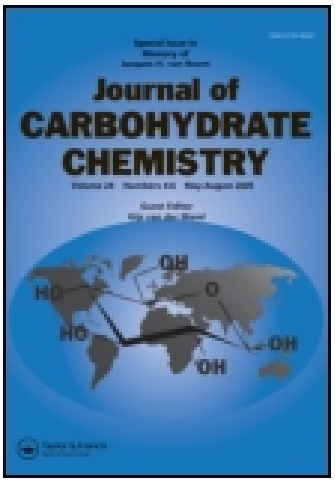

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SELECTIVE PROTECTING METHOD FOR THE INDIVIDUAL HYDROXYL GROUPS OF KDN

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ABSTRACT

Selective protection for the individual hydroxyl groups of methyl (phenyl 3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (**2**) was examined. The 4-, 5-, and 7-hydroxyl groups of methyl (phenyl 3-deoxy-8,9-*O*-isopropylidene-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (**3**) were found selectively to be protected by *t*-butyldimethylsilyl, methoxymethyl, and benzoyl groups, respectively. In order to obtain the 8- and 9-hydroxyl derivatives selectively, methyl (phenyl 4,5,7-tri-*O*-acetyl-9-*O*-*t*-butyldimethylsilyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (**12**) and methyl (phenyl 4,5,7,8-tetra-*O*-benzyl-9-*O*-triphenylmethyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (**19**) were prepared in moderate yields.

INTRODUCTION

3-Deoxy-D-*glycero*-D-*galacto*-2-nonulosonic acid (KDN) is a unique, deaminated analogue of sialic acid, and has been recently isolated from the rainbow trout egg, polysialoglycoprotein (PSGP).[1] KDN has been found in a variety of tissues such as fish eggs, fish sperm, amphibian eggs, and bacteria.[2-5] In these environments, KDN may interact with several receptor proteins which may recognize the hydroxyl groups or carboxyl group of KDN as the key polar function.[6] In order to investigate the location of the hydroxyl groups concerned with this recognition process, KDN synthetic analogues in

which the individual hydroxyl groups were masked by a protecting group or deoxygenated, could be used for bioassay, as has been performed in research concerned with the recognition process between oligosaccharides and lectin.[7] Glycosylation methodology with KDN-2-thiophenyl glycoside has been established and several ganglioside analogues containing a KDN have been synthesized.[8] Therefore, in order to synthesize modified KDN analogues, a regioselective protecting method for the individual hydroxyl groups of KDN would be essential as have been established in the case of sialic acids.[9] The Furuhata group has reported an interesting protecting method for KDN, resulting in the 5,7:8,9-di-*O*-isopropylidene derivative.[10] In addition, they also reported that the reactivity of the 5-hydroxyl group of the 8,9-*O*-isopropylidene derivative is dependent on the anomeric configuration. The 4- and 7-hydroxyl groups of the 8,9-*O*-isopropylidene derivative (β-glycoside) could be selectively protected by a benzoyl group.[10a] On the other hand, in the case of its α-glycoside, the 4- and 5-hydroxyl groups could be protected.[10b]

For the synthesis of KDN-oligosaccharide analogues, KDN derivatives should be activated as the glycosyl donors after a modification of their hydroxyl group. Therefore, we examined the use of compound **2**, which was easily prepared from KDN, for the selective protection. However, to our knowledge, there is no report on a selective protecting method for the individual hydroxyl groups of β-KDN derivatives. Here we report a selective protecting method for the individual hydroxyl groups and the reactivity of each hydroxyl group of β-KDN.

RESULTS AND DISCUSSION

Since the synthetic methods for KDN[8, 11] and its thioglycoside[8] have already been reported, we prepared methyl (phenyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-2-thio-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate ($\alpha : \beta = 1 : 8$) according to the reported method[8] and then isolated its β-glycoside **1**. After de *O*-acetylation of **1**, resulting thioglycoside **2** was treated with 2,2-dimethoxypropane to afford acetonide **3** in 92 % yield. For protection of the 4-hydroxyl groups, we used a *t*-butyldimethylsilyl group instead of the benzoyl group, because this ether protecting group can be easily deprotected by the action of the fluoride ion under moderate conditions. Silylation with 1.4 equivalents of *t*-butyldimethylsilyl chloride afforded the 4-*O*-*t*-butyldimethylsilyl derivative **4** in 88 % yield.[12] After acetylation of the 5- and 7- hydroxyl groups with acetic anhydride, de *O*-silylation by *n*-Bu4NF afforded the 4-hydroxyl derivative **6** in 64 % yield (2 steps). During this de *O*-silylation, the acetyl group at the 5-position migrated to the 4-hydroxyl group in 28 % yield.

