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The reaction of the peracetate methyl esters of *N*-acetylneuraminic acid (Neu5Ac), 3-deoxy-D-*glycero*-D-*galacto*-2-nonulosonic acid (Kdn), and 3-deoxy-D-*manno*-2-octulosonic acid (Kdo) with trimethylsilyl trifluoromethanesulfonate

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Abstract

The reaction of the peracetate methyl esters of *N*-acetylneuraminic acid (Neu5Ac), 3-deoxy-D-*glycero*-D-*galacto*-2-nonulosonic acid (Kdn), and 3-deoxy-D-*manno*-2-octulosonic acid (Kdo) with trimethylsilyl trifluoromethanesulfonate ($CF_3SO_3SiMe_3$) has been reinvestigated. We have found that the choice of solvent, reaction temperature, and reaction time dramatically influence the outcome of this reaction. © 1996 Elsevier Science Ltd.

Keywords: Carbohydrates; *N*-acetylneuraminic acid; Sialic acid; Glycal; Kdn; Kdo; Ulosonic acids

1. Introduction

5-Acetamido-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-enonic acid (Neu5Ac2en, **1**), an unsaturated ulosonic acid, was first reported some twenty-seven years ago by Meindl and Tuppy [1]. This compound was found to be, and still is, one of the most potent competitive inhibitors of sialidase (EC 3.2.1.18) from *Vibrio cholerae*. Moreover, it has been suggested [2,3] that Neu5Ac2en is a transition-state analogue for this enzyme. A wide range of analogues of **1** has since been prepared in an effort to gain

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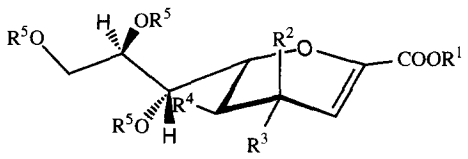
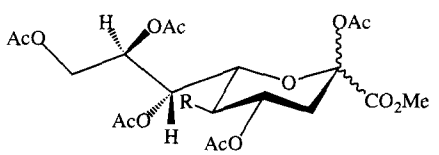
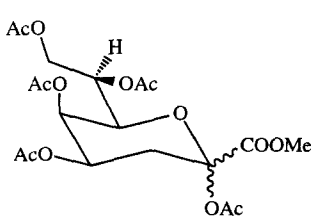
further insight into the interaction of these unsaturated *N*-acetylneuraminic acid derivatives with sialidase from viral and microbial sources [4–7]. We have recently reported the synthesis of two such unsaturated analogues [6], which have been shown to be very potent inhibitors of influenza virus sialidase. One of these compounds is currently in human clinical trials.



Compound	R^1	R^2	R^3	R^4	R^5
1	H	H	OH	NHAc	H
3	Me	H	OAc	NHAc	Ac
6	Me	H	OAc	OAc	Ac
7	Me	H	OAc	N_3	Ac
11	Me	NHAc	H	OAc	Ac
12	Me	H	NHAc	OAc	Ac
13	H	H	$NHC(NH)NH_2$	H	H
15	Me	OAc	H	OAc	Ac



2 R = NHAc
8 R = OAc



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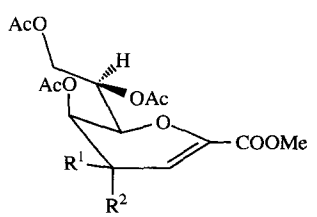
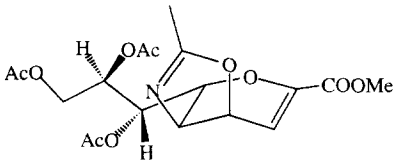


5 R^1 = OAc, R^2 = H
10 R^1 = NHAc, R^2 = H
14 R^1 = H, R^2 = OAc



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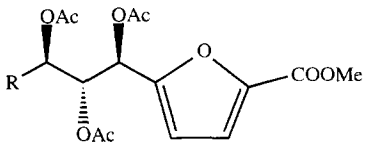

