Published in final edited form as:

J Carbohydr Chem. 2013 ; 32(5-6): 324–335. doi:10.1080/07328303.2013.804081.

Exploration of the Oxazolidinthione Protecting System for the Synthesis of Sialic Acid Glycosides

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Abstract

An N-acetyl oxazolidinthione protected sialyl thioglycoside was synthesized and its use as a sialyl donor studied. The strongly electron-withdrawing nature of the oxazolidinthione moiety is such that activation could not be achieved at -78°C . Couplings were therefore conducted at the lowest convenient temperature (-50°C). Glycosides were formed in good yield but in two out three cases studied selectivities were lower than those seen with the corresponding N-acetyl oxazolidinone protected donor. The resulting N-acetyl oxazolidinthione protected disaccharides were converted to the corresponding N-acetyl oxazolidinones by treatment with N-iodosuccinimide and triflic acid in the presence of water at 0°C .

Keywords

oxazolidinthione; isothiocyanate; sialic acid; glycosylation; oxazolidinone; stereoselectivity

Introduction

The introduction of the 4O,5N-oxazolidinone and the N-acetyl-4O,5N-oxazolidinone protecting systems (Figure 1) by the Takahashi, De Meo, and Crich laboratories,^{1–4} with subsequent variations by numerous other laboratories^{5–8} to the field of sialic acid chemistry⁹ represents a significant step forward in the stereocontrolled synthesis of complex α -sialosides in terms of stereoselectivity, yield, and avoidance of the elimination problem, as is evident from impressive syntheses of α -(2 $\rightarrow$ 8)- and α -(2 $\rightarrow$ 9)polysialic acid reported systems by the Takahashi and Wong laboratories.^{1,5,10–11} The limited mechanistic work in the area to date suggests that the beneficial effect of the oxazolidinone system arises from the high dipole moment of the heterocyclic system, as compared to simple acyclic esters and amides, in the mean plane of the pyranose ring to which it imparts a strong electron-withdrawing effect.¹² This electron-withdrawing effect destabilizes the anomeric oxocarbenium ion thereby promoting associative rather than dissociative glycosylation mechanisms. Building on this hypothesis we reasoned that stereoselectivity might be further increased if the electron-withdrawing effect of the cyclic protecting group spanning O4 and N5 could be augmented. We considered the oxazolidinthione and cyclic sulfamidate functions as candidate systems (Figure 1) and elected to pursue the former in view of the well-known powerful electron-withdrawing effect of the thiocarbonyl group, which is

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responsible for the prominence of the thioureas in organocatalysis,^{13–14} and because of potential problems arising from possible electrophilic behavior of the alternative sulfamidate system such as documented in amino acid chemistry.¹⁵

Results and Discussion

The synthesis of an oxazolidinthione protected sialyl thioglycoside **5** was achieved from the known neuraminic acid derivative **1** by treatment with HCl in ether to remove the carbamate protection giving **2** followed by treatment with phenyl thionochloroformate and sodium hydrogen carbonate in aqueous acetonitrile followed, after extractive work-up, by acetylation which was achieved through the aegis of sodium hydride and acetyl chloride (Scheme 1). The use of HCl in ether for the essentially quantitative removal of the carbamate group from **1** is a distinct improvement over the use of trifluoroacetic acid reported previously,³ which suffers from the formation of trifluoroacetamide **8** as byproduct. A byproduct of this synthesis was the isothiocyanate **6**, which arises from incomplete cyclization of the initial phenyl thionocarbamate obtained on reaction of **2** with the thionochloroformate (Scheme 1). Prolonged stirring of **2** with the mixture with phenyl thionochloroformate in the presence of sodium hydrogen carbonate resulted in the formation of the oxazolidinone **7** (Scheme 1).

