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# Sialylation reactions with 5-*N*,7-*O*-carbonyl-protected sialyl donors: unusual stereoselectivity with nitrile solvent assistance

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**Abstract**—A 5-*N*,7-*O*-carbonyl-protected sialyl donor was synthesized, and, unexpectedly, this donor showed β-selectivity (α/β = 1/2.4–1/20) on coupling with sugar acceptors in acetonitrile upon treatment with various promoter systems. For the coupling reaction in dichloromethane, a modified Ellervik's method (IBr and $AgClO_4 \cdot H_2O$) was highly effective in activating the 5-*N*,7-*O*-carbonyl donor, providing moderate α-selectivity (α/β = ~1.8/1).


*Keywords:* Sialylation; *N*,*O*-Carbonyl-protected sialyl donor; Nitrile solvent effect; Stereoselectivity

## 1. Introduction

Sialic acids are one of the biologically important sugar residues of oligosaccharides and typically occupy the distal end of glycan chains through an α-glycosic linkage to other sugar residues such as galactose, glucose, and galactosamine. The arrangement of sialic acids at the outermost positions of glycoconjugates enables their participation in carbohydrate–protein interactions that mediate various essential biological processes such as cell differentiation, cell adhesion, cellular immune response, fertilization, oncogenesis, and viral infection. It is well known that the difficulty in synthesizing α-sialosides has been a central issue in carbohydrate chemistry. This difficulty is attributable to the inherent structural disadvantages of sialic acid, namely the presence of the C-2 ketal carbon adjacent to the carboxyl group and the C-3 methylene carbon. The various methods developed to overcome these disadvantages can be classified into nitrile solvent assistance-dependent and nitrile solvent assistance-independent sialylations.[1] The former method utilizes nitrile solvents as a stereodirecting method to generate α-sialosides predominantly,[2] while the latter utilizes sialyl glycosyl donors equipped with α-directing functionality at C-3[3] or C-1.[4]

Since reporting that an *N*-Troc-protected sialyl donor exhibits high reactivity during glycosylation with the assistance of a nitrile solvent,[5] we have focused our attention on the effect of the C-5 modification of the sialyl donor on α-selective sialylation. Similarly, several reports have been published on C-5-modified sialyl donors such as *N*-trifluoroacetyl,[6] *N*,*N*-diacetyl,[7] 5-azido,[8] *N*-phthaloyl,[9] and 4-*O*,5-*N*-oxazolidinone sialyl donors.[10] Very recently, Crich's group was the first to report the synthesis of the 5-*N*,7-*O*-oxazinanone sialyl donor and its application in glycosylation reactions. Their report demonstrated that the 5-*N*,7-*O*-oxazinanone group served as a powerful disarming and β-directing element for the coupling reaction of the sialyl donor.[11] As part of our continuous investigation on the fine tuning of the reactivity of sialyl donors, we have also turned our attention to the effect of cyclic carbonate within the sialyl donor on the glycosylation reaction. Herein, we report the results of the glycosylations using a homolog of Crich's 5-*N*,7-*O*-oxazinanone sialyl donor.

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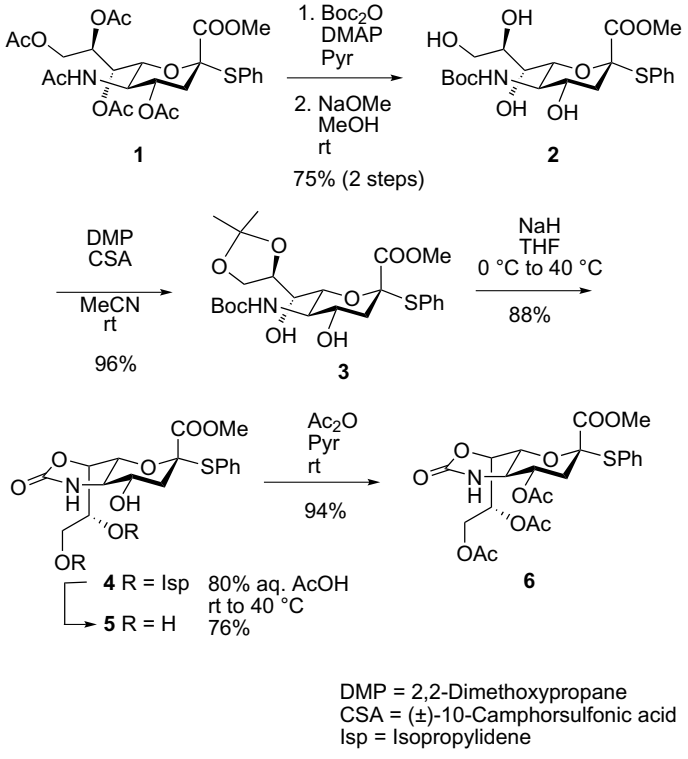
## 2. Results and discussion

### 2.1. Synthesis of sialyl donor

We have designed a phenylthioglycoside of 4,8,9-tri-*O*-acetyl-5-*N*,7-*O*-oxazinanone sialic acid (**6**) as a novel glycosyl donor to compare its donor properties with those of the corresponding 4-*O*,5-*N*-oxazolidinone derivatives reported by the De Meo[10b] and Crich groups.[10c] For the synthesis of **6**, we exploited the *N*-Boc-protected sialoside **2** as a precursor of the oxazinanone, following a reported method for synthesizing cyclic carbamates.[12] The synthesis of **6** started from the reported phenylthioglycoside of *N*-acetyl sialic acid derivative **1**[13] (Scheme 1). Thus, the Boc group was introduced at the C-5 nitrogen by the treatment of **1** with $Boc_2O$ and 4-dimethylaminopyridine in pyridine, and all acetyl groups were removed by Zemplen's method to afford *N*-Boc-protected sialoside **2** in 75% yield over the two steps. Unfortunately, the treatment of **2** with sodium hydride failed to selectively furnish the 5-*N*,7-*O*-oxazinanone structure, producing several by-products together with unreacted **2**. Therefore, **2** was treated with 2,2-dimethoxypropane and (±)-10-camphorsulfonic acid in acetonitrile to protect C-8 and C-9 hydroxyl groups as an isopropylidene acetal. The product, **3**, was again treated with 10 equiv of sodium hydride in tetrahydrofuran at 0→40 °C to produce the 5-*N*,7-*O*-oxazinanone derivative **4** in 88% yield. We have characterized 5,7-oxazinanone moiety within **4** by comparing the $^1H$ nuclear magnetic resonance (NMR) spectra of **3** and **4**. The spectra showed that the signal for C-7 in **3** was at 3.22 ppm while that in **4** was shifted downfield to 4.60 ppm. Interestingly, the ring-closing reaction exclusively afforded a six-membered ring; however, the reason underlying this process remains unclear. After the acid hydrolysis of acetonide moiety, the resulting hydroxyls were protected with acetyl groups using the conventional method to give **6** in 71% yield over the two steps

### 2.2. Glycosylation reactions

To evaluate the properties of the sialyl donor, **6** (1.0 equiv) was reacted with the known glucosyl acceptor **7** (1.0 equiv) in the presence of various glycosylation promoters for the thiosialoside donors (Table 1). Initially, glycosylation by the NIS (1.5 equiv)–TfOH (0.3 equiv) promoter system[14] at −40 °C in MeCN was explored. However, the reaction showed β-selectivity, producing a 1:3.3 mixture of the α/β-isomers of **8** in 89% yield (entry 1). On the other hand, the use of $CH_2Cl_2$ and toluene slightly improved the α-selectivity, giving an anomeric mixture in 70% (α:β = 1.1:1) and 18% (α:β = 1.6:1) yields, respectively (entries 2 and 3). The anomeric configuration of a sialyl linkage in **8** was assigned by NMR spectroscopy ($^1H$, $^{13}C$), and heteronuclear multiple bond coherence (HMBC) by comparison with the literature.[15] In addition, the H-3eq of α- and β-isomers resonated at 2.75 and 2.57 ppm, respectively (α > β); for




