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Studies on Sialic Acids. VIII. The 1,4-Lactone Derivatives of N-Acetylneuraminic Acid

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The reactions of *N*-acetylneuraminic acid with benzyl, allyl, and methyl halides in the presence of excess cesium carbonate gave the corresponding *N*-acetyl-2-*O*-alkyl-3,5-dideoxy-*D*-glycero-*D*galacto-2-noneno-1,4-lactones in good yields. The structures and stereochemistry of these 1,4lactonic sialic acid derivatives were elucidated from the infrared and proton nuclear magnetic resonance spectra and by X-ray crystal analysis.

Keywords — N-acetylneuraminic acid; ¹H-NMR; X-ray crystal analysis; 1,4-lactone; sialic acid; cesium carbonate

The sialic acids are biologically important and are widely distributed in nature in various forms. Recently, new types of sialic acids have been isolated from the lipopolysaccharides of *Pseudomonas aeruginosa* and *Shigella boydii*,¹⁾ and from egg polysialoglycoprotein of *Salmo gairdneri*.²⁾ We have been examining the synthesis of various lactone derivatives of *N*-acetylneuraminic acid with the aim of developing new strategies for the synthesis of various derivatives of sialic acid.

Several syntheses of 1,4-lactone derivatives of N-acetylneuraminic acid (1) have been reported. N-Acetylneuramino-1,4-lactone diethyldithioacetal (5-acetamido-2,2-bis(ethylthio)-2,3,5-trideoxy-D-glycero-D-galacto-nonulosono-1,4-lactone) was synthesized by Kuhn and Brossmer,³⁾ and the structure was confirmed by ¹H- and ¹³C-nuclear magnetic resonance (NMR) spectroscopic techniques by Robien $et al.^{4}$) The synthesis of 5-acetamido-3,5-dideoxy-D-glycero-D-galacto-2-noneno-1,4-lactone has been reported, but without full details.^{5,6)} In this report, we describe a new and efficient synthesis of 1,4-lactone derivatives of 1. We also describe the determination of the molecular structure of 5-acetamido-6,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-O-methyl-D-glycero-D-galacto-2-noneno-1,4-lactone (6) by X-ray crystal analysis. Benzyl esterification of the cesium salt of 1 was carried out with benzyl bromide in N,Ndimethylformamide (DMF). The reaction was completed in 2 h at room temperature to give benzyl 5-acetamido-3,5-dideoxy- β -D-glycero-D-galacto-2-nonulopyranosonate (2) as a crystalline product from 2-propanol in 80% yield. Treatment of 2 with an excess amount of cesium carbonate and benzyl bromide in DMF for 2 h at 40 °C gave 5-acetamido-2-O-benzyl-3,5-dideoxy-D-glycero-D-galacto-2-noneno-1,4-lactone (3) in 80% yield after recrystallization. Furthermore, we have found a facile method for the synthesis of 3 by the treatment of 1 with an excess amount of cesium carbonate and benzyl bromide. Thin-layer chromatography (TLC) of the reaction mixture showed three main spots of 3, the starting material (1), and benzyl bromide, together with a few trace spots. This result suggests that this lactonization for 1 is highly regioselective. The reaction mechanism is considered to involve intramolecular



