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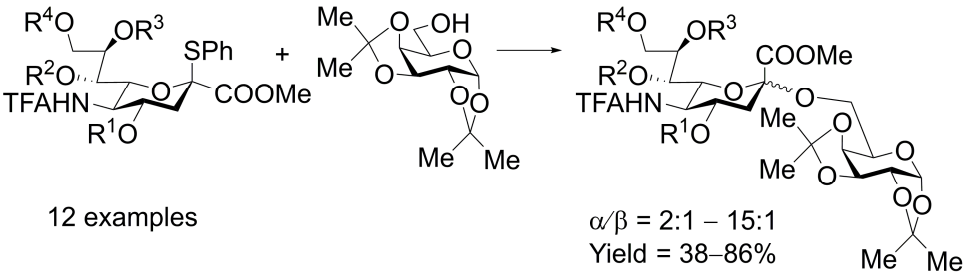

12 examples

α/β = 2:1 – 15:1
Yield = 38–86%

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Stereoselective sialylation with *O*-trifluoroacetylated thiosialosides: hydrogen bonding involved?

Nikita M. Podvalnyy, Nelly N. Malysheva, Maria V. Panova, Alexander I. Zinin, Alexander O. Chizhov, Anna V. Orlova and Leonid O. Kononov*,[1]

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Abstract

A series of novel sialyl donors containing *O*-trifluoroacetyl (TFA) groups at various positions was synthesized. The choice of protecting groups in sialyl donors was based on hypothesis that variations in ability of different acyl groups to act as hydrogen bond acceptors would influence the supramolecular structure of reaction mixture (solution structure), hence the outcome of sialylation. These glycosyl donors were examined in the model glycosylation of the primary hydroxyl group of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose in comparison with sialyl donors without *O*-TFA groups. The presence of *O*-TFA groups in a sialyl donor strongly affected the outcome of sialylation. Several sialyl donors studied showed promising results: yields of disaccharides can be as high as 86% as can be the stereoselectivities (α/β up to 15:1). The results obtained suggest that varying acyl *O*-protecting groups in sialyl donor may result in dramatic changes in the outcome of sialylation although further studies are required to dissect the influence of intermolecular hydrogen bonding and intramolecular substituent effects related to variations of electron-withdrawing properties of different acyl groups.

Keywords: neuraminic acid; glycosylation; sialylation; *O*-trifluoroacetyl group; supramer approach; hydrogen bonding.

1. Introduction

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Sialic acid-containing glycoconjugates are present in mammalian and avian tissues, in many bacteria, including pathogenic, and involved in a wide range of biological phenomena ranging from cell–cell adhesion and mobility to oncogenesis and recognition by viruses and bacteria.[1-5] Sialic acid (mostly *N*-acetylneuraminic acid (Neu5Ac)) residues are linked to other sugars by a variety of glycosidic linkages, most typically by α(2→3) and α(2→6) linkages to galactose or *N*-acetylglucosamine, as well as α(2→8) and α(2→9) linkages in homopolymers of Neu5Ac (polysialic acids).[6] The synthesis and the biomedical investigation of sialic acid-containing glycoconjugates, oligosaccharides and their analogs is very important area of research aiming at understanding their biological roles and determining their therapeutic relevance. For this reason, tremendous efforts have been made in order to develop efficient methods for the synthesis of sialo-oligosaccharides (see the recent reviews[7-19] and selected references not covered by the reviews[20-37]).

Sialic acids are attached to other carbohydrates by means of a glycosylation reaction called sialylation. Although various approaches to stereoselective α-sialylation have been suggested and substantial progress in the synthesis of sialo-oligosaccharides has recently been achieved, reliable introduction of sialic acid residues into oligosaccharides remains quite a difficult problem and poor predictability and reproducibility of yield and stereoselectivity are still typical[38, 39] of the sialylation reaction. Seemingly minor changes in the structure of reactants or in reaction conditions can dramatically influence the yield and stereoselectivity. The reason of this high sensitivity of sialylation outcome to protecting group pattern of sialyl donor is currently unknown although various hypotheses have been advanced, and several attempts to rationalize the sialylation outcome were undertaken in the last years.[8, 16, 18, 34, 35, 38-47]

Outcome of sialylation, like outcome of other glycosylation reactions, may depend on the protecting group pattern in the sialyl donor. The *O*- and *N*-protecting groups are beleived to influence the outcome of a glycosylation reaction in a variety of ways.[8, 18, 19, 43, 47] Firstly, electron donating or withdrawing effects of the *O*- and *N*-protecting groups may activate (“arm”)

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or deactivate ("disarm") a glycosyl donor, respectively.[48, 49] For sialyl donors this effect is mostly pronounced for substituents at C-5 (including protecting groups at N-5)[8, 50, 51] and for protecting groups at O-4 and O-7[43, 47, 50] that are located close to the anomeric center, a notable example[18, 52] being the use of 4-*O*,5-*N*-(thio)carbonyl-protected sialyl donors, the efficiency of which is partially attrubuted[52, 53] to destabilization of the sialyl cation by electron-withdrawing oxazolidinone group thus making an associative pathway (S_N2-like) more feasible. Note that electron-withdrawing effect of remote substituents in the side chain of sialic acids has recently been reported[54] to be surprisingly large; the consequences of this finding have yet to emerge. Secondly, it was suggested that conformations of both the side chain[55-57] and pyranose ring[43, 44, 47] of a sialyl donor (and the sialyl cation formed from it upon its activation by promoter) may be influenced by protecting groups thus modulating the stereoselectivity. A special case of such influence is the formation of extra (un)fused ring(s) (e.g., 4O,5N-oxazolidinone) by ingeniously selected protecting groups that would lock the conformation of the sialyl cation (or at least limit flexibility of the pyranose ring and the side chain).[11, 18] Finally, the outcome of sialylation may depend on intermolecular interactions that involve protecting groups in the molecules of sialyl donor and other molecules present in the reaction solution.[34, 35, 38, 40-42, 47]

We are developing a novel approach to glycosylation (including sialylation), which is based on hypothesis that such intermolecular interactions of reagents in solutions may lead to supramolecular aggregation in the reaction mixture resulting in formation of solutions with modified structure. Indeed, recent studies[58-61] revealed that commonly used solutions are not homogeneous as it is usually assumed.[45] A solute, depending on concentration, solvent, temperature and the presence of other compounds, including impurities, may exist in solutions as a variety of supramolecular species ("supramers") differing in size and structure, which may have chemical properties considerably different from those of the parent molecules comprising supramers.[38-42, 45, 62-70] The supramer approach was shown to be useful for explanation,

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prediction and discovery of a series of unexpected phenomena and allowed the development of highly efficient and stereoselective glycosylation reactions with sialyl donors that lead to formation of Neu-(α2→3)-Gal[38, 39] and Neu-(α2→6)-Gal[39, 42] glycosidic linkages found in many natural sialo-oligosaccharides of biological and medical significance.[38-42, 71]

This supramolecular aggregation may be caused by a variety of intermolecular forces[72] including (but not limited to[68]) intermolecular hydrogen bonding (H-bonding), which can often be detected by various physical methods.[38-42, 45] Indeed, the idea of possibility of intermolecular H-bonding was instrumental in developing H-bond mediated acid-base catalyzed S_N2-type glycosidation[73-77] with trichloroacetimidates and H-bond mediated aglycon delivery (HAD) methodology for efficient 1,2-*cis*-glycosylation using picolyl or picoloyl protecting groups[78-80] (as well as other related protecting groups[81, 82]) on glycosyl donor as H-bond accepting moieties. An attempt to adapt the former approach for sialyl donors was reported to result in highly stereoselective sialylation, although the standard HAD mechanism, clearly, was not operative in that case since the nitrogen atom of pyridine moiety in glycosyl donor molecule was protonated by an excess of triflic acid under the conditions used.[47] Intermolecular H-bonds involving acetamide groups of sialic acid residues were reported to reduce the reactivity in glycosylations between the two sialylated disaccharides: protection of N(5) of sialic acid as the *N*,*N*-diacetylated derivative dramatically improved the reactivity and yield although this group was fairly remote from the reacting anomeric center.[34, 35] Enhanced reactivity of monosaccharide *N*,*N*-diacetylsialyl donors is known for quite some time,[83, 84] this feature was attributed for the absence of intermolecular H-bonding between the molecules of sialyl donors.[39-41, 85]

Thus, the importance of H-bonding in modulating the outcome of glycosylation may be considered established. Therefore, a possible approach to design of new glycosyl (including sialyl) donors with modified properties may rely on regioselective introduction of protecting groups that differ in their ability to participate in H-bonding. In this proof-of-principle study, we

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provide evidence that varying acyl *O*-protecting groups in sialyl donor and, hence, modulation of intermolecular hydrogen bonding pattern in the reaction solution, may result in dramatic changes in the outcome of sialylation.

2. Results and discussion

2.1. Why sialyl donors with different patterns of protecting groups may lead to divergent sialylation outcome?

The aim of our work is to determine how acyl O-protecting groups with different ability to form H-bonds can influence the reactivity of sialyl donor and stereoselectivity of sialylation. For practical reasons a substituent at N-5 needs to be chosen and kept identical in all sialyl donors to be compared. For biological studies, both naturally occurring *N*-acetyl- and *N*-glycolyl-substituted sialo-oligosaccharides are often required. Therefore, the use of sialyl donors with a suitable temporary protection at N-5 (*e.g.,* trifluoroacetyl (TFA) group) is usually considered reasonable.[71] It is worthy of note that *N*-acetyl group at N-5 of sialic acid residue can be replaced with various functionalities after completion of oligosaccharide assembly by N-nitrosation and subsequent oxidative deamination of the *N*-nitroso-*N*-acetylsialyl glycosides formed.[54, 86] Furthermore, *N*-TFA at C-5 of sialic acid monosaccharide blocks is not only a convenient protecting group. Considerable influence of the nature of *N*-protecting group in the sialyl donor on the outcome of glycosylation has been demonstrated,[8, 17-19] and a number of syntheses of naturally occurring sialyl derivatives was efficiently performed using *N*-TFA protected sialyl donors[71, 87-91] Thus, for all the sialyl donors studied here, *N*-TFA protecting group was used.

One can envision a number of possible aggregation patterns in solutions of sialyl donors due to differences in H-bond donor and acceptor strength of various protecting groups. Trifluoroacetamide proton is the sole strong H-bond donor and may interact with carbonyl groups of methoxycarbonyl group (C-1 carbon of sialic acid) and acyl protecting groups. Among

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many acyl groups, TFA derivatives represent a special case. Carbonyl oxygens of *O*- and *N*-TFA groups are rather poor H-bond acceptors in comparison with carbonyl oxygens of Ac, Bz or CO_2Me groups.[92-95] For this reason, the possibility of their participation in H-bonding can be disregarded (at least in the first approximation). For this reason, *O*-TFA derivatives would form less dense aggregates (loose supramers) in solution than, for example, *O*-Ac and *O*-Bz derivatives, which are expected to form more tight supramers (Fig. 1).[45] The exact position of TFA groups would modulate the fine structure of the supramers formed in the solution of a sialyl donor and hence its reactivity (which is directly linked to the looseness of the supramolecular cluster determined by its fractal dimension[45]) and selectivity (which depends on accessibility of different faces of anomeric center in the reacting species). Eventually this would lead to a change in sialylation outcome.

2.2. Synthesis of sialyl donors

The first task was to synthesize a series of sialyl donors containing *O*-TFA groups at various positions. Different reactivity and steric availability of hydroxy groups in sialic acid derivatives allow access to a wide range of partially deprotected derivatives by almost routine manipulation with protecting groups.[96-98] Sialyl thiosialosides selectively substituted at oxygen atoms with various acyl, benzylidene, and benzyl protecting groups were synthesized (Schemes 1–2) in a divergent manner from the readily accessible[99] tetraol **1**. Quite a simple arsenal of methods used has led to a wide range of compounds. In some cases, the reaction conditions leading to a mixture of two products were intentionally chosen, and both products were then used for the synthesis of glycosyl donors. Thus, tetraol **1** was converted into fully acylated derivatives **2** and **3** (Scheme 1) by chloroacetylation with chloroacetic anhydride (CA_2O) and 2,4,6-collidine in MeCN and benzoylation with BzCl in pyridine, respectively. In the benzoylation reaction, product **4** containing free OH-group at C-7 was also obtained along with perbenzoate **3**. Alternatively, tetraol **1** was converted to 8,9-*O*-isopropylidene derivative **5**,

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which was then selectively acylated at O-4 to give derivatives **6**, **7** and **8** with acetyl (Ac), benzoyl (Bz) or chloroacetyl (CA) groups, respectively. Isopropylidene group was then removed to form 7,8,9-triols **9–11**. Reaction of tetraol **1** with $PhCH(OMe)_2$ catalyzed by CSA was non-regioselective and gave a mixture of stereoisomeric 8,9-*O*-benzylidene derivatives **12** along with 7,9-*O*-benzylidene acetal **14**. A mixture of epimeric 8,9-*O*-benzylidene acetals **12** without separation of stereoisomers was chloroacetylated at O-4, and the reductive opening of benzylidene group by $BH_3{\cdot}NMe_3$–$AlCl_3$ in moist[100] THF was performed to give 9-*O*-benzyl derivative **15**. Regioisomeric 7,9-*O*-benzylidene derivative **14** was converted to 4,8-bis-*O*-acetyl and 4,8-bis-*O*-chloroacetyl derivatives **16** and **17**. 4-*O*-Chloroacetyl derivative **18** with unprotected hydroxyl group at C-8 was also synthesized by chloroacetylation of diol **14** with limited amount of CA_2O. Thus, fully protected sialyl donors **2**, **3**, **16**, and **17** without *O*-TFA groups were prepared along with a number of selectively deprotected sialyl derivatives containing free OH groups at various positions ready for subsequent *O*-trifluoroacetylation.

It is important to note that *O*-TFA groups should be introduced at the last stage of the synthesis and aqueous work-up should be minimized, and especially chromatography on silica gel is best to be avoided due to reported[101] lability of *O*-TFA groups. For this reason, in most cases *O*-trifluoroacetylation was effected by trifluoroacetic anhydride (TFA_2O) in the presence of sodium trifluoroacetate (NaOTFA) as a base[99, 102] that was then removed from the reaction mixture by filtration. This method was used for the preparation of sialyl thioglycosides **19**, **20**, **21**, **22**, **23**, and **24** containing *O*-TFA groups. However, treatment of more acid-labile benzylidene derivatives **14** and **18** with TFA_2O and NaOTFA gave mixtures of products apparently due to the cleavage of benzylidene group. The target *O*-TFA derivatives **25** and **26** containing benzylidene group were cleanly obtained by acylation with TFA_2O in presence of pyridine[103] followed by aqueous work-up.

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2.3. Sialylation of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose with partially *O*-trifluoroacetylated sialyl donors

The obtained sialyl donors with *O*-TFA-protecting groups were examined in the model glycosylation reaction with equimolar amount[2] of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**27**)[104] in comparison with reference sialyl donors without *O*-TFA groups. Glycosylation reactions were performed at 0.05 M[3] concentration[4] of glycosyl donor and glycosyl acceptor in MeCN at –40 °C in the presence of 3Å molecular sieves (MS 3Å) promoted by *N*-iodosuccinimide (NIS) and catalytic triflic acid (TfOH). Minimum amount of TfOH required to initiate the reaction was taken. In the event, different amounts of TfOH had to be taken in each case to promote reaction (Table 1) apparently due to variations in basicity of acyl groups used.[41] In those cases when *O*-TFA groups were initially present in the glycosyl-donor, the mixture of products obtained after work-up was treated with NaOMe in MeOH to cleave all *O*-acyl groups and then *O*-acetylated with Ac_2O and Py. Fully protected *O*-acylated disaccharide fraction was isolated by gel permeation chromatography and analyzed by ^{1}H NMR spectroscopy to give anomeric ratio. Individual anomers of disaccharides were then separated by silica gel chromatography and the disaccharide yield was determined at this stage.

Since *O*-TFA is an electron-withdrawing group, a disarming effect[48] on the reactivity of the corresponding sialyl donors is expected. Indeed, *O*-TFA-substituted glycosyl donors, when examined under identical conditions (NIS–TfOH, MeCN, MS 3Å, –40 °C) with glycosyl acceptor **27**, required larger amount of TfOH (all other parameters being equal) and longer time

[2] We intentionally used equimolar amounts of glycosyl donor and glycosyl acceptor since this experimental design allows an easy monitoring the reaction course and correct estimation of relative reactivity of sialyl donors. The use of excess of a sialyl donor is quite a common practice; in such cases, higher yields of glycosylation products are usually obtained in line with general consensus that the competing elimination from a sialyl donor is the main reason for diminished yields in sialylation.

[3] This concentration is usually considered as “regular” and most reported glycosylations were performed at this concentration (see [68] and references cited therein).

[4] For a discussion on the influence of concentration on glycosylation outcome, which may be dramatically large and unexpectedly complex, see [38], [67], [68].

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for reaction completion in comparison with the reference *O*-TFA-free sialyl donors (Table 1). The yields of disaccharide in glycosylation reactions with *O*-TFA-protected sialyl donors were in many cases compromised in comparison with the reference glycosyl donors. Fully trifluoacetylated thioglycoside **19** (Table 1, entry 6) gave 38%[5] of α-linked disaccharide **28** while tetra-*O*-chloroacetyl and tetra-*O*-benzoyl derivatives **2** and **3** gave 86% and 61% α-linked disaccharides **32** and **29**, respectively (Table 1, entries 1 and 2). The decrease in the yield of the products of sialylation cannot be attributed to the reported relatively low stability of *O*-TFA groups[101] since the use of *O*-TFA groups for protection of hydroxyls in glycosyl donors based on mannopyranose,[103] arabinofuranose[66] or fucopyranose[105] did not reveal any substantial decrease in the yields of glycosylation products.

At the same time, it is necessary to note that the presence of *O*-TFA groups in sialyl donor increases the relative amount of α-isomer in the disaccharide fraction in comparison with almost all corresponding non-trifluoroacetylated sialyl donors with similar pattern of protecting groups (this is true even for sialyl donors containing *O*-chloroacetyl (CA) groups that are known[106] to increase α/β ratio; see below).

The presence of *O*-Bz groups in a *N*-acetyl-*N*-benzoyl-protected sialyl donor has recently been reported to drastically deteriorate the outcome of sialylation in CH_2Cl_2, β-sialosides being the major products.[50] It should be noted that *O*-benzoyl-protected *N*-acetylsialyl xanthate has earlier been used as the glycosyl donor in nitrile solvents[107, 108] to give moderate yields of α-linked sialosides. For this reason, a series of glycosyl donors containing *O*-Bz protecting groups was compared in this study (Table 1, entries 2, 9, 10). Fully *O*-benzoylated thioglycoside **3** (Table 1, entry 2) without *O*-TFA groups showed the shortest conversion time (30 min) and 61% isolated yield of α-linked disaccharide, but low stereoselectivity (α/β = 4.6:1). Addition of one *O*-TFA-group at O-7 (compound **23**, Table 1, entry 10) did not influence stereoselectivity, but

[5] Only traces of glycal, usually formed by competing elimination from a sialyl donor, were formed in this reaction suggesting alternative pathways of decomposition of the sialyl donor.

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decreased the product yield. Glycosyl donor **22** with three *O*-TFA groups in the side chain and *O*-Bz group at O-4 (Table 1, entry 9) showed the lowest reactivity in the series and somewhat higher α/β ratio in comparison with those achieved with per-*O*-benzoylated derivative **3**. This results suggest that the nature of substituent at O-4 is of vital importance for stereoselectivity of sialylation in accordance with earlier reported[43, 47] results.

