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Novel practical synthesis of Kdn2en and its C-4 nitrogen-modified derivatives

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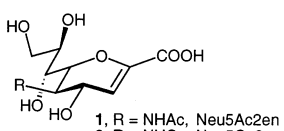
Abstract

A practical synthesis of Kdn2en and 4-amino-4-deoxy-Kdn2en has been achieved via a key intermediate, methyl 4,5,7,8,9-penta-*O*-acetyl-2,6-anhydro-3-deoxy-D-*glycero*-D-*galacto*-non-2-enonate, which has been prepared from Kdn in three steps in 91% overall yield. © 2000 Elsevier Science Ltd. All rights reserved.

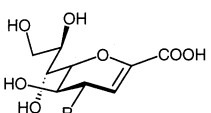
Keywords: Sialyl glycals; Kdn2en; 4-Acylamino-4-deoxy-; *iso*-Sialyl glycals

1. Introduction

2,3-Dehydro-2-deoxy-sialic acids (Neu5Ac2en, Neu5Gc2en, and their acetates) are widely distributed in nature [1] and display interesting biological activities as transition-state inhibitors of the enzyme, sialidase [2]. Recently, C-4 nitrogen-containing derivatives of *N*-acetylneuraminic acid have been shown to have significant in vivo activity against influenza virus sialidase [3,4]. On the other hand, sialyl glycals are also very important precursors for the stereoselective α-glycosylation of sialic acid [5–9]. Consequently, development of convenient routes to the glycals of sialic acid and their derivatives is of particular synthetic interest to many groups including our own. 2,3-Dehydro-2-deoxy-Kdn (Kdn-2en), which has not been isolated from nature, has been found to be a strong inhibitor of Kdnase [10]. A chemical method for preparation of Kdn on a large scale has been established in our laboratory [11], and the synthesis of Kdn2en can be achieved in 40–60% overall yield from Kdn [12,13]. However, the laborious chromatographic purification that is required after each reaction limits its large-scale preparation. As a part of the work involved in the clarification of the chemical and biological properties of Kdn2en and the synthesis of biologically active sialyl glycals, we herein report a straightforward synthesis of Kdn2en and its C-4 nitrogen-modified derivatives, which we term as '*iso*-sialyl glycals' (structures **1**–**5**).



1, R = NHAc, Neu5Ac2en
2, R = NHGc, Neu5Gc2en
3, R = OH, Kdn2en



4, R = NHAc, *iso*-Neu4Ac2en
5, R = NH_2

2. Results and discussion

The methyl ester of Kdn (**6**), prepared in almost quantitative yield [14] by reaction of

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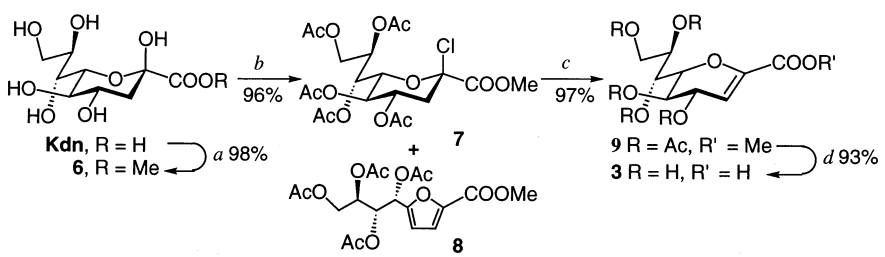
Kdn with methanol containing Dowex-50 (H^+), was dissolved in acetyl chloride, and the reaction mixture was kept for 48 h at room temperature. Concentration of the mixture gave glycosyl chloride **7** in more than 96% yield, with a trace of α-(methoxycarbonyl)-furfuryl carbinol acetate (**8**). The crude product **7** was dissolved in pyridine and stirred for 1 h at 50 °C to give the crude elimination product, methyl 4,5,7,8,9-penta-*O*-acetyl-2,6-anhydro-3-deoxy-D-*glycero*-D-*galacto*-non-2-enonate (**9**) after removal of pyridine by concentration and pyridine hydrochloride by trituration. This material could be purified by silica gel column chromatography to yield pure **9** in 91% overall yield. The physical data for compound **9** and the intermediates were in good agreement with those previously published [12,14]. The advantages of this procedure are the relatively inexpensive reagent required and the easy workup. Moreover, excess acetyl chloride was recovered as a recyclable reagent. Deprotection of **9** with LiOH in methanol and water afforded the expected compound 2,6-anhydro-3-deoxy-D-*glycero*-D-*galacto*-non-2-enonic acid (Kdn2en, **3**) in 93% yield (Scheme 1).