TABLE I. ¹H-NMR Spectral Data

	Compound					
Proton	3	4	5	6		
3-H	6.408 d	6.287 d	6.287 d	5.974 d		
	(2.0)	(2.0)	(1.8)	(2.2)		
4-H	5.436 t	5.407 t	5.420 t	4.915 t		
	(2.0)	(2.0)	(1.8)	(2.2)		
5-H	3.830 ddd	4.200 ddd	4.212 dt	4.529 dt		
	(2.0, 9.5, 10.5)	(2.0, 9.4, 10.2)	(1.8, 10.5)	(2.2, 9.9)		
6-H	3.829 dd	3.810 dd	3.831 dd	5.513 dd		
	(10.5, 8.0)	(10.2, 8.2)	(10.5, 8.1)	(2.2, 9.9)		
7-H	3.232 dd	3.233 dd	3.238 dd	5.407 dd		
	(8.0, 7.3)	(8.5, 7.5)	(8.7, 7.3)	(8.8, 2.2)		
8-H	3.498 dddd	3.487 dddd	3.500 dddd	5.090 ddd		
	(8.0, 3.0, 5.8, 5.2)	(8.5, 3.3, 6.0, 5.2)	(8.7, 3.3, 6.0, 5.5)	(8.8, 2.9, 5.5)		
9-H	3.608 ddd	3.600 ddd	3.610 ddd	4.248 dd		
	(3.0, -10.8, 5.8)	(3.3, -11.0, 5.2)	(3.3, -10.9, 5.9)	(2.9, -12.5)		
9-H′	3.370 ddd	3.380 ddd	3.398 ddd	4.012 dd		
	(3.0, -10.8, 5.8)	(6.0, -11.0, 5.2)	(6.0, -10.9, 5.9)	(5.5, -12.5)		
NH	7.745 d	7.738 d	7.735 d	5.912 d		
	(9.5)	(9.4)	(9.5)	(9.9)		
6-OH	4.708 d	4.705 d	4.700 d			
	(8.0)	(8.2)	(8.1)			
7-OH	4.288 d	4.287 d	4.285 d			
	(7.3)	(7.5)	(7.3)			
8-OH	3.498 d	4.468 d	4.458 d			
	(5.2)	(5.2)	(5.5)			
9-OH	4.370 t	4.375 t	4.362 t			
	(5.8)	(5.2)	(5.9)			
NAc	1.715 s	1.730 s	1.745 s	1.874 s		
Others	4.875 (1H, d, J =	4.4 (2H, m, allyl	3.737 (3H, s,	2.045 (3H, s, OAc)		
	12.0 Hz,CHph)	1′-H)	3-OMe)	2.077 (3H, s, OAc)		
	4.992 (1H, d, $J =$	5.30 (2H, m, allyl		2.104 (3H, s, OAc)		
	12.0 Hz, -CHph)	3'-H)		2.151 (3H, s, OAc)		
	7.390 (5H, s, ph)	5.956 (1H, m,		3.737 (3H, s,		
	· · · • • /	allyl, 2'-H)		3-OMe)		

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 δ values in DMSO-d_6 at 19 $^\circ \rm C$ and coupling constants in Hz.

lactonization, as shown in Chart 1.

The structure of 3 was established by comparison of the spectral data for 2 and 3. The field desorption-mass spectrum (FD-MS) of 3 showed the same principal ion as that of 2 at m/z 382 (M⁺+1) and the infrared (IR) absorptions at 1710 cm⁻¹ for 2 and 1765 cm⁻¹ for 3 can be assigned to an ester C=O stretching bond and a conjugated lactone C=O stretching bond, respectively.

All the signals in the ¹H-NMR spectrum of **3** were assigned by homonuclear doubleresonance studies, and the chemical shifts and coupling constants are summarized in Table I. The major differences between **2** and **3** were found to be the chemical shifts and coupling constants of protons on C-3 and C-4. Comparison of the ¹H-NMR spectra of **2** and **3** indicated that they differed by the presence of an olefinic proton at $\delta_{\rm H}$ 6.41 (1H, d, $J_{3,4}$ = 2.0 Hz) in **3** instead of the C-3 methylene protons in **2**. The value of $J_{3,4}$ =2.0 Hz of **3** suggests a five- or six-membered ring system. The resonance of H-4 in **3** is readily identified because of its characteristic shift range at the lowest field as a methine proton. These results clearly identified the structure of **3**.

In the same manner, treatment of 1 in DMF with allyl bromide or methyl iodide in the presence of an excess amount of cesium carbonate gave the corresponding 1,4-lactone compounds 4 and 5, respectively, in 70–80% yield. These structures were supported by the ¹H-NMR spectra as shown in Table I.

We attempted to confirm the 1,4-lactone structure of **6** by means of X-ray crystal structure analysis. Good crystals of 5-acetamido-6,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-methyl-D-glycero-D-galacto-2-noneno-1,4-lactone (**6**) for X-ray study were prepared by recrystallization from acetone solution. A crystal with the dimensions of $0.3 \times 0.4 \times 0.4$ mm³ was used for the structure determination. The cell dimensions and diffraction intensities were measured on a Rigaku four-circle diffractometer, using graphite-monochromated Cu K_{α} radiation.

