carboxyl group, the glucuronic acid derivative **5** was selected for the first test case. Thus, the known trityl glucoside **1** [6] was converted in 52% yield into its carboxymethyl derivative **2** via the in situ *O*-de-tritylation followed by Jones oxidation (CrO_3) in a one-pot procedure. The convenient introduction of a sulfide function into an alkenyl group has been reported by several groups via radical addition [7]. Thus, the radical addition of α-toluenethiol to the C=C double bond of the aglycon of **2** was performed in 1,3-dioxolane in the presence of AIBN as the radical initiator to afford the 3-(benzylthio)propyl glycoside **3** in an anti-Markovnikov's manner in almost quantitative yield. The structure of the sulfide **3** was confirmed by both its ^1H NMR spectrum and elemental analysis. Zemplén *O*-deacetylation of **3** gave **4** in 69% yield after purification on a column of silica gel. Saponification of the methyl ester **4** proceeded smoothly in the presence of NaOH, giving the corresponding carboxylate anion, which was converted in 95% yield into **5** by the removal of Na cations by using ion exchange resin (H^+).

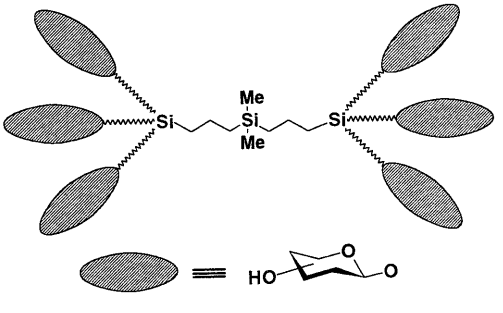
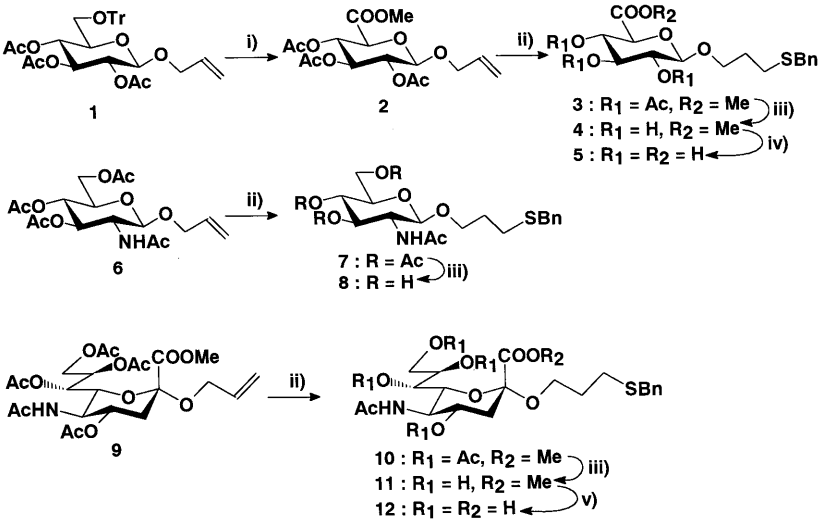


Fig. 1. An example of a carbosilane dendrimer uniformly functionalized with sugar moieties.

Since the preparation of the GlcA derivative **5** had been accomplished, we turned our attention to preparation of the 3-(benzylthio)propyl glycoside **8** of GlcNAc. For this purpose, the allyl glycoside **6** [7a] was allowed to react with α-toluenethiol in the presence of a radical initiator to provide the crystalline sulfide **7** in 98% yield. The transesterification of the acetate **7** was carried out in methanolic sodium methanoate at room temperature to give **8** in 99% yield.

Finally, we examined the preparation of a benzylthioalkyl glycoside sialic acid (which contains a carboxylic acid and an *N*-acetyl group). Thus, the known **9** was prepared as the starting material by the method previously reported [8]. Addition of a benzylsulfide moiety by a radical reaction to the allyl function of **9** also proceeded efficiently in an anti-Markovnikov's manner to afford **10** in 96% yield. Conventional *O*-de-acetylation gave the tetrol **11** in 78% yield, which was further treated with aqueous NaOH to produce the benzylthioalkyl glycoside **12** of sialic acid quantitatively (Scheme 1).