We have reported the preparation of methyl 5,7,8,9-tetra-*O*-acetyl-4-acetylamino-2,6-anhydro-3,4-dideoxy-D-*glycero*-D-*galacto*- and D-*talo*-non-2-enonates (**10** and **11**) from the peracetate of Kdn methyl ester by reaction with acetonitrile in the presence of trimethylsilyl triflate (Me_3SiOTf) at room temperature [15,16]. We postulated that the reaction occurred via an S_N1 process like the Ritter reaction via the peracetate of 2,3-unsaturated Kdn methyl ester **9**. Here, we performed the reaction of **9** with acetonitrile and Me_3SiOTf to synthesize the 4-acetylamino-4-deoxy-Kdn2en derivatives. Treatment of **9** with 2 equivalents of Me_3SiOTf in acetonitrile at 0 °C yielded two epimers of methyl 5,7,8,9-tetra-*O*-acetyl-4-acylamino-2,6-anhydro-3,4-dideoxy-D-*glycero*-D-*galacto*- and D-*talo*-2-enonates (**10** and **11**) in 88% yield. This result supported the mechanism we had postulated, and it was found that the formation of (4R)-configured amide **11** was predominant over (4S)-configured amide **10**. Interestingly, a high reaction temperature gave a high yield of the products and appeared to favor the formation of epimer **10** (Table 1). This agrees with the results reported by Kok et al. using peracetyl Kdn methyl ester [13]. In addition, similar reactions of **9** with methoxyacetonitrile or benzonitrile in the presence of Me_3SiOTf at room temperature afforded the respective 4-

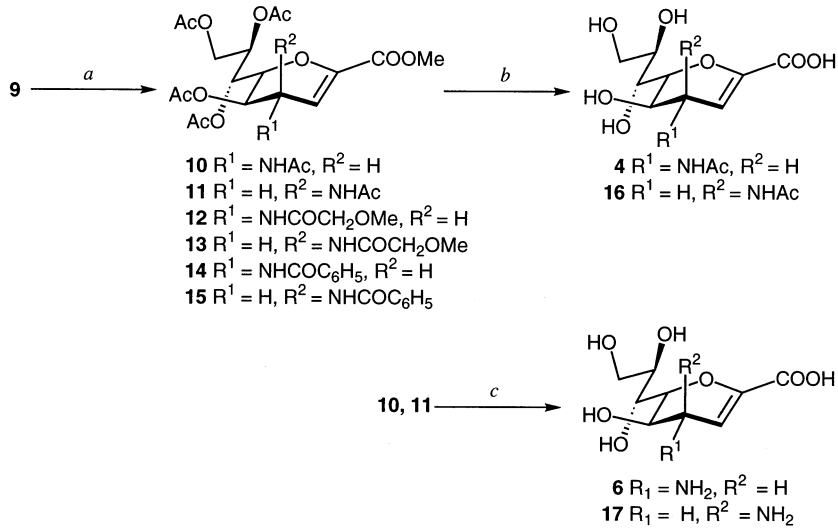


Scheme 1.

Table 1
Ritter-type reaction of peracetyl Kdn2en methyl ester with Me_3SiOTf (2.0 equiv) [a]

Run	Solvent	Temperature (°C)	Time (h)	Total yield (%)	Ratio (4*S*: to 4*R*)
1	CH_3CN	0	6	88	(1:8)
2	CH_3CN	rt	3	93	(1:6)
3	CH_3CN	70	1	94	(1:1.1)
4	CH_3OCH_2CN	rt	12	79	(1:1)
5	C_6H_5CN	rt	12	63	(1:1)

[a] Isolated yield.



Scheme 2.

acylamino-4-deoxy-Kdn2en derivatives (**12**–**15**) in high yield.

