Synthesis of neamine-derived pseudodisaccharides by stereo- and regio-selective functional group transformations†

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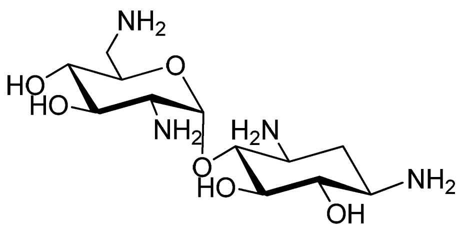
Neamine is normally found as a core structure of aminoglycoside antibiotics. In order to understand the relationship between the antibiotic activity and the configurations of the functional groups of neamine, a series of novel neamine analogues with functional group manipulations on the 2-deoxystreptamine (2-DOS) ring or the sugar ring were designed and synthesized. The synthetic approach involved the construction of 2-DOS derivatives by catalytic Ferrier II rearrangement, stereo- and regio-selective functional group transformations, glycosyl coupling reaction, and global deprotection. Of the synthetic neamine analogues, four compounds showed comparable 16S rRNA binding affinities with neamine, whereas they displayed lower binding affinities towards 18S rRNA than neamine, implying a lower toxicity to mammals. This strategy might have applications in the chemical synthesis of other neamine derivatives and new aminoglycoside antibiotics with improved biological activities.

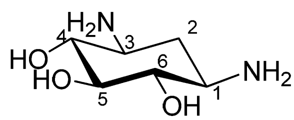
Introduction

As a group of clinically important antibiotics, 2-deoxystreptamine (2-DOS) aminoglycosides function by selectively binding to the decoding aminoacyl site (A-site) of the bacterial 16S ribosomal RNA, which leads to interference with protein biosynthesis.[1] However, the rapid spread of antibiotic resistance towards this family of antibiotics and their relatively high toxicity to mammals are critical problems that greatly limit intensive clinical use of these drugs. To overcome these problems, a wide variety of aminoglycoside modifications have been developed in the last few decades.[2] Aminoglycosides can also serve as a paradigm for exploration of small molecule–RNA interactions, which has led to further investigations into this type of compound.[3]

The main subgroup of aminoglycosides, which includes the widely used drugs gentamicin, neomycin B and kanamycin, have a pseudodisaccharide core known as neamine (Fig. 1). More generally, the carbocyclic 2-DOS core is included in most aminoglycoside antibiotics. Accordingly, numerous chemical modifications of aminoglycosides are based on neamine or 2-DOS core structures.[4–7] It was found by X-ray crystallography that neamine or 2-DOS alone indeed play a central role in the recognition of RNA with aminoglycosides.[8] The reported structural modifications vary, from different substitution on neamine (such as simple amino-containing acyclic or cyclic structures,[4] aromatic heterocyclic compounds,[5] and glycosides[6]) to dimerizations of neamine or 2-DOS.[9] The common strategy for the preparation of aminoglycoside analogues comprises the derivatization[10] of natural aminoglycosides or their substructures, thus limiting neamine or 2-DOS structures strictly to their natural forms.[11]



Neamine (**1**)



2-Deoxystreptamine (**2**)

Fig. 1 The structures of neamine (**1**) and 2-deoxystreptamine (**2**) found in most aminoglycoside antibiotics.

More structural diversity can be also achieved by changing the stereochemistry or manipulating the amino or hydroxyl functionalities on neamine or 2-DOS. Since the hydroxyl and amino groups of aminoglycosides are regarded as key binding groups for targeting RNA,[8] it is important to explore the structure–activity relationships between the configurations or changes of the functional groups of the aminoglycosides and their antibacterial activities.

For this purpose, based on the structure of neamine, a series of pseudodisaccharides **3–14**, with various configurations of amino or hydroxyl groups either on the sugar ring or on the 2-DOS ring, were designed and synthesized (Fig. 2).

As shown in Fig. 2, the natural sugar ring was retained, but the amino groups in positions 1 and 3 of 2-DOS ring were altered in configuration or changed into a series of 1,3-dihydroxyl or 1-methoxyl groups. These manipulations may mimic the natural 2-DOS structure and improve the binding affinity with RNA. In addition, to investigate the influence of glycoforms towards RNA binding, the sugar ring was changed from glucose into

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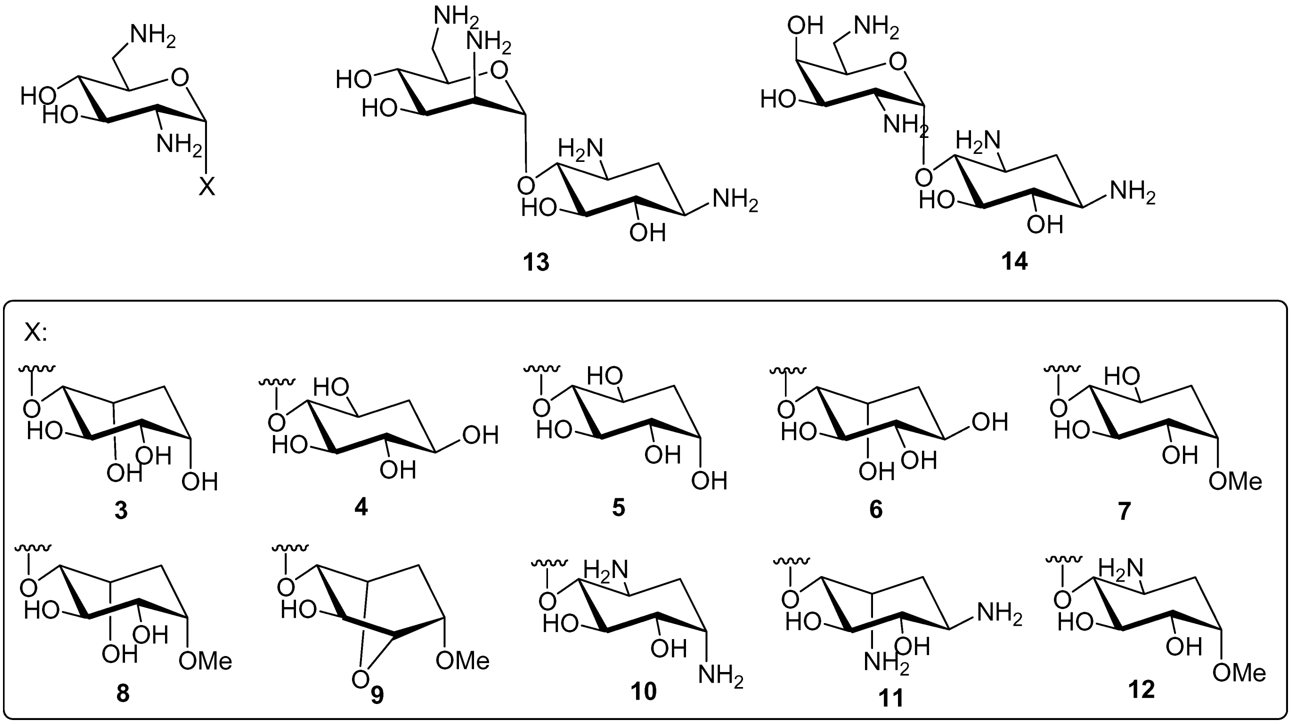


Fig. 2 The structures of pseudodisaccharides **3–14**.

galactose- or mannose-type amino sugars, with the natural 2-DOS structure unchanged. We herein report the synthesis of pseudodisaccharides **3–14** using the Ferrier II rearrangement as a key step, which can be regarded as mimic of the biosynthetic pathway of 2-DOS.[12] The RNA binding affinities and antibacterial activities of synthetic compounds **3–14** are also reported.

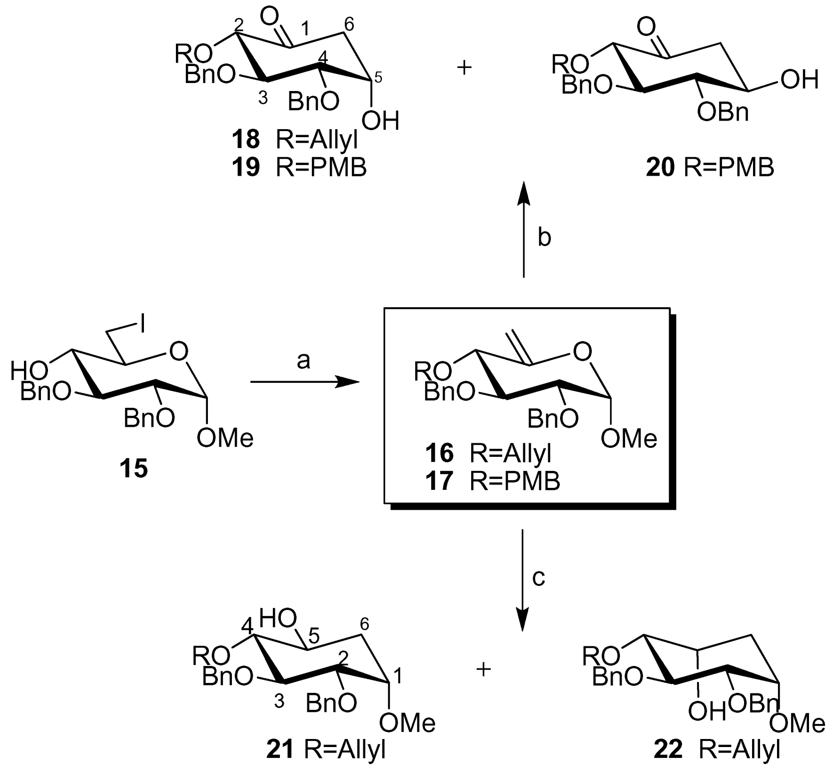
Results and discussion

Synthesis of 2-DOS and its analogues as glycosyl acceptors

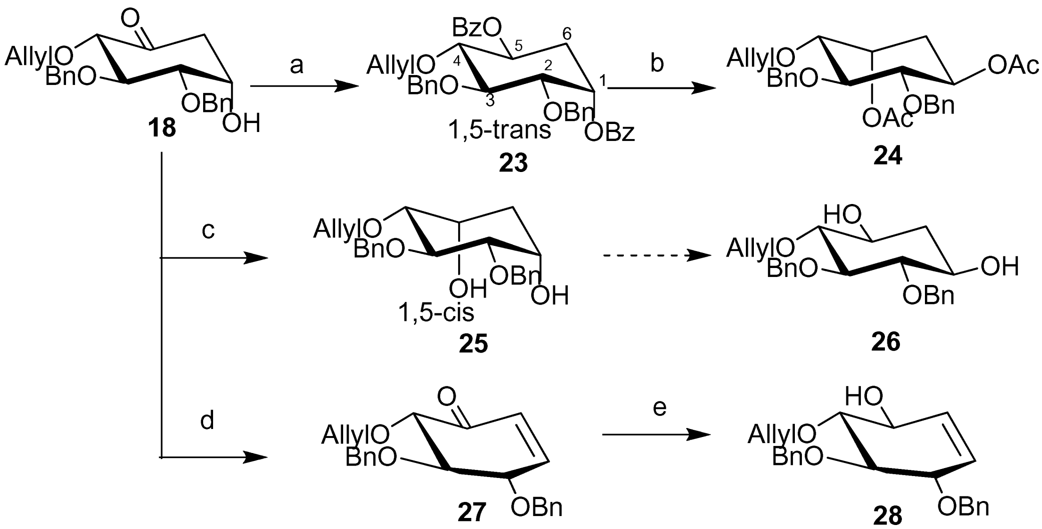
The designed pseudodisaccharides **3–14** were retrosynthetically disconnected into two building blocks: a monosaccharide moiety and a 2-DOS moiety. Coupling of these two moieties followed by global deprotection would complete the synthesis of the target molecules. According to this retrosynthetic analysis, construction of the 2-DOS moiety is the key issue. Although there are numerous methods available for the synthesis of 2-DOS and its analogues,[11] synthesis of a 2-DOS framework with various structural modifications remains a problem. Inspired by the biosynthetic route to 2-DOS,[12] we chose the Ferrier II rearrangement[13] as the key reaction to build the cyclohexanol framework starting from D-glucose, with the suitable functionalities exposed for further modifications. As shown in Scheme 1, two precursors **16** and **17** were easily prepared from compound **15** in a similar manner to the published procedure.[14] To carry out the rearrangement, various metal catalysts, including $PdCl_2$, $HgCl_2$, $Hg(OAc)_2$ and $Hg(OCOCF_3)_2$, were screened. Considering the yield, stereoselectivity, and rate of reaction, we decided to use $Hg(OCOCF_3)_2$ (0.1 equivalent) as the catalyst. In addition to allyl- and *p*-methoxybenzyl (PMB) groups, the *t*-butyldimethylsilyl (TBDMS) group was also introduced to the 4-OH position. Unfortunately, when the rearrangement precursor with the TBDMS group was treated with $PdCl_2$, a 1:1 mixture of axial and equatorial products was produced, and the total yield was low (35%). Thus, the rearrangement was performed with **16** and **17** to produce compounds **18–20**, with the 5-axial hydroxyl isomer as the major isomer.[15] To reduce the carbonyl group, triisobutylaluminium (TIBAL) was employed to promote the reaction using **16** as reactant, leading to a mixture of 1-OMe cyclohexanol products **21** and **22** in high yield with 5-axial hydroxyl isomer as the major product.

Stereoselective reduction of the Ferrier II rearrangement products provided a series of cyclitol analogues. Reduction of **18** under various conditions[16] led to 1,5-*trans* diol and 1,5-*cis* diol with high stereoselectivity (Scheme 2). To make purification easier, the 1,5-*trans* diol was benzoylated to produce **23**. Based upon the strong leaving ability of the OTf group, we considered that elimination should be suppressed in S_N2 reactions, and this was indeed the case, compound **24** being obtained after several functional group transformations *via* the triflate intermediate. However, **26** could not be obtained by a similar substitution process from **25** due to the elimination reaction, and likewise, mesylation of **18** gave the elimination product **27**. Luche reduction[17] of enone **27** afforded allylic alcohol **28** with high stereoselectivity.

The preparation of **26**, in which the 1,5-hydroxyls are established at two equatorial positions, proved to be arduous. The S_N2 reaction of the corresponding triflate of **25** by *n*-Bu_4NOAc gave elimination products exclusively. Epoxidation of **28** by either Sharpless asymmetric epoxidation or vanadium-catalyzed epoxidation provided **27**, not the epoxide which might have been further modified to give **26**. Finally, the PMB-protected cyclohexanone **20** was reduced to yield diols. After testing several reduction conditions including $NaBH_4 \cdot Et_2BOMe$, $LiAlH_4$, and $NaBH_4$ in MeOH, it was found that only $NaBH_4$ in dioxane[18] was able to reduce **20**, producing 1,5-*cis* diol **29** as the major product with moderate stereoselectivity



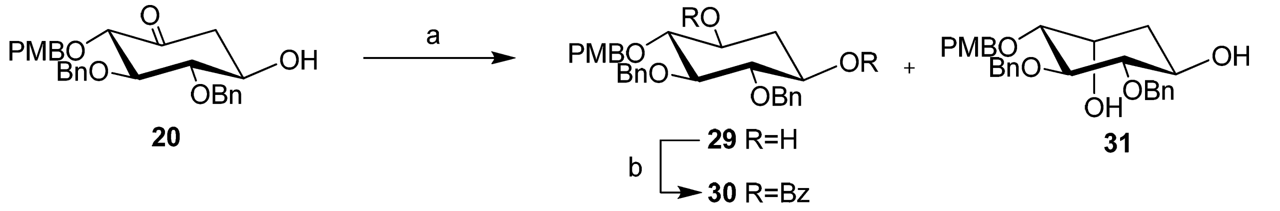
Scheme 1 Synthesis of the cyclohexanol framework by the Ferrier II rearrangement. *Reagents and conditions*: (a) allylBr, NaH, DMF, 87% for **16**; or PMBCl, NaH, DMF, 92% for **17**. (b) $Hg(OCOCF_3)_2$, acetone/water (1:1), 74% for **18**, 90% for **19** and **20** with the ratio of **19**/**20** (5:1). (c) TIBAL, PhMe, 97%, **21**/**22** (1:3).