16 R = H
17 R = CH_2OAc

One entry into these unsaturated compounds is provided by the trimethylsilyl trifluoromethanesulfonate ($CF_3SO_3SiMe_3$)-catalysed elimination reaction on the peracetylated methyl esters of these carbohydrates. This procedure was first reported by Claesson and Luthman in 1982 [8] and was subsequently modified by Zbiral and co-workers [7]. In the original procedure of Claesson and Luthman [8], catalytic amounts of $CF_3SO_3SiMe_3$ were employed. Thus, it was found that treatment of the peracetate methyl ester of *N*-acetylneuraminic acid (Neu5Ac, **2**) in acetonitrile with 0.2 M equiv of $CF_3SO_3SiMe_3$ for 5 h at room temperature gave the corresponding 2,3-unsaturated analogue **3** in high yield (90%) [8]. In the same report [8], treatment of the peracetate methyl ester of 3-deoxy-D-*manno*-2-octulosonic acid (Kdo, **4**) with 0.1 M equiv of $CF_3SO_3SiMe_3$ at room temperature for 4 h afforded the 2,3-unsaturated Kdo analogue **5** in 90% yield. In a modification [8] of this synthesis, treatment of **2** at 0 °C for 4 h with 2 M equiv of $CF_3SO_3SiMe_3$ in acetonitrile led to the formation of **3** in 95% yield. Applying analogous reaction conditions, Zbiral and co-workers [9] also prepared the peracetate methyl esters of Kdn2en (**6**) and 5-azido-5-deoxy-Kdn2en (**7**) with reported yields of 63% and 72%, respectively.

As a part of our continuing interest in ulosonic acid chemistry, and because of the biological significance of this class of carbohydrates, we required an efficient and straightforward synthesis of the glycals of these sugars. We report herein our investigations into their synthesis.

2. Results and discussion

Table 1 summarises the results of the reactions of **2**, **4**, and the peracetate methyl ester of Kdn (**8**) with $CF_3SO_3SiMe_3$ under varying conditions. Using the procedure of

Table 1
Reactions of **2**, **4**, and **8** with $CF_3SO_3SiMe_3$

Entry	Precursor	Reaction conditions				Product (s) [a]	Yield (%) [b]	Ref.
		$CF_3SO_3SiMe_3$ (equiv)	solvent	temp. (°C)	time (h)			
1	**2**	0.2	CH_3CN	RT	5	**3**	90	[8]
2	**2**	2	CH_3CN	0	4	**3**	95	[7]
3	**4**	0.1	CH_3CN	RT	4	**5**	91	[8]
4	**2**	0.2	CH_3CN	20	5	**2:3** (1:3)	99	
5	**4**	0.1	CH_3CN	RT	4	**4:5:10** (5:11:4)	99	
6	**2**	2	CH_3CN	0	4	**2:3** (2:3)	99	
7	**2**	2	CH_3CN	0	8	**3**	98 (93)	
8	**8**	2	CH_3CN	0	4	**6**	63	[9]
9	**8**	2	CH_3CN	0	0.5	**6:11** (1:1)	98	
10	**8**	2	CH_3CN	0	3.5	**6:11:12** (4:8:1)	(88)	
11	**8**	2	CH_3CN	20	20	**11:12** (8:1)	98	
12	**8**	2	CH_3CN	50	3	**11:12** (3:1)	95	
13	**8**	2	CH_3CN	70	24	**11:12** (1:1)	(85)	
14	**4**	1.2	CH_2Cl_2	0	2	**5:14** (1:1)	88 (61)	
15	**8**	1.2	CH_2Cl_2	0	1.5	**6:15** (6:1)	98 (73) [c]	
16	**8**	1.2	CH_2Cl_2	20	1.5	**6:15** (1:2)	97 (67)	
17	**2**	2	CH_2Cl_2	0	48	**3:9** (16:3)	98	

[a] Product ratio determined by ^1H NMR spectroscopy.
[b] Crude yield; isolated yield after column chromatography given in parentheses.
[c] Employing 2 equiv of $CF_3SO_3SiMe_3$ in this reaction did not significantly alter the yield or product ratio.