In order to obtain the 5-hydroxyl derivative **7**, silyl derivative **4** was treated with benzoyl chloride to afford the 7-*O*-benzoyl derivative **7** in 93 % yield.[10a]

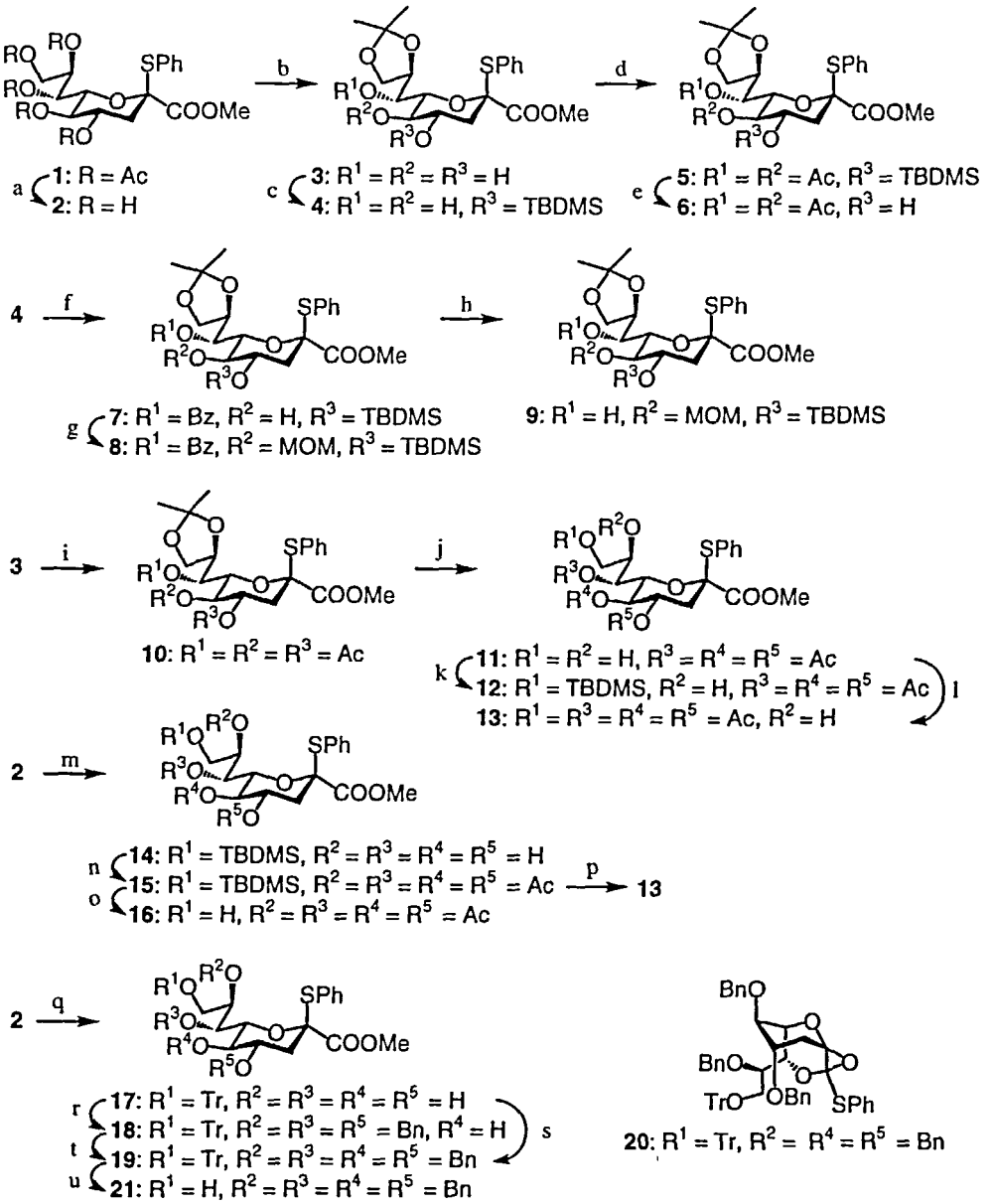
To prepare the 7-hydroxyl derivative, **9** was synthesized in 60 % yield (2 steps) by deprotection of the benzoyl group of **8** which was prepared from **7** by protection with a methoxymethyl group (MOM).

To prepare the 8-hydroxyl derivatives **12** and **13**, selective silylation and acetylation of acetyl derivative **11**, which was prepared by acetylation of **3** and then subsequent deprotection of the isopropylidene group, were performed in good yields, respectively.