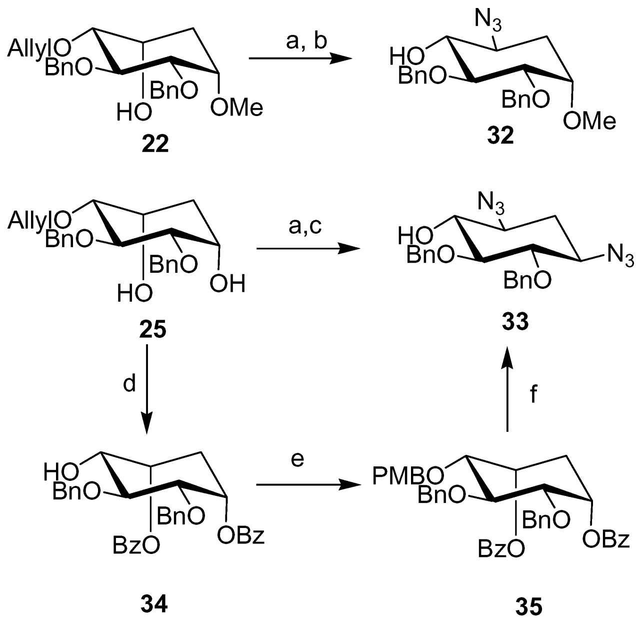
Scheme 2 Stereoselective reduction of compound **18**. *Reagents and conditions*: (a) i. Me_4NBH_4, HOAc, THF, CH_3CN; ii. BzCl, DMAP, pyridine, 80%. (b) i. NaOMe, MeOH; ii. Tf_2O, pyridine, CH_2Cl_2; iii. *n*-Bu_4NOAc, DMF, 35%. (c) $NaBH_4$, MeOH, 82%. (d) MsCl, Et_3N, CH_2Cl_2, 60%. (e) $NaBH_4$, $CeCl_3·7H_2O$, MeOH, 90%.

(Scheme 3). Compound **29** was further benzoylated to give **30**, the PMB-analogue of **26**.

Next, the hydroxyl group of the 1-OMe cyclohexanol **22** was converted to an azido group by S_N2 substitution; however, the yield for the subsequent deprotection of the allyl group was low (Scheme 4). The low efficiency of the deprotection might arise from an intramolecular cycloaddition between the azido and allyl groups. In a similar way, cyclohexanol **33** was also prepared starting from diol **25**. To avoid the low efficiency of allyl group deprotection, a PMB group was employed instead of the allyl group, and high yield of deprotected product was achieved. In the same manner, other cyclohexanols **37** and **38** with configuration changes at 1,5-positions were also obtained in acceptable yields starting from rearrangement product **19** and



Scheme 3 Selective reduction of **20** to produce diols **29** and **31**. *Reagents and conditions*: (a) $NaBH_4$, dioxane, r.t. 98%, **29**/**31** (3:1). (b) BzCl, pyridine, 89%.



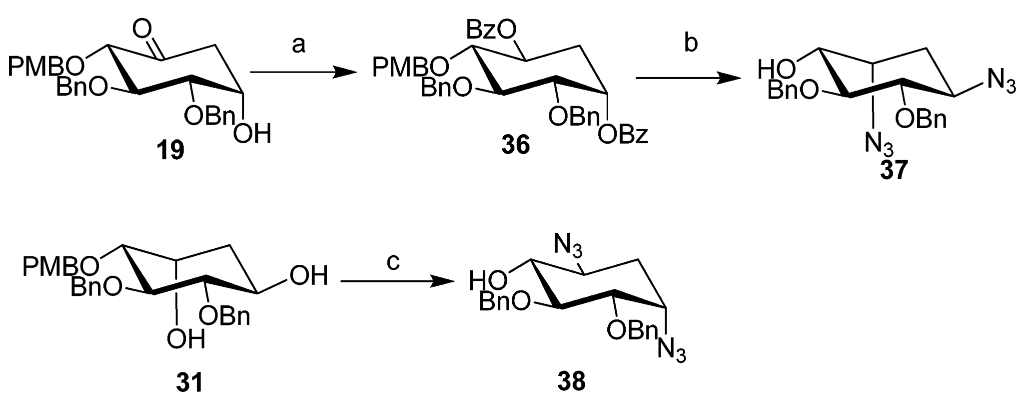
Scheme 4 Preparation of acceptors **32** and **33** starting from **22** and **25**. *Reagents and conditions*: (a) i. Tf_2O, pyridine, CH_2Cl_2, 0 °C; ii. NaN_3, DMF, 0 °C. (b) $PdCl_2$, MeOH, 35% over three steps. (c) $Pd(PPh_3)_4$, TsOH, CH_2Cl_2, r.t., 35% over three steps. (d) i. BzCl, pyridine, 0 °C to r.t.; ii. $PdCl_2$, MeOH, 88% over two steps. (e) $PMBOC(NH)CCl_3$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 56%. (f) i. NaOMe, MeOH; ii. Tf_2O, pyridine, CH_2Cl_2, 0 °C; iii. NaN_3, DMF, 0 °C; iv. DDQ, CH_2Cl_2/water (18:1), 61% over four steps.

the reduction product **31** *via* functional group manipulations (Scheme 5).

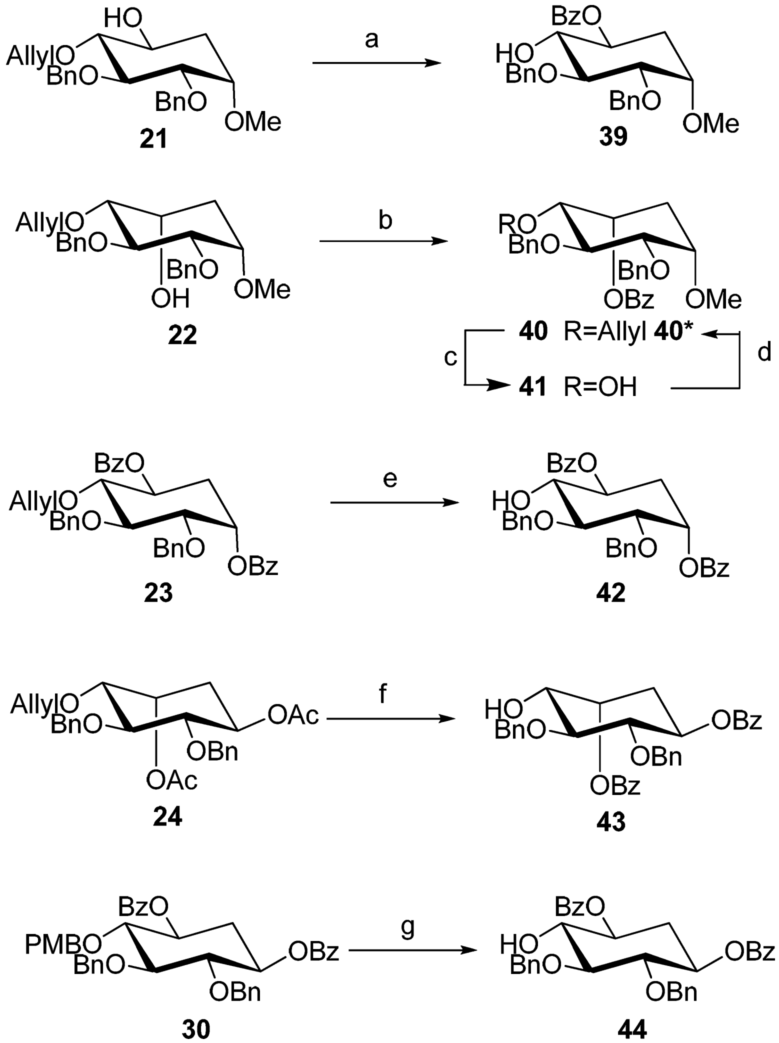
Similar to the preparation of compound **34**, other 2-DOS derivatives without amino functionalities (**39** and **41–44**) were prepared smoothly from the corresponding precursors *via* protection–deprotection operations (Scheme 6). The use of benzoyl instead of acetyl as the protective group suppressed the possible migration of the acyl group during the selective allyl or PMB group deprotection. The structures of compounds **39** and **42–44** were unambiguously identified by NMR analysis. However, the structure of compound **41** was difficult to identify by its NMR spectra due to the overlap of proton signals. To exclude the possibility of benzoyl migration and to confirm its structure, compound **41** was subjected to re-allylation to yield **40***, whose NMR spectra were identical to that of **40**. Thus the structure of cyclohexanol derivative **41** was verified.

When compound **21** was treated with triflic anhydride followed by sodium azide, the desired product **45** was not produced. Similarly, the diaxial diazide product was not obtained by starting from diol **29**, although several approaches such as using tosylate as the intermediate and sequential introduction of the azido group were tried. This might be explained by the 1,3-diaxial hindrance between the attacking azide and the OMe group or the existing azido group. However, when compound **21** was treated with triflic anhydride, the oxo-bridged product **46** was obtained (Scheme 7).

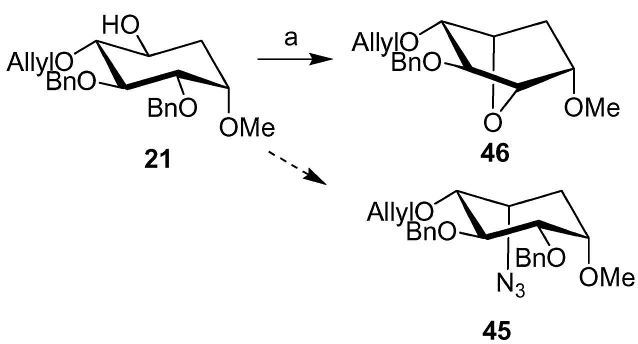
Thus, altogether ten 2-DOS analogues as glycosyl acceptors were prepared using the Ferrier II rearrangement followed by functional group manipulations (Fig. 3). The configurations of newly generated chiral centers of compounds in Fig. 3 were determined by analyzing the coupling constants in their ^{1}H NMR spectra (Table 1).



Scheme 5 Preparation of cyclohexanol derivatives **37** and **38**. *Reagents and conditions*: (a) i. Me_4NBH_4, HOAc, THF, CH_3CN; ii. BzCl, DMAP, pyridine, 88% over two steps. (b) i. NaOMe, MeOH; ii. Tf_2O, pyridine, CH_2Cl_2, 0 °C; iii. NaN_3, DMF, 0 °C, 41% over three steps. (c) i. Tf_2O, pyridine, CH_2Cl_2, 0 °C; ii. NaN_3, DMF, 0 °C; iii. DDQ, CH_2Cl_2/water (18:1), 40% over three steps.



Scheme 6 Preparation of cyclohexanols **39** and **41–44**. *Reagents and conditions*: (a) i. BzCl, DMAP, pyridine; ii. $PdCl_2$, MeOH, 98% over two steps. (b) BzCl, DMAP, pyridine, 98%. (c) $PdCl_2$, MeOH, 87%. (d) allylOC(NH)CCl_3, CH_2Cl_2/cyclohexane (1:2), TfOH, 4 Å molecular sieves, 70%. (e) $PdCl_2$, MeOH, 98%. (f) i. NaOMe, MeOH; ii. BzCl, DMAP, pyridine; iii. $PdCl_2$, MeOH, 89% over three steps. (g) DDQ, CH_2Cl_2/water (18:1), 62%.



Scheme 7 Formation of oxo-bridged compound **46**. *Reagents and conditions*: (a) Tf_2O, pyridine, CH_2Cl_2, 0 °C, 99%.

Synthesis of glycosyl donors 50–52

Scheme 8 outlines the preparation of the glycosyl donors used for the synthesis of pseudodisaccharides **3–14**. The azido-containing donor **50** was smoothly synthesized from the known thioglycoside **47**[19] by benzylation of the free hydroxyl groups. Similarly, glycosyl donors **51** and **52** were synthesized from galactosamine and mannosamine derivatives following published procedures (refs. 20 and 21, respectively). The introduction of an acetal to **51** greatly facilitated the isolation of the product from the subsequent glycosylation reactions. The use of an acetyl protecting group at positions 3 and 4 for mannosamine donor **52** proved to be better than a benzyl group in stereoselectivity control for the glycosylation reaction.

Synthesis of pseudodisaccharides 3–14

With all the glycosyl donors and acceptors in hand, we tried to assemble the pseudodisaccharides. The *N*-iodosuccinimide/triflic acid (NIS/TfOH) system was chosen as the promoter for the glycosyl coupling reactions. Thus, 2-DOS analogues **34**, **39** and **41-44** were glycosylated with thioglycoside donor **50**, providing the pseudodisaccharides **53–58** as the pure α-isomers in 70–86% yield after debenzoylation. The anomeric selectivity of glycosylations was improved by decreasing the reactivity of acceptors using the electron-withdrawing benzoyl group in place of the

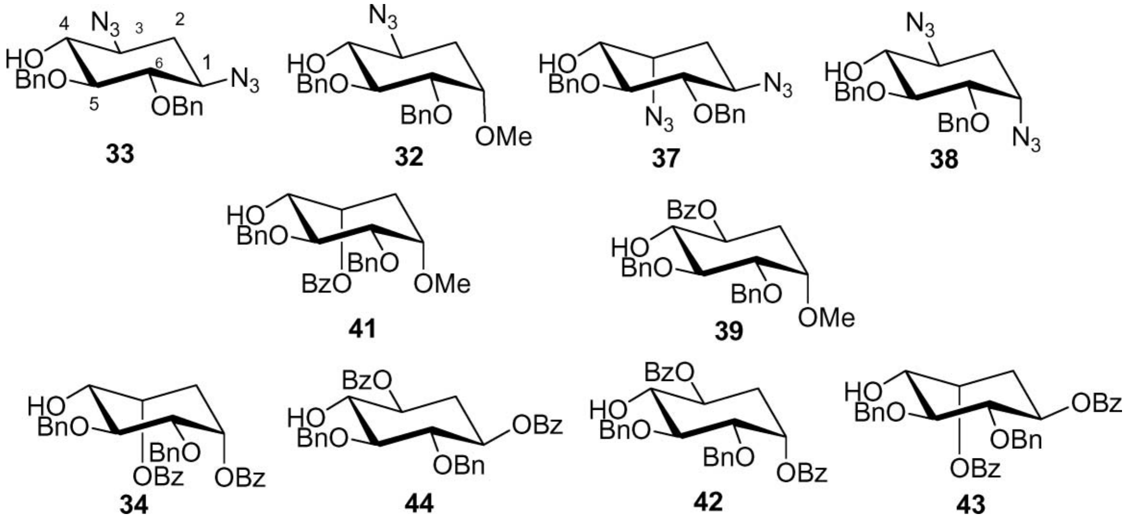
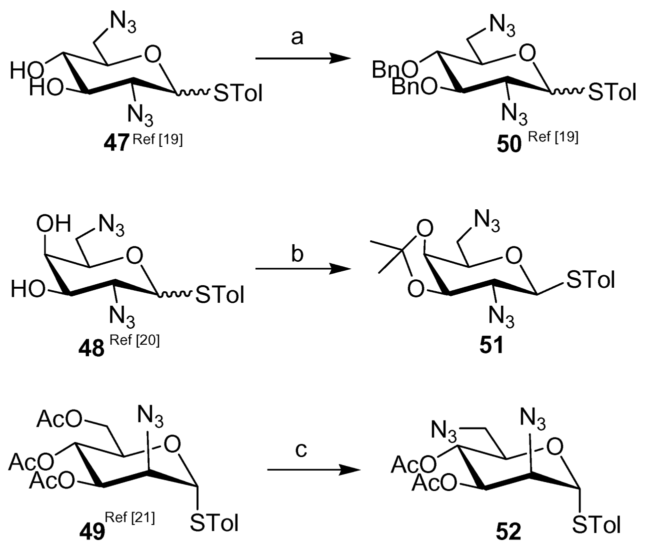


Fig. 3 2-DOS analogues as glycosyl acceptors.

