

Syntheses of $\alpha(2,8)$ Sialosides Containing NeuAc and NeuGc by Using Double Carbonyl-Protected *N*-Acyl Sialyl Donors

Yutaka Takeuchi,^[a] Kazuki Tohda,^[a] and Hiroshi Tanaka*^[a]

We report on the syntheses of NeuAc and NeuGc-containing glycosides via the use of double carbonyl-protected *N*-acetyl sialyl donors. The 7-*O*,9-*O*-carbonyl protection of an *N*-acyl-5-*N*,4-*O*-carbonyl-protected sialyl donor markedly increased the α -selectivity during glycosylation, particularly when glycosylating the C-8 hydroxyl group of sialic acids. The *N*-acyl carbamates were selectively opened with ethanethiol under basic conditions to provide *N*-acyl amines. It is noteworthy that *N*-glycolyl carbamate was more reactive to nucleophiles by comparison with the *N*-acetyl carbamate due to the electron-withdrawing oxygen in the *N*-acyl group and however, allowed selective opening of the carbamates without the loss of *N*-glycolyl

groups. To demonstrate the utility of the approach, we began by synthesizing $\alpha(2,3)$ and $\alpha(2,6)$ sialyl galactosides. Glycosylation of the hydroxy groups of galactosides at the C-6 position with the NeuAc and NeuGc donors provided the corresponding sialyl galactosides in good yields with excellent α -selectivity. However, glycosylation of the 2,3-diol galactosyl acceptor selectively provided Sia $\alpha(2,2)$ Gal. Next, we prepared a series of $\alpha(2,8)$ disialosides composed of NeuAc and NeuGc. Glycosylation of NeuGc and NeuAc acceptors at the C-8 hydroxyl group with NeuGc and NeuAc sialyl donors provided the corresponding $\alpha(2,8)$ disialosides, and no significant differences were detected in the reactivities of these acceptors.

Introduction

N-Acetyl and *N*-glycolyl neuraminic acids (NeuAc and NeuGc) are categorized as sialic acids and are widely distributed in most animals. They are often found at the non-reducing termini of glycan chains in glycoproteins and glycolipids and play important roles in biological events on cell surfaces.^[1] Humans do not biosynthetically produce *N*-glycolyl neuraminic acid (NeuGc) due to the absence of the enzyme cytidine 5'-monophosphate (CMP)-*N*-acetyl neuraminic acid hydroxylase, which converts CMP-NeuAc to CMP-NeuGc.^[2] Nevertheless, traces of NeuGc are detected in human oligosaccharides. The presence of NeuGc in humans can be traced to dietary acquisitions such as in the consumption of red meat.^[3] Notably, elevated NeuGc levels are repeatedly found in cancer tissues, cells, and serum samples. This is why NeuGc-containing antigens are exploited as a class of cancer biomarkers. The ganglioside GM3 **1** involves NeuGc $\alpha(2,3)$ Gal and is reported to be overexpressed in tumors, but it is rarely found in corresponding normal tissues (Figure 1).^[4] In addition, the ganglioside GD3 **2** that involves

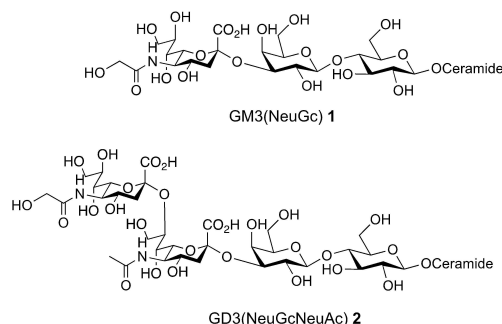


Figure 1. Structures of GM3(NeuGc) **1** and GD3(NeuGcNeuAc) **2**.

NeuGc $\alpha(2,8)$ NeuAc has been detected in human melanomas.^[5] The structural identification of this ganglioside was achieved by comparing NeuGc-containing GD3 isolated from boar erythrocyte membranes (NeuGc-NeuGc)^[6] and dolphin kidneys (NeuGc-NeuAc and NeuAc-NeuGc).^[7] Oligosaccharides sourced from natural extracts hold potential significance, but these might not be ideal for the structure determination and elucidation of biological functions due to potential heterogeneity and contamination with antigenic compounds. Consequently, it is essential to develop an effective method for the chemical synthesis of structurally defined NeuGc-containing oligosaccharides.