Claesson and Luthman [8], we found by ^1H NMR spectroscopy that treatment of **2** with 0.2 M equiv of $CF_3SO_3SiMe_3$ in acetonitrile at 20 °C for 5 h (Table 1, entry 4) gave meagre conversion (25%) to the glycal **3**. Attempts to prolong the reaction time (up to 48 h) resulted in the formation of a mixture of the desired product **3**, the oxazoline **9**, and unreacted starting material **2** in a ratio of 3:2:5, respectively. Likewise, when compound **4** was treated with a catalytic amount of $CF_3SO_3SiMe_3$ (0.1 M equiv) in acetonitrile at room temperature for 4 h [8], compound **5** was obtained in only 55% yield, and 25% of starting material was recovered (Table 1, entry 5). Furthermore, 20% of a previously unreported byproduct **10** was also isolated. This compound was identified on the basis of its ^1H NMR and mass spectral data: a broad doublet at 5.69 ppm ($J_{4,NH}$ 8.2 Hz), characteristic of an N*H* signal, and an $(M + H)^+$ peak at 402 in the mass spectrum suggested compound **10** to be methyl 4-acetamido-5,7,8-tri-*O*-acetyl-2,6-anhydro-2,3,4-trideoxy-D-*manno*-oct-2-enonate.

Following the procedure of Zbiral and co-workers [7,9] we observed that treatment of **2** with 2 M equiv of $CF_3SO_3SiMe_3$ at 0 °C for 4 h resulted in only about 60% conversion of the starting material to **3** (Table 1, entry 6). However, after an extended reaction time (a further 4 h) at 0 °C (Table 1, entry 7), a near-quantitative conversion to essentially one product (by ^1H NMR spectroscopy) was observed. Purification by column chromatography (silica gel, eluting with EtOAc) resulted in the isolation of **3** in 93% yield.

However, when **8** was subjected to the same reaction conditions, we noted that all of the starting material was consumed (by TLC) after only 0.5 h (Table 1, entry 9). The desired product **6** was formed together with an equal amount of the corresponding 4-*epi*-acetamido-4-deoxy compound **11** (as determined by ^{1}H NMR spectroscopy). The formation of this compound was also not previously noted [9]. Prolonged reaction time (3.5 h) resulted in a greatly diminished yield of **6**, with a concomitant increase in the yield of **11**, together with minor amounts of the 4-acetamido-4-deoxy compound **12** (Table 1, entry 10). When the reaction temperature was increased (Table 1, entries 11–13), no significant amount of **6** was detected (by ^{1}H NMR spectroscopy), and a mixture of only **11** and **12** was obtained. Interestingly, a higher reaction temperature appeared to favour the formation of epimer **12**.

The presence of the 4-acetamido group in **11** was confirmed by the characteristic broad doublet at 5.43 ppm in the ^{1}H NMR spectrum with an expected $J_{NH,4}$ coupling (8.2 Hz) and a resonance at 41.7 ppm (C-4) in the ^{13}C NMR spectrum. In the case of **12**, the N*H* signal also appeared, quite expectedly, as a broad doublet ($J_{NH,4}$ 7.4 Hz) at 5.75 ppm in the ^{1}H NMR spectrum. These two inseparable C-4 epimers were discerned on the basis of the H-3 signals in the ^{1}H NMR spectrum: H-3 of **11** appeared as a doublet ($J_{3,4}$ 5.3 Hz) at 5.98 ppm, whereas for **12**, the H-3 signal appeared as a doublet ($J_{3,4}$ 2.4 Hz) at 5.93 ppm. The smaller coupling is characteristically associated with an axial proton at C-4, with the larger coupling more typical of 4-*epi*-glycals of Neu5Ac [9].

The formation of compounds **10**, **11**, and **12** is ascribed to a Ritter-type reaction. This reaction involves, in the first instance, the elimation of acetic acid from the substrate. The allyl carbocation generated as a result of further elimination of the 4-acetyl group then reacts with the solvent forming an acetonitrilium ion. Upon reaction with water during workup, the corresponding 4-acetamido-2,3-unsaturated derivative is formed. The formation of allylic acetonitrilium ions via Ritter-type conditions has been previously observed in similar systems. Recently, Driguez et al. [10] reported a Ritter-like reaction on a heptulose. Also, Starkey et al. [11] have observed a Ritter-like byproduct in the synthesis of 2,6-anhydro-3,4,5-trideoxy-5-desacetamido-4-guanidinyl-D-*glycero*-D-*galacto*-non-2-enonic acid (**13**).