Table 1 The ^{1}H NMR coupling constants[a] of glycosyl acceptors **32–34**, **37–39** and **41–44**

	J_3 (Hz)			J_1 (Hz)		
Compound	$J_{3,2a}$	$J_{3,2e}$	$J_{3,4}$	$J_{1,2a}$	$J_{1,2e}$	$J_{1,6}$
32[b]	12.0	4.5	obsc[d]	—	—	—
33[c]	12.5	obsc	obsc	12.5	obsc	obsc
34[b]	3.5	obsc	3.5	—	—	—
37[c]	2.5	4.5	3.5	12.5	4.5	obsc
38[c]	12.0	4.5	9.5	2.5	4.5	7.0
39[b]	11.0	4.5	9.0	—	—	—
41[b]	3.6	obsc	3.6	—	—	—
42[b]	11.1	4.8	8.7	—	—	—
43[c]	2.5	4.5	3.0	11.2	4.5	9.0
44[b]	12.0	obsc	obsc	—	—	—

[a] The coupling constants for axial–axial coupling are in the range 8.7–12.5 Hz, whereas axial–equatorial or equatorial–equatorial couplings are in the range 2.5–4.8 Hz. To make the comparison clear, all the atom positions of compounds in this table are assigned according to compound **33**. [b] The configurations at position 1 were fixed after Ferrier rearrangement, so the configurations at position 3 were needed to determine them. [c] The two chiral centers were generated by S_N2 reaction at position 1 and 3 simultaneously. [d] "obsc" means the coupling constant was obscured by overlap with other proton signals.



Scheme 8 Synthesis of glycosyl donors **50–52**. *Reagents and conditions*: (a) BnBr, NaOH, TBAI, THF, 0 °C to r.t., 95%. (b) DMP, CSA, r.t., 50%. (c) i. NaOMe, MeOH; ii. TsCl, pyridine, 0 °C to r.t.; iii. NaN_3, DMF, 80 °C; iv. Ac_2O, pyridine, 0 °C to r.t., 51% over four steps.

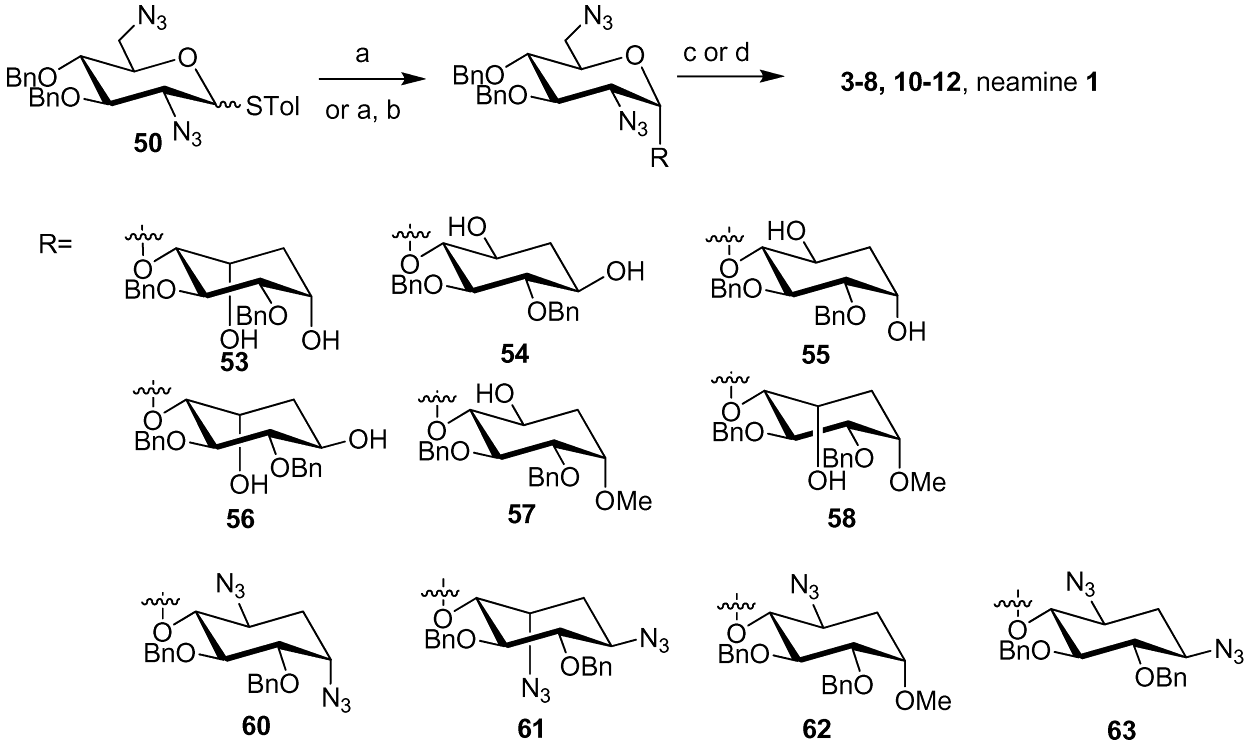
electron-donating benzyl group. The pseudodisaccharides **53–58** were subjected to catalytic hydrogenolysis over Pd/C to afford the target compounds **3–8** in 96–99% yield (Scheme 9).

As in the formation of **46** from **21** in Scheme 7, when the pseudodisaccharide **57** was treated with triflic anhydride, the oxo-bridged product **59** resulted (Scheme 10). Compound **59** was debenzylated and reduced by hydrogenolysis to provide pseudodisaccharide **9** very smoothly.

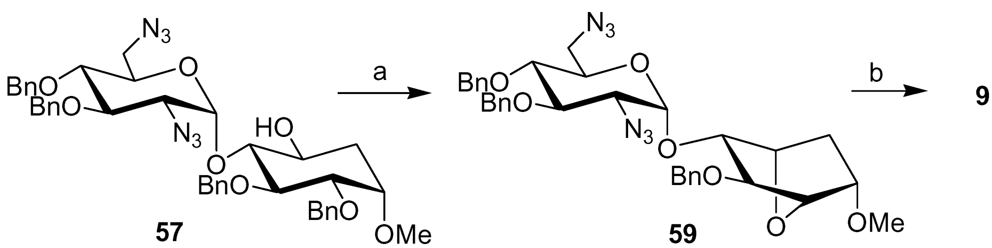
Using the same promoter (NIS/TfOH) for glycosylation, the other six pseudodisaccharides **60–65** were also assembled from other glycosyl acceptors and donors (Schemes 9 and 11). Theoretically, azido and benzyl groups could be reduced and deprotected simultaneously by hydrogenolysis. Unfortunately, this was not always true in our operations. In the case of compounds **60–65** containing more than two azido groups, complex products were obtained if azido and *O*-benzyl groups were reduced by hydrogenolysis in a single step. In these cases, a two-step protocol was used. The azido groups were first reduced with hydrogen sulfide, and the benzyl groups then cleaved by catalytic hydrogenolysis. In this manner, the target pseudodisaccharides **10–14** and neamine **1** were successfully synthesized.

RNA binding affinities and antibacterial activities

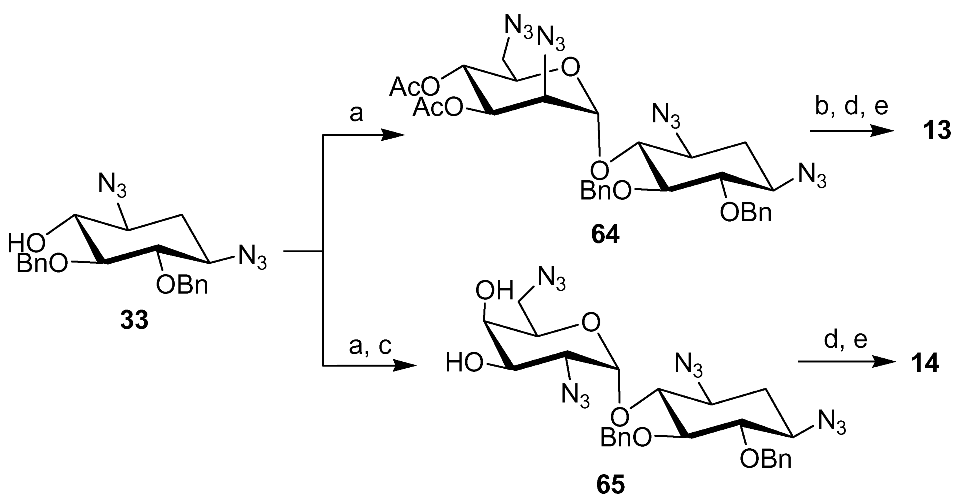
The RNA binding affinities of synthetic pseudodisaccharides **3–14** and neamine (**1**) were evaluated by surface plasmon resonance (SPR) assay with *Escherichia coli* 16S rRNA, which is implicated in the antibiotic activity, and human 18S rRNA, which may reflect the toxicity to mammals. The dissociation constants (K_d) were calculated from the equilibrium curves by a nonlinear curve-fitting method developed previously.[10,22] The resulting values are listed in Table 2. As can be seen, four compounds, **10**, **11**, **13** and **14**, showed comparable RNA binding affinities to that of



Scheme 9 Synthesis of pseudodisaccharides **3–8**, **10–12**, and neamine **1**. *Reagents and conditions*: (a) glycosyl acceptors (**32**, **33**, **34**, **39**, **37**, **38**, **41–44**), NIS, TfOH, CH_2Cl_2, 4 Å molecular sieves, −40 °C to −20 °C, 56% for **60**, 50% for **61**, 86% for **62**, 80% for **63**. (b) NaOMe, MeOH, isolated yields over two steps: **53** (80%), **54** (77%), **55** (70%), **56** (86%), **57** (70%), **58** (70%). (c) H_2, Pd/C, 1 N HCl, MeOH, isolated yields: **3** (98%), **4** (98%), **5** (99%), **6** (99%), **7** (96%), **8** (99%). (d) H_2S, pyridine/H_2O/Et_3N (3:2:1); then H_2, Pd/C, 1 N HCl, MeOH, yield over two steps: **10** (90%), **11** (90%), **12** (70%), neamine **1** (90%).



Scheme 10 Synthesis of pseudodisaccharide **9**. *Reagents and conditions*: (a) Tf_2O, pyridine, CH_2Cl_2, 0 °C, 99%. (b) H_2, Pd/C, 1 N HCl, MeOH, 96%.



Scheme 11 Synthesis of pseudodisaccharides **13** and **14**. *Reagents and conditions*: (a) glycosyl donors **51** or **52**, NIS, TfOH, CH_2Cl_2, 4 Å molecular sieves, −40 °C to −20 °C, 84% for **64** (pure α form). (b) NaOMe, MeOH. (c) 80% AcOH/H_2O, 60 °C, 60% for pure α product **65** over two steps. (d) H_2S, pyridine/H_2O/Et_3N (3:2:1). (e) H_2, Pd/C, 1 N HCl, MeOH, 96% for **13** over three steps, 95% for **14** over two steps.

Table 2 Dissociation constants of synthetic pseudodisaccharides and inhibitory effects on *Pseudomonas aeruginosa*

	K_d (μM)		Inhibition ratio (%) towards *P. aeruginosa* at 500 μg/mL
Compound	16S rRNA	18S rRNA	
1	22 ± 0.3	34 ± 0.7	100
10	26 ± 2.0	62 ± 1.7	45.5
11	6 ± 0.5	68 ± 6.0	35
13	123 ± 16	41 ± 3.0	31
14	37 ± 2.0	286 ± 29	39

neamine (**1**); the other compounds did not show any significant RNA binding affinities. It seems that the number of amino groups in the pseudodisaccharides is essential for binding to 16S rRNA. Compounds **10**, **11**, **13** and **14** displayed lower binding affinities to 18S rRNA than neamine, implying a lower toxicity.

The antibacterial activities of compounds **1**, **10**, **11**, **13**, and **14** were also evaluated against *Escherichia coli* and *Pseudomonas aeruginosa* standard strains. Neamine (**1**) is still the most active compound. The synthetic compounds did not show any inhibitory effects on the *E. coli* strain (neamine showed activity against *E. coli* with a minimum inhibitory concentration (MIC) of 65 μg/mL). For *P. aeruginosa*, compounds **10**, **11**, **13** and **14** showed 45.5, 35%, 31% and 39% inhibition when tested at the MIC of neamine (500 μg/mL) (Table 2).

Conclusion

To explore the substitution and configuration effects of neamine, neamine (**1**) and 12 analogues (pseudodisaccharides **3–14**) were designed and synthesized *via* the glycosylations of 2-DOS derivatives. The construction of 2-DOS derivatives was based on the Ferrier II rearrangement as a key step followed by a series of stereoselective functional group manipulations. In the synthetic process, linear sequences for 10 glycosyl acceptors (cyclohexanol derivatives) range from 5 to 15 steps from the common starting material, namely methyl α-D-glucoside. For the preparation of 13 target pseudodisaccharides, the number of synthetic steps range from 15 to 27. Using the synthetic strategy described here, various protected and unsymmetrical aminocyclitols and cyclitols with high stereo-variability can be prepared efficiently. The preliminary RNA binding and antibacterial results showed that four synthetic pseudodisaccharides, **10**, **11**, **13** and **14**, exhibited comparable activities with neamine, which may serve as a useful starting point in the discovery of new antibiotic entities. The approach described here may have wide applications in the chemical synthesis of other neamine derivatives and new aminoglycoside antibiotics with improved biological activities.