The formation of a glycosidic linkage in $\alpha(2,8)$ disialosides is one of the most challenging processes in synthetic carbohydrate chemistry, primarily because of two obstacles. The first involves the complexities of achieving an α -selective glycosidation of sialic acid, and the second problem relates to the low reactivity of the hydroxy group at the C-8 position during glycosylation. Numerous organic chemists have tackled these

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challenges over the years.^[8] In 2006, we developed an efficient method for the synthesis of $\alpha(2,8)$ sialosides using the 5-*N*,4-*O*-carbonyl-protected sialyl donor **3**.^[9,10] (Figure 2) Donor **3** is capable of efficient α -selective glycosidation without nitrile effects. The nitrile effect is the effect of a solvent with a cyano group coordinating from the β -face of the oxonium cation of the sialic acid, thereby promoting α -selective sialylation.^[11] We also reported on the first chemical synthesis of $\alpha(2,8)$ tetrasialic acid using the donor. In this method, the *N*-acyl groups in the sialosides are simultaneously introduced, following preparation of the glycan chain. These types of sialyl donors have been used for the synthesis of a variety of sialo-containing oligosaccharides.^[12] However, this final modification not only reduces the efficiency of the synthesis of oligosaccharides but also makes it difficult to selectively incorporate sialic acids with different acyl groups into the specific positions of oligosaccharides containing multiple sialic acids.

To avoid *N*-acylation in the final stage, the *N*-acetyl and *N*-glycolyl 5-*N*,4-*O*-carbonyl-protected sialyl donors **4** were developed.^[13] The *N*-acetyl carbamate was converted directly to

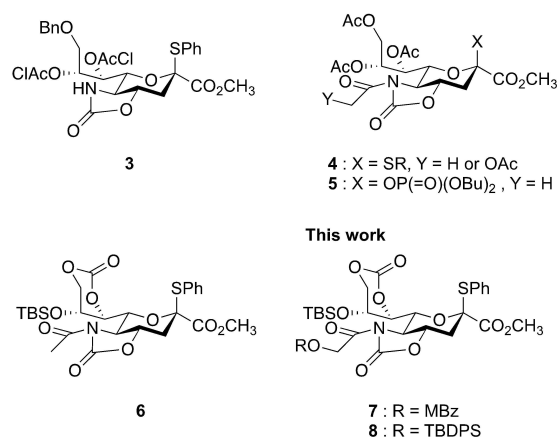


Figure 2. Historical development of 5-*N*,4-*O*-carbonyl-protected sialyl donors 3–6.

N-acyl amines under basic conditions. However, *N*-acylation of the carbamate reduced the α -selectivity of the sialyl donors. In addition, exposure of *N*-glycolyl carbamate to the same reaction conditions resulted in a significant loss of *N*-glycolyl groups.^[14] The sialyl phosphate **5** resulted in better α -selectivity compared with that achieved using thioglycoside **4**.^[15] Various sialo-containing oligosaccharides have been prepared utilizing *N*-acetyl-5-*N*,4-*O*-carbonyl-protected donors **4** and **5**.^[16] On the other hand, we have recently reported the synthesis of $\alpha(2,8)$ octasialoside, a minimum fragment of $\alpha(2,8)$ polysialic acid, via the use of double carbonyl-protected *N*-acetyl sialyl donor **6**.^[17] The 7-*O*,9-*O*-carbonyl protection not only enhanced the reactivity of the C-8 hydroxyl group toward glycosylation, but also improved α -selectivity. In addition, we have described that *N*-acetyl carbamates were selectively opened using thiols as nucleophiles, even in the presence of base-sensitive functional groups such as carbonates and esters. This method has been applied to achieve selective opening not only of *N*-acetyl carbamates in cyclic α -1,4-oligo-*N*-acetylglucosamine,^[18] but also of *N*-glycolyl carbamates in NeuGc $\alpha(2,3)$ and $\alpha(2,6)$ Gal units.^[19] Herein, we report on syntheses of NeuGc-containing disaccharides involving $\alpha(2,8)$ sialosides via the use of double carbonyl-protected *N*-glycolyl sialyl donors