**Scheme 1.** Synthesis of 5-*N*,7-*O*-carbonyl sialyl donor **6**.

H-4, the signals were assigned as 4.64 and 5.05 ppm, respectively ($\alpha < \beta$). Furthermore, the $J_{7,8}$ coupling constant of α-isomer (7.3 Hz) was greater than that of the β-isomer (3.4 Hz), which is in agreement with the reported empirical rules.[16] Although we have examined glycosylations in other solvents such as dimethylformamide and THF, a glycosylated product was not produced (entries 4 and 5). Furthermore, the use of TMSOTf (0.3 equiv) or $Cu(OTf)_2$ (1.1 equiv) as an acid partner showed no distinct enhancement of α-selectivity (18%, $\alpha:\beta = 1.4:1$; 41%, $\alpha:\beta = 1.2:1$, entries 6 and 7).

Similar results were obtained when glycosylation was promoted by PhSeOTf.[17] In MeCN–$CH_2Cl_2$, the PhSeOTf-promoted glycosylation produced the β-sialoside preferentially (38%, $\alpha:\beta = 1:2.4$, entry 8). Conversely, in $CH_2Cl_2$, the production of the α-sialoside was slightly predominant (46%, $\alpha:\beta = 1.4:1$, entry 9). On the other hand, van Boom's activation[18] ($Ph_2SO$, TTBP, $Tf_2O$) provided β-selective glycosylations when carried out both in MeCN and in $CH_2Cl_2$ (entries 10 and 11). In all the above-mentioned glycosylations, the mole quantity of the recovered sialyl donor **6** was almost consistent with that of the recovered acceptor **7**. The β-selectivity of glycosidation of **6** in MeCN is in agreement with the previous results of the 5-*N*,7-O-oxazinanone sialyl donor reported by Crich and coworkers.[11] In the above-mentioned cases of entries 3–11, the low yields of glycosylated products were attributed to the incomplete activation of **6**.

Finally, as a result of broad screening of promoter systems for sialylation, a modified Ellervik's system[19] (2.0 equiv of IBr and 3.0 equiv of $AgClO_4{\cdot}H_2O$) was proven to be highly effective in promoting the glycosidation of **6**. The modified system could complete the glycosylation of **7** with **6** in $CH_2Cl_2$ at −94 °C within 30 min to give a mixture of α:β-isomers of **8** ($\alpha:\beta = 1.2:1$) in 70% yield. In contrast, the reaction using the original promotor system (IBr and AgOTf) took 95 h to complete at temperatures between −40 °C and room temperature, producing a 1:1 α:β-mixture in 56% yield (entries 12 and 13). In EtCN, β-sialoside production was again predominant and afforded a 1:20 mixture in 21% yield (entry 14). With the modified promoter system, temperature had a small effect on α-selectivity; at −60 °C, the reaction produced a 1.3:1 mixture of **8** in 58% yield (entry 15). In addition, the corresponding 2,3-en derivative of **6** was obtained as the major by-product, which was not obtained in entries 1–11.

On the basis of these results, we chose the modified Ellervik's system for subsequent coupling reactions with a series of acceptors (Table 2). The anomeric configurations of glycosides were determined using the HMBC technique. The sialylation of the C-6 primary hydroxyl of 1,2:3,4-diacetone-galactose **9** afforded the corresponding disaccharide **14** in 83% yield as a 1:1 mixture of stereoisomers (entry 1). Analogously, along with the 4,6-dihydroxy galactoside derivative **10**, the (2→6)-sialylated product **15** was obtained as a 1:1 mixture (entry 2). In the case of the coupling with secondary hydroxyl groups, the stereoselectivity varied depending on the structure of the acceptors. Thus, **6** was glycosylated with 2-adamantanol with the optimum α-selectivity to produce a 1.8:1 mixture of α:β sialoside **16** in 38% yield (entry 3). A similar result was obtained in the case of sialylation with the galactosyl acceptor **12** containing a free 3,4-diol; a mixture of α:β-isomers of the (2→3)-linked disaccharide **17** in a ratio of 1.8:1 was produced in 35% yield (entry 4). Conversely, the 2,4,6-tribenzylated analog **13** was sialylated nonstereoselectively (entry 5).

### 2.3. Conclusions

We have synthesized the 5-*N*,7-*O*-carbonyl sialyl donor **6** and described a regioselective ring-closing reaction. The fused 5-*N*,7-*O*-oxazolidinone ring within this sialyl donor exerted a negative effect on nitrile solvent-assisted α-selective sialylation. In non-participative solvents such as $CH_2Cl_2$, the modified Ellervik's system (IBr and $AgClO_4{\cdot}H_2O$) was proven to be highly effective in promoting the glycosidation of **6**. However, good α-selectivity could not be achieved.

## 3. Experimental

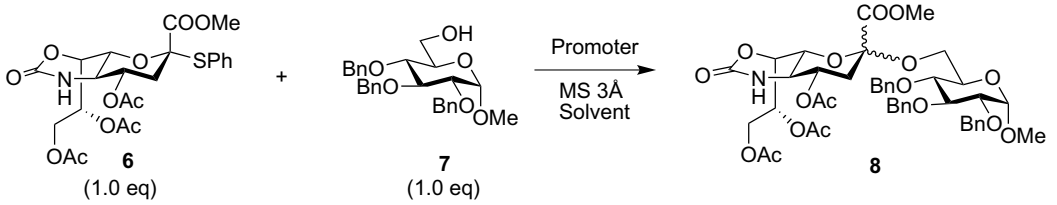
### 3.1. General procedures

$^1H$ and $^{13}C$ NMR spectra were taken by Varian Unity INOVA 400, 500, Jeol ECX 400P, and ECA 500, 600. Chemical shifts are expressed in ppm ($\delta$) relative to the signal of either $CHCl_3$ or $Me_4Si$, adjusted to 7.26 or 0.00 ppm, respectively. MALDI-TOF MS spectra were recorded in positive ion mode on a Brucker Autoflex with the use of α-cyano-4-hydroxy-cinnamic acid (CHCA) as a matrix. Molecular sieves were purchased from Wako Chemicals Inc. and dried at 300 °C for 2 h in muffle furnace prior to use. Reaction solvents were dried over molecular sieves and used without purification. TLC analysis was performed on Merck TLC (Silica Gel $60F_{254}$ on glass plate). Silica Gel 60N (spherical, neutral) manufactured by Kanto Chemical Co. Inc. was used for flash column chromatography. The quantity of silica gel was usually estimated as 100- to 150-fold weight of sample to be charged. Solvent systems in chromatography are specified in v/v. Evaporation and condensation were carried out in vacuo.