In order to circumvent the formation of these Ritter-type reaction byproducts, the solvent acetonitrile was replaced with the nonparticipating solvent, dichloromethane (Table 1, entries 14–17). When dichloromethane was used as solvent, we found that 1.2–2 equiv of $CF_3SO_3SiMe_3$ was sufficient to promote these reactions in reasonable reaction time. Thus, treatment of **4** with $CF_3SO_3SiMe_3$ in dichloromethane led to a 1:1 epimeric mixture of **5** and **14** (Table 1, entry 14). In the case of **8**, higher stereoselectivity was observed (Table 1, entry 15); a 73% recovery of a 6:1 mixture of **6** and **15** (characterised by ^{1}H NMR spectroscopy) was obtained after column chromatography. These two diastereoisomers were, however, not resolved by either TLC or silica gel column chromatography using a variety of solvent combinations. Once again, elevated temperature favoured the 4-*epi* compound **15**. Presumably the scrambling of the acetate at C-4 arises through an allyl carbonation intermediate. Importantly, it should be noted that when compound **2** was treated with $CF_3SO_3SiMe_3$ using dichloromethane as the

solvent (Table 1, entry 17), a longer reaction time was required. In addition, it also gave the oxazoline **9** as a byproduct.

In all of the reactions involving the peracetate methyl esters of the ulosonic acids **4** and **8**, the formation of small amounts (< 5%, by ^{1}H NMR spectroscopy) of the corresponding furanosonates **16** and **17** was observed. Both NMR and mass spectral data support the assignment of these structures. Similar ring-contracted furanoid byproducts have been observed in the *N*-acetylneuraminic acid series (see, for example, ref. [12]).

In summary, we have investigated the reaction of the peracetate methyl esters **2, 4**, and **8** with $CF_3SO_3SiMe_3$ in considerable detail. It is apparent from our results (Table 1) that the $CF_3SO_3SiMe_3$-mediated elimination of acetic acid from **2**, **4**, and **8** is quite sensitive to changes in solvent and temperature. Our results indicate that the peracetate methyl ester of Neu5Ac2en (**3**) is obtained in high yield (98% crude yield, 93% after column chromatography) when **2** is treated with 2 M equiv of $CF_3SO_3SiMe_3$ in acetonitrile at 0 °C for 8 h. The synthesis of the peracetate methyl ester of Kdn2en (**6**) is achieved in high yield by replacing acetonitrile with a nonparticipating solvent (in our case, dichloromethane). However, under these reaction conditions the contaminating byproduct **15** proved to be difficult to separate from the mixture. Pure **6** can be prepared at 0 °C, albeit in substantially reduced yield, by employing acetonitrile as the solvent. In the latter case, the major impurity **11** can be readily separated from the desired product by column chromatography. At elevated temperatures (> 20 °C) the desired product **6** is not observed. Rather, a mixture of **11** and **12** was isolated; the amount of **12** formed increased with temperature.

3. Experimental

General.—The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra [in δ (ppm) relative to Me_4Si] were recorded in $CDCl_3$ on a Bruker AMX 300 spectrometer at 303 K. Both low-resolution (LR) and high-resolution (HR) fast-atom bombardment (FAB) mass spectra were recorded on a Jeol JMS-DX 300 spectrometer. Optical rotations were measured at 24 °C using a JASCO DIP-370 polarimeter. All solvents were distilled and dried before use. Column chromatography was performed on Merck Silica Gel-60 (0.040–0.063 mm). Reactions were monitored by TLC on Kieselgel 60 F_{254} plate (Merck 5554), and the plates were developed by spraying with a 95% aq EtOH containing 5% H_2SO_4 and charring for several minutes. $CF_3SO_3SiMe_3$ (99% purity) was purchased from Aldrich and used without further purification. Kdn was prepared by enzyme-catalysed condensation of mannose with sodium pyruvate according to well-known procedures (see, for example, ref. [13]). The peracetate methyl esters, **2** and **8** (mixture of α and β anomers) were prepared by treating respectively Neu5Ac and Kdn sequentially with MeOH–Dowex 50W-X8 (H^+) resin and acetic anhydride–pyridine in the usual manner [14]. The peracetate methyl ester of Kdo, **4**, was prepared from Kdo following the procedure of Unger and Luthman and co-workers [14,15]. All new compounds gave satisfactory NMR and mass spectroscopic data.