Results and Discussion

Table 1 shows the glycosidation of the double carbonyl-protected *N*-acetyl and *N*-glycolyl thiosialosides **6**–**8**. 4-Methylbenzoyl (MBz) and *tert*-butyldiphenylsilyl (TBDPS) groups were used as protecting groups of *N*-glycolyl thiosialosides **7** and **8**, respectively. The *O*-triacetyl *N*-acetyl thioglycoside **9** was used for comparison. The results of glycosidation of the *N*-acetyl donor **6** to α -sialosides **11** have been previously reported.^[17] First, we examined the glycosylation of *n*-octanol (**10a**) with thiosialosides **7**–**9**. The sialyl donors **7**–**9** were treated with *n*-octanol in the presence of *N*-iodosuccinimide (NIS) and

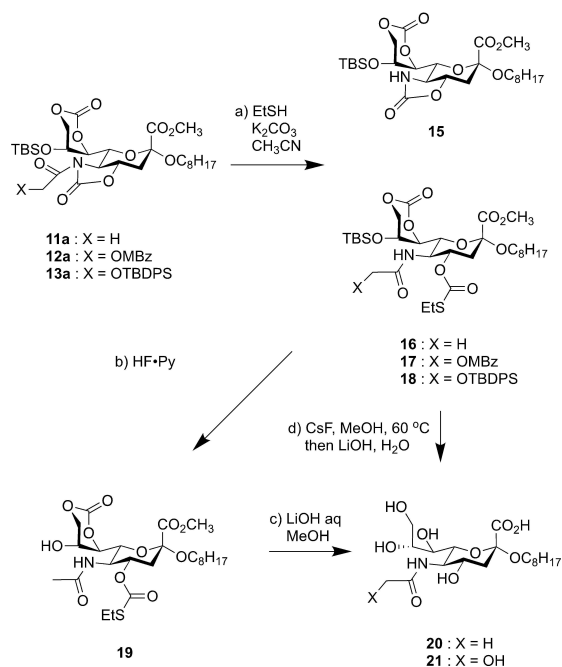
Table 1. Glycosidation of sialyl donors 6–9.

Entry	donor	Acceptor	Temp (°C)	Product	Yields of α/β mixtures of sialosides (%)	α/β ^[a]
1 ^[b]	6	10a	−45	11a	95	> 95/5
2	7	10a	−45	12a	96	> 95/5
3	8	10a	−45	13a	83	> 95/5
4	9	10a	−40	14a	96	> 95/5
5 ^[b]	6	10b	−65	11b	86	> 95/5
6	7	10b	−65	12b	87	90/10
7	8	10b	−78	13b	72	> 95/5
8	9	10b	−78	14b	81	43/57

^[a] The α/β ratios were determined via ¹H NMR spectra of the obtained sialosides. ^[b] These results were cited in the reference 17.

trifluoromethanesulfonic acid (TfOH) at -78°C . The reaction was allowed to rise to the temperatures shown in Table 1 and yielded the corresponding α -sialosides **12a–14a** in 96%, 83%, and 96% yields with complete α -selectivity, respectively. We observed no significant differences between the double carbonyl-protected *N*-acetyl and *N*-glycolyl thiosialosides **6–8** in glycosylation of the primary alcohol. Next, we examined the glycosylation of sialoside **10b** at the C-8 hydroxyl group using the glycosyl donors **7–9**. The *N*-glycolyl thiosialosides **8** possessing a TBDPS group, yielded the $\alpha(2,8)$ sialosides **13b** in 72% yield with excellent α -selectivity, respectively. The *N*-glycolyl thiosialosides **7** possessing an MBz group, provided the $\alpha(2,8)$ sialosides **12b** in 87% yield with a slightly reduced level of α -selectivity ($\alpha/\beta=90/10$). In contrast, the *O*-triacetyl thiosialoside **9** underwent glycosylation of the sialoside **10b** at the C-8 hydroxyl group to provide an anomeric mixture of disialoside **14b** in 81% ($\alpha/\beta=43/57$). These findings highlight the important role of 7-*O*,9-*O*-carbonyl protection in enhancing α -selectivity, particularly in the glycosylation of the C-8 hydroxyl group of sialic acids with 5-*N*,4-*O*-carbonyl protected sialic acid donors.

We also examined deprotection of the double carbonyl-protected *N*-acyl sialosides **11a–13a** (Scheme 1). According to the reported method, *N*-acetyl sialoside **11a** was treated with an excess amount of ethanethiol in the presence of K_2CO_3 at room temperature for 2 h to selectively provide *S*-ethyl thiocarbonate **16** in 78% yield. The *N*-glycolyl sialosides **12a** and **13a** were treated with thiol under basic conditions at -20°C for 15 h to selectively provide the corresponding *S*-ethyl thiocarbonates **17** and **18** in 85% and 80% yields, respectively.