In order to obtain the 9-hydroxyl derivative **16**, acetylation of **14** and then, de *O*-silylation under acidic conditions were performed to give **16** in 73 % yield (2 steps). However, the acetyl group at the 8-position easily migrated[13] to the 9-position on preparative TLC (3 times development). In fact, the 8-hydroxyl derivative **13** was obtained in 86 % yield under the conditions of 80% aq AcOH. Consequently, the acidic hydrolysis of **15** is a useful method for the preparation of the 8-hydroxyl derivative **13**.

Therefore, we investigated another protecting strategy as follows. Selective triphenylmethylation at the 9-position of **2** and then benzylation at the 4-, 5-, 7-, and 8-positions with excess of BaO, $Ba(OH)_2$, and BnBr were performed to give **19**. However, under these conditions, the 5-hydroxyl group did not react completely even after prolonged reaction time. The above conditions gave **18** and **19** in 71 % and 14 % yields, respectively. Therefore, benzylation with NaH and BnBr was examined for the protection of the 5-hydroxyl group. This condition successfully afforded **19** in 93 % yield from **18**, but the required compound **19** and the by-product **20** were obtained in 45 % and 33 % yields, respectively from **17**. De *O*-tritylation of **19** by acid hydrolysis afforded the 9-hydroxyl derivative **21** in 91 % yield.

From the above mentioned results, isopropylidenation at the 8- and 9-positions of β-thio glycoside **2** serves for the subsequent concise protection of the 4-hydroxyl group by the *t*-butyldimethylsilyl group. In this reaction, no by-product such as the 5- or 7-silylated derivative was obtained. Therefore, the 4-*O*-silylated derivative **4** was obtained as the sole product in high yield. Since the reactivity of the 5-hydroxyl group for the protecting reaction is relatively poor,[10a] silyl derivative **4** can be easily converted into benzoyl derivative **7** having a free hydroxyl group at only the 5-position. However, the 5-hydroxyl group also can be protected, if a simple ester such as an acetyl group or a methoxymethyl group is used. As a result, we could obtain the derivative **8** having four different protecting groups, *t*-butyldimethylsilyl-, MOM-, benzoyl-, and isopropylidene groups. As shown in the Scheme, a benzyl group could not be easily introduced at the 5-position of **17** by the use of BaO, $Ba(OH)_2$, and BnBr, resulting in tri-*O*-benzyl derivative **18**. On the



a. NaOMe, MeOH, 94 %; b. 2,2-Dimethoxypropane, Dowex 50W-X8, Acetone, 92 %; c. TBDMSCl, Imidazole, DMF, 88 %; d. Ac_2O, Pyridine, 92 %; e. *n*-Bu_4NF, THF, 70 %; f. BzCl, Pyridine, 93 %; g. Dimethoxymethane, Molecular Sieves 4A, P_2O_5, CH_2Cl_2, 63 %; h. NaOMe, MeOH, 95 %; i. Ac_2O, Pyridine, 94 %; j. 70 % aq AcOH, 95 %; k. TBDMSCl, Pyridine, 91 %; l. Ac_2O, Pyridine, 93 %; m. TBDMSCl, Pyridine, 92 %; n. Ac_2O, Pyridine, 96 %; o. AcOH/THF/H_2O (3:1:1 v/v/v), 76 %; p 80 % aq AcOH, 86 %; q. TrCl, Pyridine, 97 %; r. 1. BaO, $Ba(OH)_2$, BnBr, DMF; 2. CH_2N_2, MeOH, 71 % (2 steps); s. 1. NaH, BnBr, DMF; 2. CH_2N_2, MeOH, 45 % (2 steps); t. 1. NaH, BnBr, DMF; 2. CH_2N_2, MeOH, 93 % (2 steps); u. Dowex 50W-X8, MeOH/$CHCl_3$, 91 %.

Scheme

other hand, benzylation with NaH and BnBr, afforded tetra-*O*-benzylated derivative **19** from both **18** and **17** in 93 % and 45 % yields, respectively. These results, fortunately, afforded a concise protecting method which distinguishes between the 5- and 9-hydroxyl groups. After modification at the 5-position of **17**, we could easily perform the subsequent modification or substitution reaction at the 9-position after de *O*-triphenylmethylation. The by-product **20** has two quaternary carbons in addition to phenyl, benzyl, and triphenylmethyl groups, and has no carbonyl group as indicated from its ^{13}C NMR and IR spectra. The structure of **20** is suggested by ^{1}H NMR, ^{13}C NMR, IR and HRFABMS data.