Crystal data: $C_{20}H_{27}NO_{12}$, monoclinic, space group $P2_1$, a=13.721(2), b=8.839(1), c=9.548(1) Å, $\beta=91.05(2)^{\circ}$, V=1157.9 Å³, Z=2, $D_c=1.357$ g·cm⁻¹, $D_o=1.36$ g·cm⁻³. Two thousand seven hundred and fifty independent reflections in the range of $2\theta < 135^{\circ}$ were collected by the use of the $2\theta-\omega$ scan mode with a scanning rate of $4^{\circ}(2\theta)$ min⁻¹. A total of 2189 independent reflections with $|F_o| > 3\sigma(|F_o|)$ were obtained and corrected for Lorentz and polarization factors but not for absorption. The structure was solved by a direct method using



Fig. 1. A Perspective View of 6 and the Atomic Numbering

Atom	x	У	Z	B _{eq}	Atom	x	у	Ζ	B _{eq}
C(1)	9493 (3)	7770 (11)	11903 (11)	3.0	O(1)	9076 (4)	7279 (7)	10668 (7)	3.0
C(2)	10144 (6)	6587 (10)	12428 (10)	2.5	O(2)	9315 (5)	9007 (9)	12372 (9)	4.4
C(3)	10100 (6)	5391 (11)	11579 (10)	2.8	O(3)	10630 (5)	6876 (8)	13637 (7)	3.2
C(4)	9391 (6)	5764 (11)	10404 (10)	2.6	O(4)	8632 (6)	2561 (10)	12541 (9)	5.1
C(5)	8485 (6)	4727 (10)	10406 (10)	2.3	O(5)	8274 (4)	5011 (7)	7929 (6)	2.2
C(6)	7770 (6)	5114 (9)	9223 (9)	1.8	O(6)	7994 (6)	7474 (9)	7465 (9)	4.9
C(7)	6886 (6)	4065 (10)	9201 (10)	2.3	O(7)	7251 (4)	2509 (8)	9072 (7)	2.8
C(8)	6190 (6)	4309 (11)	7964 (11)	2.8	O(8)	6351 (6)	1813 (10)	10931 (9)	5.1
C(9)	5293 (7)	3309 (13)	8148 (13)	4.0	O(9)	5879 (4)	5907 (8)	8105 (7)	3.0
C(10)	11219 (8)	5655 (15)	14160 (12)	4.4	O(10)	5934 (7)	6212 (11)	5752 (9)	5.5
C(11)	8056 (7)	3612 (12)	12680 (11)	3.4	O(11)	4581 (4)	3770 (8)	7084 (8)	3.4
C(12)	7392 (9)	3748 (15)	13901 (12)	4.4	O(12)	3560 (5)	2046 (10)	7915 (9)	4.5
C(13)	8398 (6)	6313 (11)	7175 (11)	3.0	H(C3)	1052 (7)	437 (12)	1078 (10)	4.0
C(14)	9079 (8)	6104 (15)	5993 (11)	4.0	H(C4)	976 (6)	569 (12)	940 (10)	3.6
C(15)	6957 (7)	1540 (12)	10061 (10)	3.0	H(C5)	872 (7)	357 (12)	1027 (10)	3.9
C(16)	7494 (9)	60 (13)	9912 (14)	4.6	H(C6)	751 (6)	626 (13)	934 (10)	3.9
C(17)	5764 (7)	6659 (13)	6883 (11)	3.7	H(C7)	650 (7)	426 (12)	1016 (10)	3.7
C(18)	5467 (9)	8299 (14)	7204 (15)	5.2	H(C8)	656 (7)	400 (13)	698 (10)	3.8
C(19)	3719 (7)	3106 (13)	7146 (11)	3.5	H(C9)	547 (6)	213 (13)	801 (10)	3.9
C(20)	2995 (8)	3801 (16)	6159 (13)	4.5	H'(C9)	499 (7)	347 (12)	918 (10)	3.6
N	7986 (5)	4777 (8)	11733 (8)	2.4			()	. ,	

 TABLE II.
 Atomic Coordinates (10⁴) with Their Standard Deviations in Parentheses and Equivalent Isotropic Temperature Factors