Experimental

General procedures

Unless otherwise noted, all reactions were carried out in oven-dried glassware under an atmosphere of argon or nitrogen. Tetrahydrofuran and toluene were dried and distilled from sodium metal. Acetonitrile and dichloromethane were distilled from calcium hydride. Methanol was dried by heating under reflux with magnesium and then distilled. *N*,*N*-Dimethylformamide was dried over P_2O_5 and distilled under vacuum. Reactions were monitored by analytical thin-layer chromatography (TLC) on Merck silica gel $60F_{254}$ plates (0.25 mm), visualized by ultraviolet light and/or by staining with ceric ammonium molybdate or ninhydrin. Optical rotations were measured at ambient temperature (25 °C) using RUDOLPH AUTOPOL III. ^{1}H NMR spectra were obtained on Varian INOVA-500 or JEOL JNM-AL300 spectrometer at ambient temperature. Data were reported as follows: chemical shift on the δ scale (using either TMS or residual proton solvent as internal standard), multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, and coupling constant(s) in Hertz. ^{13}C NMR spectra were obtained with proton decoupling on a Varian INOVA-500 (125 MHz) or JEOL JNM-AL-300 (75 MHz) spectrometer and were reported in ppm with residual solvent for internal standard (77.0 for $CDCl_3$). High-resolution mass spectra were obtained on a PE SCLEX QSTAR spectrometer. Elemental analysis data were recorded on a PE-2400C elemental analyzer.

2L-(2,4,5/3)-2-*O*-(4-Methoxybenzyl)-3,4-di-*O*-benzyl-2,3,4,5-tetrahydroxycyclohexanone (19) and 2L-(2,4/5,3)-2-*O*-(4-methoxybenzyl)-3,4-di-*O*-benzyl-2,3,4,5-tetrahydroxycyclohexanone (20). To a stirred solution of **17** (4.64 g, 9.7 mmol) in acetone–water (2:1, 90 mL) was added $Hg(OCOCF_3)_2$ (0.42 g, 0.98 mmol) at room temperature. After stirring for 3 h, sat. $NaHCO_3$ was added to neutralize the mixture to pH 6–7. The mixture was partially evaporated, the suspension was extracted with EtOAc (50 mL ×2), the organic layer was collected and sequentially washed with water and brine (50 mL), dried over Na_2SO_4, filtered, concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (petroleum ether–EtOAc 3:1) to give **20** (696 mg, 15%) as a white solid: R_f = 0.42 (petroleum ether–EtOAc 1:1); $[\alpha]_D$ = –9.3 (*c* = 0.4, EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, 40 °C) δ = 7.36–7.24 (m, 12H, Ar), 6.86–6.83 (m, 2H, Ar), 4.99 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.92 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.83 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.73 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.69 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.47 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.13 (d, 1H, *J* = 8.0 Hz, H-2), 3.79 (s, 3H, OCH_3), 3.73–3.62 (m, 3H, H-3, H-4, H-5), 2.74 (dd, 1H, *J* = 4.5, 13.5 Hz, H-6eq), 2.48 (t, 1H, *J* =13.5 Hz, H-6ax), 2.43 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 203.20 (C=O), 159.43 (PMB), 138.01, 129.90, 129.47, 128.72, 128.44, 128.07, 127.98, 127.84, 113.83, 85.68, 84.65, 81.90, 75.60, 75.44, 73.30, 67.99, 55.26 (OCH_3), 44.08 (C-6); HRMS(ESI) *m*/*e* calcd for $C_{28}H_{30}O_6$ (M + Na$^+$) 485.1935, found: 485.1931. Further elution gave isomer **19** (3.33 g, 75%) as a white solid: R_f = 0.35 (petroleum ether–EtOAc 1:1); $[\alpha]_D$ = –22.4 (*c* = 0.7, EtOAc); ^{1}H NMR (500M Hz, $CDCl_3$) δ = 7.33–7.26 (m, 12H, Ar), 6.83 (d, 2H, *J* = 8.5 Hz, Ar), 4.93–4.69 (m, 6H, $PhCH_2$, H-5), 4.50 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.23–4.22 (m, 1H, H-2), 4.02–4.01 (m, 2H, H-1, H-3), 3.80–3.76 (m, 4H, H-4, OCH_3), 2.66 (dd, 1H, *J* = 4.0, 15.0 Hz, H-6eq), 2.48 (dd, 1H, *J* = 4.0, 15.0 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 203.97 (C=O), 159.28, 138.36, 137.58, 129.81, 129.71, 128.56, 128.34, 128.06, 127.88, 127.69, 113.73, 84.87, 81.67, 81.45, 75.92, 73.20, 73.09, 66.47, 55.23 (OCH_3), 42.50 (C-6); HRMS (ESI) *m*/*e* calcd for $C_{28}H_{30}O_6$ (M + Na$^+$) 485.1935, found: 485.1937.

1D-(1,2,4/3,5)-4-*O*-Allyl-2,3-di-*O*-benzyl-1-*O*-methyl-5-hydroxylcyclohexanepentol (21) and 1D-(1,2,4,5/3)-4-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-methyl-5-hydroxylcyclohexanepentol (22). To a solution of **16**[14] (1.73 g, 4.37 mmol) in toluene (10 mL), was added TIBAL (1 M in toluene, 43.7 mL) dropwise under argon at room temperature. When the addition of TIABL was finished, the mixture was heated by oil bath at 50 °C. After stirring for 3.5 h, NaOH (2M aqueous solution, 100 mL) was added to quench the reaction, the mixture was diluted with EtOAc (50 mL), washed with water (50 mL) and brine (50 mL). The organic layer was collected and dried over Na_2SO_4, concentrated and purified by column chromatography on silica gel (petroleum ether–EtOAc 4:1) to give **21** (402 mg, 24%) as a white solid: $R_f = 0.48$ (petroleum ether–EtOAc 1:2); $[\alpha]_D = +31.3$ ($c = 2.3$, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.38–7.28 (m, 10H, Ar), 5.95 (ddt, 1H, J = 5.7, 10.2, 17.4 Hz, =CH-), 5.27 (dq, 1H, J = 1.5, 17.4 Hz, =CH_2), 5.17 (dq, 1H, J = 1.5, 10.2 Hz, =CH_2), 4.94 (d, 1H, J = 10.5 Hz, $PhCH_2$), 4.75 (d, 1H, J = 10.5 Hz, $PhCH_2$), 4.71 (2d, 2H, J = 12.0 Hz, $PhCH_2$), 4.47 (ddt, 1H, J = 1.5, 5.7, 12.3 Hz, C=C-CH_2-), 4.19 (ddt, 1H, J = 1.5, 5.7, 12.3 Hz, C=C-CH_2-), 3.87–3.76 (m, 2H, H-3, H-5), 3.63–3.62 (m, 1H, H-1), 3.44–3.40 (m, 4H, H-2, OCH_3), 3.14 (t, 1H, J = 9.3 Hz, H-4), 2.41 (br, 1H, OH), 2.30 (dt, 1H, J = 4.5, 14.1 Hz, H-6eq), 1.20 (ddd, 1H, J = 2.1, 12.0, 14.1 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.72, 138.30, 135.05, 128.33, 128.05, 127.83, 127.65, 127.55, 117.02, 85.98, 82.84, 81.68, 75.67, 75.06, 74.11, 72.66, 67.82, 57.34 (OCH_3), 30.76 (C-6); HRMS (ESI) m/e calcd for $C_{24}H_{30}O_{54}$ (M + Na^+) 421.1985, found: 421.1945. Further elution gave isomer **22** (1.27 g, 73%) as a colorless oil: $R_f = 0.37$ (petroleum ether–EtOAc 1:2); $[\alpha]_D = +7.5$ ($c = 2.1$, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.41–7.26 (m, 10H, Ar), 5.97 (ddt, 1H, J = 6.0, 10.5, 17.5 Hz, =CH-), 5.30 (dq, 1H, J = 1.5, 17.5 Hz, =CH_2), 5.17 (dq, 1H, J = 1.5, 10.5 Hz, =CH_2), 4.92–4.67 (4×d, 4H, J = 12.0 Hz, $PhCH_2$), 4.23–4.20 (m, 2H, C=C-CH_2), 4.11–4.04 (m, 2H, H-3, H-5), 3.71–3.70 (m, 1H, H-1), 3.60 (d, 1H, J = 9.9 Hz, OH), 3.52 (s, 3H, OCH_3), 3.39 (dd, 1H, J = 3.0, 9.3 Hz, H-2), 3.27 (dd, 1H, J = 3.3, 9.3 Hz, H-4), 2.28 (dt, 1H, J = 3.3, 15.0 Hz, H-6eq), 1.33 (dt, 1H, J = 2.7, 15.0 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.90, 138.45, 135.18, 128.35, 128.28, 128.21, 127.75, 127.65, 127.53, 117.09, 82.47, 82.20, 78.95, 78.82, 75.97, 73.19, 71.64, 68.32, 59.01 (OCH_3), 29.54 (C-6); HRMS (ESI) m/z calcd for $C_{24}H_{30}O_5$ (M + Na^+) 421.1985, found: 421.1945.

1D-(1,2,4/3,5)-4-*O*-Allyl-1,5-di-*O*-benzoyl-2,3-di-*O*-benzyl-cyclohexanepentol (23). To one portion of powdered Me_4NBH_4 (1.16 g, 0.013 mol) in round-bottomed flask under argon, freshly distilled AcOH (2.6 ml, 0.045 mol) was added dropwise at room temperature and stirred for 30 min. THF (8 mL) was then added, the mixture was stirred at the same temperature for additional 3 h to ensure complete conversion of Me_4NBH_4 to $Me_4NBH(OAc)_3$. To the above mixture, a solution of **18** (1.108 g, 2.78 mmol) in CH_3CN (10 mL) was added dropwise. After stirring for 13 h at room temperature, sat. NH_4Cl aqueous solution was added to quench the reaction. The mixture was extracted with EtOAc (50 mL), washed with sat. $KHCO_3$ (50 mL), then dried over Na_2SO_4, concentrated to produce a colorless oil (899 mg). To a mixture of the colorless oil and DMAP (14 mg, 0.12 mmol) in pyridine (20 mL), BzCl (1.63 mL, 14.03 mmol) was added slowly at 0 °C. The mixture was allowed to stir for 6 h from 0 °C to room temperaure. The mixture was concentrated, diluted with EtOAc (50 mL), washed successively with sat. $NaHCO_3$ (50 mL) and water (50 mL). The organic layer was collected and dried over Na_2SO_4, concentrated, and purified by column chromatography on silica gel (petroleum ether–EtOAc 16:1) to give **23** (1.36 g, 80% over two steps) as colorless solids: $R_f = 0.36$ (EtOAc/petroleum ehter 1:4); $[\alpha]_D = +42$ ($c = 2.0$, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.12–8.02 (m, 4H, Ar), 7.60–7.42 (m, 7H, Ar), 7.33–7.16 (m, 9H, Ar), 5.89–5.76 (m, 2H, H-1, H-5), 5.58–5.49 (m, 1H, =CH-), 5.16 (dd, 1H, J = 1.5, 17.1 Hz, =CH_2), 5.06 (d, 1H, J = 10.2 Hz, =CH_2), 4.92–4.81 (m, 3H, $PhCH_2$), 4.60 (d, 1H, J = 11.7 Hz, $PhCH_2$), 4.37 (dd, 1H, J = 5.7, 12.0 Hz, C=C-CH_2), 4.24 (dd, 1H, J = 6.3, 12.0 Hz, C=C-CH_2), 4.00 (t, 1H, J = 9.3 Hz, H-4), 3.67–3.60 (m, 2H, H-2, H-3), 2.49 (dt, 1H, J = 4.5, 14.1 Hz, H-6eq), 1.71 (ddd, 1H, J = 2.1, 12.0, 14.1 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.65(PhCO), 165.56(PhCO), 138.53, 137.82, 134.85, 133.18, 133.08, 130.02, 129.92, 129.57, 128.46, 128.40, 128.30, 128.14, 128.00, 127.65, 117.32, 82.91, 81.52, 80.69, 76.09, 74.68, 72.15, 71.57, 66.95, 31.07 (C-6); MS (FAB) m/z calcd for $C_{37}H_{36}O_7$: 592, found: 592 (M^+); elemental analysis calcd (%) for $C_{37}H_{36}O_7$: C 74.98, H 6.12; found: C 74.70, H 6.40.

1L-(1,2,4/3,5)-1,5-Di-*O*-acetyl-2-*O*-allyl-3,4-di-*O*-benzyl-cyclohexanepentol (24). To a solution of **23** (150 mg, 0.25 mmol) in MeOH (5 mL), 30% NaOMe (0.1 mL) was added at room temperature. After stirring for 1 h, the mixture was neutralized to pH = 6–7 with ion-exchange resin (Dowex 50, strong acid form) at room temperature. The mixture was filtered and concentrated to give colorless oil. To the crude oil, CH_2Cl_2 (2 mL) and pyridine (204 μL, 2.5 mmol) were added, followed by addition of Tf_2O (174 μL, 1.0 mmol) at 0 °C. After stirring for 10 min, sat. $NaHCO_3$ (20 mL) was added to the mixture. The mixture was diluted with CH_2Cl_2 (20 mL) and washed with water (20 mL). The organic layer was collected, dried over Na_2SO_4, concentrated *in vacuo* and co-evaporated with toluene (3 mL) for three times to afford a yellow oil. The crude product was dissolved in DMF (2 mL), *n*-Bu_4NOAc (226 mg, 0.75 mmol) was added to the mixture at 0 °C under argon, and stirred for 5 h at r.t. The mixture was concentrated, the residue was purified by column chromatography on silica gel (petroleum ether–EtOAc 9:1) to give **24** (42 mg, 35% over three steps) as a white solid: $R_f = 0.32$ (petroleum ether–EtOAc 3:1); $[\alpha]_D = -2.4$ ($c = 2.5$, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.34–7.26 (m, 10H, Ar), 5.95 (ddt, 1H, J = 5.7, 10.8, 17.4 Hz, =CH-), 5.43–5.42 (m, 1H, H-1), 5.29 (ddt, 1H, J = 1.2, 1.2, 17.4 Hz, =CH_2), 5.23–5.14 (m, 2H, =CH_2, H-5), 4.92–4.67 (m, 4H, $PhCH_2$), 4.18 (dd, 1H, J = 5.7, 12.6 Hz, C=C-CH_2), 4.06 (dd, 1H, J = 6.0, 12.6 Hz, C=C-CH_2), 3.85 (t, 1H, J = 9.3 Hz, H-4), 3.51 (t, 1H, J = 9.6 Hz, H-3), 3.42 (dd, 1H, J = 3.0, 9.6 Hz, H-2), 2.20 (dt, 1H, J = 4.5, 14.1 Hz, H-6eq), 2.13 (s, 3H, $COCH_3$), 1.95 (s, 3H, $COCH_3$), 1.47 (ddd, 1H, J = 2.7, 12.3, 14.1 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.19 ($COCH_3$), 170.09 ($COCH_3$), 138.57, 138.50, 134.55, 128.37, 128.15, 127.74, 127.69, 127.64, 117.45, 83.31, 81.57, 80.36, 76.09, 75.62, 71.36, 70.69, 66.66, 30.80 (C-6), 21.14 ($COCH_3$), 21.06 ($COCH_3$); HRMS (ESI) m/z calcd for $C_{27}H_{32}O_7$ (M + Na^+) 491.2040, found: 491.2039.