For this reason, the influence of acyl group at O-4 on the sialylation outcome with glycosyl donors containing three *O*-TFA groups in the side chain was then studied (Table 1, entries 6–9). Fully trifluoroacetylated thioglycoside **19** (Table 1, entry 6) slowly reacted with glycosyl acceptor **27** to give disaccharide **28** with good stereoselectivity (α/β = 9.8:1), albeit in low yield (38%). Acetyl and benzoyl groups at O-4 (**20** and **22**, Table 1, entries 7 and 9, respectively) somewhat increased the yield but compromised the α/β ratio as expected.[43] Chloroacetyl (CA) group is known to increase the reactivity of sialyl donors and α/β ratio of glycosylation products.[106] Indeed, the presence of only one chloroacetyl group group at O-4 in otherwise trifluoroacetylated sialyl donor **21** (entry 8 in the Table 1) strongly increased both the reactivity and stereoselectivity (α/β = 15.5:1).[6]

The outcome of sialylation with sialyl donors containing 7,9-*O*-benzylidene group and various acyl groups at O-4 and O-8 were then compared. Glycosyl donor **16** with acetyl groups at O-4 and O-8 showed high reactivity but poor stereoselectivity (α/β = 2.1:1, Table 1, entry 3). The presence of two *O*-TFA or *O*-CA groups at O-4 and O-8 (**17** and **25**, respectively) and especially their combination (**26**) increased stereoselectivity of sialylation (Table 1, entries 4, 12, 13).

Summarizing the data concerning *O*-TFA and *O*-CA-substituted sialyl donors, one can see that the highest α-stereoselectivities of glycosylation were shown by glycosyl donors containing

[6] As one of the Reviewers suggested, CA group at O-4 might be a compromise between Ac and TFA groups (with respect to the electron-withdrawing properties); it would destabilize the sialyl cation moderately (leading to more S_N2-like character of the reaction pathway, hence to higher α-selectivity) without overly reducing reactivity (as observed with TFA group).

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both O-CA and *O*-TFA groups in the molecule. Glycosyl donors **21** and **26** (Table 1, entries 8 and 13) containing *O*-TFA and *O*-CA groups showed higher α/β ratios than the corresponding thioglycosides **2**, **19**, and **17**, **25** with only *O*-CA or *O*-TFA groups (Table 1, entries 1, 6 and 4, 12, respectively). Another sialyl donor **24** (Table 1, entry 11) with CA group at O-4, TFA groups at O-7 and O-8 and benzyl group at O-9 has also shown very high stereoselectivity (α/β = 12.4:1) in glycosylation reaction. It is important to note that the sialylation outcome in case of **24** is very similar to that of **21** (Table 1, entry 8) so one can conclude that substitution at O-9 does not influence the sialylation stereoselectivity significantly presumably due to low ability of both *O*-benzyl and *O*-TFA group to participate in H-bonding.

3. Conclusions

Several sialyl donors studied showed promising results: yields of α-linked disaccharides can be as high as 86% as can be the stereoselectivities (α/β up to 15:1, Table 1). The results obtained suggest that varying acyl *O*-protecting groups in sialyl donor may result in dramatic changes in the outcome of sialylation although further studies are clearly required to dissect the influence of intermolecular hydrogen bonding and intramolecular substituent effects related to variations of electron-withdrawing properties of different acyl protecting groups. The presence of *O*-TFA groups in a sialyl donor strongly affected the outcome of sialylation. The found high stereoselectivity of several *O*-TFA-substituted sialyl donors and synergetic effect of *O*-TFA and *O*-CA protecting groups in sialic acid thioglycosides should be considered when developing oligosaccharide assembling strategies.

4. Experimental

4.1. General methods

The reactions were performed with the use of commercial reagents. Solvents for reactions were distilled and purified before the use according to the standard procedures. MeCN for

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glycosylation reactions was distilled over P_2O_5 and then over CaH_2 and stored over molecular sieves (MS) 3Å. Powdered MS 4Å (Fluka) were activated before the reactions by heating at ~220 °C in high vacuum for 6 h. Column chromatography was performed on silica gel 60 (40–63 μm, Merck). Gel permeation chromatography was performed in toluene on a column (400×20 mm) packed with Bio Beads S-X3 gel (200–400 mesh, Bio-Rad) using a differential refractive index detector (Knauer). TLC was carried out on Silica Gel 60 F_{254} plates (Merck), spots were visualized under UV light and by heating plates after immersion in a 1:10 (v/v) mixture of 85% aqueous H_3PO_4 and 95% EtOH. ^{1}H, ^{13}C and ^{19}F NMR spectra of solutions in $CDCl_3$, DMSO-d_6 or acetone-d_6 were recorded on a Bruker AVANCE-600 instrument or on a Bruker AM-300 instrument. The ^{1}H chemical shifts are given relative to the signal of the residual $CHCl_3$ (δ 7.27), DMSO-d_5 (δ 2.50) or acetone-d_5 (δ 2.05), the ^{13}C chemical shifts were measured relative to the signal of $CDCl_3$ (δ 77.0), DMSO-d_6 (δ 39.51) or acetone-d_6 (δ 29.92). The ^{19}F chemical shifts are given relative to the external signal of $CFCl_3$ (δ 0.0). Assignments of the signals in the NMR spectra were performed using 2D-spectroscopy (COSY, HSQC, HMBC) and DEPT-135 experiments. ^{1}H and ^{13}C NMR data for compounds **2–26** are listed in Tables 2–4 (main chain carbons and protons) and data for all signals in the Experimental. The copies of NMR spectra of previously unknown compounds can be found in the Supplementary data section. High resolution mass spectra (electrospray ionization, ESI) were were measured in a positive mode on a Bruker micrOTOF II mass spectrometer for 2×10^{-5} M solutions in MeCN. Optical rotations were measured using a PU-07 automatic digital polarimeter (Russia) or a JASCO P-2000 automatic digital polarimeter (Japan).

4.2. Methyl (phenyl 3,5-dideoxy-2-thio-4,7,8,9-tetra-*O*-chloroacetyl-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (2)

Tetraol **1**·MeOH (6.57 g, 13.1 mmol) was co-concentrated with MeCN (2×50 mL), the residue was dried *in vacuo*, dissolved in anhydrous MeCN (100 mL), 2,4,6-collidine (17.3 mL, 131

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mmol) was added, the mixture was cooled to 0 °C (ice–water bath), and chloroacetic anhydride (13.5 g, 79 mmol) was added. The reaction mixture was stirred at 0 °C for 30 min, then allowed to warm to ~20 °C and stirred for 4 h. H_2O (5 mL) was added, the mixture was concentrated under reduced pressure, the residue was distributed between toluene (150 mL) and H_2O (250 mL), organic layer was separated, the aqueous layer was extracted with toluene (3×30 mL), and the combined extracts were washed with saturated aqueous $KHSO_4$ (200 mL). At this stage, EtOAc (50 mL) was added to the separating funnel to prevent precipitation of the product from toluene. The organic layer was further washed with H_2O (2×400 mL) and saturated aqueous $NaHCO_3$ (100 mL), and water (100 mL), additional extractions with toluene–EtOAc mixture (3:1, 2×30 mL) were performed from each aqueous layer. The combined organic extract was filtered through the mixture of powdered anhydrous Na_2SO_4 and silica gel (~1:1 v/v, ~15 mm layer), solids were washed with toluene–EtOAc mixture (3:1, 50 mL), the combined filtrate was concentrated under reduced pressure, and dried *in vacuo*. The residue was dissolved in CH_2Cl_2 (50 mL), then Et_2O (150 mL) was slowly added followed by light petroleum (150 mL). The precipitate formed was filtered off and washed with Et_2O–light petroleum mixture (1:3, 20 mL) to give **2** (colorless crystalls, 8.877 g, 87%).

$[\alpha]_D^{24}$ −108.3 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 791.0208 $[M + NH_4]^+$. Calcd for $C_{26}H_{30}Cl_4F_3N_2O_{12}S$: 791.0220. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.22 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 11.0), 2.82 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 4.8), 3.67 (s, 3H, OMe), 3.93 (d, 1H, CHCl, *J* 14.7), 3.97 (d, 1H, CHCl, *J* 14.7), 4.04 (d, 1H, CHCl, *J* 15.0), 4.08 (d, 1H, CHCl, *J* 15.0), 4.08 (d, 1H, CHCl, *J* 15.6), 4.13 (d, 1H, CHCl, *J* 15.6), 4.13 (d, 1H, CHCl, *J* 14.4), 4.16 (d, 1H, CHCl, *J* 14.4), 4.18 (dd, 1H, H-9a, $J_{9a,9b}$ 12.6, $J_{9a,8}$ 8.4), 4.23 (ddd, 1H, H-5, $J_{5,4}$ 11.0, $J_{5,6}$ 10.7, $J_{5,NH}$ 10.3), 4.61 (dd, 1H, H-9b, $J_{9b,9a}$ 12.6, $J_{9b,8}$ 1.5), 4.93 (dd, 1H, H-6, $J_{6,5}$ 10.7, $J_{6,7}$ 1.9), 5.09 (ddd, 1H, H-8, $J_{8,9a}$ 8.4, $J_{8,7}$ 2.2, $J_{8,9b}$ 1.5), 5.52 (dd, 1H, H-7, $J_{7,8}$ 2.2, $J_{7,6}$ 1.9), 5.66 (ddd, 1H, H-4, $J_{4,3a}$ 11.0, $J_{4,5}$ 11.0, $J_{4,3e}$ 4.8), 7.19 (d, 1H, NH, $J_{NH,5}$ 10.3), 7.37-7.40 (m, 2H, Ph), 7.42-7.45 (m, 3H, Ph). ^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 37.2 (C-3), 40.3, 40.4 (2C), 40.7

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(CH_2Cl), 49.9 (C-5), 53.0 (OMe), 63.3 (C-9), 70.2, 70.3 (C-4, C-7), 71.7 (C-6), 74.1 (C-8), 88.5 (C-2), 115.3 (q, $CO\underline{C}F_3$, $J_{C,F}$ 287.7), 127.9, 129.4, 130.4, 136.2 (Ph), 158.0 (q, $\underline{C}OCF_3$, $J_{C,F}$ 38.7), 166.4, 166.9, 167.6 (2C) ($\underline{C}OCH_2Cl$), 167.9 ($\underline{C}OOMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −76.62.

4.3. Methyl (phenyl 3,5-dideoxy-2-thio-4,7,8,9-tetra-*O*-benzoyl-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (3) and methyl (phenyl 3,5-dideoxy-2-thio-4,8,9-tri-*O*-benzoyl-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (4)

Tetraol **1**·MeOH (200 mg, 0.398 mmol) was coconcentrated with MeCN, the residue was dried *in vacuo*, dissolved in pyridine (4 mL), cooled to 0 ° C (ice–water bath), and benzoyl chloride (285 μL, 2.45 mmol) was added. The reaction mixture was stirred for 1.5 h, then MeOH (500 μL) was added dropwise. The mixture was stirred for 30 min, then concentrated under reduced pressure and co-concentrated with toluene (2 mL). The residue was dissolved in CH_2Cl_2 (~30 mL), washed with water (40 mL), 1 M $KHSO_4$ (30 mL), and saturated aqueous $NaHCO_3$ (30 mL). An additional extraction (2×10 mL) was performed from each aqueous layer. The combined organic extract was filtered through cotton wool plug, concentrated under reduced pressure, and dried *in vacuo*. The residue was dissolved in the mixture of benzene (10 mL) and CH_2Cl_2 (2 mL), the solution was applied onto a column with silica gel (column volume 45 mL, eluent benzene → 20% EtOAc in benzene). The fractions eluted were collected to give **3** (colorless foam, 112.8 mg, 32%) and **4** (colorless foam, 204 mg, 68%).

*4.3.1. Data for **3***

R_f 0.65 (benzene–acetone 9:1). $[\alpha]_D^{23}$ −50.8 (*c* 2.0, $CHCl_3$). HR ESI MS: found *m/z* 908.1954 [M + Na]$^+$. Calcd for $C_{46}H_{38}F_3NNaO_{12}S$: 908.1959. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.36 (dd, 1H, H-3a, $J_{3a,3e}$ 13.6, $J_{3a,4}$ 11.7), 3.01 (dd, 1H, H-3e, $J_{3e,3a}$ 13.6, $J_{3e,4}$ 4.8), 3.65 (s, 3H, OMe), 4.36 (ddd, 1H, H-5, $J_{5,6}$ 10.5, $J_{5,4}$ 10.3, $J_{5,NH}$ 9.5), 4.54 (dd, 1H, H-9a, $J_{9a,9b}$ 12.1, $J_{9a,8}$ 8.4),

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4.97 (dd, 1H, H-9b, $J_{9b,9a}$ 12.1, $J_{9b,8}$ 2.6), 5.19 (dd, 1H, H-6, $J_{6,5}$ 10.5, $J_{6,7}$ 2.4), 5.55 (ddd, 1H, H-8, $J_{8,9a}$ 8.4, $J_{8,9b}$ 2.6, $J_{8,7}$ 2.2), 5.98 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.3, $J_{4,3e}$ 4.8), 6.06 (dd, 1H, H-7, $J_{7,6}$ 2.4, $J_{7,8}$ 2.2), 7.08-7.13 (m, 2H, Ph), 7.19-7.24 (m, 2H, Ph), 7.36-7.63 (m, 14H, NH, Ph), 7.87-8.10 (m, 8H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 37.8 (C-3), 50.6 (C-5), 52.7 (OMe), 63.2 (C-9), 69.5 (C-4), 70.0 (C-7), 72.5 (C-6), 73.4 (C-8), 88.9 (C-2), 115.4 (q, CF_3, $J_{C,F}$ 287.5), 128.2, 128.5, 128.6, 129.2, 129.6, 129.9, 130.0, 132.9, 133.3, 133.5, 133.7, 136.1 (Ph), 157.6 (q, $\underline{C}OCF_3$, $J_{C,F}$ 38.0), 165.3, 165.8, 166.3, 166.7 ($\underline{C}$OPh), 168.2 ($\underline{C}$OOMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −76.18.

4.3.2. Data for ***4***

R_f 0.45 (benzene–acetone 8:1) $[\alpha]_D^{23}$ −124.8 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 804.1699 $[M + Na]^+$. Calcd for $C_{39}H_{34}F_3NNaO_{11}S$: 804.1697. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.41 (dd, 1H, H-3a, $J_{3a,3e}$ 13.6, $J_{3a,4}$ 11.6), 2.93 (dd, 1H, H-3e, $J_{3e,3a}$ 13.6, $J_{3e,4}$ 4.8), 3.52 (s, 3H, OMe), 3.93 (d, 1H, OH-7, $J_{OH,7}$ 7.0), 4.18 (ddd, 1H, H-7, $J_{7,OH}$ 7.0, $J_{7,8}$ 4.8, $J_{7,6}$ 1.5), 4.43 (ddd, 1H, H-5, $J_{5,6}$ 10.3, $J_{5,4}$ 10.3, $J_{5,NH}$ 8.4), 4.67 (dd, 1H, H-9a, $J_{9a,9b}$ 12.1, $J_{9a,8}$ 6.6), 4.71 (dd, 1H, H-6, $J_{6,5}$ 10.3, $J_{6,7}$ 1.5), 4.95 (dd, 1H, H-9b, $J_{9b,9a}$ 12.1, $J_{9b,8}$ 2.2), 5.44 (ddd, 1H, H-8, $J_{8,9a}$ 6.6, $J_{8,7}$ 4.8, $J_{8,9b}$ 2.2), 5.93 (ddd, 1H, H-4, $J_{4,3a}$ 11.6, $J_{4,5}$ 10.3, $J_{4,3e}$ 4.8), 7.09-7.22 (m, 3H, Ph), 7.34-7.63 (m, 12H, NH, Ph), 7.91-8.06 (m, 6H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 37.7 (C-3), 52.2 (C-5), 52.7 (OMe), 63.2 (C-9), 68.9, 69.0 (C-4, C-7), 73.2, 73.4 (C-6, C-8), 89.3 (C-2), 115.4 (q, CF_3, $J_{C,F}$ 287.5), 128.3, 128.4, 128.7, 129.1, 129.5, 129.7, 129.9, 132.9, 133.2, 134.0, 135.7 (Ph), 159.1 (q, $\underline{C}OCF_3$, $J_{C,F}$ 38.2), 165.9, 166.1, 167.4 ($\underline{C}$OPh), 168.1 ($\underline{C}$OOMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −75.78.

4.4. Methyl (phenyl 3,5-dideoxy-2-thio-8,9-*O*-isopropylidene-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (5)

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To the solution of tetraol **1**·MeOH (1.0 g, 1.99 mmol) in anhydrous MeCN (20 mL) 2,2-dimethoxypropane (0.46 mL, 3.74 mmol) was added followed by (1*S*)-(+)-10-camphorsulfonic acid (CSA) (36 mg, 0.154 mmol). The reaction mixture was stirred for 30 min, then NEt_3 (0.25 mL) was added. The reaction mixture was concentrated to dryness under reduced pressure, the residue was dissolved in CH_2Cl_2 (50 mL), washed with brine (100 mL), additional extractions with CH_2Cl_2 were performed from the aqueous layer (2×20 mL). The combined organic extract was filtered through cotton wool plug, concentrated under reduced pressure, and dried *in vacuo.* The residue was purified by silica gel chromatography (eluent 25% acetone in toluene) to give **5** (colorless foam, 850 mg, 84%).

R_f 0.35 (toluene–acetone 2:1). $[\alpha]_D^{25}$ −142.5 (*c* 2.0, $CHCl_3$). HR ESI MS: found *m/z* 532.1220 $[M + Na]^+$. Calcd for $C_{21}H_{26}F_3NNaO_8S$: 532.1229. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.38 (s, 3H, Me), 1.40 (s, 3H, Me), 2.11 (dd, 1H, H-3a, $J_{3a,3e}$ 13.6, $J_{3a,4}$ 11.7), 2.79 (dd, 1H, H-3e, $J_{3e,3a}$ 13.6, $J_{3e,4}$ 4.4), 3.48 (ddd, 1H, H-7, $J_{7,OH}$ 8.8, $J_{7,8}$ 8.0, $J_{7,6}$ 1.5), 3.51 (s, 3H, OMe), 3.80 (d, 1H, OH-4, $J_{OH,4}$ 6.6), 3.91 (d, 1H, OH-7, $J_{OH,7}$ 8.8), 3.98 (d, 2H, H-9a, H-9b, $J_{9,8}$ 5.9), 3.99 (ddd, 1H, H-5, $J_{5,6}$ 10.3, $J_{5,4}$ 10.0, $J_{5,NH}$ 9.0), 4.13 (dt, 1H, H-8, $J_{8,9}$ 5.9, $J_{8,7}$ 8.0), 4.30 (dddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.0, $J_{4,OH}$ 6.6, $J_{4,3e}$ 4.4), 4.53 (dd, 1H, H-6, $J_{6,5}$ 10.3, $J_{6,7}$ 1.5), 7.26-7.39 (m, 4H, NH, Ph), 7.52-7.54 (m, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 25.4, 26.4 (Me), 40.9 (C-3), 52.6 (OMe), 53.7 (C-5), 66.3 (C-4), 67.0 (C-9), 70.7 (C-7), 71.5 (C-6), 74.2 (C-8), 90.0 (C-2), 109.2 ($\underline{C}Me_2$), 115.7 (q, CF_3, $J_{C,F}$ 287.0), 128.7, 129.3, 129.7, 136.1 (Ph), 158.8 (q, $\underline{C}OCF_3$, $J_{C,F}$ 37.6), 168.9 ($\underline{C}OOMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −76.22.

4.5. Methyl (phenyl 3,5-dideoxy-2-thio-4-*O*-acetyl-8,9-*O*-isopropylidene-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (6)

Isopropylidene derivative **5** (200 mg, 0.393 mmol) was dissolved in anhydrous CH_2Cl_2, and 2,4,6-collidine (208 μL, 1.57 mmol) was added followed by Ac_2O (75 μL, 1.57 mmol). The reaction mixture was stirred for 1h at ~20 °C, then another portion of Ac_2O (75 μL, 1.57 mmol)

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was added, and the reaction mixture was kept for ~16 h. The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with water (75 mL), 1 M $KHSO_4$ (50 mL), and saturated aqueous $NaHCO_3$ (50 mL). An additional extraction with CH_2Cl_2 (10 mL) was performed from each aqueous layer. The combined organic extract was filtered through cotton wool plug and concentrated under reduced pressure. The residue was purified by silica gel chromatography (column volume 70 mL, eluent benzene → 10% acetone in benzene) to give **6** (colorless foam, 209.8 mg, 97%).