### 3.2. Methyl (phenyl 5-*tert*-butoxycarbonylamino-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosid)onate (2)

A mixture of methyl (phenyl 5-acetamido-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosid)onate **1**

**Table 1.** Glycosidations of sialyl donor **6** with glucosyl acceptor **7** under various conditions




| Entry | Promoter | Solvent | Temp (°C) | Time | Yield (%) | α:β[a] |
|---|---|---|---|---|---|---|
| 1 | NIS (1.5 equiv)<br>TfOH (0.3 equiv) | $CH_3CN$ | −40 | 4 h | 89 | 1:3.3 |
| 2 | NIS (1.5 equiv)<br>TfOH (0.3 equiv) | $CH_2Cl_2$ | −40 | 4 h | 70 | 1.1:1 |
| 3 | NIS (1.5 equiv)<br>TfOH (0.3 equiv) | Toluene | −40 | 98 h | 18 | 1.6:1 |
| 4 | NIS (1.5 equiv)<br>TfOH (0.3 equiv) | DMF | −40 to rt | 24 h | 0 | — |
| 5 | NIS (1.5 equiv)<br>TfOH (0.3 equiv) | THF | −40 to rt | 24 h | 0 | — |
| 6 | NIS (1.5 equiv)<br>TMSOTf (0.3 equiv) | $CH_2Cl_2$ | −40 to rt | 36 h | 18 | 1.4:1 |
| 7 | NIS (1.5 equiv)<br>$Cu(OTf)_2$ (1.1 equiv) | $CH_2Cl_2$ | −40 to rt | 36 h | 41 | 1.2:1 |
| 8 | PhSeBr (3.0 equiv)<br>AgOTf (3.0 equiv) | $CH_3CN$–$CH_2Cl_2$ (1:2) | −80 to rt | 24 h | 38 | 1:2.4 |
| 9 | PhSeBr (3.0 equiv)<br>AgOTf (3.0 equiv) | $CH_2Cl_2$ | −80 to rt | 24 h | 46 | 1.4:1 |
| 10 | $Ph_2SO$ (3.0 equiv)<br>$Tf_2O$ (1.1 equiv)<br>TTBP (2.0 equiv) | $CH_2Cl_2$ | −80 to rt | 24 h | 38 | 1:4.5 |
| 11 | $Ph_2SO$ (3.0 equiv)<br>$Tf_2O$ (1.1 equiv)<br>TTBP (2.0 equiv) | $CH_3CN$–$CH_2Cl_2$ (1:3) | −80 to rt | 24 h | 35 | 1:3.4 |
| 12 | IBr (2.0 equiv)<br>AgOTf (3.0 equiv) | $CH_2Cl_2$ | −40 to rt | 95 h | 56 | 1.1:1 |
| 13 | IBr (2.0 equiv)<br>$AgClO_4·H_2O$ (3.0 equiv) | $CH_2Cl_2$ | −94 | 30 min | 70 | 1.2:1 |
| 14 | IBr (2.0 equiv)<br>$AgClO_4·H_2O$ (3.0 equiv) | EtCN | −94 to rt | 20 h | 21 | 1:20 |
| 15 | IBr (2.0 equiv)<br>$AgClO_4·H_2O$ (3.0 equiv) | $CH_2Cl_2$ | −60 | 30 min | 58 | 1.3:1 |

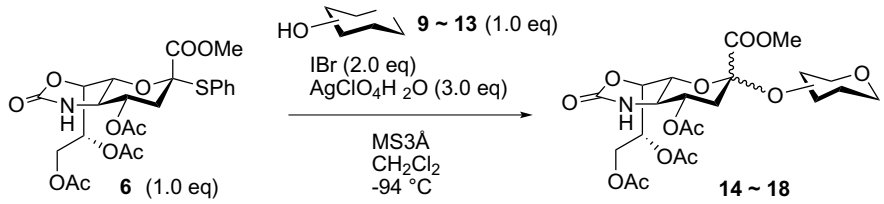
[a] Determined by $^1$H NMR analysis of the α:β mixture.

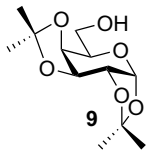
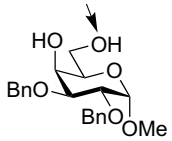
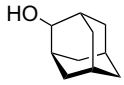
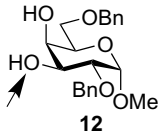
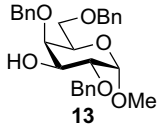
(27.4 g, 48.1 mmol), $Boc_2O$ (55.2 mL, 228 mmol), DMAP (588 mg, 4.81 mmol), and $NEt_3$ (4.9 mL, 35.2 mmol) in THF (200 mL) was heated at reflux for 17.5 h under an Ar atmosphere. The progress of the reaction was monitored by TLC ($CHCl_3$–MeOH 10:1). After cooling to rt, the reaction mixture was concentrated, extracted with EtOAc, washed with 2 M HCl, satd aq $NaHCO_3$, and brine, dried over $Na_2SO_4$, and concentrated. The residue was purified via chromatography on a short column of silica gel (EtOAc–hexane 1:3→3:2) to give a crude syrup, which was then exposed to high vacuum for 12 h. The dried syrup was dissolved in MeOH (200 mL), and 25% NaOMe in MeOH (1.04 g, 4.81 mmol) was added at rt under an Ar atmosphere. After stirring for 11 h, the mixture was acidified with Dowex ($H^+$) and filtered. The filtrate was concentrated and the residue obtained was dissolved in a minimum quantity of MeOH, and precipitated with $Et_2O$ to afford **2** as an amorphous mass (17.2 g, 75%): $[\alpha]_D$ +82.0 (*c* 0.3, $CH_3OH$); $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.56–7.34 (m, 5H, Ph), 4.86 (1H, NH), 3.80 (m, 2H), 3.63–3.47 (m, 7H), 3.34 (m, 1H), 2.84 (dd, 1H, $J_{3eq,4} = 4.6$, Hz, $J_{gem} = 12.9$ Hz, H-3eq), 1.85 (dd, 1H, $J_{3ax,4} = 11.0$ Hz, H-3ax), 1.43 (s, 9H, –$C(CH_3)_3$); $^{13}$C NMR (100 MHz, $CD_3OD$) $\delta$ 171.0, 159.5, 137.8, 131.1, 130.1, 129.8, 87.8, 80.9, 77.8, 73.0, 70.2, 68.9, 64.5, 54.3, 53.3, 41.8, 28.7; MALDI-TOFMS *m*/*z* calcd for $[C_{21}H_{31}NO_8S+K]^+$: 496.14. Found: 496.14.

### 3.3. Methyl (phenyl 5-*tert*-butoxycarbonylamino-8,9-isopropylidene-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosid)onate (3)

To a solution of compound **2** (4.70 g, 9.93 mmol) in MeCN (100 mL) were added DMP (1.41 mL, 11.5

**Table 2.** Glycosidations of sialyl donor **6** with various acceptors




| Entry | Acceptor[a] | Time (min) | Product | Yield (%) | α:β[b] |
|---|---|---|---|---|---|
| 1 |  **9** | 15 | **14** | 83 | 1:1 |
| 2 |  **10** | 20 | **15** | 62 | 1:1 |
| 3 |  **11** | 15 | **16** | 38 | 1.8:1 |
| 4 |  **12** | 15 | **17** | 35[c] | 1.8:1[c] |
| 5 |  **13** | 15 | **18** | 38 | 1:1 |

[a] Arrows point to the glycosylation site.
[b] Determined by $^1$H NMR analysis of the α:β mixture.
[c] Determined after the acetylation of the α:β mixture.