Various conditions for the activation of donor **5** were assayed including the use of the 1-benzenesulfinyl piperidine/triflic anhydride¹⁶ and diphenyl sulfoxide/triflic anhydride¹⁷ combinations, and 2,4-dinitrobenzenesulfonyl triflate.¹⁸ Unfortunately, none of these systems, each of which has been successfully in the oxazolidinone series, activated donor **5** in a satisfactory manner. The N-iodosuccinimide/triflic acid combination¹⁹ which cleanly activates the oxazolidinone-protected thiosialosides at $-78\text{ }^{\circ}\text{C}$ was not effective with **5** below $-60\text{ }^{\circ}\text{C}$, but did function effectively at $-50\text{ }^{\circ}\text{C}$. Accordingly, a number of exploratory coupling reactions were conducted with donor **5** and a series of standard acceptor alcohols at that temperature in a 2:1 mixture of dichloromethane and acetonitrile (Table 1, column 1). The anomeric stereochemistry of the coupled products was determined by measurement of the $^3J_{\text{CH}}$ coupling constants between the anomeric carboxyl carbon and the axial H3 in the usual manner,^{20–21} and by subsequent comparison with literature data after conversion to the corresponding N-acetyloxazolidinone series. For the examples presented in Table 1, coupling reactions were quenched at $-50\text{ }^{\circ}\text{C}$ before they were brought to room temperature and worked up. However, if an excess of N-iodosuccinimide was employed in the coupling and the reaction mixture allowed to warm to room temperature before quenching the products were contaminated by the corresponding N-acetyloxazolidinones. On this basis we developed a convenient protocol for conversion of the oxazolidinthiones to the oxazolidinones by treatment with N-iodosuccinimide and triflic acid in dichloromethane at $0\text{ }^{\circ}\text{C}$ in the presence of water (Table 1). Of course, it is possible to conduct the coupling and oxazolidinthione to oxazolidinone conversion in a single pot but in this study we have preferred to carry out the two operations sequentially so as to establish the activation of the thioglycoside prior to the thiocarbonyl to carbonyl conversion.

The stereoselectivities reported in Table 1 are generally no better than those reported in the literature for couplings to the adamantanyl thio N-acetyloxazolidinone protected sialyl

donor³ analogous to **5** at -78°C under otherwise analogous conditions, which we attribute to the higher temperature required for the activation of **5**, and which in turn is due to the strongly electron withdrawing, disarming nature of the oxazolidinthione moiety. Thus, as noted previously in other series,^{22–23} perceived advantages due to the presence of strongly electron withdrawing groups intended to promote associative glycosylation mechanisms can be nullified by the need to work at higher temperatures. It still remains possible that the oxazolidinthione-protected sialyl donors will be more selective than the corresponding oxazolidinones at -78°C if a suitable method can be found for their activation. Good candidates for study in this context are the sialyl phosphates so effectively deployed by the Wong group in the oxazolidinone protected series,⁵ but we have so far been unable to affect the clean conversion of **5** to the corresponding dibutyl phosphates.

The main advantage of the N-acetyl oxazolidinones introduced by our group over the oxazolidinones pursued by the Takahashi and De Meo group is their ability to undergo selective cleavage of the oxazolidinone ring, leaving in place the native acetamide group on simple treatment with methanolic sodium methoxide at room temperature. When these conditions were applied to the N-acetyl oxazolidinthione **10** the N-acetyl group was preferentially removed leaving the oxazolidinthione in place (Scheme 2). This result is consistent with observations from the asymmetric synthesis field that N-acyl oxazolidinthiones are readily deacylated with potential recovery of the oxazolidinthione chiral auxiliary.²⁴ Fortunately, the ability to convert the N-acetyl oxazolidinthione moiety cleanly to the N-acetyl oxazolidinone (Table 1) allows access to the Zemplen conditions employed in that series.

Conclusion

The strongly electron withdrawing nature of the oxazolidinthione group is such as to preclude thioglycoside activation at -78°C resulting in the need to work at higher temperatures with the anticipated loss of selectivity that this entails.

Experimental Section

Methyl (1-Adamantanyl 5-acetamido-7,8,9-tri-O-acetyl-5-N,4-O-thiocarbonyl-3,5-dideoxy-2-thio-D-glycero-β-D-galacto-non-2-ulopyranoside)onate (5) and Methyl (1-Adamantanyl 5-deamino-5-isothiocyanato-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-D-glycero-β-D-galacto-non-2-ulopyranoside)onate (6)