CONCLUSION

We have shown selective protection methodology for the individual hydroxyl groups of KDN in which the 2-position is already activated with a thiophenyl group. If we want to get the masked oligosaccharide analogues, protection would be performed before or after glycosylation. On the other hand, if we want to deoxygenate the corresponding hydroxyl group by radical reduction, the reaction would be performed after glycosylation.

KDN exists in the nonreducing end of oligosaccharides and it is deduced that KDN may play a role to protect against sialidase digestion.[14] The protection procedures described here may serve for investigation where hydroxyl groups are the key polar functions during recognition by the receptor protein or KDNase. Work is in progress to synthesize KDN-oligosaccharide analogues deoxygenated or masked.

EXPERIMENTAL

General Method. All melting points were determined using a Yanagimoto apparatus and are uncorrected. Optical rotations were measured in a 0.5 dm tube with a JASCO DIP-140 polarimeter. ^{1}H NMR spectra were recorded in chloroform-*d* unless otherwise stated, with a JEOL FX-200, JEOL EX-270, or JEOL A-500 spectrometer. IR spectra were recorded with a Hitachi 270-30 spectrometer. Elemental analyses were performed on a Perkin-Elmer 2400 II elemental analyzer. The chemical shifts, coupling constants, and IR frequencies were recorded in δ, Hz, and cm^{-1} units, respectively. Column chromatography was performed on silica gel (Silica gel 60, 70 - 230 mesh, Merck) unless otherwise stated. Thin-layer chromatography (TLC) on silica gel (Silica gel 60F254, Merck) was used to monitor the reactions and to certify the purity of the reaction products by charring after spraying with 5% H_2SO_4 in methanol. High resolution mass spectra were recorded using a Shimadzu / Kratos concept-II H spectrometer under FAB conditions.

Methyl (Phenyl 3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (2). After preparation of methyl (phenyl 4,5,7,8,9-penta-*O*-acetyl-3-deoxy-2-thio-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate, its β-anomer then isolated by silica gel chromatography with hexane/EtOAc (2:1 - 5:3 v/v). To a solution of thiophenyl derivative **1**[9] (3.50 g, 6.0 mmol) in MeOH (40 mL) was added 1.0 M NaOMe/MeOH soulution until the solution was adjusted to pH 9.0, and the mixture was stirred at 0 °C. After 2 h, the mixture was neutralized with Dowex 50W-X8 (H^+ form) and then filtered. After concentration of the filtrate, purification of the residue on a column of silica gel with $CHCl_3$/MeOH (5:1 v/v) afforded **2** (2.1 g, 94 %): $[\alpha]_D^{26}$ - 205.8 ° (*c* 1.12, MeOH); IR (cm^{-1}): 3358, 2920, 1725, 1446, 1329, 1281, 1200, 1116; ^1H NMR (270 MHz, CD_3OD) δ 7.60 - 7.31 (m, 5H, SPh), 4.46 (dd, 1H, $J_{6,7}$ = 1.0 Hz, $J_{5,6}$ = 9.9 Hz, H-6), 3.96 (ddd, 1H, H-4), 3.87 (dd, 1H, H-7), 3.83 (dd, 1H, $J_{8,9'}$ = 2.6 Hz, H-9'), 3.72 (ddd, 1H, $J_{7,8}$ = 9.2 Hz, H-8), 3.66 (dd, 1H, $J_{9,9'}$ = 10.9 Hz, $J_{8,9}$ = 5.3 Hz, H-9), 3.51 (s, 3H, COOMe), 3.48 (dd, 1H, $J_{4,5}$ = 9.2 Hz, H-5), 2.59 (dd, 1H, $J_{3eq,4}$ = 5.0 Hz, H-3eq), 1.88 (dd, 1H, $J_{3ax,3eq}$ = 13.9 Hz, $J_{3ax,4}$ = 11.9 Hz, H-3ax).

Anal. Calcd for $C_{16}H_{22}O_8S$ (374.41): C, 51.33; H, 5.92. Found: C, 51.18; H, 6.02.