mmol) and CSA (188 mg, 810 μmol) at rt under an Ar atmosphere. The progress of the reaction was monitored by TLC ($CHCl_3$–MeOH 10:1). After stirring for 10 min, the reaction mixture was quenched by the addition of $NEt_3$, and concentrated. The residue was purified by column chromatography on silica gel ($CHCl_3$–MeOH, 90:1) to give **3** as white foam (4.90 g, 96%): $[\alpha]_D$ −6.3 (*c* 0.5, $CHCl_3$); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.53–7.34 (m, 5H, Ph), 6.71 (d, 1H, $J_{5,NH} = 8.7$ Hz, NH), 5.08 (d, 1H, $J = 6.0$ Hz, –OH), 4.51 (d, 1H, $J_{5,6} = 6.4$ Hz, H-6), 4.03 (q, 1H, $J_{7,8} = J_{8,9a} = J_{8,9b} = 6.6$ Hz, H-8), 3.87 (t, 1H, $J_{gem} = 7.2$ Hz, H-9a), 3.76 (t, 1H, H-9b), 3.46–3.22 (m, 6H, H-4, H-5, H-7, COOMe), 2.57 (dd, 1H, $J_{3eq,4} = 4.3$ Hz, $J_{gem} = 12.5$ Hz, H-3eq), 1.61 (dd, 1H, $J_{3ax,4} = 11.9$ Hz, H-3ax), 1.37 (s, 9H, –$C(CH_3)_3$), 1.26, 1.17 (2s, 6H, –$C(CH_3)_2$); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 168.5, 156.3, 136.0, 129.6, 129.2, 128.6, 107.7, 86.7, 78.0, 76.3, 75.1, 69.3, 66.5, 52.6, 51.9, 41.0, 28.2, 26.7, 25.4; MALDI-TOFMS *m*/*z* calcd for $[C_{24}H_{35}NO_8S+K]^+$: 536.17. Found: 536.20.

### 3.4. Methyl (phenyl 5-amino-5-*N*,7-*O*-carbonyl-8,9-isopropylidene-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosid)onate (4)

To a solution of compound **3** (4.90 g, 9.54 mmol) in THF (500 mL) was added 60% NaH (3.82 g, 95.5 mmol) portion-wise at 0 °C under an Ar atmosphere, then the

reaction mixture was stirred at 40 °C for 27 h. The progress of the reaction was monitored by TLC ($CHCl_3$–MeOH 10:1). After cooling to 0 °C, the reaction mixture was quenched by the addition of AcOH, and the solution was extracted with EtOAc, and washed with $H_2O$ and brine. The organic layer was dried over $Na_2SO_4$, concentrated, and purified by column chromatography on silica gel ($CHCl_3$–MeOH 100:1→50:1) to give **4** as a colorless syrup (3.68 g, 88%): $[\alpha]_D$ +43.1 (*c* 0.9, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.57–7.30 (m, 5H, Ph), 7.17 (s, 1H, NH), 4.60 (t, 1H, $J_{6,7} = J_{7,8} = 5.3$ Hz, H-7), 4.48 (q, 1H, $J_{8,9a} = J_{8,9b} = 6.2$ Hz, H-8), 4.33 (br s, 1H, –OH), 4.13–4.03 (m, 2H, H-9a, H-9b), 3.67 (dd, 1H, $J_{5,6} = 10.3$ Hz, H-6), 3.58 (s, 3H, COOMe), 3.54 (m, 1H, H-4), 3.25 (t, 1H, $J_{4,5} = 9.8$ Hz, H-5), 2.85 (dd, 1H, $J_{3eq,4} = 4.3$ Hz, $J_{gem} = 13.5$ Hz, H-3eq), 1.79 (dd, 1H, $J_{3ax,4} = 11.5$ Hz, H-3ax), 1.53 and 1.44 (2s, 6H, –$C(CH_3)_2$); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 168.6, 153.1, 136.5, 130.0, 128.7, 128.6, 110.1, 88.6, 76.1, 74.4, 69.4, 68.8, 65.7, 54.0, 52.9, 26.4, 25.6; MALDI-TOFMS *m*/*z* calcd for $[C_{20}H_{25}NO_8S+Na]^+$: 462.11. Found: 462.49.

### 3.5. Methyl (phenyl 5-amino-5-*N*,7-*O*-carbonyl-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosid)onate (5)

A suspension of compound **4** (575 mg, 1.31 mmol) in 80% AcOH (13 mL) was stirred at 40 °C for 1.5 h. The progress of the reaction was monitored by TLC ($CHCl_3$–MeOH 5:1). After cooling to rt, the reaction mixture was co-evaporated with MeOH. The residue was purified by column chromatography on silica gel ($CHCl_3$–MeOH, 20:1→10:1) to give **5** as a colorless syrup (400 mg, 76%): $[\alpha]_D$ +77.7 (*c* 0.4, $CH_3OH$); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.51–7.36 (m, 5H, Ph), 7.14 (s, 1H, NH), 5.34 (m, 2H, H-7, –OH), 4.71 (t, 1H, $J_{8,9a} = J_{gem} = 4.8$ Hz, H-9a), 4.32 (t, 1H, $J_{5,6} = J_{6,7} = 4.1$ Hz, H-6), 3.96 (m, 1H, H-8), 3.66–3.52 (m, 2H, H-5, H-9b), 3.50 (s, 3H, COOMe), 3.31 (m, 1H, H-4), 2.60 (dd, 1H, $J_{3eq,4} = 4.1$ Hz, $J_{gem} = 12.8$ Hz, H-3eq), 1.62 (dd, 1H, $J_{3ax,4} = 12.2$ Hz, H-3ax); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 168.0, 151.7, 135.9, 129.9, 128.9, 128.6, 88.0, 74.9, 73.7, 70.4, 68.3, 62.4, 54.1, 52.6; MALDI-TOFMS *m*/*z* calcd for $[C_{17}H_{21}NO_8S+K]^+$: 438.06. Found: 438.77.

### 3.6. Methyl (phenyl 4,8,9-tri-*O*-acetyl-5-amino-5-*N*,7-*O*-carbonyl-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosid)onate (6)

To a solution of compound **5** (78 mg, 195 mmol) in pyridine (1.0 mL) was added $Ac_2O$ (0.5 mL) at rt under an Ar atmosphere. The progress of the reaction was monitored by TLC ($CHCl_3$–MeOH 10:1). After stirring for 3.5 h, the reaction mixture was quenched by the addition of MeOH, and concentrated with toluene. The residue was extracted with EtOAc, and washed with 2 M HCl, satd $NaHCO_3$, and brine. The organic layer was dried over $Na_2SO_4$, and concentrated. The resulting residue was purified by column chromatography on silica gel (EtOAc–Hexane 4:3) to give **6** as a colorless syrup (96 mg, 94%): $[\alpha]_D$ +37.5 (*c* 0.7, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.50–7.32 (m, 6H, NH, Ph), 5.64 (m, 1H, H-8), 4.65 (m, 2H, H-4, H-7), 4.49 (dd, 1H, $J_{8,9a} = 3.0$ Hz, $J_{gem} = 12.0$ Hz, H-9a), 4.33 (dd, 1H, $J_{8,9b} = 6.0$ Hz, H-9b), 3.90 (dd, 1H, $J_{5,6} = 10.8$ Hz, $J_{6,7} = 4.9$ Hz, H-6), 3.77 (dd, 1H, $J_{4,5} = 10.0$ Hz, H-5), 3.51 (s, 3H, COOMe), 2.94 (dd, 1H, $J_{3eq,4} = 4.6$ Hz, $J_{gem} = 14.6$ Hz, H-3eq), 2.20, 2.11 and 2.10 (3s, 9H, 3 Ac), 1.81 (dd, 1H, $J_{3ax,4} = 11.4$ Hz, H-3ax); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 170.4, 169.9, 167.3, 151.5, 135.7, 129.9, 128.8, 128.7, 88.9, 77.2, 72.8, 70.3, 70.0, 68.0, 62.9, 52.8, 50.6, 36.7, 21.2, 20.8, 20.6; MALDI-TOFMS *m*/*z* calcd for $[C_{23}H_{28}NO_{11}S+H]^+$: 526.13. Found: 526.14.