Next, selective deprotection of **10** and **11** was performed as follows. When **10** and **11** were subjected to 5% $Ba(OH)_2$ at room temperature, 4-acetylamino-4-deoxy-Kdn2en (**4**) and **16** were formed in 85 and 75% yield, respectively, whereas deprotection of **10** and **11** with 5% $Ba(OH)_2$ at 90 °C afforded 4-amino-4-deoxy-Kdn2en (**6**) and **17** in 63 and 71% yield, respectively (Scheme 2).

The structures of these products were elucidated mainly by ^{1}H NMR spectroscopy. The orientations of the 4-acylamino groups were easily deduced from the values of the coupling constants between H-3 and H-4, and H-4 and H-5. For instance, the coupling constants $J_{3,4}$ 2.3–2.7 Hz and $J_{4,5}$ 8.4–9.3 Hz indicated the (4S)-configuration for compounds **10**, **12**, and **14**, whereas the coupling constants $J_{3,4}$ 5.1–5.7 Hz and $J_{4,5}$ 4.8–5.1 Hz indicated (4R)-configuration for compounds **11**, **13**, and **15**. Moreover, an X-ray crystallographic analysis of **14** was conducted because only **14** afforded good crystals on recrystallization from hexane–ethyl acetate (Tables 2 and 3). An ORTEP drawing in Fig. 1 shows that the conformation of the pyranoid ring of **14** is a normal half chair ($^6H_5$), with similar features to those of other general glycals [17,18]. The absolute configuration at C-4 was assigned as S. Furthermore, ^{1}H NMR data for **14** indicated that the pyranoid ring has the same conformation in the crystalline state as in solution.

In conclusion, a practical synthesis of Kdn2en on a large scale, as well as *iso*-sialyl glycal, 4-acetylamino-4-deoxy-Kdn2en and 4-amino-4-deoxy-Kdn2en, was accomplished via a key intermediate per-*O*-acetyl Kdn2en methyl ester **9**, which was prepared by a new facile method from Kdn in high yield. Further, selective deprotection of the *N*-acetyl group was also established.

Table 2
Crystal structure and refinement of compound **14** [a]

Empirical formula	$C_{25}H_{29}NO_{12}$
Space group	$P2_12_12_1$
Z	4
Cell dimensions	
a (Å)	17.422(1)
b (Å)	28.225(2)
c (Å)	5.385(1)
V (Å^3)	2648(4)
Crystal dimensions (mm)	$0.20 \times 0.20 \times 0.20$
D_c (g cc^{-1})	1.642
Radiation	graphite monochromated Cu K_α
Final agreement factors	
R	6.8% ($R = \Sigma\|\|F_o\|-\|F_c\|\|/\Sigma\|F_o\|$)
R_w	6.2% ($R_w = [(\Sigma_w(\|F_o\|-\|F_c\|)/\Sigma_w F_o^2)]^{1/2}$)

[a] The data were collected using the $\omega-2\theta$ scan technique in the range $2\theta < 140.0°$. Scans of $(1.63+0.30\tan\theta)°$ were made at a speed of 16.0° min^{-1}. In total 2865 reflections were collected and corrected for Lorentz and polarization factors but not for absorption. The structure was elucidated by a direct method using TEXSAN [19]. The non-hydrogen atoms were refined anisotropically by full-matrix least-squares refinement. A difference Fourier synthesis was calculated, and the positions of all hydrogen atoms were found.

Table 3
Atomic coordinates ($Å \times 10^4$) and equivalent temperature factors (B_{eq}) for **14**