The ^{1}H NMR spectral data for compounds **2**, **4**, **8**, and **9** were found to be

indistinguishable from those previously reported [2,8,14–18]. Some of the ^{1}H NMR data for **5** were found to be inconsistent with those previously reported [15,19].

General reaction procedure.—To a solution of the peracetate (0.2 mmol) in solvent (2 mL) was added trimethylsilyl trifluoromethanesulfonate (see Table 1 for details). After additional stirring for the time specified (see Table 1), the reaction mixture was basified to pH 9 with saturated sodium bicarbonate and extracted with EtOAc. The product(s) was (were) isolated following the usual workup procedure.

*Methyl 4,5,7,8-tetra-*O*-acetyl-2,6-anhydro-3-deoxy-*D-manno*-oct-2-enonate* (**5**), *and methyl 4,5,7,8-tetra-*O*-acetyl-2,6-anhydro-3-deoxy-*D-gluco*-oct-2-enonate* (**14**).—R_f 0.60 (1:1 EtOAc–hexane); ^{1}H NMR data for **5**: δ 2.04, 2.06, 2.08 (s, 3 H, 2 × 3 H, 3 H, respectively, OCOCH_3), 3.80 (s, 3 H, COOCH_3), 4.28 (dd, 1 H, $J_{8',7}$ 7.1, $J_{8',8}$ 11.6 Hz, H-8'), 4.31 (dd, 1 H, $J_{6,5}$ 9.1, $J_{6,7}$ 3.6 Hz, H-6), 4.42 (dd, 1 H, $J_{8,7}$ 4.4 Hz, H-8), 5.26 (ddd, 1 H, $J_{5,4}$ 6.6, $J_{5,3}$ 2.7 Hz, H-5), 5.41 (ddd, 1 H, H-7), 5.54 (dd, 1 H, $J_{4,3}$ 3.0 Hz, H-4), 5.99 (dd, 1 H, H-3); ^{13}C NMR: δ 20.5, 20.7 (OCO*C*H$_3$), 52.4 (COO*C*H$_3$), 62.2 (C-8), 65.6, 66.2, 68.3, 75.5 (C-4, C-5, C-6, C-7), 107.3 (C-3), 145.2 (C-2), 161.4, 169.4, 170.1, 170.4 (carbonyls). Selected ^{1}H NMR data for **14**: δ 3.80 (s, 3 H, COOCH_3), 4.35 (dd, 1 H, $J_{6,5}$ 11.0, $J_{6,7}$ 2.1 Hz, H-6), 4.50 (dd, 1 H, $J_{8',7}$ 4.9, $J_{8',8}$ 11.8 Hz, H-8'), 4.51 (dd, 1 H, $J_{8,7}$ 4.4 Hz, H-8), 5.10 (pseudo dd, 1 H, $J_{5,4}$ 4.0 Hz, H-5), 5.45 (ddd, 1 H, H-7), 5.52 (dd, 1 H, $J_{4,3}$ 6.0 Hz, H-4), 6.06 (dd, 1 H, $J_{3,5}$ 2.3 Hz, H-3); selected ^{13}C NMR: δ 52.4 (COO*C*H$_3$), 61.5 (C-8), 64.8, 66.2, 66.9, 72.2 (C-4, C-5, C-6, C-7), 105.0 (C-3), 145.0 (C-2), 160.1 (*C*OOCH$_3$). LRFABMS for **5**/**14**: 403 $[M + H]^+$ (10%), 343 $[M - OAc]^+$ (100%).