### 3.7. General procedure for the glycosylation with 6 under the promotion of IBr–$AgClO_4$·$H_2O$

A mixture of compound **6** (100 μmol), acceptor (100 μmol), $AgClO_4$·$H_2O$ (300 μmol), and activated 3 Å molecular sieves (500 mg) in $CH_2Cl_2$ (2.0 mL) was stirred for 1 h at rt under an Ar atmosphere in the dark, and then cooled to −94 °C. After stirring for 30 min, a 1.0 M solution of IBr in $CH_2Cl_2$ (200 μmol) was added dropwise, and the mixture was stirred for 15 min. The reaction mixture was diluted with EtOAc, warmed to ambient temperature, and quenched by the addition of satd aq $NaHCO_3$. After stirring vigorously for 10 min, the mixture was filtered through a pad of Celite. The combined filtrate and washings were washed with satd aq $Na_2S_2O_3$ and brine. The organic layer was dried over $Na_2SO_4$ and concentrated. The residue was purified on Sephadex LH-20 to give an anomeric mixture of glycosidated product, which was then separated by column chromatography on silica gel.

### 3.8. Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(methyl 4,8,9-tri-*O*-acetyl-5-amino-5-*N*,7-*O*-carbonyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-α-D-glucopyranoside (8α)

$[\alpha]_D$ +29.5 (*c* 1.3, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.34–7.24 (m, 15H, 3 Ph), 6.12 (s, 1H, NH), 5.57 (m, 1H, H-8$^{Neu}$), 4.97 (d, 1H, –C$H_2$Ph), 4.87 (d, 1H, –C$H_2$Ph), 4.78 (2d, 2H, 2 –C$H_2$Ph), 4.72 (dd, 1H, $J_{6,7} = 5.2$ Hz, $J_{7,8} = 7.3$ Hz, H-7$^{Neu}$), 4.64 (m, 2H, H-4$^{Neu}$, H-9a$^{Neu}$), 4.51 (d, 1H, –C$H_2$Ph), 4.46 (m, 2H, H-1$^{Glc}$, –C$H_2$Ph), 4.23 (dd, 1H, $J_{8,9b} = 5.7$ Hz, $J_{gem} = 12.0$ Hz, H-9b$^{Neu}$), 4.02 (dd, 1H, $J_{5,6} = 10.3$ Hz, $J_{6,7} = 5.1$ Hz, H-6$^{Neu}$), 3.95 (t, 1H, $J_{2,3} = J_{3,4} = 9.2$ Hz,

H-3$^{Glc}$), 3.75–3.63 (m, 7H, H-5$^{Neu}$, COOMe, H-5$^{Glc}$, H-6a$^{Glc}$, H-6b$^{Glc}$), 3.44 (dd, 1H, $J_{1,2} = 3.5$ Hz, H-2$^{Glc}$), 3.33 (m, 4H, H-4$^{Glc}$, –OMe), 2.75 (dd, 1H, $J_{3eq,4} = 4.6$ Hz, $J_{gem} = 13.2$ Hz, H-3eq$^{Neu}$), 2.10, 2.05, 2.00 (3s, 9H, 3 Ac), 1.71 (dd, 1H, $J_{3ax,4} = 12.3$ Hz, H-3ax$^{Neu}$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 170.4, 169.9, 167.4, 150.7, 138.5, 138.1, 128.5, 128.4, 128.1, 128.0, 127.8, 127.7, 127.6, 100.3, 97.8, 81.9, 79.8, 77.8, 75.8, 74.9, 73.4, 73.0, 70.7, 69.4, 68.2, 64.3, 62.7, 55.0, 53.0, 51.2, 36.2, 20.8, 20.7, 20.6; MALDI-TOFMS *m/z* calcd for $[C_{45}H_{53}NO_{17}+Na]^+$: 902.32. Found: 902.31.

### 3.9. Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(methyl 4,8,9-tri-*O*-acetyl-5-amino-5-*N*,7-*O*-carbonyl-3,5-dideoxy-D-*glycero*-β-D-*galacto*-2-nonulopyranosylonate)-α-D-glucopyranoside (8β)

$[\alpha]_D$ +32.1 (*c* 2.0, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.38–7.26 (m, 15H, 3 Ph), 6.80 (s, 1H, NH), 5.59 (m, 1H, H-8$^{Neu}$), 5.05 (dt, 1H, $J_{3eq,4} = 4.8$ Hz, $J_{3ax,4} = J_{4,5} = 10.3$ Hz, H-4$^{Neu}$), 4.96 (d, 1H, –C$H_2$Ph), 4.91 (d, 1H, –C$H_2$Ph), 4.79 (d, 1H, –C$H_2$Ph), 4.76 (d, 1H, –C$H_2$Ph), 4.64 (2d, 2H, 2 –C$H_2$Ph), 4.61 (d, 1H, $J_{1,2} = 3.4$ Hz, H-1$^{Glc}$), 4.48 (m, 2H, H-7$^{Neu}$, H-9a$^{Neu}$), 4.28 (m, 2H, H-6$^{Neu}$, H-9b$^{Neu}$), 3.96 (t, 1H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H-3$^{Glc}$), 3.77–3.62 (m, 7H, H-5$^{Neu}$, COOMe, H-5$^{Glc}$, H-6a$^{Glc}$, H-6b$^{Glc}$), 3.55 (m, 2H, H-2$^{Glc}$, H-4$^{Glc}$), 3.36 (s, 3H, –OMe), 2.57 (dd, 1H, $J_{3eq,4} = 4.6$ Hz, $J_{gem} = 13.0$ Hz, H-3eq$^{Neu}$), 2.11, 2.10, 2.07 (3s, 9H, 3 Ac), 1.68 (dd, 1H, $J_{3ax,4} = 12.0$ Hz, H-3ax$^{Neu}$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 170.4, 170.3, 170.1, 166.5, 150.6, 138.4, 138.0, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.7, 127.6, 99.0, 98.1, 81.8, 80.4, 75.8, 74.9, 73.5, 72.9, 70.5, 69.2, 67.7, 65.4, 63.0, 62.3, 55.3, 52.7, 51.3, 36.1, 20.9, 20.7; MALDI-TOFMS *m/z* calcd for $[C_{45}H_{53}NO_{17}+Na]^+$: 902.32. Found: 902.34.

### 3.10. 1,2:3,4-Diisopropylidene-6-*O*-(methyl 4,8,9-tri-*O*-acetyl-5-amino-5-*N*,7-*O*-carbonyl-3,5-dideoxy-D-*glycero*-D-*galacto*-2-nonulopyranosylonate)-α-D-galactose (14)