Atom	*x*	*y*	*z*	B_{eq}
O(1)	0.4199(3)	0.2014(2)	0.358(1)	3.8(3)
O(2)	0.5554(4)	0.2879(2)	0.184(2)	7.1(5)
O(3)	0.4371(4)	0.2723(2)	0.058(2)	6.0(4)
O(4)	0.4666(3)	0.0949(2)	0.174(1)	3.0(3)
O(5)	0.5113(5)	0.0444(2)	0.425(1)	7.1(5)
O(6)	0.3313(3)	0.1165(2)	0.292(1)	3.2(3)
O(7)	0.3116(5)	0.0477(2)	0.500(1)	7.3(5)
O(8)	0.2638(3)	0.2044(2)	0.729(1)	3.4(3)
O(9)	0.2398(6)	0.2729(3)	0.976(2)	11.6(7)
O(10)	0.1702(3)	0.1258(2)	0.629(1)	4.8(3)
O(11)	0.0588(4)	0.1111(3)	0.436(2)	7.1(5)
O(12)	0.6242(3)	0.1276(2)	1.055(1)	4.0(3)
N(1)	0.6176(3)	0.1364(3)	0.638(2)	3.8(4)
C(1)	0.4987(6)	0.2646(3)	0.198(2)	4.5(5)
C(2)	0.4909(5)	0.2231(3)	0.361(2)	3.3(4)
C(3)	0.5503(5)	0.2069(3)	0.490(2)	3.8(4)
C(4)	0.5464(7)	0.1631(4)	0.638(2)	3.3(5)
C(5)	0.4784(5)	0.1339(3)	0.548(2)	2.8(4)
C(6)	0.4090(5)	0.1674(3)	0.554(2)	2.8(4)
C(7)	0.3318(4)	0.1441(3)	0.519(2)	2.9(4)
C(8)	0.2670(5)	0.1797(2)	0.492(2)	2.7(4)
C(9)	0.1896(5)	0.1598(3)	0.433(2)	3.6(5)
C(10)	0.4406(6)	0.3128(4)	−0.107(3)	8.4(8)
C(11)	0.4119(6)	0.0511(3)	0.634(2)	4.3(5)
C(12)	0.4904(6)	0.0153(3)	0.828(2)	6.3(6)
C(13)	0.3135(5)	0.0698(3)	0.309(2)	3.7(5)
C(14)	0.2984(7)	0.0504(3)	0.065(2)	5.5(6)
C(15)	0.2520(6)	0.2525(3)	0.711(2)	4.0(5)
C(16)	0.2458(6)	0.2720(3)	0.534(1)	3.4(4)
C(17)	0.1014(5)	0.1049(4)	0.606(2)	4.4(5)
C(18)	0.0859(5)	0.0749(3)	0.833(2)	5.8(6)
C(19)	0.6515(5)	0.1207(3)	0.849(2)	3.2(4)
C(20)	0.7260(5)	0.0947(3)	0.807(2)	3.1(4)
C(21)	0.7422(5)	0.0590(3)	0.982(2)	4.1(5)
C(22)	0.8112(6)	0.0357(3)	0.959(2)	5.7(6)
C(23)	0.8619(6)	0.0467(4)	0.777(3)	5.4(6)
C(24)	0.7771(5)	0.1049(3)	0.624(2)	4.2(5)
C(25)	0.8465(6)	0.0826(4)	0.606(2)	5.2(6)

3. Experimental

General methods.—Melting points were measured on Yanaco melting-point apparatus without correction. Optical rotations were determined with a HORIBA SEPA-200 polarimeter. ^{1}H NMR spectra were recorded at 270 MHz (JEOL EX-270) on solution in $CDCl_3$, CD_3OD (internal Me_4Si, δ 0), or D_2O (internal 3-trimethylsilyl-2,2,3,3-d_4-propionic acid sodium salt, δ 0). High-resolution fast-atom bombardment mass spectrometry (HR-FABMS) was measured on a JEOL JMS-HX-110 mass spectrometer. Electrospray ionization mass spectrometry (ESIMS) was measured on a Finnigan MATTSQ 700 mass spectrometer. Thin-layer chromatography (TLC) was performed on Silica Gel 60-F254 (E. Merck) and with detection by H_2SO_4 or molybdenum blue reagent. Column chromatography was performed on Silica Gel-60 (E. Merck, and IATROBEADS, 6RS-8060).

Preparation of methyl 3-deoxy-D-glycero-D-galacto-*2-nonulopyranosonate* (**6**).—A mixture of Kdn (5.00 g, 16.3 mmol) and Dowex-50 (H^+) resin (5.00 g) in dry MeOH (100 mL) was stirred for 18 h at room temperature (rt), then filtered and washed with MeOH. The filtrate was evaporated to dryness to give the crude methyl ester **6** (5.13 g, 99.3%), which was used directly without purification for the next step. The ^{1}H NMR spectrum was identical to that previously published [14].