Given the success of the preparation of 3-(benzylthio)propyl glycosides **5**, **8**, and **12**, we proceeded to add these derivatives to the carbosilane dendrimer **13** [5] to produce sugar clusters. We have recently reported a simple and convenient method, namely, a one-pot reaction in liquid NH_3 for Birch reduction and subsequent SN2 reaction producing thioether linkages, for the construction of a carbosilane dendrimer functionalized with β-cyclodextrin and globotriaose moieties (sugar residues lacking additional functional groups). In order to examine the broader applicability of the one-pot reaction, the 3-benzylthiopropyl glycosides of **5**, **8**, and **12** were tested. The Birch reductive removal of the benzyl group of glycoside **5** was performed in liquid NH_3 in the presence of Na, generating the thiolate anion in situ. After neutralization of the excess Na by the addition of NH_4Cl, the thiolate anion was allowed to react with the dendrimer **13**



Scheme 1. Reagents and conditions: (i) Jones oxidation, then CH_2N_2, Et_2O; (ii) α-toluenethiol, AIBN, 1,4-dioxane, 50 → 80 °C; (iii) NaOMe, MeOH, rt; (iv) 1 M aq NaOH; (v) 0.05 M aq NaOH.

carrying a bromine atom at its ω-positions to provide crude products. Purification by gel filtration for removal of the by-products, including incompletely reacted compounds, gave the carbosilane dendrimer **14** having six D-glucuronic acid moieties in 64% yield based on **13**, and which had the expected molecular-ion peak (*m*/*z* 2076). The benzyl sulfide **8** was also treated with dendrimer **13** by the method described for the preparation of **14** to afford a coupled product. Unfortunately, the crude product was found to be a mixture, including *N*-de-acetylated moieties that gave a positive ninhydrin test for the amino function. Therefore, an *N*-selective acetylation of the amino function of the product was carried out in MeOH, followed by gel filtration to give the corresponding *O*-de-acetylated glycodendrimer, accompanied by some impurities. Next, the crude *O*-de-acetylated **15** was acetylated completely to provide the corresponding dendrimer **15** having six per-*O*-acetylated *N*-acetyl-D-glucosamine moieties in 46% yield, based on **13**; it showed the expected molecular ion peak at *m*/*z* 2973.

An initial trial coupling of **12** with **13**, using the same conditions as those described for **15**, was carried out. Unfortunately, pure **16** was not obtained because of difficulties in removal of impurities. As the impurity seemed to consist of incompletely coupled products, the stoichiometric ratio of **12**:**13** was raised to 18:1 in order to enhance the efficiency of the SN2 coupling reaction. In a second trial, the coupled product **16** was obtained as acetate showing a molecular ion peak by FABMS at *m*/*z* 3838 (Scheme 2).

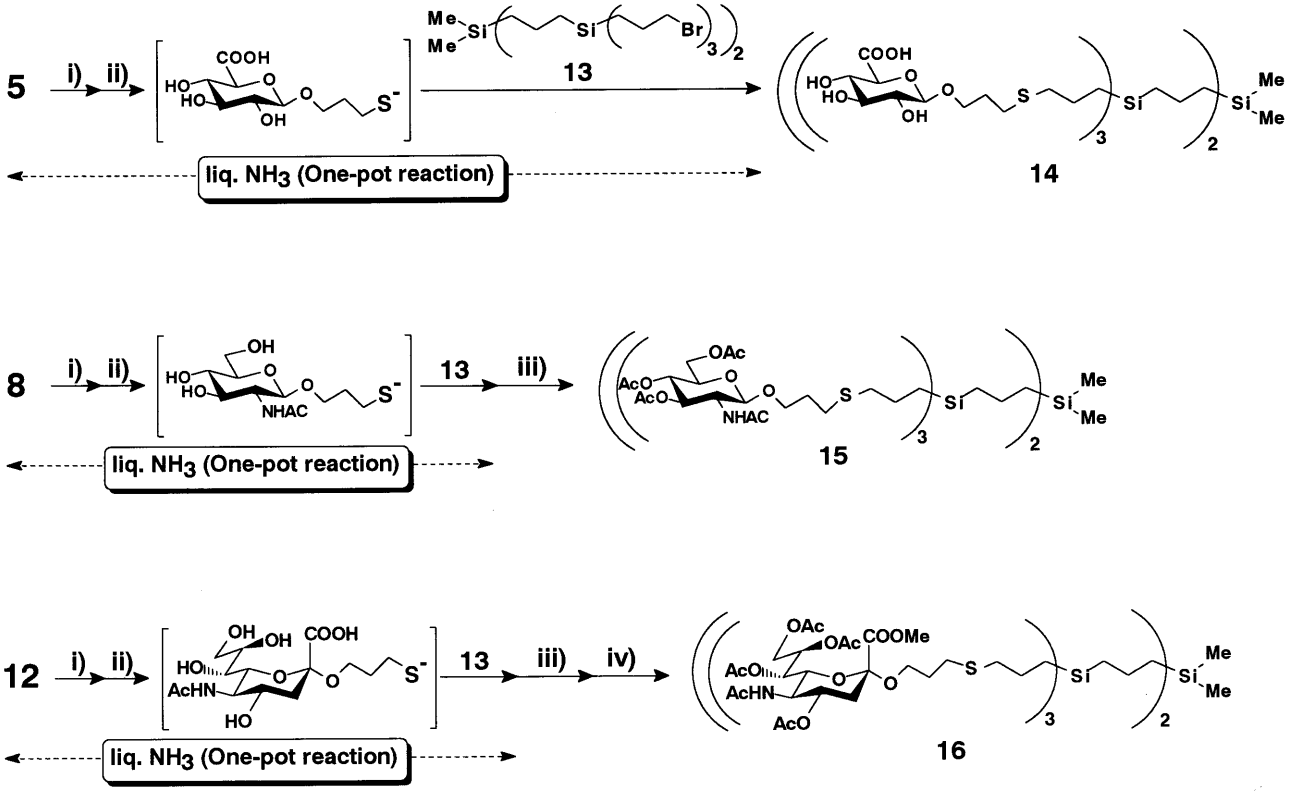
In conclusion, we have demonstrated the feasibility of a one-pot reaction in liquid NH_3 for Birch reduction and the subsequent SN2 replacement to construct carbosilane dendrimers bearing three kinds of monosaccharide derivatives containing carboxylic acid and amide functional groups. Further applications of this procedure for assembling complex oligosaccharides, using a series of carbosilane dendrimers as the core frame, are now under way.