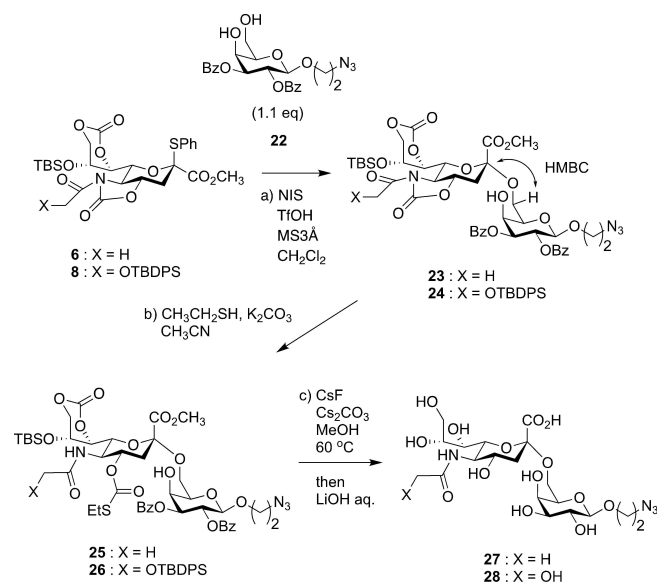


Scheme 1. Deprotection of the double carbonyl-protected α -sialosides **11a–13a**: a) $\text{CH}_3\text{CH}_2\text{SH}$, K_2CO_3 , CH_3CN , r.t. 78% for **16**, 0°C , 75% for **18**, 7% for **15**, -20°C , 85% for **17**, -20°C , 80% for **18**; b) HF-pyridine, THF, rt, 90%; c) $\text{LiOH}\cdot\text{H}_2\text{O}$, MeOH , H_2O , rt, quantitative; d) CsF , MeOH , 60°C then LiOH , H_2O , 83% for **20**, 85% for **21** from **17**, 91% for **21** from **18**.

The reaction of the *N*-glycolyl sialoside **13a** with thiol at 0°C provided a mixture of *S*-ethyl thiocarbonate **18** (75%) and deglycolyl product **15** (7%). The *N*-acetyl carbamate selectively and smoothly underwent the ring-opening with thiol at room temperature under basic conditions. Conversely, the *N*-glycolyl carbamate necessitates a low reaction temperature below -20°C to inhibit accompanying deglycolylation, thus requiring an extended reaction time. These results suggest that the electron-withdrawing oxygen functional group at the *N*-acyl group improves the reactivity of both carbonyl groups of the *N*-glycolyl carbamate. Even then, however, the reactivity of the *N*-acyl cyclic carbamate towards the ring-opening reaction was higher than that towards cleavage of the *N*-glycolyl group.

Next, we investigated the global deprotection of the resultant sialosides **16–18** bearing an (ethylthio)carbonyl group. Initially, we hydrolyzed the silyl ether of compound **16** using HF-pyridine, which resulted in an 90% yield of alcohol **19**. Alcohol **19** was then exposed to an aqueous solution of LiOH and methanol to produce the *N*-acetyl α -sialoside **20** in a quantitative yield. Desilylation of the *S*-ethyl thiocarbonate **16** via treatment with CsF in methanol at 60°C allowed a subsequent hydrolysis using an aqueous solution of LiOH in a one-pot reaction to provide the *N*-acetyl α -sialoside **20** in 83% yield. The one-pot deprotection protocol was adapted to *N*-glycolyl sialosides **17** and **18** possessing MBz and TBDPS groups to yield the *N*-glycolyl sialoside **21** in 85 and 90% yields, respectively.