Preparation of methyl 4,5,7,8,9-penta-O-*acetyl - 2 - chloro - 2,3 - dideoxy* - D - glycero - D-galacto-*2-nonulopyranosonate* (**7**).—A reaction vessel containing the crude methyl ester **6** (5.13 g, 18 mmol) in acetyl chloride (50 mL) was stoppered and left for 48 h at rt, then evaporated to dryness and coevaporated three times with toluene to give crude **7** (8.90 g,

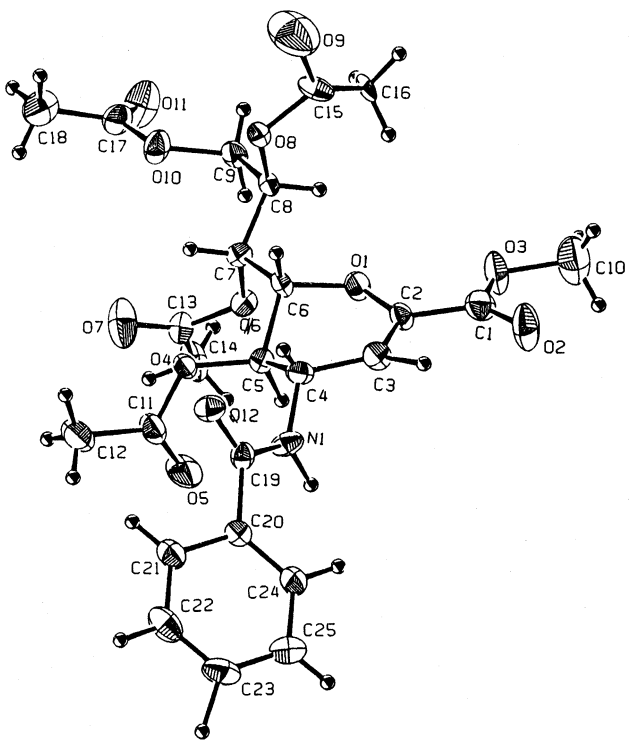


Fig. 1. ORTEP view of **14**.

96%), which was used directly without purification for the next step. The ^{1}H NMR spectrum was identical to that published [14].

Preparation of methyl 4,5,7,8,9-penta-O-acetyl-2,3-dideoxy-D-glycero-D-galacto-non-2-enopyranosonate (**9**).—Crude **7** (8.90 g, 17 mmol) was dissolved in pyridine (100 mL), and the reaction mixture was stirred for 1 h at 50 °C, then evaporated to dryness. The residue was treated with EtOAc to remove the precipitated pyridine hydrochloride, and then concentrated to give the desired product as a slightly yellow solid in 98% yield (8.11 g). It was further purified on a silica gel column with 4:3 hexane–acetone to afford **9** (8.03 g, 97%). The ^{1}H NMR spectrum was identical to that published [12].

2,6-Anhydro-3-deoxy-D-glycero-D-galacto-non-2-enonic acid (**3**).—To a solution of **9** (107 mg, 0.227 mmol) in MeOH (10 mL), was added $LiOH\cdot H_2O$ (57 mg, 1.36 mmol, 6 equiv) dissolved in water (2 mL). After stirring for 1 h at rt, the reaction mixture was acidified to pH 4 by adding cation-exchange resin (Dowex-50 (H^+)) at 0 °C. The resin was filtered off, and the filtrate was evaporated to dryness. Chromatography of the residue on Sephadex LH-20 with methanol afforded **3** (57 mg, 93%) as an amorphous powder; $[\alpha]_D^{20}$ −134° (*c* 0.78, D_2O); ^{1}H NMR (300 MHz, D_2O): δ 5.92 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-3), 4.39 (dd, 1 H, $J_{4,5}$ 7.8 Hz, H-4), 4.14 (dd, 1 H, $J_{5,6}$ 10.8 Hz, $J_{6,7}$ 1.2 Hz, H-6), 3.84 (m, 3 H, H-7, 8, 9), 3.75 (dd, 1 H, H-5), 3.64 (dd, 1 H, $J_{9,9'}$ 11.4 Hz, $J_{8,9'}$ 6.0 Hz, H-9′). ^{13}C NMR (75 MHz, D_2O): δ 69.73 (C-9), 70.05 (C-5), 70.17 (C-7), 71.83 (C-4), 72.72 (C-8), 79.59 (C-6), 114.79 (C-3), 146.09 (C-2), 168.29 (C-1). FABMS *m*/*z*: 273 [$M^+ + 1$] (*m*-NBA as matrix).