TABLE III. Bond Lengths (Å) with Their Standard Deviations in Parentheses

$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			and a second	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	C(1)-C(2)	1.46 (1)	C(10)-O(3)	1.43 (1)
C(1)-O(2) 1.21 (1) $C(11)-N$ 1.37 (1) $C(2)-C(3)$ 1.33 (1) $C(11)-O(4)$ 1.23 (1) $C(2)-O(3)$ 1.35 (1) $C(13)-C(14)$ 1.49 (1) $C(3)-C(4)$ 1.51 (1) $C(13)-O(5)$ 1.37 (1) $C(4)-C(5)$ 1.54 (1) $C(13)-O(6)$ 1.20 (1) $C(4)-O(1)$ 1.43 (1) $C(15)-C(16)$ 1.51 (2) $C(5)-C(6)$ 1.52 (1) $C(15)-O(7)$ 1.34 (1) $C(5)-N$ 1.45 (1) $C(15)-O(8)$ 1.21 (1) $C(6)-C(7)$ 1.53 (1) $C(17)-O(18)$ 1.54 (2) $C(6)-O(5)$ 1.43 (1) $C(17)-O(9)$ 1.35 (1) $C(7)-C(8)$ 1.52 (1) $C(17)-O(10)$ 1.18 (1) $C(7)-O(7)$ 1.47 (1) $C(19)-O(11)$ 1.32 (1) $C(8)-O(9)$ 1.53 (1) $C(19)-O(11)$ 1.32 (1) $C(8)-O(9)$ 1.48 (1) $C(19)-O(12)$ 1.21 (1)	C(1) - O(1)	1.37 (1)	C(11)-C(12)	1.50 (2)
$\begin{array}{c ccccc} C(2)-C(3) & 1.33 (1) & C(11)-O(4) & 1.23 (1) \\ C(2)-O(3) & 1.35 (1) & C(13)-C(14) & 1.49 (1) \\ C(3)-C(4) & 1.51 (1) & C(13)-O(5) & 1.37 (1) \\ C(4)-C(5) & 1.54 (1) & C(13)-O(6) & 1.20 (1) \\ C(4)-O(1) & 1.43 (1) & C(15)-C(16) & 1.51 (2) \\ C(5)-C(6) & 1.52 (1) & C(15)-O(7) & 1.34 (1) \\ C(5)-N & 1.45 (1) & C(15)-O(8) & 1.21 (1) \\ C(6)-C(7) & 1.53 (1) & C(17)-O(8) & 1.54 (2) \\ C(6)-O(5) & 1.43 (1) & C(17)-O(9) & 1.35 (1) \\ C(7)-C(8) & 1.52 (1) & C(17)-O(10) & 1.18 (1) \\ C(7)-O(7) & 1.47 (1) & C(19)-C(20) & 1.50 (2) \\ C(8)-C(9) & 1.53 (1) & C(19)-O(11) & 1.32 (1) \\ C(8)-O(9) & 1.48 (1) & C(19)-O(12) & 1.21 (1) \\ \end{array}$	C(1)-O(2)	1.21 (1)	C(11)–N	1.37 (1)
C(2)-O(3) $1.35(1)$ $C(13)-C(14)$ $1.49(1)$ $C(3)-C(4)$ $1.51(1)$ $C(13)-O(5)$ $1.37(1)$ $C(4)-C(5)$ $1.54(1)$ $C(13)-O(6)$ $1.20(1)$ $C(4)-O(1)$ $1.43(1)$ $C(15)-C(16)$ $1.51(2)$ $C(5)-C(6)$ $1.52(1)$ $C(15)-O(7)$ $1.34(1)$ $C(5)-N$ $1.45(1)$ $C(15)-O(8)$ $1.21(1)$ $C(6)-C(7)$ $1.53(1)$ $C(17)-C(18)$ $1.54(2)$ $C(6)-O(5)$ $1.43(1)$ $C(17)-O(9)$ $1.35(1)$ $C(7)-C(8)$ $1.52(1)$ $C(17)-O(10)$ $1.18(1)$ $C(7)-O(7)$ $1.47(1)$ $C(19)-C(20)$ $1.50(2)$ $C(8)-C(9)$ $1.53(1)$ $C(19)-O(11)$ $1.32(1)$ $C(8)-O(9)$ $1.48(1)$ $C(19)-O(12)$ $1.21(1)$	C(2)-C(3)	1.33 (1)	C(11)–O(4)	1.23 (1)
$\begin{array}{c ccccc} C(3)-C(4) & 1.51 (1) & C(13)-O(5) & 1.37 (1) \\ C(4)-C(5) & 1.54 (1) & C(13)-O(6) & 1.20 (1) \\ C(4)-O(1) & 1.43 (1) & C(15)-C(16) & 1.51 (2) \\ C(5)-C(6) & 1.52 (1) & C(15)-O(7) & 1.34 (1) \\ C(5)-N & 1.45 (1) & C(15)-O(8) & 1.21 (1) \\ C(6)-C(7) & 1.53 (1) & C(17)-C(18) & 1.54 (2) \\ C(6)-O(5) & 1.43 (1) & C(17)-O(9) & 1.35 (1) \\ C(7)-C(8) & 1.52 (1) & C(17)-O(10) & 1.18 (1) \\ C(7)-O(7) & 1.47 (1) & C(19)-C(20) & 1.50 (2) \\ C(8)-C(9) & 1.53 (1) & C(19)-O(11) & 1.32 (1) \\ C(8)-O(9) & 1.48 (1) & C(19)-O(12) & 1.21 (1) \\ \end{array}$	C(2)–O(3)	1.35 (1)	C(13)–C(14)	1.49 (1)
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$\begin{array}{c cccc} C(6)-O(5) & 1.43 (1) & C(17)-O(9) & 1.35 (1) \\ C(7)-C(8) & 1.52 (1) & C(17)-O(10) & 1.18 (1) \\ C(7)-O(7) & 1.47 (1) & C(19)-C(20) & 1.50 (2) \\ C(8)-C(9) & 1.53 (1) & C(19)-O(11) & 1.32 (1) \\ C(8)-O(9) & 1.48 (1) & C(19)-O(12) & 1.21 (1) \end{array}$	C(6)–C(7)	1.53 (1)	C(17)–C(18)	1.54 (2)
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C(8)-O(9) 1.48 (1) $C(19)-O(12)$ 1.21 (1)	C(8)C(9)	1.53 (1)	C(19)–O(11)	1.32 (1)
	C(8)–O(9)	1.48 (1)	C(19)-O(12)	1.21 (1)
C(9)–O(11) 1.45 (1)	C(9)–O(11)	1.45 (1)		