3. Experimental

Materials and methods.—Unless otherwise stated, all commercially available solvents and reagents were used without further purification. Pyridine, 1,4-dioxane, and tetrahydrofuran (THF) were stored over molecular sieves (4 Å MS), and methanol (MeOH) was stored over 3 Å MS before use. Melting points were measured with a Laboratory Devices Meltemp II apparatus and were uncorrected. The optical rotations were determined with a Jasco DIP-1000 digital polarimeter. The IR spectra were obtained using a Jasco FT/IR-300E spectrophotometer. The ^{1}H NMR spectra were recorded at 400 MHz with a Bruker

AM-400 or at 200 MHz with a Varian Gemini-2000 spectrometer in chloroform-*d* or D_2O. Tetramethylsilane (Me_4Si) and MeOH (3.3 ppm) were used as internal standards. Ring-proton assignments in NMR were made by first-order analysis of the spectra and were supported by the results of homonuclear decoupling experiments. Elemental analyses were performed with a Fisons EA1108 instrument on samples extensively dried at 50–60 °C over P_2O_5 for 4–5 h. Fast atom bombardment mass (FABMS) spectra were recorded with a Joel JMS-HX110 spectrometer. Reactions were monitored by thin-layer chromatography (TLC) on precoated plates of Silica Gel $60F_{254}$ (layer thickness, 0.25 mm; E. Merck, Darmmstadt, Germany). For detection of the intermediates, TLC sheets were sprayed with (a) a solution of 85:10:5 (v/v/v) MeOH–*p*-anisaldehyde–H_2SO_4, and heated for a few minutes (for carbohydrate) or (b) an aqueous solution of 5 wt% $KMnO_4$ and heated similarly (for C=C double bond). Column chromatography was performed on silica gel (Silica Gel 60; 63–200 μm, E. Merck). Flash column chromatography was performed on silica gel (Silica Gel 60, spherical neutral; 40–100 μm, E. Merck). All extractions were conducted below 45 °C under diminished pressure.

*Methyl (allyl 2,3,4-tri-*O*-acetyl-β-*D*-glucopyranosid)uronate* (**2**) *[9].*—To a solution of the known allyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-β-D-glucopyranoside (**1**, 5.00 g, 8.49 mmol) [6] in acetone (100 mL) was added a solution of CrO_3 (17.0 g, 170 mmol) in 3.5 M aq H_2SO_4 (23 mL) at 0 °C, and the mixture was kept warm at rt for 50 min. When TLC indicated the complete conversion of **1**, the resultant mixture was poured into ice–water and extracted with $CHCl_3$. The organic solution was washed with brine, dried ($NaSO_4$), and evaporated. The residual syrup was dissolved in CH_2Cl_2 (100 mL), and the solution was treated with ethereal CH_2N_2. Conventional work-up gave **2** (1.65 g, 51.9%) after crystallization from 2-propanol; mp 136–137 °C; IR (KBr) 2952 (ν_{C-H}), 1758 ($\nu_{C=O}$) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.02 (s, 6 H, 2 Ac), 2.05 (s, 3 H, Ac), 3.76 (s, 3 H, Me), 4.04 (m, 1 H, H-5), 4.24 (m, 2 H, OCH_2), 4.61 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 5.04 (m, 1 H, H-2), 5.45



Scheme 2. The one-pot reaction, reagents and conditions: (i) Na; (ii) NH_4Cl; (iii) acetylation; (vi) CH_2N_2, ether.