General procedure for the Ritter-type reaction.—A soln of Me_3SiOTf (0.2 mL, 1 mmol) in the appropriate nitrile (Table 1) (1 mL) was added to a solution of **9** (267 mg, 0.50 mmol) in the same nitrile (10 mL) at 0 °C. The mixture was stirred at rt for 3 h until the starting material was no longer detectable by TLC ($CHCl_3$–MeOH). Potassium carbonate (150 mg, 2 equiv) was then added, and the mixture was stirred for a further 15 min. Solids were filtered off, and concentration of the filtrate under reduced pressure gave a residue that was purified by silica gel chromatography (5:1 hexane–acetone) to yield methyl 5,7,8,9-tetra-*O*-acetyl-4-acetylamino-2,6-anhydro-3,4-dideoxy-D-*glycero*-D-*galacto*-non-2-enonate (**10**) and methyl 5,7,8,9-tetra-*O*-acetyl-4-acetylamino-2,6-anhydro-3,4-dideoxy-D-*glycero*-D-*talo*-non-2-enonate (**11**); methyl 5,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,4-dideoxy-4-methoxyacetylamino-D-*glycero*-D-*galacto*-non-2-enonate (**12**) and methyl 5,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,4-dideoxy-4-methoxyacetylamino-D-*glycero*-D-*talo*-non-2-enonate (**13**); methyl 5,7,8,9-tetra-*O*-acetyl-2,6-anhydro-4-benzoylamino-3,4-dideoxy-D-*glycero*-D-*galacto*-non-2-enonate (**14**) and methyl 5,7,8,9-tetra-*O*-acetyl-2,6-anhydro-4-benzoylamino-3,4-dideoxy-D-*glycero*-D-*talo*-non-2-enonate (**15**). Physical data of all products were identical to those published [15,16].

4-Acetylamino-2,6-anhydro-3,4-dideoxy-D-glycero-D-galacto-non-2-enonic acid (**4**) *and 4-acetylamino-2,6-anhydro-3,4-dideoxy-D-glycero-D-talo-non-2-enonic acid* (**16**).—A solution of **10** (160 mg, 0.34 mmol) in 5% aq barium hydroxide (20 mL) was stirred for 5 h at rt. The mixture was brought to pH 6.0 by addition of 1 N H_2SO_4 at 0 °C and filtered through Celite. The filtrate was brought to pH 10 by addition of 1 N NaOH and evaporated to dryness in vacuo at 60 °C. The residue was partially dissolved in water (40 mL), and the insolubles were removed by filtration. The filtrate was eluted through Amberlite IRC-50 (H+) resin (20 mL), which was washed with water (40 mL), and the combined filtrate was lyophilized to give **4** (84 mg, 85%). Compound **16** was prepared from **11** in 75% yield as described for **4**.

Compound **4**: amorphous powder; $[\alpha]_D^{20}$ +33° (*c* 0.33, H_2O); ^{1}H NMR (300 MHz, D_2O): δ 5.51 (d, 1 H, $J_{3,4}$ 2.4 Hz, H-3), 4.63 (dd, 1 H, $J_{4,5}$ 8.7, Hz, H-4), 4.18 (br. d, 1 H, $J_{6,5}$ 10.2 Hz, H-6), 3.91 (dd, 1 H, $J_{9,9'}$ 12.0, $J_{9,8}$ 2.7 Hz, H-9), 3.94–3.88 (m, 2 H, H-7, 8), 3.80 (dd, 1 H, H-5), 3.68 (dd, 1 H, $J_{9',8}$ 5.7 Hz, H-9′), 2.03 (s, 3 H, NHAc). ^{13}C NMR (75 MHz, D_2O): δ 25.50 ($COCH_3$), 53.88 (4-C), 66.59 (9-C), 69.19 (5-C), 71.15 (7-C), 73.43 (8-C), 80.23 (6-C), 109.42 (3-C), 151.18 (2-C), 172.45 (1-C), 178.02 ($COCH_3$). FABMS *m*/*z*: 292 [$M^+ + 1$] (*m*-NBA as matrix).