*Methyl 4-acetamido-5,7,8-tri-*O*-acetyl-2,6-anhydro-3,4-dideoxy-*D-manno*-oct-2-enonate* (**10**).—R_f 0.10 (1:1 EtOAc–hexane); ^{1}H NMR: δ 1.95, 2.05, 2.06, 2.07 (s, 4 × 3 H, NHCOCH_3, OCOCH_3), 3.78 (s, 3 H, COOCH_3), 4.29 (dd, 1 H, $J_{8',7}$ 7.9, $J_{8',8}$ 11.9 Hz, H-8'), 4.30 (dd, 1 H, $J_{6,5}$ 7.9, $J_{6,7}$ 2.3 Hz, H-6), 4.44 (dd, 1 H, $J_{8,7}$ 4.9 Hz, H-8), 4.90 (ddd, 1 H, $J_{4,3}$ 2.5, $J_{4,5}$ 2.5, $J_{4,NH}$ 8.2 Hz, H-4), 5.00 (m, 1 H, H-5), 5.44 (ddd, 1 H, H-7), 5.69 (d, 1 H, NH), 5.94 (pseudo d, 1 H, H-3); ^{13}C NMR: δ 20.5, 20.6, 22.9 (NHCO*C*H$_3$, OCO*C*H$_3$), 41.8 (C-4), 52.5 (COO*C*H$_3$), 62.6 (C-8), 65.2, 67.2, 72.8 (C-5, C-6, C-7), 107.2 (C-3), 145.2 (C-2), 161.7, 169.5, 170.0, 170.7 (carbonyls); LRFABMS: 402 $[M + H]^+$ (44%). HRFABMS for $C_{17}H_{24}NO_{10}$ requires 402.1400; found 402.1415.

*Methyl 4-acetamido-5,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,4-dideoxy-*D-glycero-D-talo*-non-2-enonate* (**11**), *and methyl 4-acetamido-5,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,4-dideoxy-*D-glycero-D-galacto*-non-2-enonate* (**12**).—R_f 0.44 (EtOAc); ^{1}H NMR data for **11**: δ 1.99, 2.01, 2.05, 2.07, 2.09, (s, 5 × 3 H, NHCOCH_3, OCOCH_3), 3.80 (s, 3 H, COOCH_3), 4.15 (dd, 1 H, $J_{6,5}$ 7.0, $J_{6,7}$ 2.7 Hz, H-6), 4.21 (dd, 1 H, $J_{9',8}$ 6.8, $J_{9',9}$ 12.5 Hz, H-9'), 4.67 (dd, 1 H, $J_{9,8}$ 2.6 Hz, H-9), 4.92 (ddd, 1 H, $J_{4,3}$ 5.3, $J_{4,5}$ 5.2, $J_{4,NH}$ 8.2 Hz, H-4), 5.00 (dd, 1 H, H-5), 5.36 (ddd, 1 H, $J_{8,7}$ 5.2 Hz, H-8), 5.43 (d, 1 H, NH), 5.51 (dd, 1 H, H-7), 5.98 (d, 1 H, H-3); ^{13}C NMR for **11**: δ 20.3, 20.5, 20.6, 20.8, 22.9 (OCO*C*H$_3$, NHCO*C*H$_3$), 41.7 (C-4), 52.5 (COO*C*H$_3$), 62.0 (C-9), 65.3, 67.5, 70.5, 72.3 (C-5, C-6, C-7, C-8), 107.4 (C-3), 145.1 (C-2), 161.8, 169.6, 170.0, 170.2, 170.6 (carbonyls). Selected ^{1}H NMR data for **12**: δ 3.78 (s, 3 H, COOCH_3), 4.31 (dd, 1 H, $J_{6,5}$ 10.0, $J_{6,7}$ 2.6 Hz, H-6), 4.55 (dd, 1 H, $J_{9,8}$ 2.6, $J_{9,9'}$ 12.5 Hz, H-9), 5.75 (d, 1 H, $J_{NH,4}$ 7.4 Hz, NH), 5.93 (d, 1 H, $J_{3,4}$ 2.4 Hz, H-3); selected ^{13}C NMR for **12**: δ 48.5

($COOCH_3$), 61.7 (C-9), 66.4, 66.8, 69.9, 75.7 (C-5, C-6, C-7, C-8), 110.2 (C-3), 144.3 (C-2). LRFABMS for **11/12**: 474 $[M + H]^+$ (58%); HRFABMS for $C_{20}H_{28}NO_{12}$ requires 474.1612. Found 474.1614.