To a stirred solution of **1**³ (3.0 g, 5.6 mmol) in THF (15 mL) was added 2M HCl in diethyl ether (10 mL) at 0°C . The resulting solution was stirred at room temperature for 3.5 h., and then concentrated under reduced pressure to give **2** (2.1 g) which, without further purification, was dissolved in MeCN (15 mL) and H₂O (30 mL), cooled to 0°C , and NaHCO₃ (2.1 g, 25.5 mmol) added. To the vigorously stirred mixture was slowly added *O*-phenyl chlorothionoformate (1.6 g, 9.5 mmol) in MeCN (15 mL) through a dropping funnel, after which stirring was continued for 1.0 h at 0°C and 0.5 at room temperature. Allowing the reaction to stir for longer times lead to the conversion of oxazolidinthione to the corresponding oxazolidinone derivative **7**.³ The resulting mixture was extracted with EtOAc (100 mL × 3), and the combined extracts were washed with brine and then dried over

Na₂SO₄ and concentrated. The residue was purified by column chromatography to give an approximately 2:1 mixture of **3** and **4** (2.0 g, 4.7 mmol) which was taken up in THF (15 mL) and added drop wise to a suspension of NaH (0.28 g, 7.0 mL, 60 % in mineral oil, 7 mmol) in THF (20 mL) at 0 °C followed by the addition of acetyl chloride (0.5 mL, 7.0 mmol) in THF (5 mL). After 15 min stirring, the reaction mixture was poured into saturated aqueous NH₄Cl, and was extracted with ethyl acetate (100 mL × 3). The combined organic phase was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel eluting with EtOAc/DCM (1/5) to give the N-acetyl oxazolidinethione **5** (1.3 g, 48%) and the isothiocyanate **6** (0.6 g, 23%).

N-Acetyl oxazolidinethione **5**

mp 104-105 °C; $[\alpha]_D^{20} = -56$ ($c = 0.8$, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ: 5.54 (t, $J = 3.0$ Hz, 1H), 5.35 (m, 1H), 4.79-4.72 (m, 2H), 4.67 (dd, $J = 2.0, 12.0$ Hz, 1H), 4.16 (dd, $J = 8.0, 12.0$ Hz, 1H), 3.81 (s, 3H), 3.75 (dd, $J = 9.5, 12.5$ Hz), 2.81 (dd, $J = 3.5, 12.5$ Hz, 1H), 2.71 (s, 3H), 2.17 (t, $J = 13.0$ Hz, 1H), 2.10 (s, 3H), 2.09 (s, 3H), 1.99 (s, 3H), 1.96-1.94 (m, broad, 6H), 1.85-1.83 (m, broad, 3H), 1.66-1.60 (m, broad, 6H); ¹³C NMR (150 MHz, CDCl₃) δ 186.8, 173.7, 170.9, 170.5, 169.5, 169.1, 85.4, 78.8, 74.3, 72.5, 71.9, 63.2, 62.5, 52.9, 51.3, 43.4, 38.9, 35.8, 29.8, 27.3, 21.2, 20.7, 20.6; ESIHRMS calcd for C₂₉H₃₉NO₁₁S₂Na ([M + Na]⁺) 664.18622, found 664.18550.

Isothiocyanate **6**

Mp 134-135 °C; $[\alpha]_D^{20} = -73$ ($c = 0.8$, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ: 5.48 (dd, $J = 2.0, 4.0$ Hz, 1H), 5.35 (m, 1H), 5.23 (m, 1H), 4.70 (dd, $J = 2.0, 12.5$ Hz, 1H), 4.51 (dd, $J = 2.0, 10$ Hz, 1H), 4.23 (dd, $J = 7.0, 12.5$ Hz, 1H), 3.77 (s, 3H), 3.62 (t, $J = 10$ Hz, 1H), 2.62 (dd, $J = 4.5, 13.5$ Hz, 1H), 2.14 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 2.00 (s, 3H), 1.97-1.94 (m, broad, 6H), 1.81-1.79 (m, broad, 3H), 1.73 (t, 12.5 Hz, 1H), 1.65-1.59 (m, broad, 6H); ¹³C NMR (150 MHz, CDCl₃) δ 170.5, 170.3, 169.5, 169.4, 169.3, 139.5, 85.7, 71.7, 70.9, 69.8, 69.4, 62.4, 57.1, 52.8, 50.7, 43.3, 39.3, 35.9, 29.7, 21.0, 20.9, 20.6; ESIHRMS calcd for C₂₉H₃₉NO₁₁S₂Na ([M + Na]⁺) 664.18622, found 664.18591.