MULTAN.⁷⁾ The E-map of the phase set with the highest figure of merit showed the skeleton of the molecule. The structure, thus obtained, was refined by a full-matrix least-squares method with anisotropic temperature factors. After all the hydrogen atoms had been located in the difference Fourier map, several cycles of least-squares refinement were carried out including these hydrogen atoms. The atomic scattering factors were those given by the International Tables for X-ray Crystallography.⁸⁾ The final R value was 8.0%, where $R = \Sigma ||F_o| - |F_c||/\Sigma |F_c|$.

The final atomic parameters are listed in Table II. The absolute configurations of the

C(2)–C(1)–O(1)	108.2 (8)	C(8)–C(9)–O(11)	106.8 (8)
C(2)-C(1)-O(2)	130.4 (9)	C(12)-C(11)-N	114.6 (9)
O(1)-C(1)-O(2)	121.4 (8)	C(12)-C(11)-O(4)	123.1 (10)
C(1)-C(2)-C(3)	109.8 (8)	N-C(11)-O(4)	122.2 (9)
C(1)-C(2)-O(3)	116.7 (8)	C(14)-C(13)-O(5)	112.3 (8)
C(3)-C(2)-O(3)	133.4 (8)	C(14)-C(13)-O(6)	125.4 (10)
C(2)-C(3)-C(4)	107.5 (8)	O(5)-C(13)-O(6)	122.3 (9)
C(3)-C(4)-C(5)	112.2 (7)	C(16)-C(15)-O(7)	109.5 (8)
C(3)-C(4)-O(1)	105.4 (7)	C(16)-C(15)-O(8)	125.5 (10)
C(5)-C(4)-O(1)	108.0 (6)	O(7)-C(15)-O(8)	125.1 (9)
C(5)-C(6)-C(7)	112.0 (7)	C(18)-C(17)-O(9)	108.6 (9)
C(4)-C(5)-N	112.1 (7)	C(18)-C(17)-O(10)	123.9 (11)
C(6)-C(5)-N	109.4 (6)	O(9)-C(17)-O(10)	127.3 (10)
C(5)-C(6)-C(7)	112.1 (6)	C(20)-C(19)-O(11)	112.0 (9)
C(5)-C(6)-O(5)	108.1 (6)	C(20)-C(19)-O(12)	125.2 (9)
C(7)-C(6)-O(5)	110.2 (6)	O(11)-C(19)-O(12)	122.8 (8)
C(6)-C(7)-C(8)	114.3 (7)	C(5)-N-C(11)	121.6 (7)
C(6)-C(7)-O(7)	107.3 (6)	C(1)-O(1)-C(4)	109.0 (6)
C(8)-C(7)-O(7)	106.2 (7)	C(2)-O(3)-C(10)	115.1 (7)
C(7)-C(8)-C(9)	108.9 (8)	C(6)-O(5)-C(13)	117.8 (6)
C(7)-C(8)-O(9)	104.1 (7)	C(7)-O(7)-C(15)	115.6 (6)
C(9)-C(8)-O(9)	107.9 (7)	C(8)-O(9)-C(17)	114.9 (7)