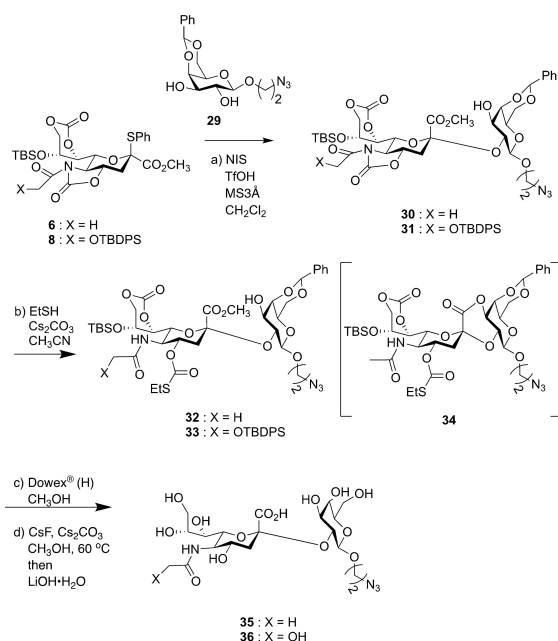
To demonstrate the utility of this method, the syntheses of $\alpha(2,6)$ and $\alpha(2,3)$ sialylgalactosides and $\alpha(2,8)$ disialosides were examined. Scheme 2 shows the syntheses of $\alpha(2,6)$ sialylgalactosides **27** and **28**. Treatment of the *N*-acetyl and *N*-glycolyl sialyl donors **6** and **8** with 1.1 equivalents of galactoside **22** that possesses two free hydroxyl groups at the C-4 and C-6 positions



Scheme 2. Syntheses of $\alpha(2,6)$ sialyl galactosides **27** and **28**: a) NIS , TfOH , $\text{MS3}\text{A}$, CH_2Cl_2 , 90%, α only for **23**, 66%, α only for **24**; b) $\text{CH}_3\text{CH}_2\text{SH}$, K_2CO_3 , CH_3CN , r.t., 76% for **25**, -20°C , 82% for **26**; c) CsF , Cs_2CO_3 , CH_3OH , 60°C , then LiOH aq., 99% for **27**, 95% for **28**.

in the presence of NIS and TfOH at -65°C provided α -sialosides **23** and **24** in 90% and 66% yields, respectively, as single isomers. The positions of the sialylated hydroxyl groups of galactosides **23** and **24** were determined to be the C-6 position due to 2D NMR experiments involving HMBC correlations between an anomeric carbon of the sialoside and a proton at the C-6 position of the galactoside. Treatment of the *N*-acyl sialosides **23** and **24** with ethanethiol under the established conditions provided the *S*-ethyl thiocarbonates **25** and **26** in 76% and 82% yields, respectively. Finally, one-pot deprotections of the *S*-ethyl thiocarbonates **25** and **26** were achieved via treatments with CsF and Cs₂CO₃ in methanol at 60°C for 14 h, which was followed by the addition of an aqueous solution of LiOH to provide sialylgalactosides **27** and **28** in 99% and 95% yields, respectively. Cs₂CO₃ accelerated solvolysis of the benzoates. Configurations of the glycosidic linkages for each of the sialic acids were determined using the coupling constants $^3J_{\text{C}1-\text{H}_{3\text{ax}}}$ (5.9 Hz for **27** and 6.3 Hz for **28**) based on their gated proton-decoupled ¹³C-NMR spectra to be α .