R_f 0.39 (benzene–EtOAc 4.2:08). $[\alpha]_D^{22}$ −162.1 (*c* 2.0, $CHCl_3$). HR ESI MS: found *m/z* 574.1326 $[M + Na]^+$. Calcd for $C_{23}H_{28}F_3NNaO_9S$: 574.1329. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.42 (s, 3H, Me), 1.43 (s, 3H, Me), 2.10 (s, 3H, CO<u>Me</u>), 2.24 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 12.1), 2.83 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 5.1), 3.32 (d, 1H, OH, $J_{OH,7}$ 8.1), 3.46 (s, 3H, OMe), 3.53 (td, 1H, H-7, $J_{7,OH}$ 8.1, $J_{7,8}$ 8.1, $J_{7,6}$ 1.5), 3.93 (dd, 1H, H-9a, $J_{9a,9b}$ 8.8, $J_{9a,8}$ 6.6), 4.04 (dd, 1H, H-9b, $J_{9b,9a}$ 8.8, $J_{9b,8}$ 5.1), 4.14 (ddd, 1H, H-8, $J_{8,7}$ 8.1, $J_{8,9a}$ 6.6, $J_{8,9b}$ 5.1), 4.24 (ddd, 1H, H-5, $J_{5,6}$ 11.0, $J_{5,4}$ 10.3, $J_{5,NH}$ 8.8), 4.55 (dd, 1H, H-6, $J_{6,5}$ 11.0, $J_{6,7}$ 1.5), 5.63 (ddd, 1H, H-4, $J_{4,3a}$ 12.1, $J_{4,5}$ 10.3, $J_{4,3e}$ 5.1), 7.28-7.42 (m, 4H, NH, Ph), 7.54-7.57 (m, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 20.7 (CO<u>Me</u>), 25.4, 26.7 (Me), 37.8 (C-3), 51.5 (C-5), 52.4 (OMe), 66.8 (C-9), 68.3 (C-4), 70.1 (C-7), 71.9 (C-6), 74.3 (C-8), 89.6 (C-2), 109.1 (<u>C</u>Me_2), 115.5 (q, CF_3, $J_{C,F}$ 287.5), 128.7, 129.0, 129.8, 136.3 (Ph), 158.5 (q, <u>C</u>OCF_3, $J_{C,F}$ 38.0), 167.8, 171.8 (<u>C</u>OMe, <u>C</u>OOMe). NMR ^{19}F (282 MHz, $CDCl_3$, δ, ppm): −76.63.

4.6. Methyl (phenyl 3,5-dideoxy-2-thio-4-*O*-benzoyl-8,9-*O*-isopropylidene-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (7)

Isopropylidene derivative **5** (165.3 mg, 0.324 mmol) was dissolved in anhydrous pyridine (3.0 mL), cooled to 0 ° C (ice-water bath), and benzoyl chloride (39 μL, 0.335 mmol) was added. The reaction mixture was stirred for 30 min at 0 ° C, then another portion of benzoyl chloride (24 μL, 0.206 mmol) was added. The mixture was stirred for 2.5 h at 0 °C until complete consumption of

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the starting material was detected by TLC. MeOH (750 μL) was added dropwise and the mixture was stirred for 30 min, then concentrated under reduced pressure and co-concentrated with toluene (2 mL). The residue was dissolved in CH_2Cl_2 (~40 mL), washed with water, 1 M $KHSO_4$, and saturated aqueous $NaHCO_3$ (50 mL each). An additional extraction (2×10 mL) was performed from each aqueous layer. The combined organic extract was filtered through cotton wool plug, concentrated under reduced pressure, and dried *in vacuo*. The residue was purified by silica gel chromatography (column volume 50 mL, eluent benzene → 20% acetone in benzene) to give **7** (colorless foam, 171.0 mg, 86%).

R_f 0.44 (benzene–EtOAc 4.2:08). $[\alpha]_D^{26}$ −141.0 (*c* 2.0, $CHCl_3$). HR ESI MS: found *m/z* 636.1481 $[M + Na]^+$. Calcd for $C_{28}H_{30}F_3NNaO_9S$: 636.1486. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.41 (s, 3H, Me), 1.42 (s, 3H, Me), 2.39 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 11.7), 2.99 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 5.1), 3.39 (d, 1H, OH, $J_{OH,7}$ 8.1), 3.48 (s, 3H, OMe), 3.57 (ddd ~td, 1H, H-7, $J_{7,OH}$ 8.1, $J_{7,8}$ 8.1, $J_{7,6}$ 1.5), 3.97 (dd, 1H, H-9a, $J_{9a,9b}$ 8.8, $J_{9a,8}$ 6.6), 4.04 (dd, 1H, H-9b, $J_{9b,9a}$ 8.8, $J_{9b,8}$ 5.1), 4.15 (ddd, 1H, H-8, $J_{8,7}$ 8.1, $J_{8,9a}$ 6.6, $J_{8,9b}$ 5.1), 4.38 (td, 1H, H-5, $J_{5,6}$ 10.3, $J_{5,4}$ 10.3, $J_{5,NH}$ 8.8), 4.62 (dd, 1H, H-6, $J_{6,5}$ 10.3, $J_{6,7}$ 1.5), 5.84 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.3, $J_{4,3e}$ 5.1), 7.28-7.33 (m, 3H, Ph), 7.37-7.46 (m, 3H, Ph, NH), 7.55-7.62 (m, 3H, Ph), 7.98-8.00 (m, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 25.4, 26.7 (Me), 38.0 (C-3), 51.8 (C-5), 52.5 (OMe), 66.9 (C-9), 69.0 (C-4), 70.3 (C-7), 72.2 (C-6), 74.4 (C-8), 89.6 (C-2), 109.1 ($\underline{C}Me_2$), 115.5 (q, CF_3, $J_{C,F}$ 287.0), 128.5, 128.6, 128.7, 129.0, 129.8, 133.8, 136.3 (Ph), 158.6 (q, $\underline{C}OCF_3$, $J_{C,F}$ 38.0), 167.2, 168.0 ($\underline{C}OMe$, $\underline{C}OOMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −75.82.

4.7. Methyl (phenyl 3,5-dideoxy-2-thio-4-*O*-chloroacetyl-8,9-*O*-isopropylidene-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (8)

To the solution of isopropylidene derivative **7** (254.3 mg, 0.499 mmol) in anhydrous CH_2Cl_2 (5.0 mL) 2,4,6-collidine (145 μL, 1.10 mmol) was added. The solution was cooled to –30 °C (acetone–dry ice bath), and the solution of chloroacetic anhydride (94 mg, 0.55 mmol) in

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anhydrous CH_2Cl_2 (2.5 mL) was added dropwise while stirring. The reaction mixture was stirred at –30 °C for 30 min, until complete consumption of the starting material (TLC monitoring). Saturated aqueous $NaHCO_3$ (5 mL) was added, and the mixture was well shaken and then allowed to warm to ~20 °C, diluted with CH_2Cl_2 (40 mL), washed with water (70 mL), 1 M $KHSO_4$ (50 mL), and saturated aqueous $NaHCO_3$ (50 mL). An additional extraction with CH_2Cl_2 (2×10 mL) was performed from each aqueous layer. The combined organic extract was filtered through cotton wool plug, concentrated under reduced pressure, and dried *in vacuo*. The residue was purified by silica gel chromatography (column volume 50 mL, eluent 5% acetone in benzene → 20% acetone in benzene) to give **8** (colorless foam, 273.4 mg, 93%).

R_f $[\alpha]_D^{26}$ −141.3 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 608.0939 $[M + Na]^+$. Calcd for $C_{23}H_{27}ClF_3NNaO_9S$: 608.0939. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.41 (s, 3H, Me), 1.42 (s, 3H, Me), 2.27 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 11.7), 2.89 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 5.1), 3.28 (d, 1H, OH, $J_{OH,7}$ 8.8), 3.46 (s, 3H, OMe), 3.51 (ddd, 1H, H-7, $J_{7,OH}$ 8.8, $J_{7,8}$ 8.1, $J_{7,6}$ 1.5), 3.98 (dd, 1H, H-9a, $J_{9a,9b}$ 8.8, $J_{9a,8}$ 6.6), 4.02 (dd, 1H, H-9b, $J_{9b,9a}$ 8.8, $J_{9b,8}$ 5.1), 4.09 (s, 2H, CH_2Cl), 4.12 (ddd, 1H, H-8, $J_{8,7}$ 8.1, $J_{8,9a}$ 6.6, $J_{8,9b}$ 5.1), 4.31 (ddd ~td, 1H, H-5, $J_{5,6}$ 10.3, $J_{5,4}$ 10.3, $J_{5,NH}$ 9.5), 4.58 (dd, 1H, H-6, $J_{6,5}$ 10.3, $J_{6,7}$ 1.5), 5.65 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.3, $J_{4,3e}$ 5.1), 7.03 (d, 1H, NH, $J_{NH,5}$ 9.5), 7.28-7.43 (m, 3H, Ph), 7.54-7.56 (m, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 25.4, 26.7 (Me), 37.6 (C-3), 40.4 (CH_2Cl), 51.0 (C-5), 52.5 (OMe), 66.9 (C-9), 70.3 (C-7), 70.4 (C-4), 71.8 (C-6), 74.2 (C-8), 89.4 (C-2), 109.3 ($\underline{C}Me_2$), 115.5 (q, CF_3, $J_{C,F}$ 287.0), 128.7, 128.8, 129.9, 136.3 (Ph), 158.4 (q, $\underline{C}OCF_3$, $J_{C,F}$ 38.0), 167.7, 168.0 ($\underline{C}OCH_2Cl$, $\underline{C}OOMe$). NMR ^{19}F (282 MHz, $CDCl_3$, δ, ppm): −76.56.

4.8. General procedure for removal of isopropylidene group

To the solution of isopropylidene derivative **6**, **7** or **8** in CH_2Cl_2 (4.5 mL per 0.1 mmol), 90% aqueous TFA (0.45 mL per 0.1 mmol, freshly prepared) was added at 0 °C (ice–water bath). The

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reaction mixture was stirred at 0 °C for 30 min. Spots with large R_f values were usually detected on TLC (apparently, they correspond to the products of O-trifluoroacetylation). The mixture was allowed to warm to ~20 °C, and co-concentrated with toluene (2 mL per 0.1 mmol). The residue was applied onto a column with silica gel and the column was kept for ~15 min without elution (to degrade undesirable O-TFA products), and then eluted with CH_2Cl_2 → 60% acetone in CH_2Cl_2 to give the desired triol (74% for **9**, 86% for **10**, 95% for **11)**.

*4.8.1. Data for methyl (phenyl 3,5-dideoxy-2-thio-4-O-acetyl-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**9**)*

R_f 0.30 ($CHCl_3$–acetone 1:1) $[\alpha]_D^{26}$ −141.5 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 534.1011 [M + Na]$^+$. Calcd for $C_{20}H_{24}F_3NNaO_9S$: 534.1016. ^{1}H NMR (300 MHz, acetone-d_6, δ, ppm, *J*, Hz): 2.00 (s, 3H, CO<u>Me</u>), 2.13 (dd, 1H, H-3a, $J_{3a,3e}$ 13.6, $J_{3a,4}$ 11.7), 2.77 (dd, 1H, H-3e, $J_{3e,3a}$ 13.6, $J_{3e,4}$ 4.8), 3.44-3.46 (m, 7H, H-7, H-8, H-9a, H-9b, OH), 4.41 (ddd, 1H, H-5, $J_{5,6}$ 10.6, $J_{5,4}$ 10.3, $J_{5,NH}$ 7.7), 4.88 (dd, 1H, H-6, $J_{6,5}$ 10.6, $J_{6,7}$ 1.1), 5.49 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.3, $J_{4,3e}$ 4.8), 7.31-7.44 (m, 3H, Ph), 7.62-7.69 (m, 2H, Ph), 8.68 (d, 1H, NH, $J_{NH,5}$ 7.7). ^{13}C NMR (75 MHz, acetone-d_6 δ, ppm, *J*, Hz): 20.9 (CO<u>Me</u>), 38.6 (C-3), 51.0 (C-5), 52.6 (OMe), 64.8 (C-9), 70.0 (C-4), 70.6 (C-8), 71.0 (C-7), 72.3 (C-6), 90.5 (C-2), 117.1 (q, CF_3, $J_{C,F}$ 288.0), 129.7, 130.4, 130.8, 137.5 (Ph), 158.2 (q, <u>C</u>OCF_3, $J_{C,F}$ 36.5), 168.5, 170.6 (<u>C</u>OMe, <u>C</u>OOMe). ^{19}F NMR (282 MHz, acetone-d_6 δ, ppm): −77.15.

*4.8.2. Data for methyl (phenyl 3,5-dideoxy-2-thio-4-O-benzoyl-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**10**)*

R_f 0.40 ($CHCl_3$–acetone 1:1). $[\alpha]_D^{23}$ −109.2 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 596.1173 [M + Na]$^+$. Calcd for $C_{25}H_{26}F_3NNaO_9S$: 596.1173. NMR ^{1}H (300 MHz, DMSO-d_6, δ, ppm, *J*, Hz): 2.20 (dd, 1H, H-3a, $J_{3a,3e}$ 13.5, $J_{3a,4}$ 11.4), 2.83 (dd, 1H, H-3e, $J_{3e,3a}$ 13.5, $J_{3e,4}$ 4.7), 3.37 (s, 3H, OMe), 3.40-3.72 (m, 4H, H-7, H-8, H-9a, H-9b), 4.39-4.52 (m, 2H, H-5, OH), 4.55 (d, 1H, OH,

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J 5.1), 4.63 (d, 1H, OH, *J* 7.6), 4.83 (d, 1H, H-6, $J_{6,5}$ 10.6), 5.52 (ddd, 1H, H-4, $J_{4,3a}$ 11.4, $J_{4,5}$ 10.5, $J_{4,3e}$ 4.7), 7.34-7.46 (m, 3H, Ph), 7.49-7.56 (m, 2H, Ph), 7.60-7.70 (m, 3H, Ph), 7.86-7.92 (m, 2H, Ph), 9.67 (d, 1H, NH, $J_{5,NH}$ 9.2). NMR ^{13}C (75 MHz, DMSO-d_6, δ, ppm, *J*, Hz): 37.3 (C-3), 49.3 (C-5), 52.1 (OMe), 63.5 (C-9), 68.6, 69.8 (C-7, C-8), 70.6 (C-4), 71.2 (C-6), 89.4 (C-2), 115.8 (q, CF_3, $J_{C,F}$ 288.0), 128.7, 128.9, 129.1, 129.2, 129.47, 129.53, 133.6, 136.1 (Ph), 156.7 (q, $\underline{C}OCF_3$, $J_{C,F}$ 36.0), 165.2, 167.2 ($\underline{C}$OPh, $\underline{C}$OOMe). NMR ^{19}F (282 MHz, DMSO-d_6, δ, ppm): −75.23.

*4.8.3. Data for methyl (phenyl 3,5-dideoxy-2-thio-4-O-chloroacetyl-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**11**)*

R_f 0.53 ($CHCl_3$–acetone 1:1). $[\alpha]_D^{26}$ −106.7 (*c* 0.83, $CHCl_3$). HR ESI MS: found *m/z* 568.0632 $[M + Na]^+$. Calcd for $C_{20}H_{23}ClF_3NNaO_9S$: 568.0626. ^{1}H NMR (600 MHz, acetone-d_6, δ, ppm, *J*, Hz): 2.18 (dd, 1H, H-3a, $J_{3a,3e}$ 13.8, $J_{3a,4}$ 11.9), 2.83 (dd, 1H, H-3e, $J_{3e,3a}$ 13.8, $J_{3e,4}$ 4.8), 3.47 (s, 3H, OMe), 3.62 (ddd ~t, 1H, H-7, $J_{7,OH}$ 9.1, $J_{7,8}$ 8.6, $J_{7,6}$ 1.4), 3.66-3.83 (m, 6H, H-8, H-9a, H-9b, OH), 4.21 (d, 1H, CHCl, $J_{CHCl,CH'Cl}$ 14.8), 4.27 (d, 1H, CH'Cl, $J_{CH'Cl,CHCl}$ 14.8), 4.42-4.49 (m, 1H, H-5), 4.90 (dd, 1H, H-6, $J_{6,5}$ 10.6, $J_{6,7}$ 1.4), 5.60 (ddd, 1H, H-4, $J_{4,3a}$ 11.9, $J_{4,5}$ 10.3, $J_{4,3e}$ 4.8), 7.35-7.42 (m, 3H, Ph), 7.65-7.68 (m, 2H, Ph), 8.73 (br. s, 1H, NH). ^{13}C NMR (151 MHz, acetone-d_6, δ, ppm, *J*, Hz): 38.4 (C-3), 41.5 (CH_2Cl), 50.9 (C-5), 52.7 (OMe), 64.9 (C-9), 70.6 (C-7), 71.0 (C-8), 72.0 (C-4), 72.4 (C-6), 90.4 (C-2), 117.1 (q, CF_3, $J_{C,F}$ 288.0), 129.8, 130.5, 130.7, 137.4 (Ph), 158.3 (q, NH$\underline{C}OCF_3$, $J_{C,F}$ 37.0), 167.7 ($\underline{C}OCH_2Cl$), 168.4 ($\underline{C}$OOMe). ^{19}F NMR (282 MHz, acetone-d_6, δ, ppm): −76.28.

4.9. Methyl (phenyl 3,5-dideoxy-2-thio-8,9-*O*-benzylidene-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (12) and methyl (phenyl 3,5-dideoxy-2-thio-7,9-*O*-benzylidene-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (14)

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To the solution of tetraol **1**·MeOH (2.0 g, 3.99 mmol) in anhydrous MeCN (80 mL) benzaldehyde dimethyl acetal (1.28 mL, 8.53 mmol) was added followed by (1*S*)-(+)-10-camphorsulfonic acid (CSA) (78 mg, 0.335). The reaction mixture was stirred for 48 h, then NEt_3 (100 μL) was added. The reaction mixture was concentrated under reduced pressure, dried *in vacuo*, the residue was purified by silica gel chromatography (column volume 80 mL, eluent benzene–CH_2Cl_2–acetone 50:50:4 → 50:50:25), the fractions were collected to give **12** (white foam, 0.7511 g, 34%) and **14** (white foam, 1.4692 g, 66%).

*4.9.1. Data for **12** (mixture of stereoisomers)*

R_f 0.22 (benzene–CH_2Cl_2–acetone 1:1:0.4). HR ESI MS: found *m/z* 580.1226 $[M + Na]^+$. Calcd for $C_{25}H_{26}F_3NNaO_8S$: 580.1223. ^{1}H NMR (300 MHz, CD_3OD, δ, ppm, *J*, Hz): 2.02 (ddd, 3H, *J* 13.7, *J* 11.6, *J* 2.2), 2.70 (dd, 3H, *J* 13.7, *J* 4.6), 3.31 (br. s., 2H), 3.66-3.81 (m, 3H), 3.93-4.14 (m, 7H), 4.15-4.31 (m, 7H), 4.52-4.68 (m, 3H), 5.81 (s, 2H), 5.90 (s, 1H), 7.13-7.22 (m, 2H), 7.28-7.52 (m, 23H), 7.53-7.60 (m, 3H). ^{13}C NMR (75 MHz, CD_3OD, δ, ppm, *J*, Hz): 42.2, 53.2, 54.4, 67.4, 67.7, 69.3, 70.9, 71.5, 73.2, 73.5, 76.5, 76.9, 91.2, 105.0, 105.8, 117.7 (q, $J_{C,F}$ 287.5), 27.7, 128.0, 129.4, 130.0, 130.3, 130.6, 130.9, 131.1, 137.5, 138.9, 139.8, 159.8 (q, $J_{C,F}$ 37.0), 170.7, 170.8. ^{19}F NMR (282 MHz, CD_3OD, δ, ppm): −76.01, −76.07.