1D-(1,2,4,5/3)-4-*O*-Allyl-2,3-di-*O*-benzyl-1,5-dihydroxy-lcyclohexanepentol (25). To a solution of **18** (571 mg, 1.49 mmol) in methanol (15 mL) at 0 °C was added portion-wise $NaBH_4$ (225 mg, 5.96 mmol). After stirring for 10 min, sat. NH_4Cl

aqueous solution was added to quench the reaction. The mixture was concentrated and extracted with EtOAc (30 mL) and water (30 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether–acetone 4:1) to give **25** (467 mg, 82%) as a colorless oil: R_f = 0.28 (petroleum ether–acetone 2:1); $[\alpha]_D$ = +15.4 (*c* = 2.6, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, D_2O exchange) δ = 7.41–7.26 (m, 10H, Ar), 5.94 (ddt, 1H, *J* = 5.4, 10.5, 17.1 Hz, =CH-), 5.29 (dd, 1H, *J* = 1.8, 17.1 Hz, $=CH_2$), 5.18 (dd, 1H, *J* =1.8, 10.2 Hz, $=CH_2$), 5.16–4.73 (m, 4H, $PhCH_2$), 4.22–4.14 (m, 4H, H-1, H-5, $=C–CH_2–$), 4.05 (t, 1H, *J* = 9.3 Hz, H-3), 3.40–3.62 (m, 2H, H-2 or H-4, OH), 3.30 (dd, 1H, *J* = 3.3, 9.3 Hz, H-2 or H-4), 2.33 (dt, 1H, *J* = 3.6, 15.0 Hz, H-6eq), 1.46 (dt, 1H, *J* = 2.7, 15.0 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.80, 138.10, 134,82, 128.39, 128.30, 128.12, 127.84, 127.75, 127.56, 117.31, 82.26, 78.66, 76.06, 72.62, 71.70, 68.53, 31.23 (C-6); HRMS (ESI) *m/z* calcd for $C_{23}H_{28}O_5$ (M + Na^+) 407.1829, found: 407.1831.

2L-(2,4/3)-2-*O*-Allyl-3,4-di-*O*-benzyl-2,3,4-trihydroxy-5-cyclohexen-1-one (27). To a solution of **18** (260 mg, 0.6 mmol) in CH_2Cl_2 (5 mL), MsCl (156 mg, 1.4 mmol) was added dropwise at 0 °C, followed by addition of triethylamine (0.5 mL, 3.6 mmol). The mixture was stirred at 0 °C for 2 h, diluted with CH_2Cl_2 (50 mL), washed successively with 0.5 M H_2SO_4, sat. $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether–EtOAc 12:1) to give **27** (148 mg, 60%) as a colorless oil: R_f = 0.28 (petroleum ether–EtOAc 3:1); $[\alpha]_D$ = +21.0 (*c* = 0.6, EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.40–7.30 (m, 10H, Ar), 6.80 (dd, 1H, *J* = 2.0, 10.5 Hz, H-6), 6.02 (dd, 1H, *J* =2.0, 10.0 Hz, H-5), 6.04–5.95 (m, 1H, =CH-), 5.35 (dd, 1H, *J* = 1.5, 17.0 Hz, $=CH_2$), 5.21 (dd, 1H, *J* = 1.5, 10.5 Hz, $=CH_2$), 4.97 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.83(d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.81 (d, 1H, *J* = 10.5 Hz, $PhCH_2$), 4.74 (d, 1H, 12.0 Hz, $PhCH_2$), 4.51 (ddt, 1H, *J* = 1.5, 5.5, 12.5 Hz, $=C–CH_2–$), 4.35 (dt, 1H, *J* = 2.0,7.5 Hz, H-4), 4.25 (ddt, 1H, *J* = 1.5, 5.5, 12.5 Hz, $=C–CH_2–$), 3.97–3.91 (m, 2H, H-2, H-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 197.34 (C=O), 148.06, 138.17, 137.62, 134.39, 128.54, 128.40, 128.19, 128.03, 127.89, 127.82, 117.80, 84.72, 83.60, 78.89, 75.76, 73.66, 29.69; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}O_4$ (M + H^+) 365.1770, found: 365.1770.

1L-(1,5/4,6)-6-*O*-Allyl-4,5-di-*O*-benzyl-cyclohex-2-en-1-ol (28). To a mixture of **27** (86 mg, 0.24 mmol) and $CeCl_3{\cdot}7H_2O$ (132 mg, 0.35 mmol) in methanol (5 mL) was added $NaBH_4$ (13 mg, 0.34 mmol) at 0 °C. After stirring for 15 min, the reaction was quenched with water and extracted with EtOAc (50 mL), washed with brine, dried over Na_2SO_4. The organic layer was concentrated and purified by column chromatography on silica gel (petroleum ether–EtOAc 4:1) to give **28** (78 mg, 90%) as a light yellow oil: R_f = 0.22 (petroleum ether–acetone 2:1); $[\alpha]_D$ = +90.3 (*c* = 3.9, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.38–7.27 (m, 10H, Ar), 5.95 (ddt, 1H, *J* = 6.0, 10.5, 17.5 Hz, =CH-), 5.72–5.67 (m, 2H, H-2, H-3), 5.28 (ddt, 1H, *J* = 1.5, 17.5 Hz, $=CH_2$), 5.19 (ddt, 1H, *J* = 1.5, 10.0 Hz, $=CH_2$), 4.89–4.65 (m, 4H, $PhCH_2$), 4.46 (ddt, 1H, *J* = 1.5, 5.0, 12.5 Hz, $=C-CH_2$), 4.30 (d, 1H, *J* = 7.0 Hz, H-1), 4.23 (dd, 1H, *J* = 5.0, 12.5 Hz, $=C-CH_2$), 4.22–4.19 (m, 1H, H-4), 3.71 (dd, 1H, *J* = 7.5, 10.5 Hz, H-5), 3.41 (dd, 1H, *J* = 7.5, 10.0 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 138.54, 138.24, 134.97 (=CH-), 129.36 (C-2), 128.42, 128.36, 127.94, 127.80, 127.72, 127.45, 127.05 (C-3), 117.32 ($=CH_2$), 84.08 (C-6), 83.27 (C-5), 80.48 (C-4), 75.24 ($PhCH_2$), 74.12 ($=C-CH_2$), 72.28 ($PhCH_2$), 71.93 (C-1); MS (ESI) *m/z* calcd. for $C_{23}H_{26}O_4$: 389 (M + Na^+), found: 389; elemental analysis calcd (%) for $C_{23}H_{26}O_4$: C 75.38, H 7.15; found: C 75.29, H 7.23.

1D-(1,3,5/2,4)-1,5-Di-*O*-benzoyl-2,3-di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-cyclohexanepentol (30) and 1L-(1,2,4/3,5)-3,4-di-*O*-benzyl-2-*O*-(4-methoxybenzyl)-1,5-dihydroxylcyclohexanepentol (31). To a solution of **20** (150 mg, 0.32 mmol) in dry dioxane (6 mL), was added $NaBH_4$ (65 mg, 1.72 mmol) under argon. After stirring for 4 h, water was added to quench the reaction at 0 °C. The reaction mixture was continued to stir until no bubble spreading out. Then the mixture was concentrated *in vacuo*, the residue was dissolved in EtOAc (20 mL), washed with water and brine, dried over Na_2SO_4, concentrated, purified by column chromatography on silica gel (CH_2Cl_2/MeOH 100:1) to give **31** (34 mg, 22%): R_f = 0.52 (CH_2Cl_2/MeOH 20:1); $[\alpha]_D$ = −2.2 (*c* = 0.5, EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.36–7.24 (m, 12H, Ar), 6.86 (d, *J* = 8.5 Hz, Ar), 5.00 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.90 (d, 1H, *J* = 10.5 Hz, $PhCH_2$), 4.82 (d, 1H, *J* = 10.5 Hz, $PhCH_2$), 4.76 (2br, 2H, OH), 4.69–4.60 (m, 3H, $PhCH_2$), 4.08 (q, 1H, *J* = 3.0 Hz, H-1), 4.95 (ddd, 1H, *J* = 5.0, 9.5, 12.0 Hz, H-5), 3.83–3.80 (m, 4H, H-3, OCH_3), 3.48 (dd, 1H, *J* = 3.0, 9.0 Hz, H-2), 3.26 (t, 1H, *J* = 9.5 Hz, H-4), 2.24 (dt, 1H, *J* = 4.5, 14.0 Hz, H-6eq), 1.37 (ddd, 1H, *J* = 2.5, 12.0, 14.0 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.42 (PMB), 138.61, 129.91, 129.52, 128.60, 128.41, 127.92, 127.83, 127.65, 113.92, 86.12, 82.93, 81.50, 75.68, 75.40, 72.45, 67.67, 65.78, 55.27 (OCH_3), 33.42 (C-6); HRMS (ESI) *m/z* calcd. for $C_{28}H_{32}O_6$ (M + Na^+) 487.2091, found: 487.2094. Another component **29** (116 mg) was collected as a colorless oil: R_f = 0.45 (CH_2Cl_2/MeOH 20:1), but its purity was not satisfactory in the ^{1}H NMR spectrum. To the above crude oil (116 mg, 0.25 mmol) in pyridine (5 mL), was added BzCl (209 mg, 1.4 mmol) at 0 °C. After stirring for 5 h, pyridine was evaporated under vacuum. The residue was diluted with EtOAc, washed with sat. $NaHCO_3$ and water. The organic layer was collected, dried over Na_2SO_4, concentrated, purified by column chromatography on silica gel (petroleum ether–EtOAc 12:1) to give **30** (150 mg, 89%) as a white solid: R_f = 0.30 (petroleum ether–EtOAc 3:1); $[\alpha]_D$ = +3.2 (*c* = 1.3, EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.14–6.66 (m, 24H, Ar), 5.30 (ddd, 2H, *J* = 4.5, 9.0, 11.5 Hz, H-1, H-5), 4.89 (d, 2H, *J* = 11.5 Hz, $PhCH_2$), 4.86–4.69 (m, 4H, $PhCH_2$), 3.82 (t, 1H, *J* = 9.0 Hz, H-2), 3.79 (t, 1H, *J* = 9.0 Hz, H-4), 3.73 (t, 1H, *J* = 9.0 Hz, H-3), 3.71 (s, 3H, OCH_3), 2.58 (dt, 1H, *J* = 5.0, 12.5 Hz, H-6eq), 1.77 (q, 1H, *J* = 12.0 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.39 (PhCO), 159.11 (PMB), 138.35, 137.94, 133.08, 130.14, 129.87, 129.62, 128.37, 128.26, 127.94, 127.70, 127.63, 113.64, 83.07, 82.71, 76.10, 75.52, 75,13, 70.85, 70.79, 55.13 (OCH_3), 32.16 (C-6). HRMS (ESI) *m/z* calcd. for $C_{42}H_{40}O_8$ (M + Na^+) 695.2615, found: 695.2615.

1D-(1,2,4/3,5)-5-Azido-2,3-di-*O*-benzyl-1-*O*-methyl-1,2,3,4-cyclohexanetetrol (32). To a solution of **22** (34 mg, 0.085 mmol) in CH_2Cl_2 (1 mL), pyridine (28 μL, 0.34 mmol) was added and followed by the addition of Tf_2O (29 μL, 0.17 mmol) at 0 °C. After stirring for 10 min, sat. $NaHCO_3$ was added to quench the reaction, diluted with EtOAc, washed with water and brine. The extract was dried over Na_2SO_4, concentrated; the residue was co-evaporated with toluene for three times before dissolved in DMF (1 mL). To the mixture, NaN_3 (1.5 mg, 0.34 mmol) was added at 0 °C. After 5 h, the mixture was evaporated *in vacuo*, diluted with EtOAc, concentrated to give a yellow oil. Mixed the oil with MeOH (1 mL), $PdCl_2$ (3 mg, 0.022 mmol) was added at r.t. After stirring for 12 h, the mixture was diluted with CH_2Cl_2, filtered, concentrated. The residue was purified by column chromatography on silica gel (petroleum ether–EtOAc 4:1) to give **32** (9 mg, 35% for 3 steps) as a colorless oil: R_f = 0.34; $[\alpha]_D$ = −9.3 (*c* = 0.4, EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.37–7.29 (m, 10H, Ar), 5.02 (d, 1H, *J* = 11.1 Hz, $PhCH_2$), 4.71 (s, 2H, $PhCH_2$), 4.69(d, 1H, *J* = 11.1 Hz, $PhCH_2$), 3.76 (t, 1H, *J* = 9.0 Hz, H-3), 3.66–3.61 (m, 2H, H-4, H-5), 3.45–3.41 (m, 4H, H-1,OCH_3), 3.39 (dd, 1H, *J* = 3.0, 9.0 Hz, H-2), 2.58 (d, 1H, *J* = 2.5 Hz, OH), 2.21 (dt, 1H, *J* = 4.0, 14.5 Hz, H-6eq), 1.19 (ddd, 1H, *J* = 2.5, 12.0, 14.5 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.51, 137.98, 128.62, 128.46, 127.99, 127.93, 127.86, 82.05, 81.40, 76.49, 75.71, 74.86, 72.46, 58.93, 57.76 (OCH_3), 29.69 (C-6); IR υ = 2103.6 cm^{-1} ($-N_3$); HRMS (ESI) *m/z* calcd. for $C_{21}H_{25}N_3O_4$ ($M + NH_4^+$) 401.2183, found: 401.2189.

General procedure for the preparation of pseudodisaccharides 53–58 and 60–65

Donor **50**[18] (0.2 mmol) and acceptor (0.3 mmol) were coevaporated twice with toluene and further dried under vacuum. To a solution of donor and acceptor in CH_2Cl_2 (5 mL), 4 Å molecular sieves (600 mg) and *N*-iodosucccinimide (0.2 mmol) were added, and the mixture was stirred for 30 min before being cooled to −40 °C under argon. Trifluoromethanesulfonic acid (0.02 mmol, 1 N in Et_2O) was added, the temperature was then allowed to rise to −20 °C, and maintained at this temperature for 30 min to 3 h until donor disappeared by TLC monitoring. Et_3N was added to quench the reaction. The reaction mixture was filtered, washed with CH_2Cl_2, and concentrated. The residue was purified by column chromatography on silica gel. To the disaccharides with a benzoyl protective group, 30% NaOMe in MeOH was added to give **53–58**. Compound **65** was obtained by the coupling of donor **51** and acceptor **33** followed by the deprotection of acetal group with 80% AcOH/H_2O at 60 °C for 2 h.