Methyl (1-Adamantanyl 5-trifluoroacetamido-3,5-dideoxy-2-thio- β -glycero- β -galacto-non-2-ulopyranoside)onate (**8**)

$[\alpha]_D^{20} = -53$ ($c = 1.3$, MeOH); ¹⁹F NMR (400 MHz, MeOH-d₄) δ: -76.0; ¹H NMR (600 MHz, MeOH-d₄) δ: 4.51 (d, $J = 10.5$ Hz, 1H), 4.11 (m, 1H), 3.9 (t, 10.3 Hz, 1H), 3.82-3.80 (m, 4H), 3.72-3.70 (m, 1H), 3.64 (dd, $J = 5.5, 11.5$ Hz, 1H), 3.38 (d, $J = 9.5$ Hz, 1H), 2.47 (dd, $J = 4.7, 13.5$ Hz, 1H), 2.00-1.95 (m, 9H), 1.77 (t, $J = 12.5$ Hz, 1H), 1.68 (s, broad, 6H); ¹³C NMR (150 MHz, MeOH-d₄) δ 172.4, 158.0, 124.0, 85.9, 70.5, 69.8, 69.6, 66.0, 63.7, 53.0, 51.9, 49.4, 48.4, 43.0, 42.8, 35.7, 29.8; ESIHRMS calcd for C₂₂H₃₂F₃NO₈SNa ([M + Na]⁺) 550.16984, found 550.16801.

General Coupling Protocol

A solution of donor (0.15 mmol), acceptor (0.23 mmol), and activated 4 Å acid-washed powdered molecular sieves (300 mg, 2.0 g/mmol) in anhydrous CH₂Cl₂:MeCN (2:1, 2 mL) was stirred for 5 h under Ar, and then cooled to -50 °C followed by addition of NIS (35 mg,

0.15 mmol) and TfOH (2 μ L, 0.02 mmol). The reaction mixture was stirred at -50°C for 4 h and then quenched with DIPEA (7 μ L). The mixture was diluted with dichloromethane, filtered through Celite, washed with 20% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution, dried over Na_2SO_4 , and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with acetone:hexane systems to afford the desired coupled products.

General protocol for the conversion of N-acetyl oxazolidinones into the corresponding N-acetyl oxazolidinones

A solution of N-acetyl oxazolidinone (0.036 mmol) in dichloromethane (0.6 mL) was cooled to 0°C followed by addition of NIS (16 mg, 0.072 mmol), TfOH (2 μ L, 0.02 mmol) and H_2O (1.5 μ L, 0.072 mmol). The reaction mixture was stirred at 0°C for 10 min and then quenched with DIPEA (7 μ L). The mixture was diluted with dichloromethane, washed with 20% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution, dried over Na_2SO_4 , and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with ethyl acetate:hexane systems.

Methyl 5-acetamido-7,8,9-tri-O-acetyl-5-N,4-O-thiocarbonyl-3,5-dideoxy- β -glycero- α -D-galacto-non-2-ulopyranosylonate-(2 $\rightarrow$ 6)-methyl 2,3,4-tri-O-benzyl- β -D-galactopyranoside (10)

Viscous oil; $[\alpha]_{\text{D}}^{20} = -5$ ($c = 1$, CHCl_3); ^1H NMR (600 MHz, CDCl_3) δ : 7.37-7.26 (m, 15H), 5.42-5.37 (m, 2H), 4.98 (d, $J = 11.0$ Hz, 1H), 4.88 (d, $J = 11.0$ Hz, 1H), 4.79-4.69 (m, 6H), 4.32-4.27 (m, 3H), 4.08-4.04 (m, 2H), 3.90-3.87 (m, 2H), 3.80-3.74 (m, 3H), 3.60 (s, 3H), 3.55 (s, 3H), 3.52 (dd, $J = 3.0, 10.0$ Hz, 1H), 2.90 (dd, $J = 3.5, 10.0$ Hz, 1H), 2.74 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.03 (s, 1H), 2.00 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 186.6, 173.3, 170.6, 170.0, 168.0, 138.8, 138.7, 138.5, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.6, 127.5, 127.3, 127.2, 104.9, 99.1, 82.0, 79.4, 78.6, 75.2, 75.1, 74.1, 73.3, 73.2, 72.9, 72.6, 71.3, 69.2, 63.6, 62.7, 61.6, 57.0, 53.0, 36.6, 27.2, 21.0, 20.8, 20.7 (C-1, $^3J_{\text{C-1,H-ax}} = 7.2$ Hz); ESIHRMS calcd for $\text{C}_{47}\text{H}_{55}\text{NO}_{17}\text{SNa}$ ($[\text{M} + \text{Na}]^+$) 960.30884, found 960.30991.