(m, 4 H, H-3, H-4, =CH_2), 5.84 (m, 1 H, CH=).

Methyl (3-benzythiopropyl 2,3,4-tri-O-acetyl-β-D-glucopyranosid)uronate (**3**).—To a stirred solution of **2** (102 mg, 0.272 mmol) and α-toluenethiol (479 μL, 4.08 mmol) in 1,4-dioxane (0.5 mL) was added 2,2′-azobisisobutyronitrile (AIBN; 22.3 mg, 0.136 mmol) at 50 °C under an Ar atmosphere. The mixture was stirred for 1.5 h at 80 °C at which time cyclohexene (413 μL, 40.8 mmol) was added, and the mixture was stirred at rt for 15 min. After evaporation, silica gel chromatography of the residual syrup (8:1 (v/v) toluene–EtOAc) yielded sulfide **3** (134 mg, 98.5%) as crystals: mp 75–77 °C, $[\alpha]_D^{28}$ −16.6° (*c* 0.44, $CHCl_3$); IR (neat) 2951 (ν_{C-H}), 1755 ($\nu_{C=O}$) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.82 (m, 2 H, CH_2), 2.00, 2.02, 2.02 (each s, 9 H, 3 Ac), 2.46 (t, 2 H, *J* 7.1 Hz, SCH_2), 3.68 (s, 3 H, Me), 3.74 (s, 2 H, CH_2Ph), 3.76 (m, 2 H, OCH_2), 4.02 (d, 1 H, $J_{4,5}$ 9.4 Hz, H-5), 4.51 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.98 (dd, 1 H, $J_{2,3}$ 9.2 Hz, H-2), 5.21 (t, 1 H, $J_{3,4}$ 9.3 Hz, H-4), 5.24 (t, 1 H, H-3), 7.22–7.33 (m, 5 H, Ph). Anal. Calcd for $C_{23}H_{30}O_{10}S$: C, 55.41; H, 6.07. Found: C, 55.67; H, 6.06.

Methyl (3-benzylthiopropyl β-D-glucopyranosid)uronate (**4**).—A solution of acetate **3** (1.60 g, 3.21 mmol) in MeOH was treated with NaOMe (52.0 mg, 0.962 mmol) at rt under an Ar atmosphere for 2 h, and then additional NaOMe (17.3 mg, 0.322 mmol) was added. After 1 h of stirring at rt, when TLC indicated the complete conversion of **3**, the reaction mixture was neutralized with IR-120B (H^+) resin until pH 7 and then filtered. The filtrate was concentrated and the residue was subjected to column chromatography on silica gel with 10:1 (v/v) $CHCl_3$–MeOH to afford pure **4** (824 mg, 69.0%) as a colorless syrup, $[\alpha]_D^{28}$ −30.0° (*c* 0.43, MeOH); IR (neat) 3399 (ν_{O-H}), 2917 (ν_{C-H}), 1746 ($\nu_{C=O}$) cm^{-1}; ^1H NMR (400 MHz, Me_2SO-d_6 with D_2O) δ 1.71 (m, 2 H, CH_2), 2.42 (t, 2 H, *J* 7.2 Hz, SCH_2), 2.99 (t, 1 H, H-2), 3.21 (t, 1 H, $J_{2,3}$ 9.0 Hz, H-3), 3.31 (t, 1 H, $J_{3,4}$ 9.3 Hz, H-4), 3.58 (m, 2 H, OCH_2), 3.62 (s, 3 H, Me), 3.65 (s, 2 H, CH_2Ph), 3.74 (d, 1 H, $J_{4,5}$ 9.7 Hz, H-5), 4.22 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 7.18–7.30 (m, 5 H, Ph). Anal. Calcd for $C_{17}H_{24}O_7S{\cdot}0.5\ H_2O$: C, 53.53; H, 6.61. Found: C, 53.70; H, 6.58.