*4.9.2. Data for **14***

R_f 0.47 (benzene–CH_2Cl_2–acetone 1:1:0.4). $[\alpha]_D^{22}$ −119.3 (*c* 1.0, acetone). HR ESI MS: found *m/z* 580.1227 $[M + Na]^+$. Calcd for $C_{25}H_{26}F_3NNaO_8S$: 580.1223. ^{1}H NMR (300 MHz, acetone-d_6, δ, ppm, *J*, Hz): 2.01 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 11.7), 2.73 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 4.4), 3.36 (s, 3H, OMe), 3.64 (dd, 1H, H-9a, $J_{9a,9b}$ 10.6, $J_{9a,8}$ 10.3), 3.79 (dd, 1H, H-7, $J_{7,8}$ 9.5, $J_{7,6}$ 1.5), 4.06 (dddd, 1H, H-8, $J_{8,9a}$ 10.3, $J_{8,7}$ 9.5, $J_{8,9b}$ 5.0, $J_{8,OH}$ 5.0), 4.27-4.38 (m, 4H, H-4, H-5, H-9b, OH-8), 4.68 (d, 1H, OH-4, $J_{OH,4}$ 4.4), 4.91 (dd, 1H, H-6, $J_{6,5}$ 10.1, $J_{6,7}$ 1.5), 5.46 (s, 1H, CH),

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7.31-7.39 (m, 6H, Ph), 7.59-7.65 (m, 4H, Ph), 8.63 (d, 1H, NH, $J_{NH,5}$ 8.4). ^{13}C NMR (75 MHz, acetone-d_6, δ, ppm, *J*, Hz): 42.2 (C-3), 52.4 (OMe), 53.6 (C-5), 61.0 (C-8), 67.3 (C-4), 70.6 (C-6), 72.4 (C-9), 80.2 (C-7), 91.3 (C-2), 101.6 (CH), 117.3 (q, CF_3, $J_{C,F}$ 288.0), 127.2, 128.6, 129.2, 129.7, 130.1, 130.4, 137.0, 139.4 (Ph), 158.2 (q, $\underline{C}OCF_3$, $J_{C,F}$ 36.0), 168.5 ($\underline{C}OOMe$). ^{19}F NMR (282 MHz, acetone-d_6, δ, ppm): −76.86.

4.10. Methyl (phenyl 3,5-dideoxy-2-thio-4,8-di-*O*-acetyl-7,9-*O*-benzylidene-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (16)

To the solution of benzylidene derivative **14** (81.1 mg, 0.145 mmol) in anhydrous pyridine (2.5 mL), Ac_2O (1.48 mL) was added in one portion, and the mixture was stirred for 30 min, then DMAP (5.0 mg, 0.041 mmol) was added. The reaction mixture was stirred for 40 min, then concentrated under reduced pressure (bath temperature 40 °C) and co-concentrated with toluene (2×3 mL). The residue was purified by silica gel chromatography (column volume 30 mL, eluent benzene–acetone 100:5) to give **16** (colorless foam, 80.8 mg, 86.6%).

R_f 0.55 (benzene–EtOAc 20:1). $[\alpha]_D^{24}$ −111.0 (*c* 2.0, $CHCl_3$). HR ESI MS: found *m/z* 664.1430 $[M + Na]^+$. Calcd for $C_{29}H_{30}F_3NNaO_{10}S$: 664.1435. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.03 (s, 3H, Me), 2.07 (s, 3H, Me), 2.19 (dd, 1H, H-3a, $J_{3a,3e}$ 13.6, $J_{3a,4}$ 12.1), 2.74 (dd, 1H, H-3e, $J_{3e,3a}$ 13.6, $J_{3e,4}$ 4.8), 3.41 (s, 3H, OMe), 3.60 (dd, 1H, H-9a, $J_{9a,9b}$ 10.6, $J_{9a,8}$ 9.5), 3.90 (dd, 1H, H-7, $J_{7,8}$ 9.9, $J_{7,6}$ 1.5), 4.51 (ddd, 1H, H-5, $J_{5,6}$ 10.3, $J_{5,4}$ 10.0, $J_{5,NH}$ 8.8), 4.61 (dd, 1H, H-6, $J_{6,5}$ 10.3, $J_{6,7}$ 1.5), 4.72 (dd, 1H, H-9b, $J_{9b,9a}$ 10.6, $J_{9b,8}$ 5.3), 5.16 (ddd, 1H, H-8, $J_{8,7}$ 9.9, $J_{8,9a}$ 9.5, $J_{8,9b}$ 5.3), 5.48 (s, 1H, CH), 5.56 (ddd, 1H, H-4, $J_{4,3a}$ 12.1, $J_{4,5}$ 10.0, $J_{4,3e}$ 4.8), 6.75 (d, 1H, NH, $J_{NH,5}$ 8.8), 7.31-7.39 (m, 8H, Ph), 7.57-7.61 (m, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 20.7, 20.9 (CO$\underline{Me}$), 37.7 (C-3), 50.3 (C-5), 52.4 (OMe), 63.1 (C-8), 67.8 (C-9), 68.5 (C-4), 70.4 (C-6), 76.4 (C-7), 89.7 (C-2), 101.6 (CH), 115.6 (q, CF_3, $J_{C,F}$ 288.0), 126.3, 128.1, 128.9, 129.0, 129.2, 129.9, 134.2, 137.0 (Ph), 157.5 (q, $\underline{C}OCF_3$, $J_{C,F}$ 37.5), 167.3 ($\underline{C}OOMe$), 169.7, 171.4 ($\underline{C}OMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −76.57.

4.11. Methyl (phenyl 3,5-dideoxy-2-thio-4-*O*-chloroacetyl-7,9-*O*-benzylidene-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (18)

To the suspension of benzylidene derivative **14** (127.5 mg, 0.223 mmol) in anhydrous CH_2Cl_2 (3.0 mL) 2,4,6-collidine (91 μL, 0.686 mmol) was added. The solution was cooled to –10 °C (acetone–dry ice bath), and the solution of chloroacetic anhydride (59 mg, 0.343 mmol) in anhydrous CH_2Cl_2 (1.0 mL) was added dropwise while stirring. Complete dissolution of the starting material was observed at this stage. The reaction mixture was stirred at –10 °C for 1 h until complete consumption of the starting material (TLC monitoring). Saturated aqueous $NaHCO_3$ (5 mL) was added, and the mixture was well shaken and then allowed to warm to ~20 °C, diluted with CH_2Cl_2 (40 mL), washed with water, 1 M $KHSO_4$, and saturated aqueous $NaHCO_3$ (50 mL each). An additional extraction with CH_2Cl_2 (2×10 mL) was performed from each aqueous layer. The combined organic extract was filtered through cotton wool plug, concentrated under reduced pressure, and dried *in vacuo*. The residue was purified by silica gel chromatography (column volume 50 mL, eluent 5% EtOAc in benzene → 30% EtOAc in benzene) to give **18** (colorless foam, 115.7 mg, 80%).

R_f 0.60 (benzene–EtOAc 6:1) $[\alpha]_D^{19}$ −142.6 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 656.0938 [M + Na]$^+$. Calcd for $C_{27}H_{27}ClF_3NNaO_9S$: 656.0939. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.82 (d, 1H, OH-8, $J_{OH,8}$ 5.5), 2.24 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 11.7), 2.76 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 5.0), 3.53 (dd, 1H, H-9a, $J_{9a,9b}$ 10.8, $J_{9a,8}$ 10.3), 3.61 (s, 3H, OMe), 3.62 (dd, 1H, H-7, $J_{7,8}$ 9.2, $J_{7,6}$ 2.2), 3.98 (dddd, 1H, H-8, $J_{8,9a}$ 10.3, $J_{8,7}$ 9.2, $J_{8,OH}$ 5.5, $J_{8,9b}$ 5.3), 4.04 (s, 2H, CH_2Cl), 4.30 (dd, 1H, H-9b, $J_{9b,9a}$ 10.8, $J_{9b,8}$ 5.3), 4.52 (ddd, 1H, H-5, $J_{5,6}$ 10.3, $J_{5,4}$ 10.0, $J_{5,NH}$ 9.5), 4.67 (dd, 1H, H-6, $J_{6,5}$ 10.3, $J_{6,7}$ 2.2), 5.38 (s, 1H, CH), 5.71 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.0, $J_{4,3e}$ 5.0), 6.80 (d, 1H, NH, $J_{NH,5}$ 9.5), 7.33-7.40 (m, 6H, Ph), 7.50-7.55 (m, 4H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 37.0 (C-3), 40.4 (CH_2Cl), 49.7 (C-5), 52.8 (OMe), 60.4 (C-8), 70.2 (C-6), 70.8 (C-9), 71.1 (C-4), 78.8 (C-7), 87.9 (C-2), 101.3 (CH), 115.5 (q, CF_3, $J_{C,F}$ 288.5),

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126.2, 128.1, 128.9, 129.1, 129.4, 129.5, 134.9, 137.1 (Ph), 157.4 (q, $\underline{C}OCF_3$, $J_{C,F}$ 38.0), 167.7, 168.1 ($\underline{C}OCH_2Cl$, $\underline{C}OOMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −76.47.

4.12. Methyl (phenyl 3,5-dideoxy-2-thio-4,8-di-*O*-chloroacetyl-7,9-*O*-benzylidene-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (17)

To the suspension of benzylidene derivative **14** (101.6 mg, 0.182 mmol) in anhydrous CH_2Cl_2 (3.0 mL) 2,4,6-collidine (145 μL, 1.093 mmol) was added. The solution was cooled to 0 °C (ice–water bath), and the solution of chloroacetic anhydride (59 mg, 0.547 mmol) in anhydrous CH_2Cl_2 (1.0 mL) was added dropwise while stirring. Complete dissolution of the starting material was observed at this stage. The reaction mixture was stirred at 0 °C for 30 min, then allowed to warm to ~20 °C, stirred at 20 C for 30 min, and then kept at –18 °C for 48 h (complete consumption of the starting material was detected by TLC). Saturated aqueous $NaHCO_3$ (5 mL) was added, and the mixture was well shaken, diluted with CH_2Cl_2 (40 mL), washed with water, 1 M $KHSO_4$, and saturated aqueous $NaHCO_3$ (40 mL each). An additional extraction with CH_2Cl_2 (2×10 mL) was performed from each aqueous layer. The combined organic extract was filtered through cotton wool plug, concentrated under reduced pressure, and dried *in vacuo*. The residue was purified by silica gel chromatography (column volume 50 mL, eluent 1% EtOAc in benzene → 10% EtOAc in benzene) to give **17** (colorless foam, 122.9 mg, 95%).

R_f 0.47 (benzene–EtOAc 10:1) $[\alpha]_D^{26}$ −147.6 (*c* 2.0, $CHCl_3$). HR ESI MS: found *m/z* 732.0654 $[M + Na]^+$. Calcd for $C_{29}H_{28}Cl_2F_3NNaO_{10}S$: 732.0655. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.23 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 12.1), 2.78 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 5.0), 3.49 (s, 3H, OMe), 3.68 (dd, 1H, H-9a, $J_{9a,9b}$ 10.8, $J_{9a,8}$ 10.3), 3.99 (dd, 1H, H-7, $J_{7,8}$ 9.5, $J_{7,6}$ 1.5), 4.00 (s, 2H, CH_2Cl), 4.05 (s, 2H, CH_2Cl), 4.60-4.72 (m, 3H, H-5, H-6, H-9b), 5.30 (ddd, 1H, H-8, $J_{8,9a}$ 10.3, $J_{8,7}$ 9.5, $J_{8,9b}$ 5.3), 5.49 (s, 1H, CH), 5.68 (ddd, 1H, H-4, $J_{4,3a}$ 12.1, $J_{4,5}$ 10.0, $J_{4,3e}$ 5.0), 6.77 (d, 1H, NH, $J_{NH,5}$ 8.1), 7.33-7.42 (m, 8H, Ph), 7.52-7.55 (m, 2H, Ph). ^{13}C NMR (75 MHz,

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$CDCl_3$, δ, ppm, *J*, Hz): 37.3 (C-3), 40.4, 40.7 (CH_2Cl), 49.8 (C-5), 52.6 (OMe), 64.2 (C-8), 67.5 (C-9), 70.7 (C-6), 70.8 (C-4), 76.7 (C-7), 89.2 (C-2), 101.8 (CH), 115.5 (q, CF_3, $J_{C,F}$ 288.5), 126.2, 128.2, 129.1, 129.2, 129.4, 129.6, 134.2, 136.6 (Ph), 157.5 (q, $\underline{C}OCF_3$, $J_{C,F}$ 37.6), 166.4, 167.2, 167.9 ($\underline{C}OCH_2Cl$, $\underline{C}OOMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −76.55.

4.13. Methyl (phenyl 3,5-dideoxy-2-thio-4-*O*-chloroacetyl-9-*O*-benzyl-5-trifluoroacetamido-D-*glycero*-*β*-D-*galacto*-nonulopyranosid)onate (15)

To the solution of benzylidene derivative **12** (117.1 mg, 0.210 mmol) in anhydrous CH_2Cl_2 (3.0 mL) 2,4,6-collidine (110 μL, 0.831 mmol) was added. The solution was cooled to –40 °C (ice–water bath), and the solution of chloroacetic anhydride (43.1 mg, 0.547 mmol) in CH_2Cl_2 (1.0 mL) was added dropwise while stirring. The reaction mixture was stirred at –40 °C for 30 min, then another portion of solution of chloroacetic anhydride (10.0 mg, 0.127 mmol) in CH_2Cl_2 (300 μL) was added, and the reaction mixture was stirred at –40 °C for additional 30 min until complete consumption of the starting material (TLC monitoring). Saturated aqueous $NaHCO_3$ (4 mL) was added, and the mixture was well shaken, diluted with CH_2Cl_2 (40 mL), washed with water, 1 M $KHSO_4$, and saturated aqueous $NaHCO_3$ (50 mL each). An additional extraction with CH_2Cl_2 (2×10 mL) was performed from each aqueous layer. The combined organic extract was filtered through cotton wool plug, concentrated under reduced pressure, and dried *in vacuo* to give crude **13** (light yellow foam, 139 mg). This product was dissolved in freshly distilled anhydrous THF (5.2 mL), cooled to 0 °C (ice-water bath), and $BH_3{\cdot}NMe_3$ (61 mg, 0.840 mmol) was added followed by $AlCl_3$ (168 mg, 1.26 mmol), then H_2O (3.8 μL, 0.210 mmol) was added *via* a syringe. The mixture was stirred at 0 °C for 30 min and at ~20 °C for 3h, then another portion of H_2O (4 μL) was added. The mixture was stirred for additional 15 min, then diluted with EtOAc (40 mL), washed with saturated aqueous NaHCO3 (50 mL; $Al(OH)_3$ precipitated at this stage), and H_2O (15 mL). The combined aqueous layer was extracted with EtOAc (3×20 mL), the combined organic extract was washed with water (15 mL), filtered through cotton wool

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plug, concentrated under reduced pressure, and dried *in vacuo*. The residue was purified by silica gel chromatography (column volume 50 mL, eluent benzene–CH_2Cl_2–acetone 25:25:1 → benzene–CH_2Cl_2–acetone 25:25:10) to give **15** (colorless foam, 89.8 mg, 67% from **12**).

R_f 0.27 (benzene–EtOAc 6:1) $[\alpha]_D^{21}$ −112.7 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 658.1092 [M + Na]$^+$. Calcd for $C_{27}H_{29}ClF_3NNaO_9S$: 658.1096. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.11 (dd, 1H, H-3a, $J_{3a,3e}$ 13.6, $J_{3a,4}$ 11.7), 2.75 (dd, 1H, H-3e, $J_{3e,3a}$ 13.6, $J_{3e,4}$ 4.8), 3.20 (d, 1H, OH-8, $J_{OH,8}$ 4.4), 3.41 (s, 3H, OMe), 3.49 (dd, 1H, H-9a, $J_{9a,9b}$ 9.5, $J_{9a,8}$ 6.6), 3.52 (ddd, 1H, H-7, $J_{7,OH}$ 9.5, $J_{7,8}$ 8.4, $J_{7,6}$ 1.1), 3.61 (d, 1H, OH-7, $J_{OH,7}$ 9.5), 3.73 (dd, 1H, H-9b, $J_{9b,9a}$ 9.5, $J_{9b,8}$ 2.9), 3.92 (dddd, 1H, H-8, $J_{8,7}$ 8.4, $J_{8,9a}$ 6.6, $J_{8,OH}$ 4.4, $J_{8,9b}$ 2.9), 3.98 (d, 1H, CHCl, $J_{CHCl,CH'Cl}$ 14.7), 4.05 (d, 1H, CH'Cl, $J_{CH'Cl,CHCl}$ 14.7), 4.41 (ddd, 1H, H-5, $J_{5,6}$ 10.6, $J_{5,4}$ 10.3, $J_{5,NH}$ 9.5), 4.51 (s, 1H, C$\underline{H}_2$Ph), 4.74 (dd, 1H, H-6, $J_{6,5}$ 10.6, $J_{6,7}$ 1.1), 5.56 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.3, $J_{4,3e}$ 4.8), 7.28-7.38 (m, 8H, Ph), 7.50-7.53 (m, 3H, NH, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 37.6 (C-3), 40.4 (CH_2Cl), 50.6 (C-5), 52.5 (OMe), 68.7 (C-8), 69.3 (C-7), 70.5 (C-4), 71.3 (C-6), 71.6 (C-9), 73.3 ($\underline{C}H_2Ph$), 89.5 (C-2), 115.6 (q, CF_3, $J_{C,F}$ 287.5), 127.7, 127.7, 128.3, 128.8, 129.4, 129.6, 135.7, 137.8 (Ph), 158.4 (q, $\underline{C}OCF_3$, $J_{C,F}$ 38.0), 167.3, 167.9 ($\underline{C}OCH_2Cl$, $\underline{C}OOMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −76.65.

4.14. General procedure for *O*-trifluoroacetylation of triols

The starting material was dried *in vacuo* (0.1 Torr, 1 h) dissolved in TFA_2O (1.6 mL per 0.1 mmol), then sodium trifluoroacetate (11.8 mg per 0.1 mmol, freshly dried *in vacuo* (0.1 Torr, 1 h) at 80 °C) was added. The mixture was stirred at room temperature (~20 °C) until complete consumption of the starting material (TLC monitoring). The reaction mixture was coconcentrated with anhydrous benzene (2×10 mL per 0.1 mmol) and with anhydrous CCl_4 (2×10 mL per 0.1 mmol) under reduced pressure, the residue was triturated with anhydrous benzene or with anhydrous CCl_4 (3 mL per 0.1 mmol), than the extract was filtered through a PTFE microfilter (Iso-Disk, 0.45μm, 13 mm, Supelco). The solids were washed with the solvent

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(3×2 mL per 0.1 mmol), and the combined filtrate was concentrated under reduced pressure, the residue was dried *in vacuo* to give trifluoroacetylated product (90% for **20**, 87% for **21**, and 89% for **22**). The obtained trifluoroacetylated thiosialosides were used in the sialylation reactions without further purification.