1L-(1,2,4,5/3)-2-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-3,4-di-*O*-benzyl-1,2,3,4,5-cyclohexanepentol (53). A mixture of donor **50** (85 mg, 0.16 mmol), acceptor **34** (149 mg, 0.27 mmol), *N*-iodosucccinimide (37 mg, 0.16 mmol), and powdered 4 Å molecular sieves (600 mg) in CH_2Cl_2 (5 mL) was stirred at room temperature for 30 min. The reaction mixture was cooled to −40 °C and trifluoromethanesulfonic acid (16 μL, 1 N in Et_2O) was added. The reaction temperature was allowed to rise to −20 °C. After stirring at −20 °C for 1 h, the reaction was diluted with CH_2Cl_2 (10 mL) and Et_3N (0.1 mL) was added to quench the reaction, filtered, and washed successively with sat. $Na_2S_2O_3$ (10 mL) and sat. $NaHCO_3$ (10 mL). The organic layer was collected, dried over Na_2SO_4, concentrated, purified by column chromatography on silica gel (petroleum ether–EtOAc 8:1) to give the glycosylation product (124 mg). To a solution of the glycosylation product (124 mg) in MeOH (5 mL), 30% NaOMe (0.1 mL) was added at room temperature. After stirring for 1 h, the mixture was neutralized to pH = 6–7 with ion-exchange resin (Dowex 50, strong acid form) at room temperature, filtered, and concentrated to give **53** (96 mg, 80% for two steps) as a white solid: R_f = 0.5 (petroleum ether–EtOAc 1:2); $[\alpha]_D$ = +19.9 (*c* = 3.2, EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.41–7.25 (m, 20H, Ar), 5.28 (d, 1H, *J* = 3.5 Hz, H-1′), 5.02 (d, 1H, *J* = 10.0 Hz, $PhCH_2$), 4.92–4.85 (m, 4H, $PhCH_2$), 4.74 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.69 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.59 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.18–4.10 (m, 4H, H-1 or H-5, H-2 or H-4, H-3 H-5′), 4.05 (dd, 1H, *J* = 9.0, 10.0 Hz, H-3′), 3.58 (dd, 1H, *J* = 3.5, 10.0 Hz, H-2′), 3.52–3.44 (m, 5H, H-1 or H-5, H-2 or H-4, H-4′, H-6a′, OH), 3.33 (dd, 1H, *J* = 6.0, 13.5 Hz, H-6b′), 3.12 (d, 1H, *J* = 2.5 Hz, OH), 2.32 (dt, 1H, *J* = 3.5, 15.5 Hz, H-6eq), 1.53 (d, 1H, *J* =15.5 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.74, 137.75, 137.58, 128.53, 128.36, 128.12, 127.98, 127.90, 127.83, 127.74, 127.53, 99.14 (C-1′), 82.10, 82.16, 80.37, 78.94, 78.18, 75.84, 75.59, 75.13, 72.78, 70.93, 70.34, 68.50, 63.86, 51.10, 31.52 (C-6); MS (ESI-TOF) *m/z* calcd. for $C_{40}H_{44}N_6O_8$ 754 ($M + NH_4^+$), found 754; elemental analysis calcd (%) for $C_{40}H_{44}N_6O_8$: C 65.20, H 6.02, N 11.41, found: C, 65.09, H, 6.00, N, 11.19.

1D-(1,3,5/2,4)-2-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-3,4-di-*O*-benzyl-1,2,3,4,5-cyclohexanepentol (54). Yield: 77%; $[\alpha]_D$ = +0.6 (*c* = 0.3, EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.38–7.27 (m, 20H, Ar), 5.37 (d, 1H, *J* = 3.5 Hz, H-1′), 5.02 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.94 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.88–4.86 (m, 4H, $PhCH_2$), 4.67 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.59 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.21 (ddd, 1H, *J* = 2.5, 5.5, 10.0 Hz, H-5′), 3.97 (dd, 1H, *J* = 9.0, 10.0 Hz, H-4′), 3.64–3.46 (m, 7H, H-1, H-2, H-3 or H-4, H-5, H-2′, H-3′, H-6a′), 3.37–3.33 (m, 2H, H-3 or H-4, H-6b′), 2.96 (br, 1H, OH), 2.24 (dt, 1H, *J* = 4.5, 12.5 Hz, H-6eq), 1.62 (br, 1H, OH), 1.48 (q, 1H, *J* = 12.5 Hz, H-6ax); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 138.36, 138.20, 137.44, 137.38, 128.69, 128.59, 128.49, 128.42, 128.16, 128.10, 128.02, 127.92, 127.87, 127.54, 127.29, 98.28 (C-1′), 86.17, 85.48, 82.68, 80.27, 78.74, 75.57 (×2), 75.47, 75.28, 70.82, 68.51, 68.26, 63.76, 51.22, 36.43 (C-6); HRMS (ESI) *m/z* calcd. for $C_{40}H_{44}N_6O_8$ ($M + Na^+$) 759.3113, found: 759.3124.

1D-(1,2,4/3,5)-4-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-2,3-di-*O*-benzyl-1,2,3,4,5-cyclohexanepentol (55). Yield: 70%; $[\alpha]_D$ = +76.5 (*c* = 0.3, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.40–7.24 (m, 20H, Ar), 5.39 (d, 1H, *J* = 3.6 Hz, H-1′), 4.97–4.85 (m, 4H, $PhCH_2$), 4.71–4.66 (m, 2H, $PhCH_2$), 4.56 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.26–4.22 (m, 1H, H-5′), 4.13–4.07 (m, 1H, H-1), 4.12–3.96 (m, 2H, H-3 or H-4, H-3′), 3.85 (t, 1H, *J* = 9.0 Hz, H-4′), 3.56–3.43 (m, 5H, H-2, H-3 or H-4, H-5, H-2′, H-6a′), 3.33 (dd, 1H, *J* = 5.1, 13.2 Hz, H-6b′), 2.25 (dt, 1H, *J* = 4.2, 13.8 Hz, H-6eq), 1.53 (ddd, 1H, *J* = 2.4, 13.0, 13.8 Hz, H-6ax). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.70, 137.65, 137.50, 137.43, 128.56, 128.49, 128.34, 128.11, 128.01, 127.87, 127.52, 127.45, 98.14 (C-1′), 85.13, 83.01, 80.49, 80.24, 78.75, 75.55, 75.24, 72.73, 70.74, 67.41, 65.60, 63.76, 51.13, 34.47 (C-6); MS (ESI-TOF) *m/z* calcd. for $C_{40}H_{44}N_6O_8$ 754 ($M + NH_4^+$), found: 754; elemental analysis calcd (%) for $C_{40}H_{44}N_6O_8$: C 65.20, H 6.02, N 11.41, found: C 65.07, H 5.99, N 11.19.

1L-(1,2,4/3,5)-2-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-3,4-di-*O*-benzyl-1,2,3,4,5-cyclohexanepentol (56). Yield: 86%; $[\alpha]_D$ = +8.7 (*c* = 0.3, EtOAc); ^{1}H NMR

(300 MHz, $CDCl_3$) δ = 7.39–7.25 (m, 20H, Ar), 5.35 (d, 1H, *J* = 3.9 Hz, H-1′), 5.02–4.95 (m, 2H, $PhCH_2$), 4.91–4.84 (m, 4H, $PhCH_2$), 4.70 (d, 1H, *J* = 11.7 Hz, $PhCH_2$), 4.58 (d, 1H, *J* = 11.1 Hz, $PhCH_2$), 4.11–4.12 (m, 1H, H-1), 4.03–3.89 (m, 4H, H-3 or H-4, H-3′, H-4′, H-5′), 3.72 (dd, 1H, *J* = 2.7, 9.6 Hz, H-2), 3.50–3.42 (m, 3H, H-3 or H-4, H-5, H-6a′), 3.34–3.27 (m, 2H, H-2′, H-6b′), 2.39-2.33 (2×br, 2H, OH), 2.22 (dt, 1H, *J* = 4.2, 13.8 Hz, H-6eq), 1.45 (ddd, 1H, *J* = 2.0, 12.0, 13.5 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.43, 138.38, 137.33, 137.19, 128.59, 128.49, 128.40, 128.18, 128.05, 127.88, 127.74, 127.50, 98.59 (C-1′), 86.54, 81.20, 81.10, 80.22, 78.76, 75.58, 75.44, 75.38, 75.29, 71.23, 68.10, 67.76, 63.59, 51.09, 34.24 (C-6); HRMS (ESI) *m/z* calcd. for $C_{40}H_{44}N_6O_8$ (M + Na^+) 759.3113, found: 759.3116.

1D-(1,2,4/3,5)-4-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-2,3-di-*O*-benzyl-1-*O*-methyl-1,2,3,4,5-cyclohexanepentol (57). Yield: 70%; $[\alpha]_D$ = +72.7 (*c* = 4.4, EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.38–7.26 (m, 20H, Ar), 5.37 (d, 1H, *J* = 3.6 Hz, H-1′), 4.99–4.84 (m, 5H, $PhCH_2$), 4.74–4.65 (m, 2H, $PhCH_2$), 4.59 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.18 (ddd, 1H, *J* = 2.4, 5.1, 10.2 Hz, H-5′), 4.00 (dd, 1H, *J* = 9.0, 10.2 Hz, H-4′), 3.91 (t, 1H, *J* = 9.0 Hz, H-3′), 3.84–3.80 (m, 1H, H-1), 3.60 (m, 1H, H-5), 3.56–3.41 (m, 8H, H-2, H-3, H-4, H-2′, H-6a′, OCH_3), 3.33 (dd, 1H, *J* = 5.1, 13.2 Hz, H-6b′), 2.90 (d, 1H, *J* = 3.9 Hz, OH), 2.28 (dt, 1H, *J* = 4.5, 14.4 Hz, H-6eq), 1.23 (t, 1H, *J* = 14.4 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.85, 138.13, 137.47, 137.42, 128.56, 128.49, 128.36, 128.27, 128.12, 127.99, 127.90, 127.86, 127.71, 127.63, 127.34, 98.21 (C-1′), 85.97, 82.70, 80.44, 80.14, 78.76, 75.53, 75.21, 74.75, 72.69, 70.75, 67.62, 63.76, 57.54 (OCH_3), 51.17, 31.97 (C-6); HRMS (ESI) *m/z* calcd. for $C_{41}H_{46}N_6O_8$ (M + Na^+) 773.3269, found: 773.3262.

1L-(1,2,4,5/3)-2-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-3,4-di-*O*-benzyl-5-*O*-methyl-1,2,3,4,5-cyclohexanepentol (58). Yield: 70%; $[\alpha]_D$ = +34.8 (*c* = 2.4, EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.42–7.24 (m, 20H, Ar), 5.23 (d, 1H, *J* = 3.6 Hz, H-1′), 5.02 (d, 1H, *J* = 10.5 Hz, $PhCH_2$), 4.91–4.83 (m, 4H, $PhCH_2$), 4.77 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.67 (d, 1H, *J* = 11.7 Hz, $PhCH_2$), 4.59 (d, 1H, *J* = 11.4 Hz, $PhCH_2$), 4.22–4.06 (m, 4H, H-1 or H-3, H-3′, H-4′, H-5′), 3.70–3.65 (m, 2H, H-1 or H-3, OH), 3.54–3.41 (m, 8H, H-4, H-5, H-6, H-2′, H-6a′, OCH_3), 3.34 (dd, 1H, *J* = 5.1, 13.2 Hz, H-6b′), 2.27 (d, 1H, *J* = 15.0 Hz, H-6eq), 1.23 (d, 1H, *J* = 14.4 Hz, H-6ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.80, 138.14, 137.66, 128.41, 128.28, 128.09, 127.92, 127.87, 127.82, 127.75, 127.64, 127.44, 99.33 (C-1′), 82.99, 82.70, 80.35, 78.99, 78.61, 78.35, 75.77, 75.52, 75.00, 73.13, 70.76, 70.17, 63.97, 59.06 (OCH_3), 51.10, 29.71 (C-6); HRMS (ESI) *m/z* calcd. for $C_{41}H_{46}N_6O_8$ (M + Na^+) 773.3269, found: 773.3254.

1L-(1,3,4/2,6)-1-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-2,3-di-*O*-benzyl-4,6-diazido-1,2,3-cyclohexanetriol (60). Yield: 56%; $[\alpha]_D$ = +60.0 (*c* = 0.3, EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ = 7.37–7.24 (m, 20H, Ar), 5.59 (d, 1H, *J* = 4.0 Hz, H-1′), 5.05 (d, 1H, *J* = 10.5 Hz, $PhCH_2$), 4.91–4.86 (m, 4H, $PhCH_2$), 4.70 (s, 2H, $PhCH_2$), 4.61 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.07 (ddd, 1H, *J* = 2.5, 4.0, 9.5 Hz, H-5′), 4.01 (dd, 1H, *J* = 9.0, 10.0 Hz, H-3′), 3.99 (dd, 1H, *J* = 3.5, 7.7 Hz, H-2′), 3.95 (t, 1H, *J* = 9.5 Hz, H-4′), 3.65–3.58 (m, 2H, H-1 or H-2, H-4), 3.53–3.46 (m, 3H, H-1 or H-2, H-6, H-6a′), 3.36 (dd, 1H, *J* = 4.5, 13.0 Hz, H-6b′), 3.31 (dd, 1H, *J* = 4.0, 10.0 Hz, H-3), 2.15 (dt, 1H, *J* = 4.5, 14.5 Hz, H-5eq), 1.47 (ddd, 1H, *J* = 3.0, 12.0, 14.5 Hz, H-5ax); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 138.24, 137.68 (×2), 137.22, 128.59, 128.48, 128.41, 128.14, 128.05, 128.01, 127.90, 127.74, 127.58, 127.45, 97.74 (C-1′), 82.93, 81.71, 80.04, 78.71, 78.26, 75.47, 75.35, 75.00, 73.19, 70.89, 63.28, 58.28, 57.27, 51.00, 31.17 (C-5); HRMS (ESI) *m/z* calcd. for $C_{40}H_{42}N_{12}O_6$ (M + Na^+) 809.3242, found: 809.3241.

1L-(1,3,6/2,4)-1-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-4,6-diazido-2,3-di-*O*-benzyl-1,2,3-cyclohexanetriol (61). Yield: 50%; $[\alpha]_D$ = +82.1 (*c* = 0.6, EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ = 7.36–7.25 (m, 20H, Ar), 5.37 (d, 1H, *J* = 4.0 Hz, H-1′), 5.01 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.93 (d, 1H, *J* = 10.5 Hz, $PhCH_2$), 4.88–4.82 (m, 5H, $PhCH_2$), 4.56 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.06 (dd, 1H, *J* = 3.0, 6.0 Hz, H-6), 4.03 (dd, 1H, *J* = 9.0, 10.5 Hz, H-3′), 3.97 (t, 1H, *J* = 9.0 Hz, H-4′), 3.91 (ddd, 1H, *J* = 2.5, 7.0, 9.5 Hz, H-5′), 3.85 (dd, 1H, *J* = 3.5, 9.5 Hz, H-2′), 3.71 (ddd, 1H, *J* = 4.5, 9.5, 12.5 Hz, H-4), 3.45–3.32 (m, 4H, H-1, H-2, H-3, H-6a′), 3.27 (dd, 1H, *J* = 7.0, 12.5 Hz, H-6b′), 2.11 (dt, 1H, *J* = 4.0, 14.0 Hz, H-5eq), 1.45 (ddd, 1H, *J* = 2.0, 11.5, 13.5 Hz, H-5ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.24, 137.56, 137.44, 137.39, 128.56, 128.44, 128.16, 128.05, 127.88, 127.60, 127.32, 99.02 (C-1′), 85.04, 81.64, 79.79, 79.41, 78.72, 75.81, 75.61, 75.53, 75.06, 71.87, 63.27, 59.96, 59.43, 51.10, 31.72 (C-5); HRMS (ESI) *m/z* calcd. for $C_{40}H_{42}N_{12}O_6$ (M + Na^+) 809.3242, found: 809.3232.