3-Benzylthiopropyl β-D-glucopyranosyluronic acid (**5**).—A solution of methyl ester **4** (389 mg, 1.04 mmol) in 1 M aq NaOH (5 mL) was stirred for 15 min at rt. To the solution was added an IR-120B (H^+) resin to remove Na^+, and the suspension was filtered and concentrated to give **5** (354 mg, 94.7%) as an amorphous solid, $[\alpha]_D^{27}$ −33.4° (*c* 1.13, MeOH); IR (KBr) 3304 (ν_{O-H}), 2923 (ν_{C-H}), 1741 ($\nu_{C=O}$) cm^{-1}; ^1H NMR (400 MHz, Me_2SO-d_6 with D_2O) δ 1.74 (m, 2 H, CH_2), 2.46 (t, 2 H, *J* 7.2 Hz, SCH_2), 2.95 (t, 1 H, $J_{2,3}$ 8.6 Hz, H-2), 3.15 (t, 1 H, H-3), 3.26 (t, 1 H, $J_{3,4}$ 9.3, $J_{4,5}$ 9.4 Hz, H-4), 3.70 (s, 2 H, CH_2Ph), 4.18 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 7.22–7.30 (m, 5 H, Ph). Anal. Calcd for $C_{16}H_{22}O_7S{\cdot}0.2\ H_2O$: C, 53.08; H, 6.24. Found: C, 53.09; H, 6.17.

3-Benzylthiopropyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside (**7**).—Allyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (**6**) (1.30 g, 3.36 mmol) [7a] was treated with α-toluenethiol (5.91 mL, 50.3 mmol) in the same way as that previously described for the preparation of **3** to afford white crystalline **7** (1.68 g, 97.8%), mp 136–137 °C, $[\alpha]_D^{28}$ −1.77° (*c* 0.55, $CHCl_3$); IR (KBr) 2922 (ν_{C-H}), 1742 ($\nu_{C=O}$), 1663 ($\nu_{C=O}$; amide I), 1538 (δ_{N-H}; amide II) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.83 (m, 2 H, CH_2), 1.90 (s, 3 H, NAc), 2.03, 2.03, 2.08 (each s, 9 H, 3 Ac), 2.48 (t, 2 H, *J* 7.4 Hz, SCH_2), 3.69 (s, 2 H, CH_2Ph), 4.12 (dd, 1 H, $J_{5,6a}$ 2.6, $J_{6a,6b}$ 12.4 Hz, H-6a), 4.23 (dd, 1 H, $J_{5,6b}$ 4.8 Hz, H-6b), 4.58 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 5.06 (t, 1 H, $J_{3,4}$ 9.4, $J_{4,5}$ 9.6 Hz, H-4), 5.24 (t, 1 H, $J_{2,3}$ 10.6 Hz, H-3), 5.41 (d, 1 H, $J_{2,NH}$ 8.8 Hz, NH), 7.22–7.34 (m, 5 H, Ph). Anal. Calcd for $C_{24}H_{33}O_9NS$: C, 56.35; H, 6.50; N, 2.74. Found: C, 56.60; H, 6.50; N, 2.74.

3-Benzylthiopropyl 2-acetamido-2-deoxy-β-D-glucopyranoside (**8**).—A solution of acetate **7** (1.50 g, 2.93 mmol) in MeOH (30 mL) was treated with NaOMe (47.5 mg, 0.88 mmol) at rt for 1.5 h under an Ar atmosphere. To the resulting mixture was added IR-120B (H^+) resin for neutralization, and then the mixture was filtered. The filtrate was evaporated in vacuo to give **8** (1.12 g, 99.0%) as white crystals, mp 160–162 °C, $[\alpha]_D^{27}$ −23.8° (*c* 0.99,

Me_2SO); IR (KBr) 3277 (ν_{O-H}), 2921 (ν_{C-H}), 1653 ($\nu_{C=O}$; amide I), 1550 (δ_{N-H}; amide II) cm^{-1}; ^1H NMR (200 MHz, CD_3OD) δ 1.76 (m, 2 H, CH_2), 1.94 (s, 3 H, NAc), 2.47 (t, 2 H, J 7.2 Hz, SCH_2), 3.70 (s, 2 H, CH_2Ph), 4.36 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 7.24–7.30 (m, 5 H, Ph). Anal. Calcd for $C_{18}H_{27}O_6NS{\cdot}0.5\ H_2O$: C, 54.80; H, 7.15; N, 3.55. Found: C, 55.05; H, 7.17; N, 3.51.