*4.14.1. Data for methyl (phenyl 3,5-dideoxy-2-thio-4-O-acetyl-7,8,9-tri-O-trifloroacetyl-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**20**)*

R_f 0.59 (benzene–EtOAc 10:1) $[\alpha]_D^{28}$ −105.2 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 838.0229 $[M + K]^+$. Calcd for $C_{26}H_{21}F_{12}KNO_{12}S$: 838.0224. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.14 (s, 3H, Me), 2.25 (dd, 1H, H-3a, $J_{3a,3e}$ 14.1, $J_{3a,4}$ 11.7), 2.78 (dd, 1H, H-3e, $J_{3e,3a}$ 14.1, $J_{3e,4}$ 5.0), 3.74 (s, 3H, OMe), 4.13 (ddd, 1H, H-5, $J_{5,6}$ 10.5, $J_{5,4}$ 10.3, $J_{5,NH}$ 9.5), 4.28 (dd, 1H, H-9a, $J_{9a,9b}$ 12.5, $J_{9a,8}$ 9.2), 4.74 (dd, 1H, H-9b, $J_{9b,9a}$ 12.5, $J_{9b,8}$ 2.4), 4.81 (dd, 1H, H-6, $J_{6,5}$ 10.5, $J_{6,7}$ 2.4), 4.98 (ddd, 1H, H-8, $J_{8,9a}$ 9.2, $J_{8,7}$ 1.8, $J_{8,9b}$ 2.4), 5.54 (dd, 1H, H-7, $J_{7,8}$ 1.8, $J_{7,6}$ 2.4), 5.77 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.3, $J_{4,3e}$ 5.0), 7.12 (d, 1H, NH, $J_{NH,5}$ 9.5), 7.35-7.46 (m, 5H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 20.6 (CO<u>Me</u>), 37.2 (C-3), 50.2 (C-5), 53.1 (OMe), 63.9 (C-9), 67.9 (C-4), 71.7, 71.7 (2 C, C-6, C-7), 75.4 (C-8), 88.1 (C-2), 114.0 (q, CF_3, $J_{C,F}$ 285.3), 114.1 (q, CF_3, $J_{C,F}$ 284.7), 114.2 (q, CF_3, $J_{C,F}$ 285.3), 115.2 (q, CF_3, $J_{C,F}$ 288.0), 127.5, 129.6, 130.8, 136.0 (Ph), 156.2 (q, O<u>C</u>OCF_3, $J_{C,F}$ 43.7), 156.4 (q, O<u>C</u>OCF_3, $J_{C,F}$ 43.7), 158.0 (q, NH<u>C</u>OCF_3, $J_{C,F}$ 38.7), 167.7, 172.2 (<u>C</u>OMe, <u>C</u>OOMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −77.05, −75.94, −75.76, −75.25.

*4.14.2. Data for methyl (phenyl 3,5-dideoxy-2-thio-4-O-chloroacetyl-7,8,9-tri-O-trifloroacetyl-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**21**)*

R_f 0.68 (benzene–EtOAc 9:1). $[\alpha]_D^{25}$ −97.9 (*c* 2.0, $CHCl_3$). HR ESI MS: found *m/z* 760.0276 $[M + Na]^+$. Calcd for $C_{26}H_{20}ClF_{12}NNaO_{12}S$: 760.0272. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.28 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 11.7), 2.84 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 4.8), 3.76 (s, 3H,

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OMe), 4.07 (d, 1H, CHCl, $J_{CHCl,CH'Cl}$ 15.4), 4.12 (d, 1H, CH'Cl, $J_{CH'Cl,CHCl}$ 15.4), 4.17 (ddd, 1H, H-5, $J_{5,6}$ 10.6, $J_{5,4}$ 10.3, $J_{5,NH}$ 9.9), 4.27 (dd, 1H, H-9a, $J_{9a,9b}$ 12.5, $J_{9a,8}$ 9.2), 4.72 (dd, 1H, H-9b, $J_{9b,9a}$ 12.5, $J_{9b,8}$ 2.6), 4.87 (dd, 1H, H-6, $J_{6,5}$ 10.6, $J_{6,7}$ 2.2), 5.02 (ddd, 1H, H-8, $J_{8,9a}$ 9.2, $J_{8,7}$ 1.8, $J_{8,9b}$ 2.6), 5.56 (dd, 1H, H-7, $J_{7,8}$ 1.8, $J_{7,6}$ 2.2), 5.83 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.3, $J_{4,3e}$ 4.8), 6.98 (d, 1H, NH, $J_{NH,5}$ 9.9), 7.37-7.46 (m, 5H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 36.9 (C-3), 40.3 (CH_2Cl), 49.9 (C-5), 53.2 (OMe), 63.8 (C-9), 70.0 (C-4), 71.5 (C-6), 71.6 (C-7), 75.1 (C-8), 87.9 (C-2), 114.0 (q, CF_3, $J_{C,F}$ 285.3), 114.1 (q, CF_3, $J_{C,F}$ 285.3), 114.2 (q, CF_3, $J_{C,F}$ 285.3), 115.1 (q, CF_3, $J_{C,F}$ 288), 127.2, 129.7, 131.0, 136.0 (Ph), 156.2 (q, O<u>C</u>OCF_3, $J_{C,F}$ 43.7), 156.3 (q, O<u>C</u>OCF_3, $J_{C,F}$ 44.2), 156.8 (q, O<u>C</u>OCF_3, $J_{C,F}$ 44.2), 158.0 (q, NH<u>C</u>OCF_3, $J_{C,F}$ 39.3), 167.5 (<u>C</u>OOMe), 168.5 (<u>C</u>OCH_2Cl). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −76.87, −75.88, −75.73, −75.19.

*4.14.3. Data for methyl (phenyl 3,5-dideoxy-2-thio-4-O-benzoyl-7,8,9-tri-O-trifloroacetyl-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**22**)*

R_f 0.79 (benzene–EtOAc 9:1). $[\alpha]_D^{23}$ −89.3 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 884.0639 [M + Na]$^+$. Calcd for $C_{31}H_{23}F_{12}NNaO_{12}S$: 884.0642. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.45 (dd, 1H, H-3a, $J_{3a,3e}$ 14.1, $J_{3a,4}$ 11.7), 2.95 (dd, 1H, H-3e, $J_{3e,3a}$ 14.1, $J_{3e,4}$ 5.0), 3.80 (s, 3H, OMe), 4.29 (dd, 1H, H-9a, $J_{9a,9b}$ 12.5, $J_{9a,8}$ 9.2), 4.34 (ddd, 1H, H-5, $J_{5,6}$ 10.3, $J_{5,4}$ 10.3, $J_{5,NH}$ 9.5), 4.71 (dd, 1H, H-9b, $J_{9b,9a}$ 12.5, $J_{9b,8}$ 2.6), 4.83 (ddd, 1H, H-8, $J_{8,9a}$ 9.2, $J_{8,7}$ 1.8, $J_{8,9b}$ 2.6), 4.90 (dd, 1H, H-6, $J_{6,5}$ 10.3, $J_{6,7}$ 2.2), 5.62 (dd, 1H, H-7, $J_{7,8}$ 1.8, $J_{7,6}$ 2.2), 6.20 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.3, $J_{4,3e}$ 5.0), 7.25-7.42 (m, 6H, NH, Ph), 7.50-7.55 (m, 2H, Ph), 7.62-7.72 (m, 1H, Ph), 7.99-8.03 (m, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 37.2 (C-3), 50.1 (C-5), 53.2 (OMe), 63.8 (C-9), 68.8 (C-4), 71.6 (C-7), 71.8 (C-6), 75.5 (C-8), 87.8 (C-2), 114.0 (q, CF_3, $J_{C,F}$ 285.3), 114.1 (q, CF_3, $J_{C,F}$ 285.8), 114.2 (q, CF_3, $J_{C,F}$ 285.3), 115.1 (q, CF_3, $J_{C,F}$ 287.5), 127.3, 127.8, 129.1, 129.6, 129.9, 130.8, 134.6, 136.0 (Ph), 156.2 (q, O<u>C</u>OCF_3, $J_{C,F}$ 43.1), 156.5 (q,

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O<u>C</u>OCF$_3$, $J_{C,F}$ 44.8), 157.0 (q, O<u>C</u>OCF$_3$, $J_{C,F}$ 44.2), 158.1 (q, NH<u>C</u>OCF$_3$, $J_{C,F}$ 38.7), 167.8 (<u>C</u>OPh, <u>C</u>OOMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −77.28, −75.89, −75.72, −75.17.

4.15. General procedure for trifluoroacetylation of compounds containing one or two OH groups

The starting material was dried *in vacuo* (0.1 Torr, 1 h), dissolved in anhydrous CH_2Cl_2 (1.5 mL per 0.1 mmol), then TFA_2O (1.5 mL per 0.1 mmol) was added followed by sodium trifluoroacetate (15.0 mg per 0.1 mmol, freshly dried *in vacuo* (0.1 Torr, 1 h) at 80 °C) was added. The mixture was stirred at room temperature (~20 °C) until complete consumption of the starting material (TLC monitoring). The reaction mixture was further processed as described above in section 4.14 to give trifluoroacetylated product (94% for **23**, quantitative for **24**).The obtained trifluoroacetylated thiosialosides were used in the sialylation reactions without further purification.

*4.15.1. Data for methyl (phenyl 3,5-dideoxy-2-thio-4,8,9-O-tri-O-benzoyl-7-O-trifloroacetyl-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**23**)*

R_f 0.77 (benzene–EtOAc 8:1). $[\alpha]_D^{23}$ −96.1 (*c* 1.97, $CHCl_3$). HR ESI MS: found *m/z* 900.1519 $[M + Na]^+$. Calcd for $C_{41}H_{33}F_6NNaO_{12}S$: 900.1520. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.43 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 11.7), 3.01 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 4.8), 3.67 (s, 3H, OMe), 4.37 (dd, 1H, H-9a, $J_{9a,9b}$ 12.5, $J_{9a,8}$ 8.8), 4.40 (ddd, 1H, H-5, $J_{5,6}$ 10.6, $J_{5,4}$ 10.3, $J_{5,NH}$ 9.5), 4.82 (dd, 1H, H-9b, $J_{9b,9a}$ 12.5, $J_{9b,8}$ 2.4), 5.09 (dd, 1H, H-6, $J_{6,5}$ 10.6, $J_{6,7}$ 2.2), 5.42 (ddd, 1H, H-8, $J_{8,9a}$ 8.8, $J_{8,7}$ 1.8, $J_{8,9b}$ 2.4), 5.81 (dd, 1H, H-7, $J_{7,8}$ 1.8, $J_{7,6}$ 2.2), 6.02 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.3, $J_{4,3e}$ 4.8), 7.04-7.09 (m, 1H, Ph), 7.15-7.20 (m, 2H, Ph), 7.34 (d, 1H, NH, $J_{NH,5}$ 9.5), 7.37-7.65 (m, 11H, Ph), 7.87-7.90 (m, 2H, Ph), 7.98-8.05 (m, 4H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 37.6 (C-3), 50.4 (C-5), 52.9 (OMe), 62.5 (C-9), 69.2 (C-4), 72.1 (C-6), 73.0 (C-8), 73.8 (C-7), 88.8 (C-2), 114.4 (q, CF_3, $J_{C,F}$ 285.8), 115.2 (q, CF_3, $J_{C,F}$ 288.0), 127.9,

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128.3, 128.6, 128.8, 129.0, 129.3, 129.5, 129.7, 129.8, 129.9, 130.1, 133.1, 133.7, 134.1, 136.1 (Ph), 156.7 (q, O<u>C</u>OCF$_3$, $J_{C,F}$ 43.7), 158.0 (q, NH<u>C</u>OCF$_3$, $J_{C,F}$ 38.7), 165.6, 166.3, 167.3, 167.9 (<u>C</u>OPh, <u>C</u>OOMe,). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −77.04, −75.14.

*4.15.2. Data for methyl (phenyl 3,5-dideoxy-2-thio-4-O-chloroacetyl-7,8-di-O-trifloroacetyl-9-O-benzyl-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**24**)*

R_f 0.60 (benzene–EtOAc 10:1). $[\alpha]_D^{29}$ −62.3 (*c* 0.5, $CHCl_3$). HR ESI MS: found *m/z* 850.0741 $[M + Na]^+$. Calcd for $C_{31}H_{27}ClF_9NNaO_{11}S$: 850.0742. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.22 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 11.7), 2.80 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 5.1), 3.57 (dd, 1H, H-9a, $J_{9a,9b}$ 11.4, $J_{9a,8}$ 7.3), 3.63 (s, 3H, OMe), 3.92 (dd, 1H, H-9b, $J_{9b,9a}$ 11.4, $J_{9b,8}$ 3.3), 4.03 (s, 2H, CH_2Cl), 4.17 (ddd, 1H, H-5, $J_{5,6}$ 10.6, $J_{5,4}$ 10.6, $J_{5,NH}$ 9.5), 4.31 (d, 1H, CHPh, $J_{CHPh,CH'Ph}$ 11.7), 4.36 (d, 1H, CH'Ph, $J_{CH'Ph,CHPh}$ 11.7), 4.86 (dd, 1H, H-6, $J_{6,5}$ 10.6, $J_{6,7}$ 2.6), 5.36 (ddd, 1H, H-8, $J_{8,9a}$ 7.3, $J_{8,7}$ 3.3, $J_{8,9b}$ 3.3), 5.56 (ddd, 1H, H-7, $J_{7,8}$ 3.3, $J_{7,6}$ 2.6), 5.64 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 10.6, $J_{4,3e}$ 5.1), 6.79 (d, 1H, NH, $J_{NH,5}$ 9.5), 7.21-7.23 (m, 2H, Ph), 7.30-7.37 (m, 6H, Ph), 7.43-7.46 (m, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 37.1 (C-3), 40.2 (CH_2Cl), 50.3 (C-5), 52.9 (OMe), 66.7 (C-9), 70.1 (C-4), 71.3 (C-6), 72.1 (C-7), 73.3 (<u>C</u>H$_2$Ph), 75.8 (C-8), 88.6 (C-2), 114.2 (q, CF_3, $J_{C,F}$ 285.8), 119.0 (q, CF_3, $J_{C,F}$ 288), 127.5, 127.9, 128.4, 129.4, 129.5, 130.4, 135.7, 137.1 (Ph), 156.3 (q, O<u>C</u>OCF$_3$, $J_{C,F}$ 44.2), 156.4 (q, O<u>C</u>OCF$_3$, $J_{C,F}$ 44.2), 157.9 (q, NH<u>C</u>OCF$_3$, $J_{C,F}$ 38.2), 167.2, 167.9 (<u>C</u>OCH$_2$Cl, <u>C</u>OOMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −76.76, −75.67, −75.35.

4.16. General procedure for trifluoroacetylation of compounds containing benzylidene group

The starting material was dried *in vacuo* (0.1 Torr, 1 h), dissolved in anhydrous CH_2Cl_2, the solution was cooled to 0 °C, then pyridine (33 μL per 0.1 mmol for derivatives with one hydroxy group, 48 μL per 0.1 mmol of diol) followed by TFA_2O (28 μL per 0.1 mmol for derivatives

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with one hydroxy group, 41 μL per 0.1 mmol of diol) was added. The mixture was stirred at 0 °C until complete consumption of the starting material (TLC monitoring). The reaction mixture was coconcentrated with anhydrous toluene (2×5 mL per 0.1 mmol), the residue was dissolved in benzene (~50 mL per 0.1 mmol), the solution was washed with water (2×~50 mL per 0.1 mmol). The organic layer was filtered through cotton wool plug, concentrated under reduced pressure and dried *in vacuo* to give desired trifluoroacetyl derivative (98% for **25**, quantitative for **26**). The obtained trifluoroacetylated thiosialosides were utilized in the sialylation reactions without further purification.

*4.16.1. Data for methyl (phenyl 3,5-dideoxy-2-thio-4,8-di-O-trifluoroacetyl-7,9-O-benzylidene-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**25**)*

R_f 0.74 (benzene–EtOAc 9:1) $[\alpha]_D^{27}$ −88.5 (*c* 0.5, $CHCl_3$). HR ESI MS: found *m/z* 772.0873 [M + NH_4]$^+$. Calcd for $C_{29}H_{28}F_9N_2O_{10}S$: 772.0869. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.27 (dd, 1H, H-3a, $J_{3a,3e}$ 13.8, $J_{3a,4}$ 11.7), 2.79 (dd, 1H, H-3e, $J_{3e,3a}$ 13.8, $J_{3e,4}$ 4.8), 3.55 (s, 3H, OMe), 3.77 (dd, 1H, H-9a, $J_{9a,9b}$ 10.6, $J_{9a,8}$ 9.5), 4.06 (dd, 1H, H-7, $J_{7,8}$ 9.5, $J_{7,6}$ 2.2), 4.61 (ddd, 1H, H-5, $J_{5,6}$ 10.3, $J_{5,4}$ 9.9, $J_{5,NH}$ 8.8), 4.66 (dd, 1H, H-9b, $J_{9b,9a}$ 10.6, $J_{9b,8}$ 5.3), 4.69 (dd, 1H, H-6, $J_{6,5}$ 10.3, $J_{6,7}$ 2.2), 5.39 (ddd~td, 1H, H-8, $J_{8,7}$ 9.5, $J_{8,9a}$ 9.5, $J_{8,9b}$ 5.3), 5.52 (s, 1H, CH), 5.68 (ddd, 1H, H-4, $J_{4,3a}$ 11.7, $J_{4,5}$ 9.9, $J_{4,3e}$ 4.8), 6.48 (d, 1H, NH, $J_{NH,5}$ 8.8), 7.33-7.43 (m, 8H, Ph), 7.53-7.56 (m, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 36.6 (C-3), 40.3 (CH_2Cl), 49.6 (C-5), 52.8 (OMe), 66.0 (C-8), 66.7 (C-9), 70.2 (C-6), 72.8 (C-4), 75.8 (C-7), 88.7 (C-2), 101.9 (CH), 110.7-118.1 (m, 3×CO<u>C</u>F_3), 126.2, 128.3, 128.9, 129.3, 129.4, 129.9, 134.8, 136.1 (Ph), 154.4-159.0 (m, 3×<u>C</u>OCF_3), 167.1 (<u>C</u>OOMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): −75.76, −77.52, −75.37.

*4.16.1. Data for methyl (phenyl 3,5-dideoxy-2-thio-4-O-chloroacetyl-8-O-trifloroacetyl-7,9-O-benzylidene-5-trifluoroacetamido-D-glycero-β-D-galacto-nonulopyranosid)onate (**26**)*

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R_f 0.58 (benzene–EtOAc 9:1). $[\alpha]_D^{23}$ −99.4 (*c* 1.0, $CHCl_3$). HR ESI MS: found *m/z* 752.0656 [M + Na]$^+$. Calcd for $C_{29}H_{26}ClF_6NNaO_{10}S$: 752.0762. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 2.21 (dd, 1H, H-3a, $J_{3a,3e}$ 13.9, $J_{3a,4}$ 12.1), 2.78 (dd, 1H, H-3e, $J_{3e,3a}$ 13.9, $J_{3e,4}$ 5.1), 3.47 (s, 3H, OMe), 3.76 (dd, 1H, H-9a, $J_{9a,9b}$ 10.6, $J_{9a,8}$ 9.5), 4.04 (s, 2H, CH_2Cl), 4.06 (dd, 1H, H-7, $J_{7,8}$ 9.9, $J_{7,6}$ 1.5), 4.60 (ddd, 1H, H-5, $J_{5,6}$ 10.3, $J_{5,4}$ 9.9, $J_{5,NH}$ 8.4), 4.61 (dd, 1H, H-6, $J_{6,5}$ 10.3, $J_{6,7}$ 1.5), 4.68 (dd, 1H, H-9b, $J_{9b,9a}$ 10.6, $J_{9b,8}$ 5.1), 5.39 (ddd, 1H, H-8, $J_{8,7}$ 9.9, $J_{8,9a}$ 9.5, $J_{8,9b}$ 5.1), 5.53 (s, 1H, CH), 5.73 (ddd, 1H, H-4, $J_{4,3a}$ 12.1, $J_{4,5}$ 9.9, $J_{4,3e}$ 5.1), 6.91 (d, 1H, NH, $J_{NH,5}$ 8.4), 7.31-7.42 (m, 8H, Ph), 7.55-7.58 (m, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 37.3 (C-3), 40.3 (CH_2Cl), 49.7 (C-5), 52.6 (OMe), 66.2 (C-8), 66.6 (C-9), 70.4 (C-6), 70.7 (C-4), 75.8 (C-7), 89.3 (C-2), 101.8 (CH), 114.2 (q, OCO$\underline{C}F_3$, $J_{C,F}$ 285.8), 115.5 (q, NHCO$\underline{C}F_3$, $J_{C,F}$ 288.0), 126.2, 128.2, 129.1, 129.2, 129.4, 129.6, 134.6, 136.3 (Ph), 156.3 (q, O$\underline{C}OCF_3$, $J_{C,F}$ 43.1), 157.7 (q, NH$\underline{C}OCF_3$, $J_{C,F}$ 37.6), 167.1, 168.1 ($\underline{C}OCH_2Cl$, $\underline{C}OOMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm): –75.5, –74.4.