*Preparation of methyl 4,5,7,8,9-penta-*O*-acetyl-2,6-anhydro-3-deoxy-*D-glycero-D-galacto-*non-2-enonate* (**6**), *and methyl 4,5,7,8,9-penta-*O*-acetyl-2,6-anhydro-3-deoxy-*D-glycero-D-talo-*non-2-enonate* (**15**).—R_f 0.55 (1:1 EtOAc–hexane); ^{1}H NMR data for **6** is consistent with that previously reported [9]; ^{13}C NMR for **6**: δ 20.5, 20.7, 20.8 ($OCOCH_3$), 52.5 ($COOCH_3$), 61.8 (C-9), 65.6, 66.8, 68.8, 69.9, 75.5 (C-4, C-5, C-6, C-7, C-8), 107.6 (C-3), 145.3 (C-2), 161.3, 169.6, 169.8, 170.4 (carbonyls). ^{1}H NMR data for **15**: δ 1.98, 2.03, 2.04, 2.07, 2.08 (s, 5 × 3 H, $OCOCH_3$), 3.78 (s, 3 H, $COOCH_3$); 4.21 (dd, 1 H, $J_{9',8}$ 6.6, $J_{9',9}$ 12.7 Hz, H-9′), 4.39 (dd, 1 H, $J_{6,5}$ 11.0, $J_{6,7}$ 2.0 Hz, H-6), 4.68 (dd, 1 H, $J_{9,8}$ 2.3 Hz, H-9), 5.02 (dd, 1 H, $J_{5,4}$ 4.0 Hz, H-5), 5.42 (ddd, 1 H, $J_{8,7}$ 6.5 Hz, H-8), 5.50 (dd, 1 H, H-7), 5.54 (dd, 1 H, $J_{4,3}$ 5.9 Hz, H-4), 6.05 (d, 1 H, H-3); selected ^{13}C NMR for **15**: δ 52.4 ($COOCH_3$), 61.7 (C-9), 64.7, 67.1, 70.3, 71.8, 104.9 (C-3), 146.5 (C-2).

*Methyl 5-[(*D-erythro-*1,2,3-trihydroxypropyl)-2-furanosid]onate* (**16**).—R_f 0.65 (1:1 EtOAc–hexane); ^{1}H NMR: δ 2.03, 2.10 (s, 3 H, 2 × 3 H, respectively, $OCOCH_3$), 3.88 (s, 3 H, $COOCH_3$), 4.35 (dd, 1 H, $J_{8',7}$ 7.8, $J_{8',8}$ 12.1 Hz, H-8′), 4.46 (dd, 1 H, $J_{8',7}$ 4.0 Hz, H-8), 5.58 (ddd, 1 H, $J_{7,6}$ 6.7 Hz, H-7), 6.10 (pseudo dd, 1 H, $J_{6,4}$ 5.3 Hz, H-6), 6.50 (dd, 1 H, $J_{4,3}$ 3.5 Hz, H-4), 7.11 (dd, 1 H, $J_{3,6}$ 1.4 Hz, H-3); FABMS: 343 $[M + H]^+$ (68%), 283 $[M - OAc]^+$ (36%).

*Methyl 5-[(*D-erythro-*1,2,3,4-tetrahydroxybutyl)-2-furanosid]onate* (**17**).—R_f 0.63 (1:1 EtOAc–hexane); $[\alpha]_D$ −32° (*c* 1.2, $CHCl_3$) ^{1}H NMR: δ 2.04, 2.07, 2.10 (s, 4 × 3 H, $OCOCH_3$), 3.87 (s, 3 H, $COOCH_3$), 4.13 (dd, 1 H, $J_{9',8}$ 4.7, $J_{9',9}$ 12.5 Hz, H-9′), 4.25 (dd, 1 H, $J_{9,8}$ 2.6 Hz, H-9), 5.23 (ddd, 1 H, $J_{8,7}$ 7.5 Hz, H-8), 5.58 (dd, 1 H, $J_{7,6}$ 3.3 Hz, H-7), 6.12 (d, 1 H, H-6), 6.44 (d, 1 H, $J_{4,3}$ 3.4 Hz, H-4), 7.08 (d, 1 H, H-3); ^{13}C NMR: δ 20.6 ($OCOCH_3$), 51.9 ($COOCH_3$), 61.6 (C-9), 65.8, 68.2, 69.4 (C-6, C-7, C-8), 111.2, 118.3 (C-3, C-4), 145.0 (C-2), 153.0 (C-5), 169.3, 169.7, 170.5 (carbonyls); LRFABMS: 415 $[M + H]^+$ (49%), 355 $[M - OAc]^+$ (100%).

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