3 - Benzylthiopropyl 5 - acetamido - 4,7,8,9-tetra - O - *acetyl* - *3,5* - *dideoxy* - *β* - D - glycero - D-galacto-*2-nonulopyranosonic acid methyl ester* (**10**).—Allyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosonic acid methyl ester (**9**) (1.30 g, 2.45 mmol) [8] was allowed to react with α-toluenethiol (4.31 mL, 36.7 mmol) in the same way as described for the preparation of **3** to afford amorphous **10** (1.54 g, 96.2%), $[\alpha]_D^{27}$ −20.6° (*c* 1.56, $CHCl_3$); IR (KBr) 2959 (ν_{C-H}), 1748 ($\nu_{C=O}$), 1660 ($\nu_{C=O}$; amide I), 1549 (δ_{N-H}; amide II) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.80 (m, 2 H, OCH_2CH_2), 1.88 (s, 3 H, NAc), 1.93 (dd, 1 H, $J_{3ax,3eq}$ 12.8, $J_{3ax,4}$ 12.4 Hz, H-3ax), 2.03, 2.04, 2.12, 2.15 (each s, 12 H, 4 Ac), 2.48 (t, 2 H, J 7.2 Hz, SCH_2), 2.56 (dd, 1 H, $J_{3eq,4}$ 4.6 Hz, H-3eq), 3.56 (m, 2 H, OCH_2), 3.70 (s, 2 H, CH_2Ph), 3.77 (s, 3 H, Me), 4.06 (q, 1 H, H-5), 4.09 (dd, 1 H, $J_{8,9b}$ 5.5, $J_{9a,9b}$ 12.5 Hz, H-9b), 4.11 (dd, 1 H, $J_{5,6}$ 10.6, $J_{6,7}$ 2.2 Hz, H-6), 4.30 (dd, 1 H, $J_{8,9a}$ 2.7 Hz, H-9a), 4.84 (ddd, 1 H, $J_{4,5}$ 9.8 Hz, H-4), 5.17 (d, 1 H, $J_{5,NH}$ 9.6 Hz, NH), 5.32 (dd, 1 H, $J_{7,8}$ 8.4 Hz, H-7), 5.40 (ddd, 1 H, H-8), 7.15–7.33 (m, 5 H, Ph). Anal. Calcd for $C_{30}H_{41}O_{13}NS$: C, 54.95; H, 6.30; N, 2.14. Found: C, 54.91; H, 6.29; N, 2.14.

3-Benzylthiopropyl5-acetamido-3,5-dideoxy-β - D - glycero - D - galacto - *2* - *nonulopyranosonic acid methyl ester* (**11**).—A solution of acetate **10** (1.30 g, 1.98 mmol) in MeOH (15 mL) was stirred in the presence of NaOMe (43.0 mg, 0.793 mmol) at rt for 2 h under an Ar atmosphere. The resulting mixture was treated with IR-120B (H^+) resin, filtered, and concentrated. The residual syrup was chromatographed on silica gel with 5:1 (v/v) $CHCl_3$–MeOH to give pure **11** (755 mg, 78.1%) as white crystals: mp 148–150 °C, $[\alpha]_D^{27}$ −27.4° (*c* 1.77, Me_2SO); IR (KBr) 3352 (ν_{O-H}), 2935 (ν_{C-H}), 1724 ($\nu_{C=O}$), 1625 ($\nu_{C=O}$; amide I), 1561 (δ_{N-H}; amide II) cm^{-1}; ^1H NMR (200 MHz, Me_2SO-d_6 with D_2O) δ 1.52 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4}$ 11.8 Hz, H-3ax), 1.64 (m, 2 H, OCH_2CH_2), 1.84 (s, 3 H, NAc), 2.34 (t, 2 H, J 7.1 Hz, SCH_2), 2.46 (dd, 1 H, $J_{3eq,4}$ 1 > Hz, H-3eq), 3.63 (s, 2 H, CH_2Ph), 3.68 (s, 3 H, Me), 7.19–7.28 (m, 5 H, Ph). Anal. Calcd for $C_{22}H_{33}O_9NS$: C, 54.20; H, 6.82; N, 2.87. Found: C, 54.24; H, 6.86; N, 2.80.

3-Benzylthiopropyl5-acetamido-3,5-dideoxy-α - D - glycero - D - galacto - *2* - *nonulopyranosonic acid* (**12**).—A solution of methyl ester **11** (796 mg, 1.63 mmol) in 0.05 M aq NaOH (80 mL) was stirred at rt for 1 h, at which time an IR-120B (H^+) resin was added to the mixture. After filtration, the filtrate was concentrated in vacuo to give amorphous **12** in quantitative yield, $[\alpha]_D^{23}$ −18.6° (*c* 1.12, Me_2SO); IR (KBr) 3415 (ν_{O-H}), 2933 (ν_{C-H}), 1635 ($\nu_{C=O}$; amide I), 1562 (δ_{N-H}; amide II) cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 1.60 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4}$ 12 Hz, H-3ax), 1.79 (m, 2 H, OCH_2CH_2), 2.00 (s, 3 H, NAc), 2.50 (t, 2 H, J 7.3 Hz, SCH_2), 2.69 (dd, 1 H, $J_{3eq,4}$ 4.7 Hz, H-3eq), 3.74 (s, 2 H, CH_2Ph), 7.28–7.39 (m, 5 H, Ph). Anal. Calcd for $C_{21}H_{31}O_9NS{\cdot}0.7\ H_2O$: C, 51.88; H, 6.72; N, 2.88. Found: C, 51.84; H, 6.64; N, 2.89.