Compound **16**: amorphous powder; $[\alpha]_D^{20}$ −163° (*c* 0.33, H_2O). ^1H NMR (300 MHz, D_2O): δ 5.75 (d, 1 H, $J_{3,4}$ 5.7 Hz, H-3), 4.71 (dd, 1 H, $J_{4,5}$ 4.8, Hz, H-4), 4.11 (dd, 1 H, $J_{6,5}$ 9.9 Hz, H-5), 4.06 (dd, 1 H, $J_{6,7}$ 1.2 Hz, H-6), 3.94 (dd, 1 H, $J_{8,9}$ 2.7, $J_{8,7}$ 9.1, $J_{8,9'}$ 6.6 Hz, H-8), 3.90 (dd, 1 H, $J_{9,9'}$ 11.7 Hz, H-9), 3.83 (dd, 1 H, H-7), 3.69 (dd, 1 H, H-9′), 2.04 (s, 3 H, NHAc). ^{13}C NMR (75 MHz, D_2O): δ 25.45 ($COCH_3$), 47.76 (C-4), 66.51 (C-9), 67.93 (C-5), 71.66 (C-7), 73.62 (C-8), 76.90 (C-6), 107.62 (C-3), 151.05 (C-2), 171.78 (C-1), 177.65 ($COCH_3$). FABMS *m*/*z*: 292 [$M^+ + 1$] (*m*-NBA as matrix).

4-Amino-2,6-anhydro-3,4-dideoxy-D-glycero-D-galacto-*non-2-enonic acid* (**5**) *and 4-amino-2,6-anhydro-3,4-dideoxy*-D-glycero-D-talo-*non-2-enonic acid* (**17**).—A solution of **10** (123 mg, 0.26 mmol) in 5% aq barium hydroxide (20 mL) was stirred for 5 h at 90 °C. The mixture was brought to pH 6.0 by addition of 1 N H_2SO_4 at 0 °C and filtered through Celite. The filtrate was brought to pH 10 by addition of 1 N NaOH and evaporated to dryness in vacuo at 60 °C. The residue was partially dissolved in water (40 mL), and the precipitate was removed by filtration. The filtrate was eluted through Amberlite IRC-50 (H^+) resin (20 mL), which was washed with water (40 mL), and the combined filtrate was lyophilized to give **5** (41 mg, 63%).

Compound **17** was prepared from **11** in 71% yield as described for **5**.

Compound **5**: amorphous powder; $[\alpha]_D^{20}$ −5.7° (*c* 0.28, H_2O); ^1H NMR (300 MHz, D_2O): δ 5.83 (d, 1 H, $J_{3,4}$ 2.4 Hz, H-3), 4.26 (br. d, 1 H, $J_{6,5}$ 10.2 Hz, H-6), 4.14 (dd, 1 H, $J_{4,5}$ 8.7 Hz, H-4), 4.02 (dd, 1 H, H-5), 4.01–3.90 (m, 3 H, H-7, 8, 9), 3.71 (dd, 1 H, $J_{9,9'}$ 11.7, $J_{9',8}$ 5.9 Hz, H-9′). ^{13}C NMR (75 MHz, D_2O): δ 55.04 (C-4), 66.49 (C-9), 67.62 (C-5), 70.83 (C-7), 73.19 (C-8), 79.89 (C-6), 102.98 (C-3), 153.69 (C-2), 171.90 (C-1). FABMS *m*/*z*: 250 [$M^+ + 1$] (*m*-NBA as matrix).