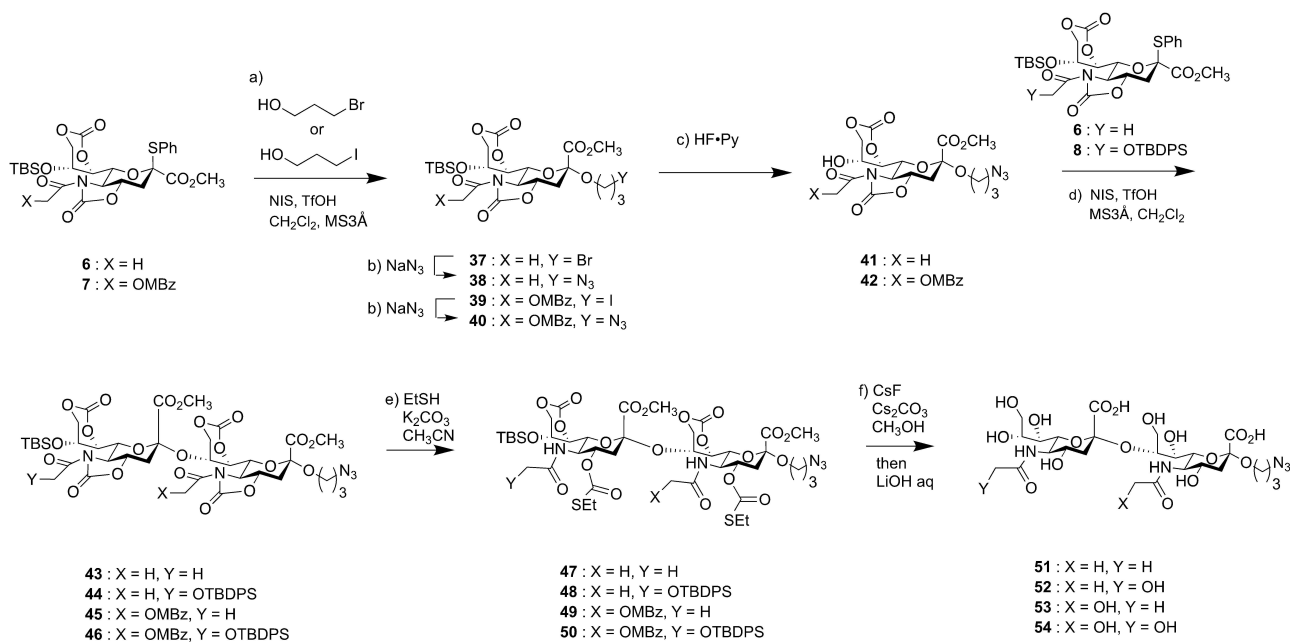
The syntheses of $\alpha(2,3)$ sialylgalactosides was examined (Scheme 3). The galactoside **29** with two hydroxy groups at the C-2 and C-3 positions was used as an acceptor for $\alpha(2,3)$ sialylation. The hydroxy group at the C-3 would exhibit higher reactivity than that at C-2 position due to its reduced steric hindrance via the axially orientated C4 hydroxy group. The sialyl donors **6** and **8** were reacted with 1.1 equivalents of β -galactoside **29**. The reactions were achieved in the presence of NIS and TfOH to unexpectedly provide the disaccharides **30** and **31** composed of Sia $\alpha(2,2)$ Gal in 58% and 52% yields, respectively, both as single α -isomers. The positions of the sialylated hydroxyl groups on disaccharides **30** and **31** were



Scheme 3. Syntheses of $\alpha(2,2)$ sialyl galactosides **35** and **36**: a) NIS, TfOH, MS3 A, CH₂Cl₂, 58%, α only for **30**, 52%, α only for **31**; b) EtSH, Cs₂CO₃, CH₃CN, rt, 50% for **32** and 18% for **34**, -10°C , 71% for **32**; -20°C , 88% for **33**; c) Dowex® resin, CH₃OH, rt; d) CsF, Cs₂CO₃, CH₃OH, 60°C , then LiOH·H₂O, 82% for **35**, quantitative for **36**.

identified at the C-2 position of the galactoside, as determined via 2D NMR experiments involving H–H COSY spectra and deuterium replacement of the acidic proton of the remaining hydroxy group. Danishefsky et. al have reported an unexpected glycosylation of a 1- β -galactosyl-2-azido- sphingosine derivative at the C-2 hydroxy group with a sialyl donor.^[20] Although the reason for a C2 glycosylation was not mentioned by Danishefsky, one common feature is that the β -galactosides contain 2-azidoethyl groups as their aglycons. These results suggest that the azido group might be responsible for the selective glycosylation at the C-2 hydroxy group. Further, treatment of sialosides **30** and **31** with ethanethiol under basic conditions at -10 and -20°C selectively provided the *S*-ethyl thiocarbonates **32** and **33** in 71% and 88% yields, respectively. In the reaction at 0°C , a byproduct was observed. The HRMS mass spectra of the byproduct indicated it was lactone **34**.^[21,22] The global deprotections of *S*-ethyl thiocarbonates **32** and **33** were then explored. Initially, the *S*-ethyl thiocarbonates **32** and **33** were subjected to treatment with strong cation exchange resins (Dowex® 50Wx4 (H)) in methanol at room temperature, which led to solvolysis of the benzylidene acetal. After the resin was removed via filtration, the reaction mixture was concentrated in vacuo. The resultant substances were further reacted with CsF and Cs₂CO₃ in methanol, and then an aqueous solution of LiOH was added. These operations provided the *N*-acyl α -sialosides **35** and **36** in 82% and quantitative isolated yields, respectively. Finally, the configurations of the glycosidic linkages of sialosides **35** and **36** were established as α via coupling constants $^3J_{\text{C}1-\text{H}_{3\text{ax}}}$ (5.2 Hz for **35** and 5.8 Hz for **36**).