4.17. Typical glycosylation procedure

A mixture of thioglycoside sialyl donor (0.044–0.10 mmol, 1 equiv.) and alcohol **27**[104] (1 equiv.) was dried *in vacuo* for 2 h, then anhydrous MeCN (2.0 mL per 0.1 mmol of sialyl donor) was added under argon. Freshly activated powdered MS 3Å (Fluka; 100 mg per 1 mL of solvent) were added to the resulting solution. The suspension was stirred under argon at ~20 °C for 1 h, then cooled to –40 °C (dry ice–MeCN bath). Solid NIS (1.5 equiv. per 1 equiv. of glycosyl donor) was added. Neat triflic acid was added portionwise by a syringe in 15 min intervals until persistent iodine color was visible (~2–3 μL, 1 to 3 additions were required for various sialyl donors; see Table 1). The reaction mixture was stirred under argon at –40 °C until complete consumption of the starting thioglycoside (TLC monitoring; the time is specified in Table 1), then diluted with $CHCl_3$ (20 mL) and filtered through Celite pad. The solids were thoroughly washed with $CHCl_3$ (100 mL) and the filtrate was successively washed with 20% aqueous

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$Na_2S_2O_3$ (2 × 50 mL) and water (2 × 50 mL), filtered through a cotton wool plug and concentrated. In those cases when *O*-TFA groups were present in the molecule of sialyl donor, the residue was dissolved in anhydrous MeOH (3 mL per 0.1 mmol of sialyl donor) and MeONa (0.3 mL of 1 M solution in methanol per 0.1 mmol of sialyl donor) followed by ethyl trifluoroacetate (0.1 mL per 0.1 mmol of sialyl donor) was added. The reaction mixture was kept at room temperature overnight, then quenched by addition of dry ice and concentrated under reduced pressure.[7] The residue was co-concentrated with toluene (3 mL), dried *in vacuo*, dissolved in anhydrous pyridine (3 mL per 0.1 mmol of sialyl donor), and acetic anhydride (3 mL per 0.1 mmol of sialyl donor) was added. The reaction mixture was kept at room temperature overnight, then quenched by addition of methanol (3 mL), concentrated under reduced pressure, the residue was coconcentrated with toluene (3 mL), dissolved in CH_2Cl_2 (40 mL), washed with water (40 mL), the organic layer was filtered through cotton wool plug and concentrated under reduced pressure. The residue was dried *in vacuo*, dissolved in toluene (2 mL) and separated by gel permeation chromatography on Bio-Beads S-X3 (toluene). The first eluted fraction contained disaccharides **28–33**, which was analyzed by NMR spectroscopy to give anomeric ratio values (α : β, see Table 1; for determination of ratio of anomers of disaccharides **28–33** integral intensities of signals of α-H-3eq and β-H-3eq of neuraminic residue were used). The disaccharide fraction was chromatographed on a silica gel 60 column to give pure α-linked isomer of disaccharides **28–33** (for the yields see Table 1; all yields were calculated with respect to the glycosyl donor taken).

*4.17.1. Data for methyl [1,2:3,4-di-O-isopropylidene-6-(3,5-dideoxy-2-thio-4,7,8,9-tetra-O-acetyl-5-trifluoroacetamido-D-glycero-α-D-galacto-nonulopyranosyl)-α-D-galactopyranose)]onate (**28**)*

[7] For glycosyl donor **25**, the residue after work-up of the reaction mixture was dissolved in MeOH (3.0 mL), and NEt_3 (0.5 mL) and ethyl trifluoroacetate (100 μL) were added. The reaction mixture was stirred at room temperature overnight, then concentrated under reduced pressure and co-concentrated with toluene (3.0 mL).

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R_f 0.53 (benzene–EtOAc 4:1) $[\alpha]_D^{25}$ −38.0 (*c* 1.5, $CHCl_3$). HR ESI MS: found *m/z* 810.2401 [M + Na]$^+$. Calcd for $C_{32}H_{44}F_3NO_{18}$: 810.2403. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.33 (s, 3H, CMe), 1.33 (s, 3H, CMe), 1.42 (s, 3H, CMe), 1.54 (s, 3H, CMe), 2.02 (s, 3H, COMe), 2.03 (s, 3H, COMe), 2.13 (s, 3H, COMe), 2.14 (s, 3H, COMe), 1.98 (dd, 1H, H-3a Neu, $J_{3a,3e}$ 12.8, $J_{3a,4}$ 12.2), 2.67 (dd, 1H, H-3e Neu, $J_{3e,3a}$ 12.8, $J_{3e,4}$ 4.8), 3.61 (dd, 1H, H-6a Gal, $J_{6a,6b}$ 9.5, $J_{6a,5}$ 7.3), 3.79 (s, 3H, OMe), 3.85 (dd, 1H, H-6b Gal, $J_{6b,6a}$ 9.5, $J_{6b,5}$ 5.7), 3.88 (ddd, 1H, H-5 Gal, $J_{5,6a}$ 7.3, $J_{5,6b}$ 5.7, $J_{5,4}$ 1.9), 4.00 (ddd ~td, 1H, H-5 Neu, $J_{5,6}$ 10.7, $J_{5,4}$ 10.3, $J_{5,NH}$ 9.8), 4.21 (dd, 1H, H-9a Neu, $J_{9a,9b}$ 12.5, $J_{9a,8}$ 5.5), 4.23 (dd, 1H, H-4 Gal, $J_{4,3}$ 7.8, $J_{4,5}$ 1.9), 4.28 (dd, 1H, H-6 Neu, $J_{6,5}$ 10.7, $J_{6,7}$ 2.2), 4.30 (dd, 1H, H-2 Gal, $J_{2,1}$ 5.0, $J_{2,3}$ 2.5), 4.32 (dd, 1H, H-9b Neu, $J_{9b,9a}$ 12.5, $J_{9b,8}$ 2.7), 4.59 (dd, 1H, H-3 Gal, $J_{3,4}$ 7.8, $J_{3,2}$ 2.5), 5.02 (ddd, 1H, H-4 Neu, $J_{4,3a}$ 12.2, $J_{4,5}$ 10.3, $J_{4,3e}$ 4.8), 5.30 (dd, 1H, H-7 Neu, $J_{7,8}$ 7.2, $J_{7,6}$ 2.2), 5.38 (ddd, 1H, H-8 Neu, $J_{8,7}$ 7.2, $J_{8,9a}$ 5.5, $J_{8,9b}$ 2.7), 5.51 (d, 1H, H-1 Gal, $J_{1,2}$ 5.0), 6.71 (d, 1H, NH, $J_{NH,5Neu}$ 9.8). ^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 20.5, 20.58, 20.64, 21.0 (COMe), 24.6, 24.9, 25.97, 26.03 (CMe_2), 37.6 (C-3 Neu), 50.2 (C-5 Neu), 52.7 (OMe), 62.0 (C-9 Neu), 63.3 (C-6 Gal), 66.4 (C-5 Gal), 67.4 (C-7 Neu), 68.6 (C-4 Neu), 69.4 (C-8 Neu), 70.61, 70.62 (C-2 Gal, C-3 Gal), 70.7 (C-4 Gal), 71.9 (C-6 Neu), 96.3 (C-1 Gal), 98.7 (C-2 Neu), 108.5, 109.2 (CMe_2), 115.5 (q, $COCF_3$, $J_{C,F}$ 288.0), 157.5 (q, $COCF_3$, $J_{C,F}$ 37.6), 167.9 (COOMe), 169.9, 170.2, 170.6, 171.0 (COMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm) –77.02.

*4.17.2. Data for methyl [1,2:3,4-di-O-isopropylidene-6-(3,5-dideoxy-2-thio-4,7,8,9-tetra-O-benzoyl-5-trifluoroacetamido-D-glycero-α-D-galacto-nonulopyranosyl)-α-D-galactopyranose)]onate (**29**)*

R_f 0.40 (benzene–acetone 9:1). $[\alpha]_D^{25}$ +12.3 (*c* 3.82, $CHCl_3$). HR ESI MS: found *m/z* 1058.3027 [M + Na]$^+$. Calcd for $C_{52}H_{52}F_3NNaO_{18}$: 1058.3029. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.33 (s, 3H, CMe), 1.34 (s, 3H, CMe), 1.44 (s, 3H, CMe), 1.55 (s, 3H, CMe), 2.09 (dd, 1H, H-3a Neu, $J_{3a,3e}$ 12.8, $J_{3a,4}$ 11.9), 2.88 (dd, 1H, H-3e Neu, $J_{3e,3a}$ 12.8, $J_{3e,4}$ 5.1), 3.51 (s, 3H, OMe), 3.86

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(dd, 1H, H-6a Gal, $J_{6a,6b}$ 9.6, $J_{6a,5}$ 6.5), 3.97 (ddd, 1H, H-5 Gal, $J_{5,6a}$ 6.5, $J_{5,6b}$ 6.1, $J_{5,4}$ 1.9), 4.02 (dd, 1H, H-6b Gal, $J_{6a,6b}$ 9.6, $J_{6a,5}$ 6.1), 4.10 (ddd, 1H, H-5 Neu, $J_{5,6}$ 10.6, $J_{5,4}$ 10.2, $J_{5,NH}$ 9.3), 4.27 (dd, 1H, H-4 Gal, $J_{4,3}$ 7.9, $J_{4,5}$ 1.9), 4.33 (dd, 1H, H-2 Gal, $J_{2,1}$ 5.0, $J_{2,3}$ 2.4), 4.53 (dd, 1H, H-9a Neu, $J_{9a,9b}$ 12.5, $J_{9a,8}$ 5.1), 4.62 (dd, 1H, H-3 Gal, $J_{3,4}$ 7.9, $J_{3,2}$ 2.4), 4.70 (dd, 1H, H-6 Neu, $J_{6,5}$ 10.6, $J_{6,7}$ 1.5), 4.38 (dd, 1H, H-9b Neu, $J_{9b,9a}$ 12.5, $J_{9b,8}$ 2.6), 5.52 (ddd, 1H, H-4 Neu, $J_{4,3a}$ 11.9, $J_{4,5}$ 10.2, $J_{4,3e}$ 5.1), 5.56 (d, 1H, H-1 Gal, $J_{1,2}$ 5.0), 5.94 (dd, 1H, H-7 Neu, $J_{7,8}$ 7.6, $J_{7,6}$ 1.5), 5.98 (ddd, 1H, H-8 Neu, $J_{8,7}$ 7.6, $J_{8,9a}$ 5.1, $J_{8,9b}$ 2.6), 6.89 (d, 1H, NH, $J_{NH,5\ Neu}$ 9.3), 7.35-7.41 (m, 6H, Ph), 7.48-7.55 (m, 5H, Ph), 7.60-7.63 (m, 1H, Ph), 7.91-7.93 (m, 2H, Ph), 7.96-7.97 (m, 2H, Ph), 8.00-8.01 (m, 2H, Ph), 8.13-8.15 (m, 2H, Ph). ^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 24.6, 24.9, 26.0, 26.1 (C<u>Me</u>$_2$), 37.6 (C-3 Neu), 51.0 (C-5 Neu), 52.7 (OMe), 62.6, 63.5 (C-6 Gal, C-9 Neu), 66.8 (C-5 Gal), 68.5, 69.1, 70.0 (C-4 Neu, C-7 Neu, C-8 Neu), 70.7 (2C), 70.9 (C-2 Gal, C-3 Gal, C-4 Gal), 71.8 (C-6 Neu), 96.3 (C-1 Gal), 98.9 (C-2 Neu), 108.5, 109.3 (<u>C</u>Me$_2$), 115.4 (q, CO<u>C</u>F$_3$, $J_{C,F}$ 288.0), 128.3, 128.4, 128.5, 128.6, 128.9, 129.1, 129.7, 129.8 (2C), 129.9, 130.2, 132.9, 133.1, 133.5, 133.6 (Ph), 157.4 (q, <u>C</u>OCF$_3$, $J_{C,F}$ 37.6), 165.3, 165.5, 166.0, 166.1 (<u>C</u>OPh), 168.1 (<u>C</u>OOMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm) −77.02.

*4.17.3. Data for methyl [1,2:3,4-di-O-isopropylidene-6-(3,5-dideoxy-2-thio-4,8-di-O-acetyl-7,9-O-benzylidene-5-trifluoroacetamido-D-glycero-α-D-galacto-nonulopyranosyl)-α-D-galactopyranose)]onate (**30**)*

R_f 0.46 (benzene–acetone 4:1). $[\alpha]_D^{25}$ −88.0 (*c* 1.47, $CHCl_3$). HR ESI MS: found *m/z* 814.2496 $[M + Na]^+$. Calcd for $C_{35}H_{44}F_3NNaO_{16}$: 814.2504. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.33 (s, 6H, C<u>Me</u>), 1.41 (s, 3H, C<u>Me</u>), 1.52 (s, 3H, C<u>Me</u>), 2.00 (dd, 1H, H-3a Neu, $J_{3a,3e}$ 12.8, $J_{3a,4}$ 12.3), 2.05 (s, 3H, CO<u>Me</u>), 2.14 (s, 3H, CO<u>Me</u>), 2.62 (dd, 1H, H-3e Neu, $J_{3e,3a}$ 12.8, $J_{3e,4}$ 4.8), 3.60 (dd, 1H, H-9a Neu, $J_{9a,9b}$ 10.5, $J_{9a,8}$ 10.3), 3.64 (dd, 1H, H-6a Gal, $J_{6a,6b}$ 9.5, $J_{6a,5}$ 7.6), 3.75 (dd, 1H, H-7 Neu, $J_{7,8}$ 9.7, $J_{7,6}$ 1.9), 3.78 (s, 3H, OMe), 3.84 (dd, 1H, H-6b Gal, $J_{6a,6b}$ 9.5, $J_{6a,5}$ 5.8), 3.89 (ddd, 1H, H-5 Gal, $J_{5,6a}$ 7.6, $J_{5,6b}$ 5.8, $J_{5,4}$ 1.8), 4.04 (dd, 1H, H-6 Neu, $J_{6,5}$ 10.5,

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$J_{6,7}$ 1.9), 4.21 (dd, 1H, H-4 Gal, $J_{4,3}$ 7.9, $J_{4,5}$ 1.8), 4.27 (dd, 1H, H-2 Gal, $J_{2,1}$ 5.0, $J_{2,3}$ 2.4), 4.38 (ddd, 1H, H-5 Neu, $J_{5,6}$ 10.5, $J_{5,4}$ 10.4, $J_{5,NH}$ 9.2), 4.49 (dd, 1H, H-9b Neu, $J_{9b,9a}$ 10.5, $J_{9b,8}$ 5.3), 4.56 (dd, 1H, H-3 Gal, $J_{3,4}$ 7.9, $J_{3,2}$ 2.4), 5.03 (ddd, 1H, H-4 Neu, $J_{4,3a}$ 12.3, $J_{4,5}$ 10.4, $J_{4,3e}$ 4.8), 5.28 (ddd, 1H, H-8 Neu, $J_{8,9a}$ 10.3, $J_{8,7}$ 9.7, $J_{8,9b}$ 5.3), 5.44 (s, 1H, CH), 5.49 (d, 1H, H-1 Gal, $J_{1,2}$ 5.0), 6.29 (d, 1H, NH, $J_{NH,5\ Neu}$ 9.2), 7.33-7.40 (m, 3H, Ph), 7.52-7.59 (m, 2H, Ph). ^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 20.6, 20.7 (CO<u>Me</u>), 24.6, 24.9, 26.0, 26.2 (C<u>Me</u>$_2$), 37.0 (C-3 Neu), 50.1 (C-5 Neu), 52.6 (OMe), 61.9 (C-6 Gal), 62.8 (C-8 Neu), 66.3 (C-5 Gal), 68.0 (C-9 Neu), 68.8 (C-4 Neu), 70.6 (2C), 70.7, 70.9 (C-2 Gal, C-3 Gal, C-4 Gal, C-6 Neu), 76.4 (C-7 Neu), 96.2 (C-1 Gal), 98.6 (C-2 Neu), 101.4 (CH), 108.6, 109.1 (<u>C</u>Me$_2$), 115.6 (q, CO<u>C</u>F$_3$, $J_{C,F}$ 288.3), 126.3, 128.1, 128.8, 137.1 (Ph), 157.3 (q, <u>C</u>OCF$_3$, $J_{C,F}$ 37.3), 168.0 (<u>C</u>OOMe), 169.2, 171.3 (<u>C</u>OMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm) –76.65.

*4.17.4. Data for methyl [1,2:3,4-Di-O-isopropylidene-6-(3,5-dideoxy-2-thio-4,8-di-O-chloroacetyl-7,9-O-benzylidene-5-trifluoroacetamido-D-glycero-α-D-galacto-nonulopyranosyl)-α-D-galactopyranose)]onate (**31**)*

R_f 0.68 (benzene–acetone 9:1). $[\alpha]_D^{25}$ −83.8 (*c* 4.3, $CHCl_3$). HR ESI MS: found *m/z* 877.2172 [M + NH_4]$^+$. Calcd for $C_{35}H_{46}Cl_2F_3N_2O_{16}$: 877.2172. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.32 (s, 6H, C<u>Me</u>), 1.42 (s, 3H, C<u>Me</u>), 1.51 (s, 3H, C<u>Me</u>), 2.03 (dd, 1H, H-3a Neu, $J_{3a,3e}$ 12.8, $J_{3a,4}$ 12.0), 2.70 (dd, 1H, H-3e Neu, $J_{3e,3a}$ 12.8, $J_{3e,4}$ 4.9), 3.64 (dd, 1H, H-6a Gal, $J_{6a,6b}$ 9.4, $J_{6a,5}$ 7.4), 3.68 (dd, 1H, H-9a Neu, $J_{9a,9b}$ 10.5, $J_{9a,8}$ 10.0), 3.79 (s, 3H, OMe), 3.83 (dd, 1H, H-6b Gal, $J_{6a,6b}$ 9.4, $J_{6a,5}$ 5.9), 3.84 (dd, 1H, H-7 Neu, $J_{7,8}$ 9.4, $J_{7,6}$ 2.2), 3.87 (ddd, 1H, H-5 Gal, $J_{5,6a}$ 7.4, $J_{5,6b}$ 5.9, $J_{5,4}$ 1.9), 4.02 (d, 1H, CHCl, *J* 15.0), 4.05 (d, 1H, CHCl, *J* 15.0), 4.11 (dd, 1H, H-6 Neu, $J_{6,5}$ 10.5, $J_{6,7}$ 2.2), 4.16 (d, 1H, CHCl, *J* 15.0), 4.21 (dd, 1H, H-4 Gal, $J_{4,3}$ 7.9, $J_{4,5}$ 1.9), 4.25 (d, 1H, CHCl, *J* 15.0), 4.29 (dd, 1H, H-2 Gal, $J_{2,1}$ 5.0, $J_{2,3}$ 2.4), 4.42 (ddd, 1H, H-5 Neu, $J_{5,6}$ 10.5, $J_{5,4}$ 10.4, $J_{5,NH}$ 9.2), 4.49 (dd, 1H, H-9b Neu, $J_{9b,9a}$ 10.5, $J_{9b,8}$ 5.3), 4.58 (dd, 1H, H-3 Gal, $J_{3,4}$ 7.9, $J_{3,2}$ 2.4), 5.18 (ddd, 1H, H-4 Neu, $J_{4,3a}$ 12.0, $J_{4,5}$ 10.4, $J_{4,3e}$ 4.9), 5.39 (ddd, 1H, H-8 Neu, $J_{8,9a}$

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10.0, $J_{8,7}$ 9.4, $J_{8,9b}$ 5.3), 5.45 (s, 1H, CH), 5.49 (d, 1H, H-1 Gal, $J_{1,2}$ 5.0), 6.44 (d, 1H, NH, $J_{NH,5\ Neu}$ 9.2), 7.34-7.41 (m, 3H, Ph), 7.54-7.56 (m, 2H, Ph). ^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 24.7, 24.9, 26.0, 26.1 ($C\underline{Me}_2$), 36.9 (C-3 Neu), 40.4, 40.7 (CH_2Cl), 49.6 (C-5 Neu), 52.8 (OMe), 63.0 (C-6 Gal), 63.3 (C-8 Neu), 66.3 (C-5 Gal), 67.7 (C-9 Neu), 70.4 (C-6 Neu), 70.6 (2C, C-3 Gal, C-4 Gal), 70.7 (C-2 Gal), 70.9 (C-4 Neu), 76.1 (C-7 Neu), 96.2 (C-1 Gal), 98.4 (C-2 Neu), 101.6 (CH), 108.6, 109.2 ($\underline{C}Me_2$), 115.5 (q, $CO\underline{C}F_3$, $J_{C,F}$ 288.5), 126.3, 128.1, 129.0, 136.7 (Ph), 157.3 (q, $\underline{C}OCF_3$, $J_{C,F}$ 37.7), 165.9, 167.7 ($\underline{C}OCH_2Cl$) 167.9 ($\underline{C}OOMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm) −76.55.