**3.10.1. α-Isomer.** $[\alpha]_D$ −9.7 (*c* 1.1, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.99 (s, 1H, NH), 5.58 (m, 1H, H-8$^{Neu}$), 5.45 (d, 1H, $J_{1,2} = 5.0$ Hz, H-1$^{Gal}$), 4.69 (m, 2H, H-4$^{Neu}$, H-7$^{Neu}$), 4.57 (dd, 1H, $J_{2,3} = 7.8$ Hz, $J_{3,4} = 2.3$ Hz, H-3$^{Gal}$), 4.48 (dd, 1H, $J_{8,9a} = 3.0$ Hz, $J_{gem} = 12.1$ Hz, H-9a$^{Neu}$), 4.27 (m, 2H, H-9b$^{Neu}$, H-2$^{Gal}$), 4.16 (dd, 1H, $J_{4,5} = 7.8$ Hz, H-4$^{Gal}$), 4.06 (dd, 1H, $J_{5,6} = 10.5$ Hz, $J_{6,7} = 5.0$ Hz, H-6$^{Neu}$), 3.84 (m, 4H, COOMe, H-5$^{Gal}$), 3.75 (m, 2H, H-5$^{Neu}$, H-6a$^{Gal}$), 3.56 (dd, 1H, $J_{5,6b} = 5.9$ Hz, $J_{gem} = 9.6$ Hz, H-6b$^{Gal}$), 2.78 (dd, 1H, $J_{3eq,4} = 4.5$ Hz, $J_{gem} = 13.2$ Hz, H-3eq$^{Neu}$), 2.11, 2.10, 2.08 (3s, 9H, 3 Ac), 1.78 (dd, 1H, $J_{3ax,4} = 11.5$ Hz, H-3ax$^{Neu}$), 1.50, 1.39 and 1.31 (3s, 12H, 2 –C(C$H_3$)$_2$); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.7, 170.6, 170.0, 167.8, 151.6, 109.4, 108.7, 100.3, 96.3, 72.9, 70.9, 70.6, 70.5, 68.4, 66.6, 64.0, 62.8, 53.1, 51.1, 36.6, 26.1, 26.0, 25.0, 24.6, 21.0, 20.9, 20.8; MALDI-TOFMS *m/z* calcd for $[C_{29}H_{41}NO_{17}+Na]^+$: 698.22. Found: 698.29.

**3.10.2. β-Isomer.** $[\alpha]_D$ −8.8 (*c* 1.0, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.85 (s, 1H, NH), 5.60 (m, 1H, H-8$^{Neu}$), 5.49 (d, 1H, $J_{1,2} = 5.1$ Hz, H-1$^{Gal}$), 4.97 (dt, 1H, $J_{3eq,4} = 4.4$ Hz, $J_{3ax,4} = J_{4,5} = 10.2$ Hz, H-4$^{Neu}$), 4.64 (dd, 1H, $J_{2,3} = 7.8$ Hz, $J_{3,4} = 2.3$ Hz, H-3$^{Gal}$), 4.57 (m, 1H, H-6$^{Neu}$, H-7$^{Neu}$), 4.49 (dd, 1H, $J_{8,9a} = 3.0$ Hz, $J_{gem} = 12.1$ Hz, H-9a$^{Neu}$), 4.33 (m, 2H, H-2$^{Gal}$, H-4$^{Gal}$), 4.28 (dd, 1H, $J_{8,9b} = 5.5$ Hz, H-9b$^{Neu}$), 4.03 (m, 1H, H-5$^{Gal}$), 3.75 (m, 5H, H-5$^{Neu}$, COOMe, H-6a$^{Gal}$), 3.42 (dd, 1H, $J_{5,6b} = 5.2$ Hz, $J_{gem} = 8.0$ Hz, H-6b$^{Gal}$), 2.57 (dd, 1H, $J_{gem} = 13.0$ Hz, H-3eq$^{Neu}$), 2.11, 2.09 and 2.08 (3s, 9H, 3 Ac), 1.66 (dd, 1H, H-3ax$^{Neu}$), 1.57, 1.45, 1.34, 1.33 (4s, 12H, 2 –C(C$H_3$)$_2$); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.4, 170.1, 166.5, 151.2, 109.2, 108.7, 99.0, 96.1, 72.7, 70.6, 70.5, 70.3, 67.5, 67.3, 64.9, 62.9, 60.8, 52.7, 5.07, 36.1, 26.0, 25.7, 24.8, 23.9, 20.8, 20.6; MALDI-TOFMS *m/z* calcd for $[C_{29}H_{41}NO_{17}+Na]^+$: 698.22. Found: 698.24.

### 3.11. Methyl 2,3-di-*O*-benzyl-6-*O*-(methyl 4,8,9-tri-*O*-acetyl-5-amino-5-*N*,7-*O*-carbonyl-3,5-dideoxy-D-*glycero*-D-*galacto*-2-nonulopyranosylonate)-α-D-galactopyranoside (15)

**3.11.1. α-Isomer.** $[\alpha]_D$ +29.4 (*c* 0.8, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36–7.26 (m, 10H, 2Ph), 6.84 (s, 1H, NH), 5.58 (m, 1H, H-8$^{Neu}$), 4.79 (m, 2H, 2 –C$H_2$Ph), 4.67 (m, 4H, H-4$^{Neu}$, H-7$^{Neu}$, 2 –C$H_2$Ph), 4.58 (d, 1H, $J_{1,2} = 3.2$ Hz, H-1$^{Gal}$), 4.46 (dd, 1H, $J_{8,9a} = 3.0$ Hz, $J_{gem} = 12.1$ Hz, H-9a$^{Neu}$), 4.25 (dd, 1H, $J_{8,9b} = 5.9$ Hz, H-9b$^{Neu}$), 4.06 (dd, 1H, $J_{5,6} = 10.5$ Hz, $J_{6,7} = 5.0$ Hz, H-6$^{Neu}$), 3.94 (br s, 1H, H-4$^{Gal}$), 3.86-3.68 (m, 8H, H-5$^{Neu}$, COOMe, H-2$^{Gal}$, H-3$^{Gal}$, H-5$^{Gal}$, H-6a$^{Gal}$), 3.58 (dd, 1H, $J_{5,6b} = 5.5$ Hz, $J_{gem} = 9.1$ Hz, H-6b$^{Gal}$), 3.32 (s, 3H, –OMe), 2.75 (dd, 1H, $J_{3eq,4} = 4.7$ Hz, $J_{gem} = 13.0$ Hz, H-3eq$^{Neu}$), 2.44 (s, 1H, –OH$^{Gal}$), 2.10, 2.07 and 2.06 (3s, 9H, 3 Ac), 1.73 (dd, 1H, $J_{3ax,4} = 11.9$ Hz, H-3ax$^{Neu}$); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.5, 170.4, 169.8, 167.6, 151.3, 138.2, 138.0, 128.5, 128.4, 128.0, 127.9, 127.8, 127.7, 100.1, 98.3, 75.6, 73.5, 72.9, 72.8, 70.2, 68.3, 68.2, 67.8, 67.4, 63.9, 62.6, 55.2, 53.2, 51.1, 36.3, 20.7, 20.6; MALDI-TOFMS *m/z* calcd for $[C_{38}H_{47}NO_{17}+Na]^+$: 812.27. Found: 812.31.

**3.11.2. β-Isomer.** $[\alpha]_D$ +13.5 (*c* 1.1, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36–7.26 (m, 11H, NH, 2Ph), 5.58 (m, 1H, H-8$^{Neu}$), 5.03 (dt, 1H, $J_{3eq,4} = 4.6$ Hz, $J_{3ax,4} = J_{4,5} = 10.5$ Hz, H-4$^{Neu}$), 4.75 (m, 3H, 3 –C$H_2$Ph), 4.63 (m, 3H, H-7$^{Neu}$, H-1$^{Gal}$, –C$H_2$Ph), 4.46 (dd, 1H, $J_{8,9a} = 3.0$ Hz, $J_{gem} = 12.2$ Hz, H-9a$^{Neu}$), 4.26

(m, 2H, H-6$^{Neu}$, H-9b$^{Neu}$), 4.01 (br s, 1H, H-4$^{Gal}$), 3.86–3.68 (m, 8H, H-5$^{Neu}$, COOMe, H-2$^{Gal}$, H-3$^{Gal}$, H-5$^{Gal}$, H-6a$^{Gal}$), 3.38 (dd, 1H, $J_{5,6b} = 5.9$ Hz, $J_{gem} = 8.7$ Hz, H-6b$^{Gal}$), 3.34 (s, 3H, –OMe), 3.21 (s, 1H, –OH$^{Gal}$), 2.34 (dd, 1H, $J_{gem} = 13.2$ Hz, H-3eq$^{Neu}$), 2.12, 2.09 and 2.08 (3s, 9H, 3 Ac), 1.73 (dd, 1H, H-3ax$^{Neu}$); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.1, 170.4, 170.0, 166.5, 151.9, 138.3, 138.1, 128.5, 128.3, 128.0, 127.8, 127.7, 127.6, 99.2, 98.6, 77.5, 75.4, 73.5, 72.7, 72.6, 70.0, 67.5, 66.8, 66.6, 65.5, 62.7, 61.1, 55.4, 52.7, 51.0, 36.2, 21.0, 20.8, 20.7; MALDI-TOFMS *m/z* calcd for $[C_{38}H_{47}NO_{17}+Na]^+$: 812.27. Found: 812.32.