Finally, we synthesized a set of $\alpha(2,8)$ disialosides **51–54** containing NeuAc and NeuGc (Scheme 4). Initially, the preparation of the glycosyl acceptors **42** and **44** for $\alpha(2,8)$ sialylation was examined. Treatment of the *N*-acetyl sialyl donor **6** with 2.0 equivalents of 3-bromopropanol in the presence of NIS and TfOH at -78°C provided the α -sialoside **37** in 92% yield with complete α -selectivity. Bromide **37** was treated with sodium azide at room temperature to provide azide **38** in 92% yield. Subsequent cleavage of TBS ether **38** with HF-pyridine provided alcohol **41** as a glycosyl acceptor in a good total yield. The preparation of alcohol **42** possessing an *N*-glycolyl group was achieved in the following manner. Glycosylation of 3-iodopropanol with the *N*-glycosyl sialyl donor **7** under the same reaction conditions provided α -sialoside **39** along with a trace amount of a β -isomer ($\alpha/\beta = 94/6$). The mixture was purified by column chromatography on silica gel to provide the α -sialoside **39** in 87% yield. The obtained iodide **39** was reacted with sodium azide in DMF at 0°C to provide azide **40** in 79% yield. Keeping the reaction temperature below 0°C was important to inhibit the opening of the *N*-glycolyl carbamate with sodium azide. Subsequent hydrolysis of the silyl ether **40** with HF-pyridine provided a version of alcohol **42** that possessed an *N*-glycolyl group. Glycosylation of the sialosides **41** and **42** with the *N*-acetyl and *N*-glycolyl sialyl donors **6** and **8** were examined. The *N*-acetyl and *N*-glycolyl sialyl acceptors **41** and **42** were reacted with 1.5 equivalents of the *N*-acetyl and *N*-glycolyl sialyl donors **6** and **8** to provide $\alpha(2,8)$ disialosides **43–46** in 91%, 74%, 80%, and 91% yields with complete α -



Scheme 4. Syntheses of $\alpha(2,8)$ disaccharides **51–54**: a) NIS, TfOH, MS3 Å, CH₂Cl₂, -78°C , 92%, for **37**, -78°C to -65°C , 87% for **39**; b) NaN₃, DMF, rt, 92% for **37**, 0°C , 89%, for **40**; c) HF·Pyridine, THF, rt, 93% for **41**, 94% for **42**; d) NIS, TfOH, MS3 Å, CH₂Cl₂, 91% for **43**, 74% for **44**, 80% for **45**, 91% for **46**; e) EtSH, K₂CO₃, CH₃CN, rt, 77% for **47**, -20°C then rt, 97% for **48**, 73% for **49**, -20°C , 78% for **50**; f) CsF, Cs₂CO₃, CH₃OH then LiOH aq., 92% for **51**, 90% for **52**, 89% for **53**, 90% for **54**.

selectivity, respectively. There were no significant differences in either reactivity or stereoselectivity among these coupling reactions. These results suggest that the 4-methylbenzyloxy group at the α position of the *N*-acetyl group exerts little effect on the reactivity of the hydroxyl group at the C-8 position for glycosylation. Finally, the removal of all protection groups from disaccharides **43–46** was conducted based on the established method. The treatment of $\alpha(2,8)$ disialoside **43** with two *N*-acetyl groups with ethanethiol at room temperature provided the *S*-ethyl thiocarbonate **47** in 77% yield. The $\alpha(2,8)$ sialosides **46** with two *N*-glycolyl groups were reacted with ethanethiol at -20°C to provide *S*-ethyl thiocarbonate **50** in 78% yield. On the other hand, versions of $\alpha(2,8)$ disialosides **44** and **45** that possessed both *N*-acetyl and *N*-glycolyl groups were initially reacted with thiol at -20°C to selectively open the *N*-glycolyl carbamate. After the starting materials were completely consumed, the reaction temperature was raised to room temperature, which led to the production of the 4,4'-*O*-bis(*S*-ethyl thiocarbonyl) disialosides **48** and **49** in 97% and 73% yields, respectively. Finally, disialosides **47–50** were treated with CsF and Cs₂CO₃ in CH₃OH at 60°C . Subsequently, a solution of LiOH aq was added to the reaction mixtures to yield $\alpha(2,8)$ sialosides **51–54** in 92%, 90%, 89%, and 90% yields, respectively.