*4.17.5. Data for methyl [1,2:3,4-di-O-isopropylidene-6-(3,5-dideoxy-2-thio-4,7,8,9-tetra-O-chloroacetyl-5-trifluoroacetamido-D-glycero-α-D-galacto-nonulopyranosyl)-α-D-galactopyranose)]onate (**32**)*

R_f 0.53 (benzene–acetone 4:1). $[\alpha]_D^{25}$ −35.9 (*c* 1.34, $CHCl_3$). HR ESI MS: found *m/z* 941.1285 $[M + NH_4]^+$. Calcd for $C_{32}H_{44}Cl_4F_3N_2O_{18}$: 941.1290. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.33 (s, 6H, C$\underline{Me}$), 1.43 (s, 3H, C$\underline{Me}$), 1.53 (s, 3H, C$\underline{Me}$), 2.04 (dd, 1H, H-3a Neu, $J_{3a,3e}$ 13.4, $J_{3a,4}$ 11.4), 2.74 (dd, 1H, H-3e Neu, $J_{3e,3a}$ 13.4, $J_{3e,4}$ 4.8), 3.59 (dd, 1H, H-6a Gal, $J_{6a,6b}$ 9.5, $J_{6a,5}$ 6.7), 3.81 (s, 3H, OMe), 3.82 (dd, 1H, H-6b Gal, $J_{6a,6b}$ 9.5, $J_{6a,5}$ 5.7), 3.88 (ddd, 1H, H-5 Gal, $J_{5,6a}$ 6.7, $J_{5,6b}$ 5.7, $J_{5,4}$ 1.9), 4.00 (d, 1H, CHCl, *J* 15.3), 4.03 (d, 1H, CHCl, *J* 15.3), 4.07 (s, 2H, CH_2Cl), 4.10 (ddd ~td, 1H, H-5 Neu, $J_{5,6}$ 10.5, $J_{5,4}$ 9.5, $J_{5,NH}$ 9.5), 4.16 (d, 1H, CHCl, *J* 15.3), 4.20 (d, 1H, CHCl, *J* 15.3), 4.21 (d, 1H, CHCl, *J* 15.3), 4.25 (d, 1H, CHCl, *J* 15.3), 4.21 (dd, 1H, H-4 Gal, $J_{4,3}$ 8.6, $J_{4,5}$ 1.9), 4.31 (dd, 1H, H-2 Gal, $J_{2,1}$ 4.8, $J_{2,3}$ 1.9), 4.32 (dd, 1H, H-9a Neu, $J_{9a,9b}$ 12.9, $J_{9a,8}$ 5.7), 4.34 (dd, 1H, H-6 Neu, $J_{6,5}$ 10.5, $J_{6,7}$ 2.4), 4.56 (dd, 1H, H-9b Neu, $J_{9b,9a}$ 12.9, $J_{9b,8}$ 2.4), 4.60 (dd, 1H, H-3 Gal, $J_{3,4}$ 8.6, $J_{3,2}$ 1.9), 5.12 (ddd, 1H, H-4 Neu, $J_{4,3a}$ 11.4, $J_{4,5}$ 9.5, $J_{4,3e}$ 4.8), 5.38 (dd, 1H, H-7 Neu, $J_{7,8}$ 7.2, $J_{7,6}$ 2.4), 5.52 (d, 1H, H-1 Gal, $J_{1,2}$ 4.8), 5.52 (ddd, 1H, H-8 Neu, $J_{8,7}$ 7.2, $J_{8,9a}$ 5.7, $J_{8,9b}$ 2.4), 6.94 (d, 1H, NH, $J_{NH,5\ Neu}$ 9.5). ^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 24.6, 24.8, 26.0 (2C) ($C\underline{Me}_2$), 37.3 (C-3 Neu), 40.3, 40.4, 40.5, 40.9 (CH_2Cl),

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49.8 (C-5 Neu), 53.1 (OMe), 63.0, 63.6 (C-6 Gal, C-9 Neu), 66.5 (C-5 Gal), 68.6, 70.3 (2C) (C-4 Neu, C-7 Neu, C-8 Neu), 70.5, 70.6, 70.7 (C-2 Gal, C-3 Gal, C-4 Gal), 71.5 (C-6 Neu), 96.3 (C-1 Gal), 98.6 (C-2 Neu), 108.6, 109.3 ($\underline{C}Me_2$), 115.3 (q, $CO\underline{C}F_3$, $J_{C,F}$ 288.0), 157.8 (q, $\underline{C}OCF_3$, $J_{C,F}$ 38.0), 166.6, 166.8, 167.0, 167.5 ($\underline{C}OCH_2Cl$), 167.9 ($\underline{C}OOMe$). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm) –76.72.

*4.17.6. Data for methyl [1,2:3,4-Di-O-isopropylidene-6-(3,5-dideoxy-2-thio-4,7,8-tri-O-acetyl-9-O-benzyl-5-trifluoroacetamido-D-glycero-α-D-galacto-nonulopyranosyl)-α-D-galactopyranose)]onate (**33**)*

R_f 0.23 (benzene–acetone 9:1) $[\alpha]_D^{25}$ −30.2 (*c* 3.9, $CHCl_3$). HR ESI MS: found *m/z* 858.2767 [M + Na]$^+$. Calcd for $C_{37}H_{48}F_3NNaO_{17}$: 858.2767. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 1.32 (s, 3H, C$\underline{Me}$), 1.33 (s, 3H, C$\underline{Me}$), 1.41 (s, 3H, C$\underline{Me}$), 1.54 (s, 3H, C$\underline{Me}$), 2.02 (s, 3H, CO$\underline{Me}$), 2.05(s, 3H, CO$\underline{Me}$), 2.12 (s, 3H, CO$\underline{Me}$), 1.97 (dd, 1H, H-3a Neu, $J_{3a,3e}$ 12.9, $J_{3a,4}$ 12.4), 2.68 (dd, 1H, H-3e Neu, $J_{3e,3a}$ 12.9, $J_{3e,4}$ 4.8), 3.54-3.57 (m, 1H, H-9a Neu), 3.64 (dd, 1H, H-6a Gal, $J_{6a,6b}$ 11.4, $J_{6a,5}$ 9.1), 3.77 (s, 3H, OMe), 3.80-3.82 (m, 1H, H-9b Neu), 3.89 (dd, 1H, H-6b Gal, $J_{6a,6b}$ 11.4, $J_{6a,5}$ 5.7), 3.90 (ddd, 1H, H-5 Gal, $J_{5,6a}$ 9.1, $J_{5,6b}$ 5.7, $J_{5,4}$ 1.4), 4.00 (ddd ~td, 1H, H-5 Neu, $J_{5,6}$ 10.5, $J_{5,4}$ 10.5, $J_{5,NH}$ 9.9), 4.20 (dd, 1H, H-4 Gal, $J_{4,3}$ 8.1, $J_{4,5}$ 1.4), 4.28 (dd, 1H, H-6 Neu, $J_{6,5}$ 10.5, $J_{6,7}$ 1.4), 4.31 (dd, 1H, H-2 Gal, $J_{2,1}$ 5.0, $J_{2,3}$ 2.4), 4.45 (d, 1H, C$\underline{H}$Ph, *J* 11.8), 4.54 (d, 1H, C$\underline{H}$Ph, *J* 11.8), 4.60 (dd, 1H, H-3 Gal, $J_{3,4}$ 8.1, $J_{3,2}$ 2.4), 5.04 (ddd, 1H, H-4 Neu, $J_{4,3a}$ 12.4, $J_{4,5}$ 10.5, $J_{4,3e}$ 4.8), 5.35-3.38 (m, 2H, H-7 Neu, H-8 Neu), 5.52 (d, 1H, H-1 Gal, $J_{1,2}$ 5.0), 6.87 (d, 1H, NH, $J_{NH,5Neu}$ 9.9), 7.25-7.28 (m, 1H, *p*-CH(Ph)), 7.30-7.34 (m, 2H, *m*-CH(Ph)), 7.36-7.37 (m, 2H, *o*-CHPh). ^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm, *J*, Hz): 20.5, 20.6, 21.1 (CO$\underline{Me}$), 24.6, 24.9, 26.0, 26.1 ($C\underline{Me}_2$), 37.7 (C-3 Neu), 50.3 (C-5 Neu), 52.7 (OMe), 63.3 (C-6 Gal), 66.5 (C-5 Gal), 68.2 (C-7 Neu), 68.5 (C-9 Neu), 68.5 (C-4 Neu), 70.5 (C-8 Neu), 70.6, 70.7 (C-2 Gal, C-3 Gal), 70.7 (C-4 Gal), 72.2 (C-6 Neu), 73.2 ($\underline{C}H_2Ph$), 96.3 (C-1 Gal), 98.7 (C-2 Neu), 108.5, 109.2 ($\underline{C}Me_2$), 115.5 (q, $CO\underline{C}F_3$, $J_{C,F}$ 288.0), 127.6 (*p*-CH(Ph)), 127.8 (*m*-CH(Ph)),

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128.3 (*o*-CH(Ph)), 137.9 (C(Ph)), 157.5 (q, <u>C</u>OCF$_3$, $J_{C,F}$ 38.0), 167.9 (<u>C</u>OOMe), 169.9, 170.6, 170.9 (<u>C</u>OMe). ^{19}F NMR (282 MHz, $CDCl_3$, δ, ppm) –76.99.

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6. Supplementary data

Supplementary data section contains the copies of NMR spectra of prepared compounds. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.xxxxxx.

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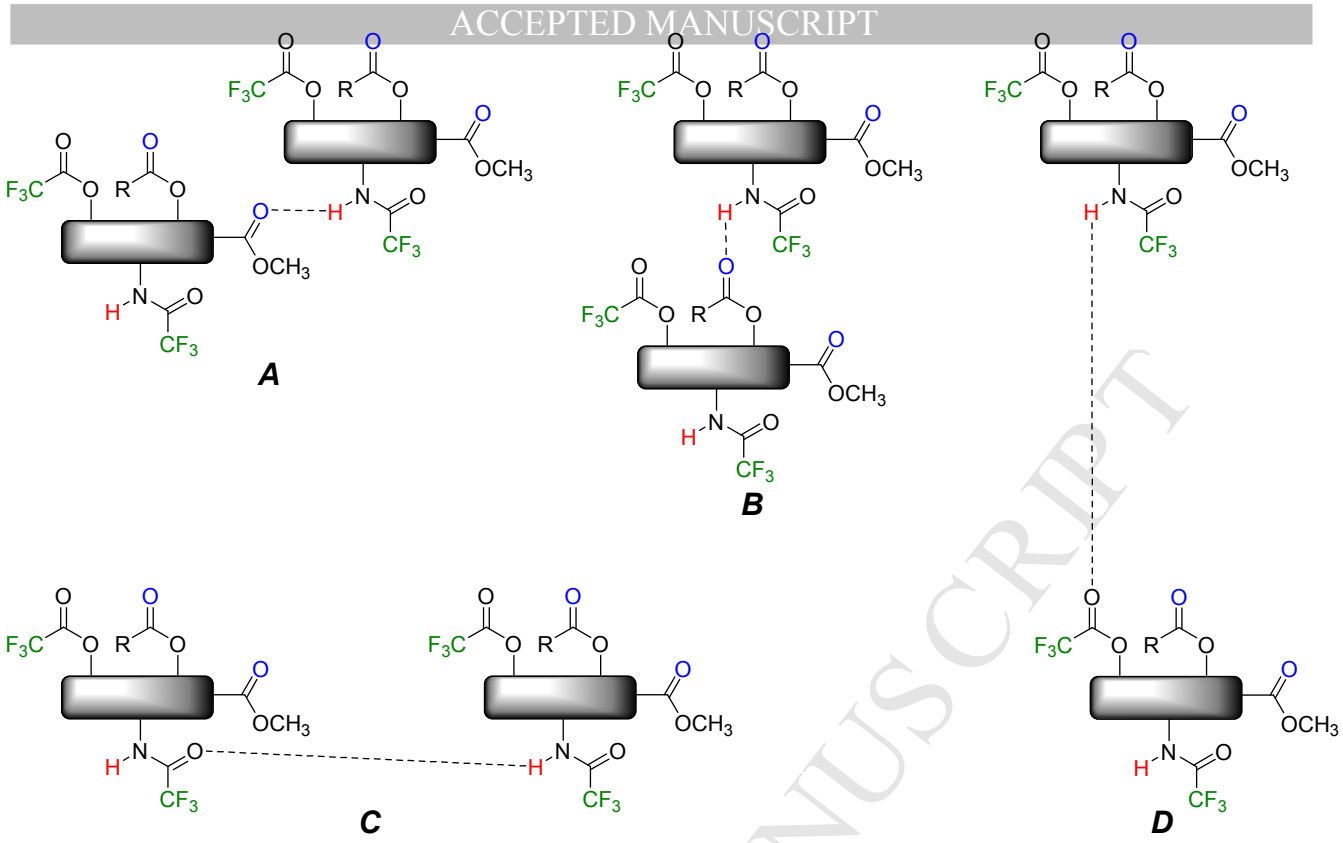

Fig. 1. Possible types of hydrogen-bonded supramers formed in the solutions of sialyl donors with *N*- and *O*-trifluoroacetyl groups. Structures ***A*** and ***B***, which involve methoxycarbonyl or *O*-acetyl/benzoyl/chloroacetyl groups as hydrogen-bond acceptors, correspond to more tight supramers than structures ***C*** and ***D***, which involve carbonyls of *N*- and *O*-trifluoroacetyl groups, since hydrogen bond with carbonyl of TFA group is rather weak. Dashed lines represent hydrogen bonds, the shorter is the length of the line the stronger is the hydrogen bond. Dimers are shown for clarity.

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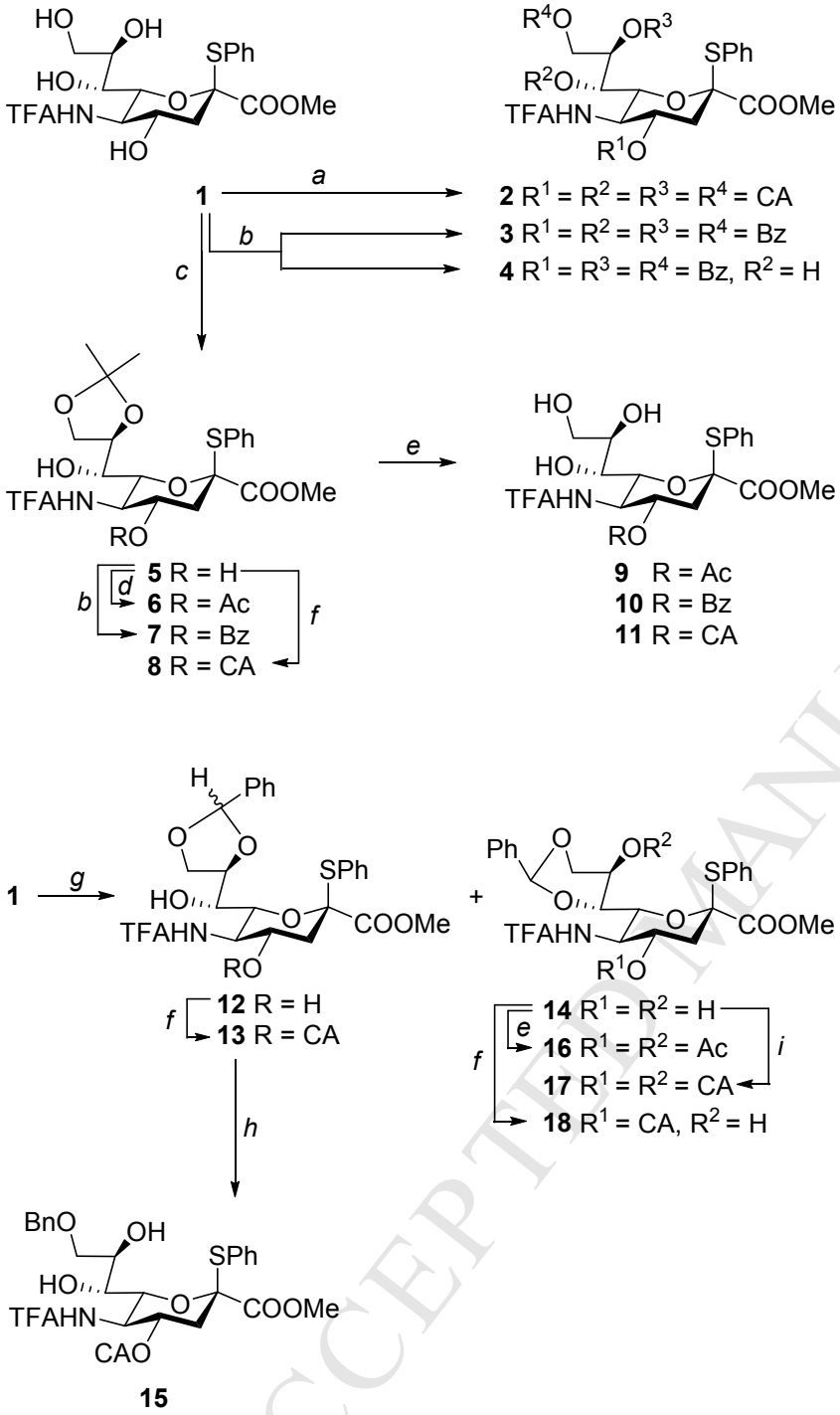

Scheme 1. Synthesis of sialyl donors and their prucursors without *O*-TFA groups. <u>*Reagents and conditions*</u>: *a.* 3 equiv. CA_2O, 2,4,6-collidine, MeCN (87%). *b.* BzCl, Py (**3** (68%) + **4** (32%); **7** (86%)). *c.* $Me_2CH(OMe)_2$, CSA, MeCN (84%). *d.* Ac_2O, Py (97% for **6**, 87% for **16**). *e*. 90% aq. CF_3CO_2H, CH_2Cl_2, 0 °C (74% for **9**, 86% for **10**, 95% for **11**). *f.* 1.5 equiv. CA_2O, 2,4,6-collidine, CH_2Cl_2 (94% for **8**, 80% for **18**). *g.* $PhCH(OMe)_2$, CSA, MeCN (**12** (34%) + **14** (66%)). *h.* $BH_3{\cdot}NMe_3$, $AlCl_3$, THF, H_2O (67% of **15** from **12**). *i.* 3 equiv. CA_2O, 2,4,6-collidine, CH_2Cl_2 (95%). Ac = CH_3CO, Bz = PhCO, CA = $ClCH_2CO$, TFA = CF_3CO.