1L-(1,3,4/2,5)-1-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-6-azido-2,3-di-*O*-benzyl-4-*O*-methyl-1,2,3,4-cyclohexanetetrol (62). Yield: 86%; $[\alpha]_D$ = +47.7 (*c* = 0.3, EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.37–7.26 (m, 20H, Ar), 5.62 (d, 1H, *J* = 4.0 Hz, H-1′), 5.07 (d, 1H, *J* = 10.5 Hz, $PhCH_2$), 4.91–4.86 (m, 4H, $PhCH_2$), 4.70–4.60 (m, 3H, $PhCH_2$), 4.28 (ddd, 1H, *J* = 2.5, 4.0, 10.0 Hz, H-5′), 4.03 (t, 1H, *J* = 9.0 Hz, H-3′), 4.00 (t, 1H, *J* = 9.0 Hz, H-4′), 3.67–3.36 (m, 10H, H-1, H-2, H-3, H-4, H-6, H-2′, H-6a′, OCH_3), 3.30 (dd, 1H, *J* = 4.0, 10.5 Hz, H-6b′), 2.32 (dt, 1H, *J* = 4.0, 14.0 Hz, H-5eq), 1.32 (ddd, 1H, *J* = 2.0, 13.5, 14.0 Hz, H-5ax); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.52, 137.82, 137.70, 128.44, 128.35, 128.03, 127.93, 127.87, 127.73, 127.45, 97.74 (C-1′), 82.86, 81.75, 79.98, 78.70, 78.61, 75.43, 75.15, 74.98, 74.35, 72.73, 70.74, 63.23, 58.28, 57.90 (OCH_3), 50.97, 29.74 (C-5); HRMS (ESI) *m/z* calcd. for $C_{41}H_{45}N_9O_7$ (M + NH_4^+) 793.3780, found: 793.3786.

5,6,3′,4′-Tetra-*O*-benzyl-1,3,2′,6′-tetraazidoneamine (63). Yield: 80%; $[\alpha]_D$ = +55.1 (*c* = 1.3, EtOAc); 1H NMR (300 MHz, CDCl3) δ = 7.38–7.26 (m, 20H, Ar), 5.58 (d, 1H, *J* = 3.9 Hz, H-1′), 5.02 (d, 1H, *J* = 11.1 Hz, $PhCH_2$), 4.94–4.80 (m, 6H, $PhCH_2$), 4.61 (d, 1H, *J* = 11.1 Hz, $PhCH_2$), 4.27 (m, 1H, H-5′), 4.00 (t, 1H, *J* = 9.0 Hz, H-3′), 3.65–3.29 (m, 9H, H-1, H-3, H-4, H-5, H-6, H-2′, H-4′, H-6a′, H-6b′), 2.32 (dt, 1H, *J* = 4.2, 13.2 Hz, H-2eq), 1.49 (q, 1H, *J* = 13.2 Hz, H-2ax). The ^1H NMR data coinside with the previous report.[23]

4-*O*-(2′,6′-Diazido-2′,6′-dideoxy-3′4′-di-*O*-acetyl-α-D-mannopyranosyl)-1,3-diazido-5,6-di-*O*-benzyl-2-deoxystreptamine (64). Yield: 84%; $[\alpha]_D$ = +68.9 (*c* = 0.9, EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ = 7.39–7.26 (m, 10H, Ar), 5.29–5.21(m, 2H, H-3′, H-4′), 5.18 (d, 1H, *J* = 2.5 Hz, H-1′), 5.02 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.90 (d, 1H, *J* = 10.5 Hz, $PhCH_2$), 4.83 (d, 1H, *J* = 10.5 Hz, PhCH$_2$), 4.62 (d, 1H, J = 11.5 Hz, PhCH$_2$), 4.32 (ddd, 1H, J = 3.0, 6.0, 9.0 Hz, H-5′), 3.53–3.46 (m, 4H, H-2′, H-4, H-5, H-6), 3.43–3.37 (m, 2H, H-1, H-3), 3.33 (dd, 1H, J = 6.5, 13.5 Hz, H-6a′), 3.25 (dd, 1H, J = 3.0, 13.5 Hz, H-6b′), 2.34 (dt, 1H, J = 4.5, 13.0 Hz, H-2eq), 2.05 (s, 3H, COCH$_3$), 2.04 (s, 3H, COCH$_3$), 1.50 (q, 1H, J = 13.0 Hz, H-2ax); ^{13}C NMR (75 MHz, CDCl$_3$) δ = 169.94 (COCH$_3$), 169.65 (COCH$_3$), 137.35, 137.09, 128.72, 128.52, 128.26, 128.11, 128.05, 127.22, 98.76 (C-1′), 84.38, 84.10, 79.51, 75.91 (×2), 70.70, 70.30, 66.76, 61.01, 60.18, 58.79, 51.01, 32.15 (C-2), 20.68 (COCH$_3$), 20.45 (COCH$_3$); HRMS (ESI) m/z calcd. for $C_{30}H_{34}N_{12}O_8$ (M + Na$^+$) 713.2515, found: 713.2506.

4-*O*-(2′,6′-Diazido-2′,6′-dideoxy-α-D-galactopyranosyl)-1,3-diazido-5,6-di-*O*-benzyl-2-deoxystreptamine (65). Yield: 60% over two steps; $[\alpha]_D$ = +20.7 (c = 0.3, EtOAc); ^{1}H NMR (500 MHz, CDCl$_3$) δ = 7.35–7.25 (m, 10H, Ar), 5.68 (d, 1H, J = 4.0 Hz, H-1′), 5.02 (d, 1H, J = 11.0 Hz, PhCH$_2$), 4.89–4.86 (m, 2H, PhCH$_2$), 4.82 (d, 1H, J = 10.0 Hz, PhCH$_2$), 4.39 (t, 1H, J = 5.5 Hz, H-3′), 4.13 (dd, 1H, J = 3.0, 5.5 Hz, H-2′), 4.03 (d, 1H, J = 2.0 Hz, H-4′), 3.67–3.57 (m, 3H, H-4, H-5, H-6), 3.53–3.39 (m, 5H, H-1, H-3, H-5′, H-6a′, H-6b′), 2.52 (br, 2H, OH), 2.31 (dt, 1H, J = 4.5, 13.0 Hz, H-2eq), 1.50 (q, 1H, J = 12.5 Hz, H-2ax); ^{13}C NMR (75 MHz, CDCl$_3$) δ = 137.75, 137.23, 128.49, 128.13, 128.05, 127.69, 127.06, 97.80 (C-1′), 84.62, 84.40, 77.19, 75.95, 75.20, 69.65, 69.04, 68.13, 60.24, 59.72, 59.51, 51.22, 32.30 (C-2); HRMS (ESI) m/z calcd. for $C_{26}H_{30}N_{12}O_6$ (M + Na$^+$) 629.2304, found: 629.2307.

2-*O*-(2′,6′-Diazido-3′,4′-di-*O*-benzyl-2′,6′-dideoxy-α-D-glucopyranosyl)-3-*O*-benzyl-5-*O*-methyl-(2*R*,3*S*,4*R*,5*R*)-7-oxa-bicyclo-[2.2.1]heptane (59). To a solution of **57** (39 mg, 0.052 mmol) in CH$_2$Cl$_2$ (2 mL), was added pyridine (42 μL, 0.52 mmol) and Tf$_2$O (35 μL, 0.21 mmol) at 0 °C. After stirring for 40 min, sat. NaHCO$_3$ was added to quench the reaction. The mixture was diluted with CH$_2$Cl$_2$ and washed with brine. The organic layer was collected, dried over Na$_2$SO$_4$, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether–EtOAc 3:1) to give **59** (33 mg, 99%) as a white solid: R_f = 0.23 (petroleum ether–EtOAc 3:1); $[\alpha]_D$ = +64.0 (c = 2.9, EtOAc); ^{1}H NMR (500 MHz, CDCl$_3$) δ = 7.39–7.24 (m, 15H, Ar), 4.92 (d, 1H, J = 3.5 Hz, H-1′), 4.90–4.84 (m, 3H, PhCH$_2$), 4.62–4.55 (m, 4H, PhCH$_2$, H-1), 4.51 (d, 1H, J = 5.0 Hz, H-2), 4.05 (dd, 1H, J = 2.5, 7.0 Hz, H-5), 4.02–3.98 (m, 2H, H-3′, H-5′), 3.93 (d, 1H, J = 5.5 Hz, H-3), 3.59 (d, 1H, J = 1.5 Hz, H-4), 3.54 (t, 1H, J = 9.5 Hz, H-4′), 3.50 (dd, 1H, J = 2.5, 13.5 Hz, H-6a′), 3.35 (dd, 1H, J = 5.0, 13.5 Hz, H-6b′), 3.31 (dd, 1H, J = 3.5, 10.0 Hz, H-2′), 3.26 (s, 3H, OCH$_3$), 1.90 (dd, 1H, J = 7.0, 13.5 Hz, H-6eq), 1.74 (ddt, 1H, J = 1.5, 7.0, 13.5 Hz, H-6ax); ^{13}C NMR (125 MHz, CDCl$_3$) δ = 137.97, 137.88, 137.67, 128.82, 128.78, 128.35, 128.31, 128.23, 128.11, 127.97, 98.30 (C-1′), 86.91, 84.56, 81.09, 79.99, 79.51, 79.05, 77.56, 75.68, 75.45, 73.23, 71.20, 63.49, 56.76 (OCH$_3$), 51.30, 35.60 (C-6); HRMS (ESI) m/z calcd. for $C_{34}H_{38}N_6O_7$ (M + Na$^+$) 665.2694, found: 665.2697.

General procedure for the preparation of compounds 3–14 from 53–62, and 64–65

The preparation of compounds **3–9**: to a solution of the pseudodisaccharide (**53–59**) in methanol, 10% Pd/C (1.5 times the weight of the starting material) was added. The mixture was stirred for 18 h under an atmosphere of H$_2$. The mixture was filtered and concentrated. The residue was purified by ion-exchange chromatography (Amberlite CG-50, NH$_4^+$ form) with a linear gradient of aqueous ammonia. Gradient ammonia aqueous solution (0–10%, 0–15%, 0–20%) was used. The fractions were collected and concentrated *in vacuo*. The products were dissolved in water, and 0.1 N HCl was used to adjust the pH values to 3–4. The final products were obtained after lyophilization. The preparation of compounds **10–14**: H$_2$S gas was introduced into the solution of pseudodisaccharide (**60–62**, **64–65**) in a mixed solvent of pyridine/H$_2$O/Et$_3$N (3:2:1) to reduce the azido groups to amino groups. The solvent was removed and the residue was purified by column chromatography on silica gel (EtOAc or CHCl$_3$/methanol/NH$_4$OH as eluents) to give benzyl-protected pseudodisaccharides. Finally, the benzyl groups were removed under Pd/C/H$_2$ conditions as described above to provide target compounds.

1L-(1,2,4,5/3)-2-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-1,2,3,4,5-cyclohexanepentol (3). 32 mg, yield: 98%; $[\alpha]_D$ = +95.0 (c = 0.6, H$_2$O); ^{1}H NMR (500 MHz, D$_2$O) δ = 5.52 (d, 1H, J = 3.5 Hz, H-1′), 4.22–4.21 (m, 1H, H-1), 4.11–4.05 (m, 3H, H-4, H-5, H-5′), 3.98 (dd, 1H, J = 9.0, 11.0 Hz, H-3), 3.71 (dd, 1H, J = 3.0, 9.5 Hz, H-2′), 3.57 (dd, 1H, J = 2.5, 9.0 Hz, H-2), 3.46–3.41 (m, 3H, H-3′, H-4′, H-6a′), 3.20 (dd, 1H, J = 8.5, 13.5 Hz, H-6b′), 2.16 (dt, 1H, J = 4.0, 15.5 Hz, H-6eq), 1.78 (dt, 1H, J = 3.0, 15.5 Hz, H-6ax); ^{13}C NMR (125 MHz, D$_2$O) δ = 97.09 (C-1′), 82.12 (×2), 74.47, 71.81, 70.53(×2), 69.84, 69.31, 54.78, 40.88, 32.45 (C-6); HRMS (ESI) m/z calcd. for $C_{12}H_{24}N_2O_8$ (M + H$^+$) 325.1605, found: 325.1672.

1D-(1,3,5/2,4)-2-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-1,2,3,4,5-cyclohexanepentol (4). 25 mg, yield: 98%; $[\alpha]_D$ = +70.0 (c = 0.9, H$_2$O); ^{1}H NMR (500 MHz, D$_2$O) δ = 5.54 (d, 1H, J = 4.0 Hz, H-1′), 4.29 (ddd, 1H, J = 3.0, 8.5, 11.0 Hz, H-5′), 3.92 (dd, 1H, J = 9.0, 11.0 Hz, H-3 or H-4), 3.71 (ddd, 1H, J = 5.0, 9.5, 12.5 Hz, H-5), 3.57–3.51 (m, 2H, H-1, H-3′), 3.48–3.39 (m, 4H, H-2, H-3 or H-4, H-2′, H-6a′), 3.31 (t, 1H, J = 9.0 Hz, H-4′), 3.20 (dd, 1H, J = 8.5, 13.5 Hz, H-6b′), 2.23 (dt, 1H, J = 4.5, 12.5 Hz, H-6eq), 1.51 (q, 1H, J = 12.5 Hz, H-6ax); ^{13}C NMR (125 MHz, D$_2$O) δ = 96.67 (C-1′), 83.93, 77.53, 75.17, 71.69, 69.97, 68.85, 68.75, 67.56, 54.79, 40.84, 37.92 (C-6); HRMS (ESI) m/z calcd. for $C_{12}H_{24}N_2O_8$ (M + H$^+$) 325.1605, found: 325.1615.

1D-(1,2,4/3,5)-4-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-1,2,3,4,5-cyclohexanepentol (5). 17 mg, yield: 99%; $[\alpha]_D$ = +169.2 (c = 0.6, H$_2$O); ^{1}H NMR (500 MHz, D$_2$O) δ = 5.56 (d, 1H, J = 3.5 Hz, H-1′), 4.29 (ddd, 1H, J = 3.0, 9.0 Hz, H-5), 4.07 (dd, 1H, J = 3.0, 6.0 Hz, H-1), 3.93 (dd, 1H, J = 9.0, 9.5 Hz, H-3′), 3.88 (ddd, 1H, J = 5.0, 9.0, 12.0 Hz, H-5′), 3.77 (t, 1H, J = 9.0 Hz, H-4), 3.54–3.39 (m, 5H, H-2, H-3, H-2′, H-4′, H-6a′), 3.20 (dd, 1H, J = 8.5, 13.5 Hz, H-6b′), 2.14 (dt, 1H, J = 4.5, 13.5 Hz, H-6eq), 1.62 (ddd, 1H, J = 2.5, 12.0, 13.5 Hz, H-6ax); ^{13}C NMR (125 MHz, D$_2$O) δ = 96.66 (C-1′), 84.36, 74.34, 73.85, 71.73, 70.00, 68.76, 68.73, 67.28, 54.84, 40.87, 36.30 (C-6); HRMS (ESI) m/z calcd. for $C_{12}H_{24}N_2O_8$ (M + H$^+$) 325.1605, found: 325.1619.