### 3.12. Methyl (2-adamantyl 4,8,9-tri-*O*-acetyl-5-amino-5-*N*,7-*O*-carbonyl-3,5-dideoxy-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (16)

**3.12.1. α-Isomer.** $[\alpha]_D$ +23.2 (*c* 0.6, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.81 (s, 1H, NH), 5.60 (m, 1H, H-8), 4.73 (t, 1H, $J_{6,7} = J_{7,8} = 5.8$ Hz, H-7), 4.76 (m, 1H, H-4), 4.43 (dd, 1H, $J_{8,9a} = 3.5$ Hz, $J_{gem} = 12.1$ Hz, H-9a), 4.24 (dd, 1H, $J_{8,9b} = 6.9$ Hz, H-9b), 3.96 (m, 2H, H-6, Adam), 3.83 (s, 3H, COOMe), 3.68 (t, 1H, $J_{4,5} = J_{5,6} = 10.0$ Hz, H-5), 2.87 (dd, 1H, $J_{3eq,4} = 4.6$ Hz, $J_{gem} = 13.2$ Hz, H-3eq), 2.12, 2.08 and 2.07 (3s, 9H, 3 Ac), 2.03–1.43 (m, 15H, H-3ax, Adam); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 170.7, 170.5, 169.6, 168.6, 151.6, 100.5, 78.0, 74.0, 70.6, 69.5, 68.0, 62.6, 53.0, 53.0, 51.7, 37.5, 37.4, 36.7, 34.1, 33.0, 31.5, 31.5, 27.2, 26.9, 21.0, 20.9, 20.8; MALDI-TOFMS *m/z* calcd for $[C_{27}H_{37}NO_{12}+Na]^+$: 590.22. Found: 590.22.

**3.12.2. β-Isomer.** $[\alpha]_D$ +8.5 (*c* 0.4, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.53 (s, 1H, NH), 5.60 (m, 1H, H-8), 5.09 (dt, 1H, $J_{3eq,4} = 4.6$ Hz, $J_{3ax,4} = J_{4,5} = 10.5$ Hz, H-4), 4.60 (t, 1H, $J_{6,7} = 5.2$ Hz, $J_{7,8} = 8.6$ Hz, H-7), 4.49 (dd, 1H, $J_{8,9a} = 2.8$ Hz, $J_{gem} = 12.0$ Hz, H-9a), 4.29 (dd, 1H, $J_{8,9b} = 5.7$ Hz, H-9b), 4.20 (dd, 1H, $J_{5,6} = 10.3$ Hz, H-6), 3.77 (m, 2H, H-5, Adam), 3.73 (s, 3H, COOMe), 2.68 (dd, 1H, $J_{gem} = 12.9$ Hz, H-3eq), 2.13, 2.11 and 2.09 (3s, 9H, 3 Ac), 1.85–1.47 (m, 15H, H-3ax, Adam); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 170.6, 170.5, 170.3, 167.7, 151.1, 99.7, 78.6, 73.0, 70.6, 67.9, 66.4, 63.1, 52.5, 51.4, 37.3, 37.2, 36.8, 36.6, 34.3, 32.7, 31.8, 31.4, 27.1, 26.9, 21.0, 20.9, 20.8; MALDI-TOFMS *m/z* calcd for $[C_{27}H_{37}NO_{12}+Na]^+$: 590.22. Found: 590.19.

### 3.13. Methyl 4-*O*-acetyl-2,6-di-*O*-benzyl-3-*O*-(methyl 4,8,9-tri-*O*-acetyl-5-amino-5-*N*,7-*O*-carbonyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-α-D-galactopyranoside (17)

**3.13.1. α-Isomer.** $[\alpha]_D$ +33.6 (*c* 0.6, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.33–7.26 (m, 10H, 2Ph), 6.67 (s, 1H, NH), 5.59 (dt, 1H, $J_{7,8} = J_{8,9a} = 3.7$ Hz, $J_{8,9b} = 7.5$ Hz, H-8$^{Neu}$), 5.24 (d, 1H, $J_{3,4} = 3.4$ Hz, H-4$^{Gal}$) 4.79 (dt, 1H, $J_{3eq,4} = 4.4$ Hz, $J_{3ax,4} = J_{4,5} = 10.7$ Hz, H-4$^{Neu}$), 4.73 (dd, 1H, $J_{6,7} = 5.8$ Hz, H-7$^{Neu}$), 4.67 (m, 3H, H-1$^{Gal}$, 2 –C$H_2$Ph), 4.53 (m, 3H, H-3$^{Gal}$, 2 –C$H_2$Ph), 4.43 (m, 2H, H-9a$^{Neu}$, –C$H_2$Ph), 4.27 (dd, 1H, $J_{gem} = 12.0$ Hz, H-9b$^{Neu}$), 4.07 (t, 1H, $J_{5,6a} = J_{5,6b} = 5.7$ Hz, H-5$^{Gal}$), 3.86 (s, 3H, COOMe), 3.77 (dd, 1H, $J_{5,6} = 9.8$ Hz, H-6$^{Neu}$), 3.67 (dd, 1H, $J_{1,2} = 3.5$ Hz, $J_{2,3} = 10.3$ Hz, H-2$^{Gal}$), 3.64 (t, 1H, H-5$^{Neu}$), 3.47 (dd, 1H, $J_{gem} = 9.8$ Hz, H-6a$^{Gal}$), 3.42 (dd, 1H, H-6b$^{Gal}$), 3.37 (s, 3H, –OMe), 2.73 (dd, 1H, $J_{gem} = 13.4$ Hz, H-3eq$^{Neu}$), 2.07, 2.03 and 2.01 (3s, 12H, 4 Ac), 1.91 (dd, 1H, H-3ax$^{Neu}$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 170.5, 170.4, 169.9, 169.5, 167.7, 151.3, 138.1, 138.0, 128.4, 128.3, 128.0, 127.8, 127.6, 100.2, 98.5, 75.0, 74.9, 73.3, 70.9, 70.7, 70.1, 70.0, 69.0, 67.9, 67.5, 62.4, 55.3, 53.4, 51.7, 35.4, 20.9, 20.8, 20.7, 20.6; MALDI-TOFMS *m/z* calcd for $[C_{40}H_{49}NO_{18}+Na]^+$: 854.28. Found: 854.28.