Methyl 5-acetamido-7,8,9-tri-O-acetyl-5-N,4-O-carbonyl-3,5-dideoxy- β -glycero- α -D-galacto-non-2-ulopyranosylonate-(2 $\rightarrow$ 6)-methyl 2,3,4-tri-O-benzyl- β -D-galactopyranoside (11)

This compound was obtained from **10** by the standard procedure and had physical data consistent with the literature.²

Methyl 5-acetamido-7,8,9-tri-O-acetyl-5-N,4-O-thiocarbonyl-3,5-dideoxy- β -glycero- α -D-galacto-non-2-ulopyranosylonate-(2 $\rightarrow$ 3)-methyl 2,6-di-O-benzyl- β -D-galactopyranoside (13a)

Viscous oil; $[\alpha]_{\text{D}}^{20} = -8$ ($c = 0.7$, CHCl_3); ^1H NMR (600 MHz, CDCl_3) δ : 7.35-7.23 (m, 10H), 5.46-5.44 (m, 2H), 4.80 (d, $J = 12.0$ Hz, 1H), 4.69 (d, $J = 12.0$ Hz, 1H), 4.56-4.54 (m, 3H), 4.37 (dd, $J = 2.0, 12.5$ Hz, 1H), 4.33 (d, $J = 8.0$ Hz, 1H), 4.09-4.03 (m, 2H), 3.97-3.94 (dd, $J = 5.5, 12.5$ Hz, 1H), 3.83-3.79 (m, 2H), 3.76 (s, 3H), 3.75-3.69 (m, 2H), 3.61 (t, $J = 5.5$ Hz, 1H), 3.55 (s, 3H), 3.54-3.52 (m, 1H), 2.86 (dd, $J = 3.5, 12.0$ Hz, 1H), 2.75 (d, $J =$

3.0 Hz, 1H), 2.72 (s, 3H), 2.21 (t, $J = 12.5$ Hz, 1H), 2.10 (s, 3H), 2.02 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 186.5, 173.1, 170.6, 170.2, 169.8, 168.2, 138.8, 138.0, 128.3, 128.1, 127.8, 127.7, 127.5, 98.6, 78.7, 76.3, 75.1, 74.6, 73.6, 72.6, 71.2, 69.3, 69.0, 68.2, 62.9, 61.4, 56.9, 53.2, 35.3, 29.7, 27.2, 21.1, 20.7, 20.5 (C-1, $^3J_{\text{C-1,H-ax}} = 6.8$ Hz); ESIHRMS calcd for $\text{C}_{40}\text{H}_{49}\text{NO}_{17}\text{SNa}$ ($[\text{M} + \text{Na}]^+$) 870.26189, found 870.26312.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-5-*N*,4-*O*-thiocarbonyl-3,5-dideoxy- β -glycero- β -galacto-non-2-ulopyranosylonate-(2 $\rightarrow$ 3)-methyl 2,6-di-*O*-benzyl- β -galactopyranoside (13 β)

Viscous oil; $[\alpha]_{\text{D}}^{20} = +2$ ($c = 0.9$, CHCl_3); ^1H NMR (600 MHz, CDCl_3) δ : 7.32-7.26 (m, 10H), 5.47 (s, broad, 1H), 5.38 (dd, $J = 2.5, 4.5$ Hz, 1H), 4.77 (d, $J = 11.0$ Hz, 1H), 4.65 (dd, $J = 3.5, 12.5$ Hz, 1H), 4.62-4.55 (m, 5H), 4.54-4.52 (dd, $J = 2.5, 9.0$ Hz, 1H), 4.26-4.25 (d, $J = 8.0$ Hz), 4.05-4.01 (m, 2H), 3.84-3.76 (m, 4H), 3.56-3.53 (m, 5H), 3.50 (s, 3H), 2.88 (dd, $J = 3.5, 12.5$ Hz), 2.72 (s, 3H), 2.11 (t, $J = 13.0$ Hz, 1H), 2.06 (s, 3H), 2.05 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 187.0, 174.0, 170.7, 170.6, 169.6, 166.2, 138.2, 137.7, 132.5, 128.3, 128.2, 127.7, 127.6, 104.9, 99.1, 78.3, 75.3, 74.8, 73.7, 72.6, 72.0, 70.5, 70.0, 69.4, 63.2, 61.7, 60.0, 57.0, 52.8, 36.2, 29.6, 27.3, 21.0, 20.8, 20.7 (C-1, $^3J_{\text{C-1,H-ax}} = 1.0$ Hz); ESIHRMS calcd for $\text{C}_{40}\text{H}_{49}\text{NO}_{17}\text{SNa}$ ($[\text{M} + \text{Na}]^+$) 870.26189, found 870.26322.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-5-*N*,4-*O*-carbonyl-3,5-dideoxy- β -glycero- α -galacto-non-2-ulopyranosylonate-(2 $\rightarrow$ 3)-methyl 2,6-di-*O*-benzyl- β -galactopyranoside (14)