Carbosilane dendrimer carrying six D-*glucuronic acid moieties* (**14**).—To a stirred solution of **5** (229 mg, 0.639 mmol) in liquid NH_3 (~30 mL) was added Na (147 mg, 6.39 mmol) at −30 °C, and the mixture was stirred for 1 h. The stirred mixture was treated with NH_4Cl (273 mg, 5.11 mmol) for 10 min, and then a solution of bis[(3-bromopropylsilyl)propyl]dimethylsilane (**13**) (53 mg, 57 μmol) [5] in THF (2 mL) was added dropwise. The mixture was stirred overnight and then evaporated to dryness. The residue was purified by Sephadex G-25 with 5% aq AcOH as an eluent to give **14** (80 mg, 64.0%) as an amorphous solid. An analytical sample was treated with IR-120B (H^+) resin for 20 min at rt. After filtration, the filtrate was lyophilized to give pure **14** as white powder, $[\alpha]_D^{22}$ −36.4° (*c* 0.98, water); IR (KBr) 3377 (ν_{O-H}), 2913 (ν_{C-H}), 1732 ($\nu_{C=O}$) cm^{-1}; ^1H NMR (400 MHz, D_2O) δ −0.05 (s, 6 H, 2 Me), 0.65 (m, 20 H, 10 $SiCH_2$), 1.37 (m, 4 H, 2 CH_2), 1.61 (m, 12 H, 6 CH_2), 1.93 (m, 12 H, 6 CH_2), 2.61 (m, 24 H, 12 SCH_2), 3.39 (t, 6 H, $J_{2,3}$ 8.5 Hz, H-2),

3.56 (t, 6 H, $J_{3,4}$ 9.1 Hz, H-3), 3.62 (t, 6 H, $J_{4,5}$ 9.2 Hz, H-4), 3.85 (m, 12 H, 6 OCH_2), 3.99 (d, 6 H, H-5), 4.50 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1); ^{13}C NMR (100.6 MHz, D_2O) δ −2.19 (Me), 12.02 [SiC (G1)], 17.52 [CH_2 (G0)], 18.70 [CH_2 (G0)], 20.34 [CH_2 (G0)], 24.28, 28.32, 29.56, 35.79, 69.29 (C-4), 71.49 (C-2), 72.92, 74.90, 75.43, 102.65 (C-1), 172.27 (C-6); FABMS Calcd for [M^+]: 2076.7. Found: m/z 2076.5. Anal. Calcd for $C_{80}H_{144}O_{42}S_6Si_3 \cdot 2\ H_2O$: C, 45.96; H, 7.14. Found: C, 46.05; H, 7.07.

Carbosilane dendrimer carrying six N-*acetyl*-D-*glucosamine moieties* (**15**).—A mixture of **8** (254 mg, 0.658 mmol), Na (151 mg, 6.58 mmol) in liquid NH_3 ($\sim$30 mL) was stirred for 1 h at −30 °C. After adding NH_4Cl (317 mg portionwise, 5.92 mmol), the dendrimer **13** (51 mg, 57 μmol) in THF (1 mL) was injected dropwise to the stirred mixture and the stirring was continued for 19 h. When the TLC of the reaction mixture indicated *N*-de-acetylation of products, as judged by the results of a ninhydrin test, the reaction mixture was acetylated in the conventional way in MeOH after removal of NH_3. Chromatographic purification by Sephadex G-25 eluting with 5% aq AcOH gave crude products. Further manipulation of the products into the complete acetates was accomplished by Ac_2O with pyridine. Chromatography of the resulting acetates on silica gel with 10:1 (v/v) $CHCl_3$–MeOH afforded pure **15** (75 mg, 46.0%) as an amorphous solid, $[\alpha]_D^{25}$ −3.0° (*c* 0.63, $CHCl_3$); IR (KBr) 2920 (ν_{C-H}), 1748 ($\nu_{C=O}$), 1661 ($\nu_{C=O}$; amide I), 1557 (δ_{N-H}; amide II) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ −0.10 (s, 6 H, 2 CH_3), 0.53 (m, 20 H, 10 $SiCH_2$), 1.23 (m, 4 H, 2 CH_2), 1.50 (m, 12 H, 6 CH_2), 1.80 (m, 12 H, 6 CH_2), 1.92 (s, 18 H, 6 NAc), 1.98, 2.00, 2.04 (each s, 54 H, 18 Ac), 2.45 (t, 12 H, *J* 7.1 Hz, 6 SCH_2), 2.51 (t, 12 H, *J* 7.0 Hz, 6 SCH_2), 3.72 (ddd, 6 H, $J_{4,5}$ 9.7, $J_{5,6a}$ 2.4, $J_{5,6b}$ 4.7 Hz, H-5), 3.74 (m, 12 H, 6 OCH_2), 3.88 (q, 6 H, H-2), 4.09 (dd, 6 H, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.23 (dd, 6 H, H-6b), 4.66 (d, 6 H, $J_{1,2}$ 8.3 Hz, H-1), 5.03 (t, 6 H, $J_{3,4}$ 9.6 Hz, H-4), 5.26 (t, 6 H, $J_{2,3}$ 9.9 Hz, H-3), 6.44 (d, 6 H, $J_{2,NH}$ 8.9 Hz, NH); FABMS Calcd for [M^+]: 2973.15. Found: m/z 2973.07. Anal. Calcd for $C_{128}H_{210}O_{54}N_6S_6Si_3$: C, 51.70; H, 7.12; N, 2.83. Found: C, 52.20; H, 7.19; N, 2.62.