**3.13.2. β-Isomer.** $[\alpha]_D$ +17.7 (*c* 0.3, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.37–7.26 (m, 10H, 2Ph), 5.75 (s, 1H, NH), 5.57 (m, 1H, H-8$^{Neu}$), 5.31 (d, 1H, $J_{3,4} = 2.3$ Hz, H-4$^{Gal}$), 4.93 (dt, 1H, $J_{3eq,4} = 4.4$ Hz, $J_{3ax,4} = J_{4,5} = 10.7$ Hz, H-4$^{Neu}$), 4.81 (dd, 1H, $J_{5,6} = 10.3$ Hz, $J_{6,7} = 5.1$ Hz, H-6$^{Neu}$), 4.68 (dd, 1H, $J_{7,8} = 8.6$ Hz, H-7$^{Neu}$), 4.63 (d, 1H, –C$H_2$Ph), 4.60 (dd, 1H, $J_{2,3} = 10.3$ Hz, H-3$^{Gal}$), 4.54 (d, 1H, $J_{1,2} = 3.4$ Hz, H-1$^{Gal}$), 4.52 (d, 1H, –C$H_2$Ph), 4.48 (dd, 1H, $J_{8,9a} = 2.8$ Hz, $J_{gem} = 12.7$ Hz, H-9a$^{Neu}$), 4.40 (2d, 2H, 2 –C$H_2$Ph), 4.27 (dd, 1H, $J_{8,9b} = 5.7$ Hz, H-9b$^{Neu}$), 4.06 (t, 1H, $J_{5,6a} = J_{5,6b} = 6.0$ Hz, H-5$^{Gal}$), 3.72 (t, 1H, H-5$^{Neu}$), 3.67 (dd, 1H, H-2$^{Gal}$), 3.54 (s, 3H, COOMe), 3.46 (dd, 1H, $J_{gem} = 9.5$ Hz, H-6a$^{Gal}$), 3.40 (dd, 1H, H-6b$^{Gal}$) 3.31 (s, 3H, –OMe), 2.73 (dd, 1H, $J_{gem} = 13.7$ Hz, H-3eq$^{Neu}$), 2.11, 2.09, 2.06, 2.01 (4s, 12H, 4 Ac), 1.71 (dd, 1H, H-3ax$^{Neu}$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 170.7, 170.5, 170.3, 170.0, 165.9, 150.7, 138.1, 137.6, 128.5, 128.4, 128.1, 127.9, 127.8, 100.3, 98.6, 75.7, 75.6, 73.5, 72.8, 70.9, 70.1, 69.9, 68.2, 67.8, 67.7, 66.2, 63.0, 55.5, 52.4, 51.0, 36.6, 20.9, 20.7, 20.6; MALDI-TOFMS *m/z* calcd for $[C_{40}H_{49}NO_{18}+Na]^+$: 854.28. Found: 854.30.

### 3.14. Methyl 2,4,6-tri-*O*-benzyl-3-*O*-(methyl 4,8,9-tri-*O*-acetyl-5-amino-5-*N*,7-*O*-carbonyl-3,5-dideoxy-D-*glycero*-D-*galacto*-2-nonulopyranosylonate)-α-D-galactopyranoside (18)

**3.14.1. α-Isomer.** $[\alpha]_D$ +24.4 (*c* 0.5, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.33–7.25 (m, 15H, 3 Ph), 6.22 (s, 1H, NH), 5.59 (m, 1H, H-8$^{Neu}$), 4.85 (d, 1H, –C$H_2$Ph), 4.79 (dt, 1H, $J_{3eq,4} = 4.6$ Hz, $J_{3ax,4} = J_{4,5} = 10.1$ Hz, H-4$^{Neu}$), 4.73 (dd, 1H, $J_{6,7} = 6.0$ Hz, $J_{7,8} = 3.2$ Hz, H-7$^{Neu}$), 4.69 (m, 2H, H-1$^{Gal}$, –C$H_2$Ph), 4.58–4.50 (3d, 3H, 3 –C$H_2$Ph), 4.41 (m, 3H, H-9a$^{Neu}$, H-3$^{Gal}$, –C$H_2$Ph), 4.15 (dd, 1H, $J_{8,9a} = 7.8$ Hz, $J_{gem} = 11.9$ Hz, H-9b$^{Neu}$),

3.90 (m, 3H, H-6$^{Neu}$, H-2$^{Gal}$, H-5$^{Gal}$), 3.82 (s, 3H, COOMe), 3.76 (m, 1H, H-4$^{Gal}$), 3.70 (dd, 1H, $J_{4,5} = J_{5,6}$ =10.1 Hz, H-5$^{Neu}$), 3.54 (dd, 1H, $J_{5,6a} = 6.8$ Hz, $J_{gem} = 9.6$ Hz, H-6a$^{Gal}$), 3.46 (dd, 1H, $J_{5,6b} = 5.0$ Hz, H-6b$^{Gal}$), 3.39 (s, 3H, OMe), 2.78 (dd, 1H, $J_{gem} =$ 13.8 Hz, H-3eq$^{Neu}$), 2.17 (dd, 1H, H-3ax$^{Neu}$), 2.07, 1.99 and 1.96 (3s, 9H, 3 Ac); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.6, 170.5, 169.3, 167.7, 151.0, 138.7, 138.3, 138.0, 128.6, 128.4, 128.3, 128.2, 128.1, 127.8, 127.6, 127.5, 101.6, 98.4, 76.1, 74.6, 73.4, 73.3, 70.9, 69.6, 69.4, 67.5, 62.7, 55.1, 53.3, 51.7, 34.2, 20.9, 20.8, 20.5; MALDI-TOFMS *m/z* calcd for $[C_{45}H_{53}NO_{17}+Na]^+$: 902.32. Found: 902.34.

**3.14.2. β-Isomer.** $[\alpha]_D$ +11.7 (*c* 0.5, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.39–7.28 (m, 15H, 3 Ph), 5.73 (s, 1H, NH), 5.54 (m, 1H, H-8$^{Neu}$), 4.83 (dt, 1H, $J_{3eq,4} =$ 4.5 Hz, $J_{3ax,4} = J_{4,5} = 10.5$ Hz, H-4$^{Neu}$), 4.75 (d, 1H, –C$H_2$Ph), 4.65 (m, 2H, 2 –C$H_2$Ph), 4.56 (m, 3H, H-7$^{Neu}$, H-1$^{Gal}$, –C$H_2$Ph), 4.47 (m, 4H, H-9a$^{Neu}$, H-3$^{Gal}$, 2 –C$H_2$Ph), 4.24 (m, 3H, H-6$^{Neu}$, H-9b$^{Neu}$), 3.97 (dd, 1H, $J_{5,6a} = J_{5,6b} = 6.9$ Hz, H-5$^{Gal}$), 3.91 (dd, 1H, $J_{1,2} = 3.5$ Hz, $J_{2,3} = 10.4$ Hz, H-2$^{Gal}$), 3.81 (m, 1H, H-4$^{Gal}$), 3.72 (dd, 1H, $J_{4,5} = J_{5,6} = 10.1$ Hz, H-5$^{Neu}$), 3.63–3.53 (m, 5H, COOMe, H-6a$^{Gal}$, H-6b$^{Gal}$), 3.30 (s, 3H, OMe), 2.84 (dd, 1H, $J_{gem} = 13.7$ Hz, H-3eq$^{Neu}$), 2.10, 2.04 and 2.03 (3s, 9H, 3 Ac), 1.75 (dd, 1H, H-3ax$^{Neu}$); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.4, 170.1, 170.0, 166.0, 150.1, 138.2, 138.1, 137.7, 128.6, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.1, 100.5, 98.6, 78.3, 75.1, 75.0, 73.4, 73.3, 72.8, 70.6, 69.3, 68.3, 67.5, 66.6, 62.9, 55.4, 52.5, 51.1, 36.3, 20.9, 20.7, 20.6; MALDI-TOFMS *m/z* calcd for $[C_{45}H_{53}NO_{17}+Na]^+$: 902.32. Found: 902.33.

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## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2008.05.005.

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