This compound was obtained from **13a** by the standard procedure and had physical data consistent with the literature.²

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-5-*N*,4-*O*-thiocarbonyl-3,5-dideoxy- β -glycero- α -galacto-non-2-ulopyranosylonate-(2 $\rightarrow$ 3)-methyl 2,4,6-tri-*O*-benzyl- β -galactopyranoside (16a)

Viscous oil; $[\alpha]_{\text{D}}^{20} = -12$ ($c = 1.1$, CHCl_3); ^1H NMR (600 MHz, CDCl_3) δ : 7.36-7.22 (m, 15H), 5.54 (t, $J = 7.5$ Hz, 1H), 5.46 (d, $J = 9.0$ Hz, 1H), 4.89 (d, $J = 11.5$ Hz, 1H), 4.80 (d, $J = 12.0$, 1H), 4.70 (d, $J = 12.0$ Hz, 1H), 4.54 (d, $J = 11.5$ Hz, 1H), 4.48-4.42 (m, 2H), 3.76 (d, $J = 2.5$ Hz, 1H), 3.73-3.69 (m, 2H), 3.67 (s, 3H), 3.62-3.56 (m, 2H), 3.53 (s, 3H), 2.73 (s, 3H), 2.71 (dd, $J = 4.0, 13.0$ Hz, 1H), 2.29 (t, $J = 13.0$ Hz, 1H), 2.10 (s, 3H), 1.99 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 186.7, 173.2, 170.5, 169.8, 169.6, 168.0, 139.2, 138.7, 137.9, 128.3, 128.2, 128.0, 127.9, 127.7, 127.5, 127.4, 127.0, 105.0, 99.2, 78.9, 74.9, 74.7, 74.5, 73.5, 73.1, 70.9, 68.9, 68.3, 62.6, 61.4, 57.1, 52.9, 34.7, 27.2, 21.0, 20.7, 20.6 (C-1, $^3J_{\text{C-1,H-ax}} = 7.5$ Hz); ESIHRMS calcd for $\text{C}_{47}\text{H}_{55}\text{NO}_{17}\text{SNa}$ ($[\text{M} + \text{Na}]^+$) 960.30884, found 960.30732.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-5-*N*,4-*O*-thiocarbonyl-3,5-dideoxy- β -glycero- β -galacto-non-2-ulopyranosylonate-(2 $\rightarrow$ 3)-methyl 2,4,6-tri-*O*-benzyl- β -galactopyranoside (16 β)

Viscous oil; $[\alpha]_{\text{D}}^{20} = +1$ ($c = 0.9$, CHCl_3); ^1H NMR (600 MHz, CDCl_3) δ : 7.36-7.18 (m, 15H), 5.25 (s, broad, 1H), 5.15 (d, $J = 8.0$ Hz, 1H), 4.75-4.71 (m, 2H), 4.67-4.62 (m, 2H), 4.58-4.49 (m, 3H), 4.24 (d, 7.5 Hz, 1H), 4.16-4.11 (m, 2H), 3.98 (dd, $J = 8.0, 12.0$ Hz, 1H),