TABLE IV. Bond Angles (°) with Their Standard Deviations in Parentheses

asymmetric centers agree with those of a related molecule, methyl β -glycosidic neuraminic acid.⁹⁾ Figure 1 shows a perspective drawing of **6**. Bond lengths and angles are shown in Tables III and IV. No abnormal lengths or angles were found in the structure.

The absolute configuration at C-4 was assigned as S. Torsional angles C(3)–C(4)–C(5)–C(6), C(4)–C(5)–C(6)–C(7), C(5)–C(6)–C(7)–C(8), and C(6)–C(7)–C(8)–C(9) are 180°, 170°, -175°, and -174°, respectively. The vicinal coupling constants between the hydrogen atoms on the side chain of 6, shown in Table I, indicate that the side chain has the same zigzag conformation both in the crystal and in solution.

Experimental

General Methods—Melting points were determined in a capillary tube and are uncorrected. ¹H-NMR spectra were measured on a Varian XL-400 spectrometer with Me₄Si (TMS) as an internal standard in CDCl₃ or Me₃Si(CH₂)₃SO₃Na(DSS) in D₂O. The FD-MS were obtained on a JEOL JMS-DX 300 instrument, and IR spectra on a JASCO-A2 spectrometer. Optical rotations were measured with a JASCO-JIP-4 digital polarimeter. Column chromatography was performed on Wakogel C-200, and TLC was performed on Kieselgel 60 GF₂₅₄ (Merck) with detection by ultraviolet (UV) light and by carrying with sulfuric acid.

Benzyl 5-Acetamido-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosonate (2)—A solution of 1 (2g, 6.47 mmol) in water (10 ml) was neutralized with 10% Cs₂CO₃ aqueous solution. The solution was lyophilized and dried over P₂O₅ to give the cesium salt of 1, which was dissolved in dry DMF (20 ml). Then BnBr (5 ml) was added to the stirred solution, and the reaction mixture was stirred under argon for 2 h at room temperature. The reaction mixture was filtered and evaporated to a syrup, which was purified by recrystallization from 2-propanol to give 2.0 g (80%) of 2 as colorless needles. mp 183–185 °C, $[\alpha]_{Da}^{2B} - 43^{\circ}$ (*c*=1, H₂O). Anal. Calcd for C₁₇H₂₅NO₉: C, 52.71; H, 6.51; N, 3.28. Found: C, 52.68; H, 6.55; N, 3.24. IR v_{max}^{KBr} cm⁻¹: 1710, 1620, 1520. ¹H-NMR (400 MHz, D₂O) $\delta_{\rm H}$ (DSS): 1.822 (1H, dd, *J*=11.5, 13.0 Hz, 3-H_{ax}), 1.960 (3H, s, NAc), 2.233 (1H, dd, *J*=5.0, 13.0 Hz, 3-H_{eq}), 3.982 (1H, ddd, *J*=5.0, 10.5 Hz, 4-H), 3.827 (1H, ddd, *J*=10.2, 10.2 Hz, 5-H), 3.985 (1H, dd, *J*=10.5, 1.2 Hz, 6-H), 3.469 (1H, dd, *J*= 1.2, 9.4 Hz, 7-H), 3.634 (1H, ddd, *J*=2.8, 6.1, 9.4 Hz, 8-H), 3.573 (1H, dd, *J*=6.1, 12.0 Hz, 9-H), 3.473 (1H, dd, *J*= 2.8, 12.0 Hz, 9-H'), 5.219 (1H, d, *J*=12.0 Hz, phenyl-CH–), 5.230 (1H, *J*=12.0 Hz, phenyl-CH–), 7.038 (phenyl group).