Conclusions

In conclusion, we've successfully developed a novel method for synthesizing NeuAc and/or NeuGc-containing oligosaccharides by employing double carbonyl-protected *N*-acetyl and *N*-glycolyl sialyl donors **6–8**. A key advancement was the

incorporation of a cyclic carbonate into the side chain of the sialyl donors, which significantly enhanced their α -selectivity of the glycosylation. Notably, this improvement was particularly pronounced during glycosylation of the C-8 hydroxyl group of sialic acids. The *N*-acetyl and *N*-glycolyl carbamates could be selectively cleaved to yield *N*-acyl amines containing an (alkylthio)carbonyloxy group. This transformation was facilitated using ethanethiol under basic conditions. The *N*-glycolyl carbamate displayed greater sensitivity to nucleophiles compared with that of its *N*-acetyl counterpart and still allowed chemoselective opening of the carbamate without the loss of an *N*-glycolyl group. This increased sensitivity is attributed to the electron-withdrawing oxygen functional group at the *N*-glycolyl group. To further validate the potential of our approach, we synthesized the $\alpha(2,6)$ sialyl galactosides **27** and **28**, in addition to a series of $\alpha(2,8)$ disialosides **51–54** that contain either NeuAc or NeuGc or both. However, glycosylation of galactosyl acceptor **29** with two hydroxyl groups at the C-2 and C-3 position unexpectedly provided the disaccharide composed of Sia $\alpha(2,2)$ Gal. The azido group in the reducing end might promote the unexpected glycosylation at the C-2 hydroxyl group. Overall, our method, which employs double carbonyl-protected *N*-acyl sialyl donors, has the potential to transform the study of both NeuGc-containing and NeuAc-containing oligosaccharides. It significantly improves the efficiency of synthesizing a broad range of NeuGc-containing oligosaccharides, thereby aiding in their functional analysis

Experimental Section

All experiments were performed under argon atmosphere. All reactions were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plates (60F-254) with UV light, visualized by *p*-anisaldehyde solution or ceric sulfate. Purification of the crude materials was performed by column chromatography separations on silica gel (Merck silica gel 60, 0.063–0.200 mm) and gel permeation chromatography (GPC) on a Japan Analytical Industry Model RI-5 refractive index detector and 301 ultra violet detector with a polystyrene gel column (JAIGEL-1H, 20 mm×600 mm), using CHCl₃ as solvent (3.5 mL / min). NMR spectra were recorded on a Bruker AVANCE III HD (400 MHz for ¹H, 100 MHz for ¹³C) instrument in the indicated solvent. IR spectra was recorded on a Perkin-Elmer Spectrum One FT-IR spectrophotometer. JASCO FT/IR-4200 spectrophotometer. Only the strongest and/or structurally important peaks are reported as the IR data given in cm⁻¹. Optical rotations were measured on a JASCO model P-1020 polarimeter. High-resolution mass spectrometry (HRMS) (ESI) was carried out using a Q Exactive equipped with an UltiMate 3000 HPLC system (Thermo Fisher Scientific, Waltham, MA) LC-plus (JMS-T100LP, JEOL) and QSTAR Elite (Sciex).

Supporting Information

The authors have cited additional references within the Supporting Information.^[22]

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Biomarkers · Glycosidation · *N*-acyl carbamates · *N*-glycolyl neuraminic acids · Thiocarbamates

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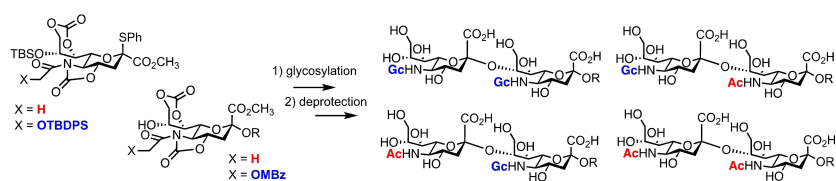
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Syntheses of $\alpha(2,8)$ Sialosides Containing NeuAc and NeuGc by Using Double Carbonyl-Protected *N*-Acyl Sialyl Donors



Double carbonyl-protected *N*-acetyl and *N*-glycoyl sialyl donors underwent efficient $\alpha(2,8)$ sialylation in dichloromethane, allowing for the chemical synthesis of $\alpha(2,8)$ disialosides involving the compounds containing both NeuAc and NeuGc. The selective

ring-opening of the *N*-glycolylcarbamate in these sialosides without losing the *N*-glycoyl group was accomplished under a lower reaction temperature than that required for *N*-acetyl carbamate.