Compound **17**: amorphous powder; $[\alpha]_D^{20}$ −141° (*c* 0.21, H_2O); ^1H NMR (300 MHz, D_2O): δ 5.77 (d, 1 H, $J_{3,4}$ 5.1 Hz, H-3), 4.32 (dd, 1 H, $J_{4,5}$ 5.1, $J_{5,6}$ 9.6 Hz, H-5), 4.23 (dd, 1 H, $J_{6,7}$ 1.2 Hz, H-6), 4.12 (t, 1 H, H-4), 3.94 (ddd, 1 H, $J_{8,7}$ 9.3, $J_{8,9'}$ 6.3, $J_{8,9}$ 2.7 Hz, H-8), 3.91 (dd, 1 H, $J_{9,9'}$12.3 Hz, H-9), 3.86 (dd, 1 H, H-7), 3.69 (dd, 1 H, H-9′). ^{13}C NMR (75 MHz, D_2O): δ 49.44 (C-4), 64.88 (C-5), 66.45 (C-9), 71.56 (C-7), 73.43 (C-8), 76.57 (C-6), 102.24 (C-3), 153.95 (C-2), 171.32 (C-1). FABMS *m*/*z*: 250 [$M^+ + 1$] (*m*-NBA as matrix).

References

[1] A.K. Schukla, C. Schroder, U. Nohle, R. Shauer, *Glycoconjugates*, Lund–Ronneby, Sweden, 1983, pp. 155–156.
[2] C.A. Miller, P. Wang, M. Flasher, *Biochem. Biophys. Res. Commun.*, 83 (1978) 1479–1487.
[3] M. von Itzstein, W.-Y. Wu, G.B. Kok, M.S. Pegg, J.C. Dyason, B. Jin, T.V. Phan, M.I. Smythe, H.F. White, S.W. Oliver, P.M. Colman, J.N. Varghese, D.M. Ryan, J.M. Woods, R.C. Bethell, V.J. Hotham, J.M. Cameron, C.R. Penn, *Nature*, 363 (1993) 418–423.
[4] F.G. Hayden, J.C. Treanor, R.F. Betts, M. Lobo, J. Esinhart, E. Hussey, *J. Am. Med. Assoc.*, 275 (1996) 295–299.
[5] Y. Ito, M. Numata, M. Sigimoto, T. Ogawa, *J. Am. Chem. Soc.*, 111 (1989) 8508–8510.
[6] T. Ercegovie, G. Magnusson, *J. Org. Chem.*, 60 (1995) 3378–3384.
[7] T. Tomoo, T. Kondo, H. Abe, S. Tsukamoto, M. Isobe, T. Goto, *Carbohydr. Res.*, 284 (1996) 207–222.
[8] V. Marchitonok, G.M. Whitesides, *Carbohydr. Res.*, 302 (1997) 123–129.
[9] J.C. Castro-Palomino, Y.E. Tsvetkov, R.R. Schmidt, *J. Am. Chem. Soc.*, 120 (1989) 5434–5440.
[10] S. Nishino, H. Kuroyanagi, T. Terada, S. Inoue, F.A. Troy, K. Kitajima, *J. Biol. Chem.*, 271 (1996) 2909–2913.
[11] M. Nakamura, K. Furuhata, K. Yamazaki, H. Ogura, *Chem. Pharm. Bull.*, 39 (1991) 3140–3144.
[12] X.-L. Sun, T. Kai, H. Takayanagi, K. Furuhata, *J. Carbohydr. Chem.*, 16 (1997) 541–547.
[13] G.B. Kok, B. Mackey, M. von Itzstein, *Carbohydr. Res.*, 289 (1996) 67–75.
[14] M. Nakamura, H. Takayanagi, K. Furuhata, H. Ogura, *Chem. Pharm. Bull.*, 40 (1992) 879–885.
[15] X.-L. Sun, T. Kai, H. Takayanagi, K. Furuhata, *Chem. Pharm. Bull.*, 43 (1995) 1654–1658.
[16] X.-L. Sun, T. Kai, H. Takayanagi, K. Furuhata, *Carbohydr. Res.*, 298 (1997) 181–189.
[17] K. Furuhata, S. Sato, M. Goto, H. Ogura, *Chem. Pharm. Bull.*, 36 (1988) 1872–1876.
[18] V. Kumar, J. Kessier, M.E. Scott, B.H. Patcuardhan, S.W. Tanenbaum, M. Flashner, *Carbohydr. Res.*, 94 (1981) 123–130.
[19] TEXRAY: Structure Analysis Package, Molecular Structure Corporation, 1985.