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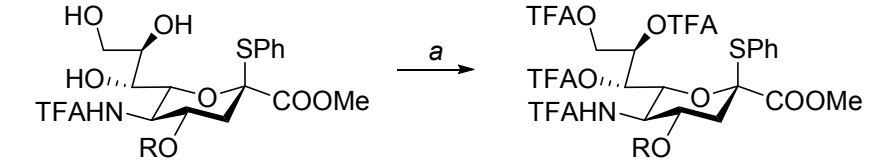
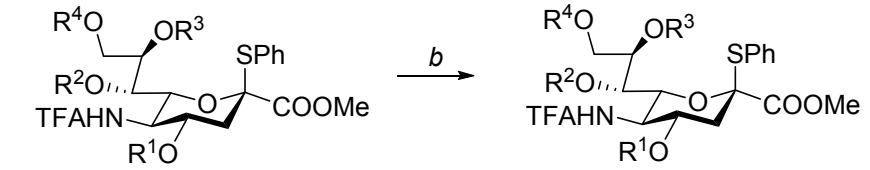


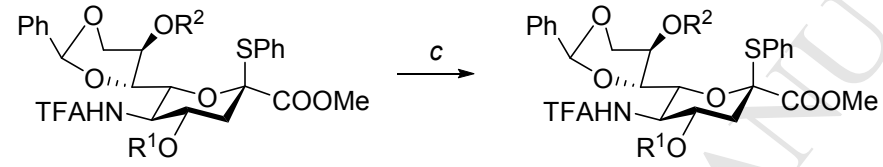
1 R = H
9 R = Ac
11 R = CA
10 R = Bz

19 R = TFA
20 R = Ac
21 R = CA
22 R = Bz



4 $R^1 = R^3 = R^4 = Bz$, $R^2 = H$
15 $R^1 = CA$, $R^2 = R^3 = H$, $R^4 = Bn$

23 $R^1 = R^3 = R^4 = Bz$, $R^2 = TFA$
24 $R^1 = CA$, $R^2 = R^3 = TFA$, $R^4 = Bn$



14 $R^1 = R^2 = H$
18 $R^1 = CA$, $R^2 = H$

25 $R^1 = R^2 = TFA$
26 $R^1 = CA$, $R^2 = TFA$

Scheme 2. *O*-Trifluoroacetylation. *Reagents and conditions*: *a*. TFA_2O, TFAONa (~100% for **19**, 89% for **20**, 87% for **21**, 89% for **22**). *b*. TFA_2O, NaOTFA, CH_2Cl_2 (94% for **23**, ~100% for **24**). *c*. TFA_2O, Py, CH_2Cl_2 (98% for **25**, ~100% for **26**).

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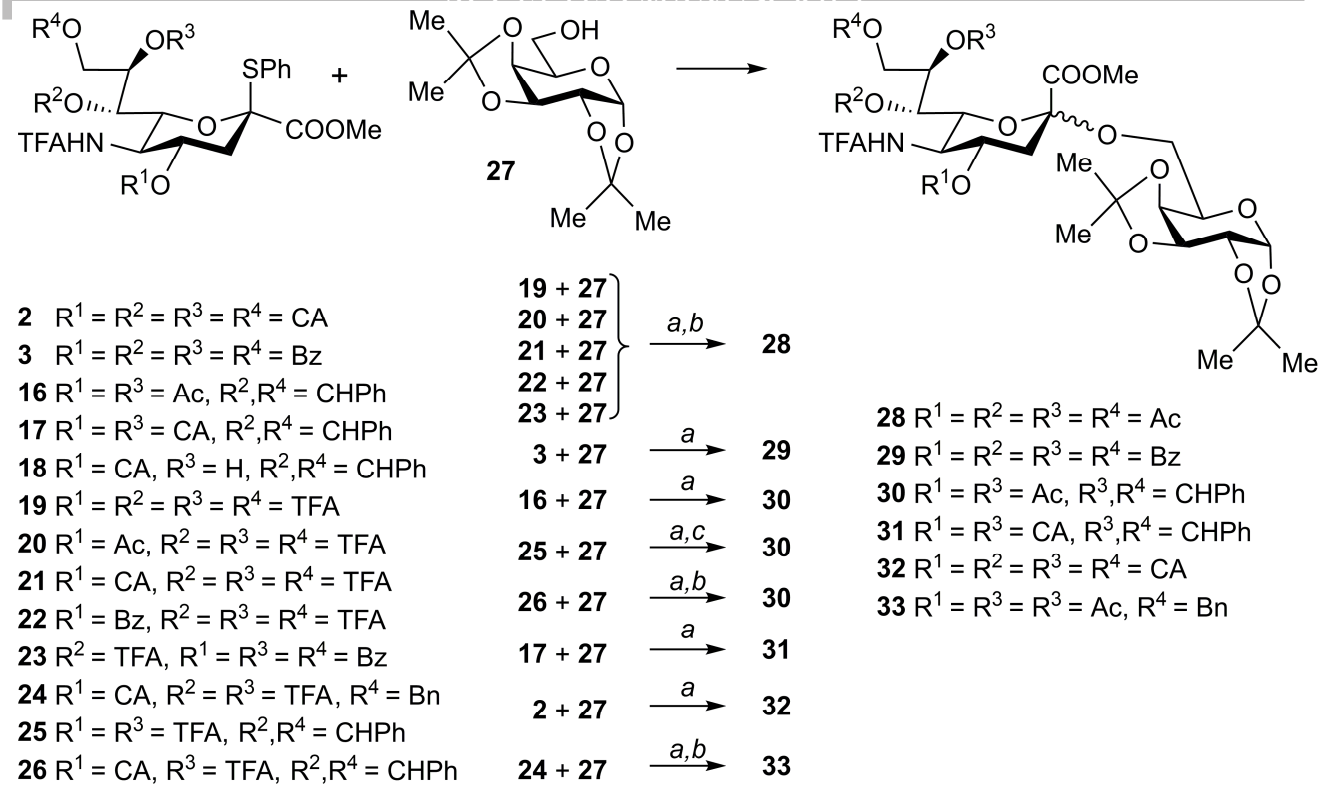

2 $R^1 = R^2 = R^3 = R^4 = CA$
3 $R^1 = R^2 = R^3 = R^4 = Bz$
16 $R^1 = R^3 = Ac$, $R^2,R^4 = CHPh$
17 $R^1 = R^3 = CA$, $R^2,R^4 = CHPh$
18 $R^1 = CA$, $R^3 = H$, $R^2,R^4 = CHPh$
19 $R^1 = R^2 = R^3 = R^4 = TFA$
20 $R^1 = Ac$, $R^2 = R^3 = R^4 = TFA$
21 $R^1 = CA$, $R^2 = R^3 = R^4 = TFA$
22 $R^1 = Bz$, $R^2 = R^3 = R^4 = TFA$
23 $R^2 = TFA$, $R^1 = R^3 = R^4 = Bz$
24 $R^1 = CA$, $R^2 = R^3 = TFA$, $R^4 = Bn$
25 $R^1 = R^3 = TFA$, $R^2,R^4 = CHPh$
26 $R^1 = CA$, $R^3 = TFA$, $R^2,R^4 = CHPh$

19 + **27**
20 + **27**
21 + **27**
22 + **27**
23 + **27** —*a,b*→ **28**

3 + **27** —*a*→ **29**
16 + **27** —*a*→ **30**
25 + **27** —*a,c*→ **30**
26 + **27** —*a,b*→ **30**
17 + **27** —*a*→ **31**
2 + **27** —*a*→ **32**
24 + **27** —*a,b*→ **33**

28 $R^1 = R^2 = R^3 = R^4 = Ac$
29 $R^1 = R^2 = R^3 = R^4 = Bz$
30 $R^1 = R^3 = Ac$, $R^3,R^4 = CHPh$
31 $R^1 = R^3 = CA$, $R^3,R^4 = CHPh$
32 $R^1 = R^2 = R^3 = R^4 = CA$
33 $R^1 = R^3 = R^3 = Ac$, $R^4 = Bn$

Scheme 3. Glycosylation of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**27**) with sialyl donors. *Reagents and conditions*: *a*. NIS, TfOH, MeCN, MS 3Å, –40 °C. *b*. 1) MeONa, MeOH; 2) Ac_2O, Py. *c*. 1) Et_3N, MeOH; 2) Ac_2O, Py.

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Table 1. Conditions and products of glycosylation[a]

Entry	Glycosyl donor	*O*-Bz present[b]	*O*-Ac present[b]	*O*-CA present[b]	*O*-TFA present[b]	Addition of TfOH (equiv.)[c]	Reaction time / h	Disaccharide	Yield (%)[d]	Anomeric ratio (α:β)[e]
1	**2**	–	–	++++ (4,7,8,9)	–	1 (0.26)	16	**32**	86	10.9:1
2	**3**	++++ (4,7,8,9)	–	–	–	1 (0.30)	0.5	**29**	61	4.6:1
3	**16**	–	++ (4,8)	–	–	1 (0.26)	3	**30**	60	2.1:1
4	**17**	–	–	++ (4,8)	–	2 (0.52)	2	**31**	57	5.8:1
5	**18**	–	–	+ (4)	–	1 (0.38)	3	n.a.[f]	n.a.[f]	n.a.
6	**19**	–	–	–	++++ (4,7,8,9)	3 (0.78)	21	**28**	38	9.8:1
7	**20**	–	+ (4)	–	+++ (7,8,9)	2 (0.53)	16	**28**	59	7.2:1
8	**21**	–	–	+ (4)	+++ (7,8,9)	2 (0.32)	2.5	**28**	55	15.5:1
9	**22**	+ (4)	–	–	+++ (7,8,9)	2 (0.52)	21	**28**	49	6.3:1
10	**23**[g]	+++ (4,8,9)	–	–	+ (7)	2 (0.59)	4	**28**	45	4.6:1
11	**24**	–	–	+ (4)	++ (7,8)	1 (0.30)	19	**33**	52	12.4:1
12	**25**	–	–	–	++ (4,8)	1 (0.31)	19	**30**[h]	49	7.7:1
13	**26**	–	–	+ (4)	+ (8)	1 (0.60)	19	**30**	70	9.2:1

[a] 1 equiv. of glycosyl donor (0.05 mol·L^{-1}), 1 equiv. of glycosyl acceptor (0.05 mol·L^{-1}), NIS, TfOH, MeCN, MS 3Å, –40 °C. Reaction was quenched after complete consumption of glycosyl donor (TLC control). In those cases when *O*-TFA groups were initially present in the glycosyl-donor, the mixture of products obtained after work-up was treated with NaOMe in MeOH to cleave all *O*-acyl groups and then *O*-acetylated with Ac_2O and Py. Fully protected *O*-acylated disaccharide fraction was isolated by gel permeation chromatography on BioBeads S-X3 (toluene).and analyzed by ^{1}H NMR to give anomeric ratio. Individual anomers of disaccharides were then separated by silica gel chromatography and the disaccharide yield was determined at this stage.

[b] Minus sign (–) indicates that these *O*-acyl groups were absent while the number of plus signs (+) denotes the number of the corresponding *O*-acyl (Bz, Ac, CA or TFA) groups. Numbers in parentheses indicate positions of the respective *O*-acyl groups.

[c] Number of additions of TfOH and the total amount of added TfOH (equiv.) are given.

[d] Isolated yield of α-isomer of disaccharide after silica gel chromatography is given.

[e] ^{1}H NMR data for the disaccharide fraction isolated by gel permeation chromatography on BioBeads S-X3 (toluene).

[f] Multiple products were formed.

[g] Glycosylation was performed at 36 mM concentration of glycosyl donor and glycosyl acceptor.

[h] Treatement with NEt_3 in MeOH was used for cleavage of *O*-TFA groups from the disaccharide prior to acetylation with Ac_2O and Py.

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Table 2. ^{1}H NMR chemical shifts (300 MHz, δ_H) of thioglycosides **2–26** in $CDCl_3$.[a]

Compound	H-3ax	H-3eq	H-4	H-5	H-6	H-7	H-8	H-9a	H-9b
2	2.22	2.82	5.66	4.23	4.93	5.52	5.09	4.18	4.61
3	2.36	3.01	5.98	4.36	5.19	6.06	5.55	4.54	4.97
4	2.41	2.93	5.93	4.43	4.71	4.18	5.44	4.67	4.95
5	2.11	2.79	4.30	3.99	4.53	3.48	4.13	3.98	
6	2.24	2.83	5.63	4.24	4.55	3.53	4.14	3.97	4.04
7	2.39	2.99	5.84	4.38	4.62	3.57	4.15	3.97	4.04
8	2.27	2.89	5.65	4.31	4.58	3.51	4.12	3.98	4.02
9[b]	2.13	2.77	5.49	4.41	4.88		3.53–3.91 (m)		
10[c]	2.20	2.83	5.52	4.46	4.83		4.40–4.72 (m)		
11[b]	2.18	2.83	5.60	4.46	4.90		3.66–3.83 (m)		
14[b]	2.01	2.73	~4.32[d]	~4.28[d]	4.91	3.79	4.06	3.64	~4.36[d]
15	2.11	2.75	5.56	4.41	4.74	3.52	3.92	3.49	3.73
16	2.19	2.74	5.56	4.51	4.61	3.90	5.16	3.60	4.72
17	2.23	2.78	5.68	~4.66[d]	~4.62[d]	3.99	5.30	3.68	~4.65[d]
18	2.24	2.76	5.71	4.52	4.67	3.62	3.98	3.53	4.30
19	2.36	2.92	5.75	4.18	4.92	5.55	5.01	4.29	4.72
20	2.25	2.78	5.77	4.13	4.81	5.54	4.98	4.28	4.74
21	2.28	2.84	5.83	4.17	4.87	5.56	5.02	4.27	4.72
22	2.45	2.95	6.20	4.34	4.90	5.62	4.83	4.29	4.71
23	2.43	3.01	6.02	4.40	5.09	5.81	5.42	4.37	4.82
24	2.22	2.80	5.64	4.17	4.86	5.56	5.36	3.57	3.92
25	2.27	2.79	5.68	4.61	4.69	4.06	5.39	3.77	4.66
26	2.21	2.78	5.73	4.60	4.61	4.06	5.39	3.76	4.68

[a] Chemical shifts of signals of protecting groups can be found in the Experimental and in the Supplementary data section.

[b] In acetone-d_6.

[c] In DMSO-d_6.

[d] Chemical shift was determined from ^{1}H,^{1}H-COSY experiment.

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Table 3. ^{1}H NMR coupling constants (*J*, Hz) of thioglycosides **2–26** in $CDCl_3$.

Compound	3ax,3eq	3ax,4	3eq,4	4,5	5,6	6,7	7,8	8,9a	8,9b	9a,9b
2	13.9	11.0	4.8	11.0	10.7	1.9	2.2	8.4	1.5	12.6
3	13.6	11.7	4.8	10.3	10.5	2.4	2.2	8.4	2.6	12.1
4	13.6	11.6	4.8	10.3	10.3	1.5	4.8	6.6	2.2	12.1
5	13.6	11.7	4.4	10.0	10.3	1.5	8.0	5.9		n.d.[a]
6	13.9	12.1	5.1	10.3	11.0	1.5	8.1	6.6	5.1	8.8
7	13.9	11.7	5.1	10.3	10.3	1.5	8.1	6.6	5.1	8.8
8	13.9	11.7	5.1	10.3	10.3	1.5	8.1	6.6	5.1	8.8
9[b]	13.6	11.7	4.8	10.3	10.6	1.1	n.d.	n.d.	n.d.	n.d.
10[c]	13.5	11.4	4.7	10.5	10.6	n.d.	n.d.	n.d.	n.d.	n.d.
11[b]	13.8	11.9	4.8	10.3	10.6	1.4	8.6	n.d.	n.d.	n.d.
14[b]	13.9	11.7	4.4	n.d.	10.1	1.5	9.2	10.3	5.3	10.6
15	13.6	11.7	4.8	10.3	10.6	1.1	8.4	6.6	2.9	9.5
16	13.6	12.1	4.8	10.0	10.3	1.5	9.9	9.5	5.3	10.6
17	13.9	12.1	5.0	10.0	n.d.	1.5	9.5	10.3	5.3	10.8
18	13.9	11.7	5.0	10.0	10.3	2.2	9.2	10.3	5.3	10.8
19	13.9	11.4	5.1	10.3	10.6	2.2	1.8	9.2	2.6	12.5
20	14.1	11.7	5.0	10.3	10.5	2.4	1.8	9.2	2.4	12.5
21	13.9	11.7	4.8	10.3	10.6	2.2	1.8	9.2	2.6	12.5
22	14.1	11.7	5.0	10.3	10.3	2.2	1.8	9.2	2.6	12.5
23	13.9	11.7	4.8	10.3	10.6	2.2	1.8	8.8	2.4	12.5
24	13.9	11.7	5.1	10.6	10.6	2.6	3.3	7.3	3.3	11.4
25	13.8	11.7	4.8	9.9	10.3	2.2	9.5	9.5	5.3	10.6
26	13.9	12.1	5.1	9.9	10.3	1.5	9.9	9.5	5.1	10.6

[a] Not determined.

[b] In acetone-d_6.

[c] In DMSO-d_6.

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Table 4. ^{13}C NMR chemical shifts (75 MHz, δ_C) of thioglycosides **2–26** in $CDCl_3$.[a]

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
2	167.9	88.5	37.2	70.3[b]	49.9	71.7	70.2[b]	74.1	63.3
3	168.2	88.9	37.8	69.5	50.6	72.5	70.0	73.4	63.2
4	168.1	89.3	37.7	68.9[c]	52.2	73.2[d]	69.0[c]	73.4[d]	63.2
5	168.9	90.0	40.9	66.3	53.7	71.5	70.7	74.2	67.0
6	167.8	89.6	37.8	68.3	51.5	71.9	70.1	74.3	66.8
7	167.8	89.6	38.0	69.0	51.8	72.2	70.3	74.4	66.9
8	167.7	89.4	37.6	70.4	51.0	71.8	70.3	74.2	66.9
9[f]	168.5	90.5	38.6	70.0	51.0	72.3	71.0	70.6	64.8
10[g]	167.2	89.4	37.3	70.6	49.3	71.2	69.8[e]	68.6[e]	63.5
11[f]	168.4	90.4	38.4	72.0	50.9	72.4	70.6	71.8	64.9
14[f]	168.5	91.3	42.2	67.3	53.6	70.6	80.2	61.0	72.4
15	167.9	89.5	37.6	70.5	50.6	71.3	69.3	68.7	71.6
16	167.3	89.7	37.7	68.5	50.3	70.4	76.4	63.1	67.9
17	167.2	89.2	37.3	70.8	49.8	70.7	76.7	64.2	67.5
18	167.7	87.9	37.0	71.1	49.7	70.2	78.8	60.4	70.8
19	167.4	87.5	36.5	71.9	49.8	71.1	71.5	75.0	63.8
20	167.7	88.1	37.2	67.9	50.2	71.7	71.7	75.4	63.9
21	167.5	87.9	36.9	70.0	49.9	71.5	71.6	75.1	63.8
22	167.8	87.8	37.2	68.8	50.1	71.8	71.6	75.5	63.8
23	167.9	88.8	37.6	69.2	50.4	72.1	73.8	73.0	62.5
24	167.9	88.6	37.1	70.1	50.3	71.3	72.1	75.8	66.7
25	167.1	88.7	36.6	72.8	49.6	70.2	75.8	66.0	66.7
26	167.1	89.3	37.3	70.7	49.7	70.4	75.8	66.2	66.6

[a] Chemical shifts of signals of protecting groups can be found in the Experimental and in the Supplementary data section.

[b–e] Signals may have to be interchanged.

[f] In acetone-d_6.

[g] In DMSO-d_6.

- Varying protecting groups may change solution structure and sialylation outcome.
- Influence of O-protecting group pattern on the sialylation outcome was studied.
- A series of novel sialyl donors containing *O*-TFA groups was synthesized.
- The presence of *O*-TFA groups strongly influenced the sialylation outcome.
- Combination of *O*-TFA and *O*-CA groups is the key to stereoselective sialylation.

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