1L-(1,2,4/3,5)-2-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-1,2,3,4,5-cyclohexanepentol (6). 13 mg, yield: 99%; $[\alpha]_D$ = +26.7 (c = 0.6, H$_2$O); ^{1}H NMR (500 MHz, D$_2$O) δ = 5.52 (d, 1H, J = 3.5 Hz, H-1′), 4.21 (dd, 1H, J = 3.0, 5.5 Hz, H-1), 4.01 (ddd, 1H, $J = 3.0, 7.5, 10.5$ Hz, H-5′), 3.95 (dd, 1H, $J = 9.5, 10.5$ Hz, H-3′), 3.81–3.76 (m, 2H, H-4, H-5), 3.71 (dd, 1H, $J = 3.0, 10.0$ Hz, H-2), 3.46–3.39 (m, 3H, H-3, H-2′, H-6a′), 3.29 (t, 1H, $J = 9.0$ Hz, H-4′), 3.22 (dd, 1H, $J = 8.0, 13.5$ Hz, H-6b′), 2.11 (dt, 1H, $J = 4.5, 14.5$ Hz, H-6eq), 1.58 (ddd, 1H, $J = 2.5, 12.0, 13.5$ Hz, H-6ax); ^{13}C NMR (125 MHz, D_2O) $\delta = 97.56$ (C-1′), 81.68, 77.99, 73.08, 71.66, 69.73, 69.34, 68.65, 68.51, 54.72, 40.86, 35.74 (C-6); HRMS (ESI) *m/z* calcd. for $C_{12}H_{24}N_2O_8$ (M + H$^+$) 325.1605, found: 325.1585.

1D-(1,2,4/3,5)-4-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-1-*O*-methyl-1,2,3,4,5-cyclohexanepentol (7). 18 mg, yield: 96%; $[\alpha]_D = +93.3$ ($c = 0.6$, H_2O); ^{1}H NMR (500 MHz, D_2O) $\delta = 5.60$ (d, 1H, $J = 4.0$ Hz, H-1′), 4.32 (ddd, 1H, $J = 3.0, 7.5, 10.5$ Hz, H-5), 3.97 (dd, 1H, $J = 9.5, 10.5$ Hz, H-3′), 3.82 (ddd, 1H, $J = 4.5, 9.5, 12.0$ Hz, H-5′), 3.76–3.72 (m, 1H, H-1, H-4), 3.62 (dd, 1H, $J = 3.5, 10.0$ Hz, H-2), 3.57–3.42 (m, 7H, H-3, H-2′, H-4′, H-6a′, OCH_3), 3.24 (dd, 1H, $J = 8.0, 13.5$ Hz, H-6b′), 2.42 (dt, 1H, $J = 4.5, 14.5$ Hz, H-6b), 1.51 (ddd, 1H, $J = 2.5, 12.0, 13.5$ Hz, H-6a); ^{13}C NMR (125 MHz, D_2O) $\delta = 96.67$ (C-1′), 84.24, 78.53, 74.24, 74.08, 71.71, 69.99, 68.76, 67.19, 57.64 (OCH_3), 54.82, 40.85, 32.21 (C-6); HRMS (ESI) *m/z* calcd. for $C_{13}H_{26}N_2O_8$ (M + H$^+$) 339.1767, found: 339.1759.

1L-(1,2,4,5/3)-2-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-5-*O*-methyl-1,2,3,4,5-cyclohexanepentol (8). 19 mg, yield: 99%; $[\alpha]_D = +57.5$ ($c = 0.6$, H_2O); ^{1}H NMR (500 MHz, D_2O) $\delta = 5.51$ (d, 1H, $J = 3.5$ Hz, H-1′), 4.18–4.17 (m, 1H, H-1), 4.11 (td, 1H, $J = 2.5, 9.0$ Hz, H-2), 4.06 (t, 1H, $J = 9.0$ Hz, H-3′), 3.99 (t, 1H, $J = 9.0$ Hz, H-4′), 3.74–4.73 (m, 1H, H-5), 3.68–3.63 (m, 2H, H-2′, H-5′), 3.46–3.42 (m, 6H, H-3, H-4, H-6a′, OCH_3), 3.20 (dd, 1H, $J = 8.5, 13.5$ Hz, H-6b′), 2.35 (d, 1H, $J = 15.0$ Hz, H-6eq), 1.65 (d, 1H, $J = 15.0$ Hz, H-6ax); ^{13}C NMR (125 MHz, D_2O) $\delta = 97.01$ (C-1′), 81.92, 79.98, 73.83 (×2), 71.82, 70.61, 69.85, 69.30, 58.11 (OCH_3), 54.77, 40.87, 28.72 (C-6); HRMS (ESI) *m/z* calcd. for $C_{13}H_{26}N_2O_8$ (M + H$^+$) 339.1767, found: 339.1761.

2-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-5-*O*-methyl-(2*R*,3*S*,4*R*,5*R*)-7-oxa-bicyclo[2.2.1]heptane (9). 37 mg, yield: 96%; $[\alpha]_D = +60.0$ ($c = 1.0$, H_2O); ^{1}H NMR (500 MHz, D_2O) $\delta = 5.36$ (d, 1H, $J = 3.5$ Hz, H-1′), 4.67 (t, 2H, $J = 6.0$ Hz, H-4), 4.18–4.16 (m, 2H, H-5, H-3′), 3.94 (ddd, 1H, $J = 3.0, 8.5, 9.5$ Hz, H-5′), 3.89 (dd, 1H, $J = 9.0, 10.5$ Hz, H-4′), 3.76 (d, 1H, $J = 1.0$ Hz, H-2), 3.48–3.40 (m, 3H, H-1, H-2′, H-6a′), 3.33 (s, 3H, OCH_3), 3.22 (dd, 1H, $J = 8.5, 13.5$ Hz, H-6b′), 2.10 (dd, 1H, $J = 7.0, 14.0$ Hz, H-6ax), 1.76 (ddt, 1H, $J = 2.0, 6.5, 14.0$ Hz, H-6eq); ^{13}C NMR (125 MHz, D_2O) $\delta = 94.30$ (C-1′), 85.14, 82.54, 81.40, 77.82, 76.36, 71.76, 69.88, 69.30, 56.66 (OCH_3), 54.21, 40.88, 35.00 (C-6); HRMS (ESI) *m/z* calcd. for $C_{13}H_{24}N_2O_7$ (M + H$^+$) 321.1656, found: 321.1647.

1L-(1,3,4/2,6)-1-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-4,6-diamino-1,2,3-cyclohexanetriol (10). 18 mg, yield: 90%; $[\alpha]_D = +84.2$ ($c = 0.6$, H_2O); ^{1}H NMR (500 MHz, D_2O) $\delta = 5.80$ (d, 1H, $J = 3.5$ Hz, H-1′), 4.14–4.12 (m, 3H, H-5′, H-2, H-1 or H-3), 4.06–4.01 (m, 2H, H-3′, H-1 or H-3), 3.94–3.92 (m, 1H, H-4 or H-6), 3.83–3.81 (m, 1H, H-4 or H-6), 3.55–3.51 (m, 3H, H-2′, H-4′, H-6a′), 3.31 (dd, 1H, $J = 7.5, 13.5$ Hz, H-6b′), 2.53 (ddd, 1H, $J = 4.5, 7.0, 15.0$ Hz, H-5eq), 2.22 (ddd, 1H, $J = 4.5, 9.0, 15.0$ Hz, H-5ax); ^{13}C NMR (125 MHz, D_2O) $\delta = 95.68$ (C-1′), 75.17, 71.46, 70.78, 69.83, 69.25, 69.19, 54.24, 48.71, 47.66, 40.84, 25.68 (C-5); HRMS (ESI) *m/z* calcd. for $C_{12}H_{26}N_4O_6$ (M + H$^+$) 323.1925, found: 323.1954.

1L-(1,3,6/2,4)-1-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-4,6-diamino-1,2,3-cyclohexanetriol (11). 21 mg, yield: 90%; $[\alpha]_D = +68.3$ ($c = 0.6$, H_2O); ^{1}H NMR (500 MHz, D_2O) $\delta = 5.76$ (d, 1H, $J = 3.5$ Hz, H-1′), 4.20 (dd, 1H, $J = 4.5, 10.0$ Hz, H-1), 4.08 (m, 1H, H-6), 4.02 (t, 1H, $J = 9.0$ Hz, H-3′), 3.96 (ddd, 1H, $J = 3.0, 7.5, 9.0$ Hz, H-5′), 3.86 (t, 1H, $J = 9.0$ Hz, H-4′), 3.61 (t, 1H, $J = 9.0$ Hz, H-3), 3.52–3.42 (m, 4H, H-2, H-4, H-2′, H-6′a), 3.25 (dd, 1H, $J = 8.0, 13.5$ Hz, H-6b′), 2.46 (dt, 1H, $J = 3.0, 15.5$ Hz, H-5eq), 2.16 (ddd, 1H, $J = 4.0, 14.0, 16.0$ Hz, H-5ax); ^{13}C NMR (125 MHz, D_2O) $\delta = 97.55$ (C-1′), 75.24, 73.38, 73.22, 71.60, 69.73, 69.16, 54.34, 50.08, 49.06, 40.90, 27.81 (C-5); HRMS (ESI) *m/z* calcd. for $C_{12}H_{26}N_4O_6$ (M + H$^+$) 323.1925, found: 323.1924.

1L-(1,3,4/2,6)-1-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-glucopyranosyl)-6-amino-4-*O*-methyl-1,2,3,4-cyclohexanetetrol (12). 16 mg, yield: 70%; $[\alpha]_D = +89.2$ ($c = 0.6$, H_2O); ^{1}H NMR (500 MHz, D_2O) $\delta = 5.92$ (d, 1H, $J = 4.0$ Hz, H-1′), 4.02 (ddd, 1H, $J = 3.5, 7.0, 10.0$ Hz, H-5′), 3.99 (dd, 1H, $J = 9.0, 11.0$ Hz, H-3′), 3.88 (t, 1H, $J = 9.0$ Hz, H-4′), 3.83 (t, 1H, $J = 9.0$ Hz, H-2 or H-1), 3.79 (dd, 1H, $J = 3.5, 5.5$ Hz, H-4), 3.63 (dd, 1H, $J = 3.0, 9.5$ Hz, H-2′), 3.53–3.45 (m, 4H, H-1 or H-2, H-3, H-6, H-6a′), 3.41 (s, 3H, OCH_3), 3.30 (dd, 1H, $J = 7.0, 13.5$ Hz, H-6b′), 2.51 (dt, 1H, $J = 4.5, 14.0$ Hz, H-5eq), 1.71 (ddd, 1H, $J = 2.0, 14.0, 14.5$ Hz, H-5ax); ^{13}C NMR (125 MHz, D_2O) $\delta = 96.75$ (C-1′), 79.61, 77.34, 74.38, 73.69, 71.41, 69.83, 69.10, 57.76 (OCH_3), 54.28, 48.33, 40.84, 27.94 (C-5); HRMS (ESI) *m/z* calcd. for $C_{13}H_{27}N_3O_7$ (M + H$^+$) 338.1922, found: 338.1914.

4-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-mannopyranosyl)-2-deoxystreptamine (13). 17 mg, yield: 96% over three steps; $[\alpha]_D = +53.3$ ($c = 0.6$, H_2O); ^{1}H NMR (500 MHz, D_2O) $\delta = 5.67$ (d, 1H, $J = 4.0$ Hz, H-1′), 4.26 (dd, 1H, $J = 4.0, 7.5$ Hz, H-3′), 4.19 (dt, 1H, $J = 5.0, 7.5$ Hz, H-5′), 4.01 (t, 1H, $J = 9.5$ Hz, H-4 or H-5), 3.84 (t, 1H, $J = 4.0$ Hz, H-2′), 3.72 (t, 1H, $J = 7.5$ Hz, H-4′), 3.68 (t, 1H, $J = 9.0$ Hz, H-4 or H-5), 3.61–3.52 (m, 2H, H-1 or H-3, H-6), 3.47–3.41 (m, 2H, H-6a′, H-6b′), 3.35 (dt, 1H, $J = 4.0, 12.0$ Hz, H-1 or H-3), 2.51 (dt, 1H, $J = 4.0, 12.5$ Hz, H-2eq), 1.92 (q, 1H, $J = 12.5$ Hz, H-2ax); ^{13}C NMR (125 MHz, D_2O) $\delta =$ 96.41 (C-1′), 79.13, 75.50, 73.29, 72.48, 68.40, 67.25, 53.61, 50.45, 49.27, 40.50, 28.82 (C-2); HRMS (ESI) *m/z* calcd. for $C_{12}H_{26}N_4O_6$ (M + H$^+$) 323.1925, found: 323.1921.

4-*O*-(2′,6′-Diamino-2′,6′-dideoxy-α-D-galactopyranosyl)-2-deoxystreptamine (14). 14 mg, yield: 95% over two steps; $[\alpha]_D = +31.7$ ($c = 0.6$, H_2O); ^{1}H NMR (500 MHz, D_2O) $\delta = 5.99$ (d, 1H, $J = 4.0$ Hz, H-1′), 4.32 (td, 1H, $J = 1.0, 5.0$ Hz, H-5′), 4.23 (dd, 1H, $J = 3.0, 11.0$ Hz, H-3′), 4.13 (dd, 1H, $J = 1.5, 3.0$ Hz, H-4′), 4.00 (dd, 1H, $J = 9.0, 10.0$ Hz, H-4), 3.71 (t, 1H, $J = 9.0$ Hz, H-5), 3.67 (dd, 1H, $J = 4.0, 11.5$ Hz, H-2′), 3.61 (t, 1H, $J = 9.5$ Hz, H-6), 3.57 (ddd, 1H, $J = 4.0, 10.0, 12.5$ Hz, H-1 or H-3), 3.39–3.34 (m, 3H, H-1 or H-3, H-6a′, H-6b′), 2.52 (dt, 1H, $J = 4.0, 12.5$ Hz, H-2eq), 1.92 (q, 1H, $J = 12.5$ Hz, H-2ax); ^{13}C NMR (125 MHz, D_2O) $\delta = 96.95$ (C-1′), 78.13, 75.97, 73.25, 70.02, 68.22, 65.81, 50.83, 50.45, 49.27, 41.29, 28.99 (C-2); HRMS (ESI) *m/z* calcd. for $C_{12}H_{26}N_4O_6$ (M + H$^+$) 323.1925, found: 323.1925.

SPR binding studies

Biotin-labelled RNA fragments were purchased at Bioneer (Korea). SPR measurements were conducted on a Biocore 3000 system from Biocore AB and performed as described in the literature.[20] Streptavidin-coated sensor-chips (SA-chips) were obtained from Biocore and loaded with RNA fragments to 591–648 RU. An empty cell was used as reference surface. Calculation of dissociation constants by fitting the steady-state responses was performed using the formula $R = R_{max}[c/(K_d + c)]$, where R = response, R_{max} = maximum response of one binding site occupied, and c = concentration.

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