Carbosilane dendrimer carrying six N-*acetylneuraminic acid moieties* (**16**).—Sodium (148 mg, 6.45 mmol) was added to a solution of **12** (305 mg, 0.645 mmol) in liquid NH_3 ($\sim$30 mL) at −55 °C, and the dark blue mixture was stirred for 1 h. The mixture was treated with NH_4Cl (276 mg, 5.16 mmol) for 5 min, and then a solution of dendrimer **13** (25 mg, 27 μmol) in THF (2 mL) was added dropwise to the mixture at −30 °C. The mixture was stirred overnight and evaporated. The white residue was allowed to react with Ac_2O (5 mL) in pyridine (15 mL) at rt overnight. After evaporation in vacuo, the residue was treated with CH_2N_2 in diethyl ether. A combination of a gel filtration with Sephadex LH-20 eluted with MeOH and silica gel chromatography of the concentrated reactant mixture gave **16** as a colorless solid (42 mg, 40.8%): ^1H NMR (400 MHz, $CDCl_3$) δ −0.68 (s, 6 H, 2 CH_3), 0.56 (m, 20 H, 10 $SiCH_2$), 1.25 (m, 4 H, 2 CH_2), 1.52 (m, 12 H, 6 CH_2), 1.80 (m, 12 H, 6 CH_2), 1.86 (s, 18 H, 6 NAc), 1.92 (t, 6 H, $J_{3ax,4}$ 12.6 Hz, H-3ax), 2.00, 2.03, 2.12, 2.13 (each s, 72 H, 24 Ac), 2.48 (t, 12 H, *J* 7.3 Hz, 6 SCH_2), 2.53 (t, 12 H, *J* 7.2 Hz, 6 SCH_2), 2.56 (dd, 6 H, $J_{3ax,3eq}$ 13.2, $J_{3eq,4}$ 4.6 Hz, H-3eq), 3.56 (m, 12 H, 6 OCH_2), 3.78 (s, 18 H, Me), 4.05 (q, 6 H, H-5), 4.10 (m, 6 H, H-6), 4.12 (dd, 6 H, H-9b), 4.29 (dd, 6 H, $J_{8,9a}$ 2.3, $J_{9a,9b}$ 12.4 Hz, H-9a), 4.83 (ddd, 6 H, $J_{4,5}$ 9.5 Hz, H-4), 5.30 (d, 6 H, $J_{5,NH}$ 8.9 Hz, NH), 5.32 (dd, 6 H, $J_{6,7}$ 1.9, $J_{7,8}$ 8.4 Hz, H-7), 5.38 (ddd, 6 H, $J_{8,9b}$ 5.7 Hz, H-8); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ −3.30 (SiMe), 12.11 [SiC (G1)], 20.76 [CH_2 (G0)], 20.82 [CH_2 (G0)], 20.86 [CH_2 (G0)], 21.08, 23.13, 24.23, 28.43, 29.67, 35.88, 38.02, 49.36 (OMe), 52.70, 62.28, 63.36, 67.25, 68.54, 69.10, 72.43, 77.20, 98.76 (C-2), 168.43 (C=O), 169.96 (C=O), 170.06 (C=O), 170.21 (C=O), 170.62 (C=O), 170.94 (C=O); FABMS Calcd for [$M + H^+$]: 3838.42. Found: m/z 3838.20.

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