3.79 (d, $J = 2.5$ Hz, 1H), 3.71–3.63 (m, 4H), 3.53 (s, 3H), 3.51 (dd, $J = 3.5, 12.0$ Hz, 1H), 3.46 (s, 3H), 2.70 (s, 3H), 2.68 (d, $J = 3.0$ Hz, 1H), 2.06 (s, 3H), 2.03 (d, $J = 2.5$ Hz, 1H), 2.02 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 186.8, 172.1, 171.0, 170.49, 169.1, 166.0, 138.7, 138.1, 138.0, 129.1, 128.4, 128.1, 127.8, 127.7, 127.0, 105.2, 99.1, 78.7, 77.7, 76.4, 76.0, 74.8, 74.7, 73.7, 73.4, 73.0, 72.4, 68.6, 63.0, 61.4, 56.9, 52.6, 36.3, 27.2, 20.9, 20.7, 20.6 (C-1, $^3J_{\text{C-1,H-ax}} = 0$ Hz); ESIHRMS calcd for $\text{C}_{47}\text{H}_{55}\text{NO}_{17}\text{SNa}$ ($[\text{M} + \text{Na}]^+$) 960.30884, found 960.30923.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-5-*N*,4-*O*-carbonyl-3,5-dideoxy- D -glycero- α - D -galactonon-2-ulopyranosylonate-(2 $\rightarrow$ 3)-methyl 2,4,6-tri-*O*-benzyl- β - D -galactopyranoside (17)

This compound was obtained from **16a** by the standard procedure and had physical data consistent with the literature.²

Methyl 5-*N*,4-*O*-thiocarbonyl-3,5-dideoxy- D -glycero- α - D -galactonon-2-ulopyranosylonate-(2 $\rightarrow$ 6)-methyl 2,3,4-tri-*O*-benzyl- β - D -galactopyranoside (18)

To a solution of **10** (75 mg, 0.08 mmol) in methanol (2 mL) was added a few drops of sodium methoxide solution in methanol (~50 μL , 0.2 mmol) at room temperature. The mixture was stirred at room temperature for 30 min followed by treatment with Amberlyst 15 ion-exchange resin for 5 min. The mixture was diluted with methanol and filtered through a sintered funnel packed with Celite and silica gel. The filter pad was rinsed with methanol (3 X 5 mL) after filtration. The combined filtrates were concentrated under reduced pressure to afford **18** in 96% yield. $[\alpha]_{\text{D}}^{20} = +5$ ($c = 0.6$, MeOH); ^1H NMR (500 MHz, MeOH-d^4) δ : 7.37–7.26 (m, 15H), 4.78–4.70 (m, 4H), 4.60 (m, 1H), 4.32 (m, 1H), 4.02–3.96 (m, 3H), 3.87–3.78 (m, 2H), 3.76–3.60 (m, 8H), 3.55–3.50 (m, 4H), 3.36 (s, 3H), 2.72–2.66 (m, 1H), 1.78–1.70 (m, 1H); ^{13}C NMR (125 MHz, MeOH-d^4) δ 205.9, 138.5, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 127.1, 104.7, 81.7, 79.1, 74.5, 74.3, 72.5, 70.9, 60.0, 56.0, 55.9, 52.1, 48.2; ESIHRMS calcd for $\text{C}_{47}\text{H}_{55}\text{NO}_{17}\text{SNa}$ ($[\text{M} + \text{Na}]^+$) 792.26658, found 792.26702.

Acknowledgments

We thank the NIH (GM 62160) for support of this work.

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X = H, oxazolidinone

X = Ac, N-acetyloxazolidinone

X = H, oxazolidinthione

X = Ac, N-acetyloxazolidinthione

X = H, cyclic sulfamidate

X = Ac, N-acetylsulfamidate

Figure 1.
Existing and Potential 5-Membered Cyclic Protecting Groups for Sialyl Donors

J Carbohydr Chem. Author manuscript; available in PMC 2016 January 22.

Scheme 2.

Selective deacetylation of an N-Acetyloxazolidinthione.

Table 1

Exploratory Coupling Reactions with Donor **5**, and Oxazolidinone to Oxazolidinone Conversion.

Entry	Acceptor	Coupled Product ^a	Oxazolidinone ^b
		% Yield, $\alpha:\beta$ ratio	% Yield
1		 10, 81%, α -only	 11, 82%
2		 13, 74%, $\alpha:\beta$ 7:1	 14, 73%
3		 16, 78%, $\alpha:\beta$ 1:1	 17, 75%

^a Unreacted donor **5** was recovered from all reactions following work-up and chromatography. Glycal formation was not observed.^b Only the isolated pure α -anomers were subjected to the oxazolidinone to oxazolidinone conversion