5-Acetamido-2-O-benzyl-3,5-dideoxy-\beta-D-glycero-p-galacto-2-noneno-1,4-lactone (3)—1: Cs₂CO₃ (4.89 g, 15 mmol) and BnBr (2.38 g, 20 mmol) were added to a solution of 1 (1.55 g, 5 mmol) in DMF (20 ml) with stirring. After

2 h at 40 °C, insoluble materials were removed through Celite, and the filtrate was evaporated. The residue was purified by recrystallization from ethanol to give 1.42 g (78%) of 3 as colorless crystals. mp 195–196 °C, $[\alpha]_D^{24}$ – 64 ° (*c*=1, MeOH). MS (FD) *m/z*: 382 (M⁺ + 1). Anal. Calcd for C₁₈H₂₃NO₈: C, 56.29; H, 6.04; N, 3.67. Found: C, 56.83; H, 6.07; N, 3.64. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1765, 1650, 1535. ¹H-NMR data are shown on Table I.

2: A solution of 2 (0.11 g, 0.3 mmol) in DMF (10 ml) was treated with BnBr (0.5 ml). Work-up as described above afforded 3 (0.09 g, 80%). The physical constants were identical with those of 3 prepared above.

5-Acetamido-2-O-allyl-3,5-dideoxy-β-D-glycero-D-galacto-2-noneno-1,4-lactone (4)—Cs₂CO₃ (4.89 g, 15 mmol) and allyl bromide (2.19 ml, 20 mmol) were added to a solution of 1 (1.55 g, 5 mmol) in DMF (20 ml). The mixture was stirred for 3 h at 40 °C, insoluble materials were removed through Celite and the filtrate was evaporated. The residue was triturated with ethanol (100 ml), and the resulting insoluble materials were removed by filtration. After evaporation of the filtrate, the crude product was purified by silica gel column chromatography, with chloroform-methanol (4:1), and the product was recrystallized from ethanol to give 0.72 (42%) of 4 as colorless needles. mp 151—152 °C. [α]₂^B – 77 ° (*c* = 1, MeOH). MS (FD) *m/z*: 332 (M⁺ + 1). Anal. Calcd for C₁₄H₂₁NO₈: C, 50.76; H, 6.34; N, 4.23. Found: C, 50.28; H, 6.53; N, 4.18. IR ν_{max}^{Bar} cm⁻¹: 1775, 1640, 1540. ¹H-NMR data are given in Table I.

5-Acetamido-3,5-dideoxy-2-O-methyl-\beta-D-glycero-D-galacto-2-noneno-1,4-lactone (5)—Cs₂CO₃ (4.89 g, 15 mmol) and MeI (1.25 ml, 20 mmol) were added to a stirred solution of 1 (1.55 g, 5 mmol) in DMF. The mixture was stirred for 1.5 h at 40 °C, insoluble materials were removed through Celite and the filtrate was evaporated. The residue was triturated with ethanol (100 ml), and the resulting insoluble materials were removed by filtration. After evaporation of the filtrate, the crude product was purified by silica gel column chromatography with chloroform-methanol (4:1), and the product was recrystallized from ethanol to give 0.76 g (50%) of **5** as colorless prisms. mp 169.0—169.5 °C. [α] $_{D}^{24}$ -79 ° (c=1, MeOH). MS (FD) m/z: 306 (M⁺ +1). Anal. Calcd for C₁₂H₁₉NO₈: C, 47.21; H, 6.28; N, 4.59. Found: C, 47.06; H, 6.29; N, 4.59. IR ν_{max}^{RBF} cm⁻¹: 1770, 1650, 1535. ¹H-NMR data are given in Table I.

5-Acetamido-6,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-O-methyl-β-D-glycero-D-galacto-2-noneno-1,4-lactone (6) Acetic anhydride (1 ml) was added to a solution of 5 (0.31 g, 1 mmol) in pyridine (1 ml). The reaction mixture was stirred overnight at room temperature, ethanol (10 ml) was added, and the whole was evaporate to dryness. The residue was purified by recrystallization from acetone to give 0.35 g (75%) of 6 as colorless prisms. mp 181–182 °C. $[\alpha]_{D}^{27}$ +13.8 ° (c=1, CHCl₃). Anal. Calcd for C₂₀H₂₇NO₁₂: C, 50.74; H, 5.71; N, 2.96. Found: C, 50.64; H, 5.75; N, 2.90. IR ν_{max}^{KBr} cm⁻¹: 1770 (sh), 1750, 1660, 1530. ¹H-NMR data are given in Table I.

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