Methyl (Phenyl 3-deoxy-8,9-*O*-isopropylidene-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (3). To a solution of the thiophenyl derivative **2** (2.2 g, 5.88 mmol) in acetone (60 mL) containing 2,2-dimethoxypropane (3.0 mL) was added Dowex 50W-X8 (H^+ form, 2.4 g), and the mixture was stirred for 6 h at room temperature. After filtration, the filtrate was concentrated *in vacuo*. Purification of this residue on a column of silica gel with $CHCl_3$/MeOH (8:1 - 6:1 v/v) afforded **3** (2.3 g, 92%): $[\alpha]_D^{26}$ - 237.6 ° (*c* 0.86, MeOH); mp 149 - 151 °C (EtOH - hexane); IR (cm^{-1}); 3416, 2912, 1746, 1442, 1324, 1266, 1214; ^1H NMR (270 MHz, CD_3OD) δ 7.49 - 7.18 (m, 5H, SPh), 4.23 (dd, 1H, $J_{6,7}$ = 1.0 Hz, H-6), 4.07 (ddd, 1H, $J_{8,9}$ = 5.9 Hz, $J_{8,9'}$ = 6.3 Hz, H-8), 3.88 (ddd, 1H, H-4), 3.87 (m, 2H, H-9 and H-9'), 3.82 (dd, 1H, $J_{7,8}$ = 8.3 Hz, H-7), 3.46 (s, 3H, COOMe), 3.42 (dd, 1H, $J_{4,5}$ = 9.2 Hz, H-5), 2.52 (dd, 1H, $J_{3eq,4}$ = 4.6 Hz, H-3eq), 1.81 (dd, 1H, $J_{3ax,3eq}$ = 13.9 Hz, $J_{3ax,4}$ = 11.9 Hz, H-3ax), 1.31, 1.33 (each s, each 3H, 2 x CH_3).

Anal. Calcd for $C_{19}H_{26}O_8S$ (414.48): C, 55.06; H, 6.32. Found: C, 54.95; H, 6.16.

Methyl (Phenyl 4-*O*-*t*-butyldimethylsilyl-3-deoxy-8,9-*O*-isopropylidene-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (4). To a solution of acetonide **3** (800 mg, 1.93 mmol) in DMF (20 mL) were added *t*-butyldimethylsilyl chloride (407 mg, 2.7 mmol) and imidazole (171 mg, 2.51 mmol), and the mixture was stirred at room temperature. After 4 h, the mixture was diluted with ether

and washed with aq $NaHCO_3$ solution. After drying with $MgSO_4$, the organic phase was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (8:1 - 6:1 v/v) afforded **4** (896 mg, 88 %): $[\alpha]_D^{26}$ - 175.4 ° (*c* 1.01, $CHCl_3$); IR (cm^{-1}): 3448, 2932, 1734, 1440, 1374, 1257, 1212; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 - 7.16 (m, 5H, SPh), 4.38 (dd, 1H, $J_{6,7}$ = 1.5 Hz, $J_{5,6}$ = 9.8 Hz, H-6), 4.12 (ddd, 1H, H-4), 4.07 (dd, 1H, $J_{7,8}$ = 7.6 Hz, $J_{8,9'}$ = 5.8 Hz, $J_{8,9}$ = 6.1 Hz, H-8), 4.02 (dd, 1H, $J_{9,9'}$ = 8.6 Hz, H-9), 3.97 (bdd, 1H, H-7), 3.94 (dd, 1H, H-9'), 3.58 (ddd, 1H, $J_{4,5}$ = 8.9 Hz, $J_{5,OH}$ = 3.3 Hz, H-5), 3.54 (s, 3H, COOMe), 2.76 (d, 1H, 5-OH), 2.57 (dd, 1H, $J_{3eq,4}$ = 4.9 Hz, H-3eq), 2.35 (s, 1H, 7-OH), 1.96 (dd, 1H, $J_{3ax,3eq}$ = 13.7 Hz, $J_{3ax,4}$ = 11.6 Hz, H-3ax), 1.45, 1.41 (each s, each 3H, 2 x CH_3), 0.91 (s, 9H, Si*t*Bu), 0.16, 0,15 (each s, each 3H, $Si(CH_3)_2$).

Anal. Calcd for $C_{25}H_{40}O_8SSi$ (528.74): C, 56.79; H, 7.63. Found: C, 56.88; H, 7.51.

Methyl (Phenyl 5,7-di-*O*-acetyl-4-*O*-*t*-butyldimethylsilyl-3-deoxy-8,9-*O*-isopropylidene-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (5). To a solution of silyl derivative **4** (100 mg, 0.19 mmol) in pyridine (2.0 mL) was added acetic anhydride (2.0 mL), and the mixture was stirred at room temperature. After 3 h, the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (3:1 - 1:1 v/v) afforded **5** (106 mg, 92 %): $[\alpha]_D^{26}$ - 95.7 ° (*c* 0.93, $CHCl_3$); IR (cm^{-1}): 2932, 1743, 1464, 1371, 1233, 1131; ^1H NMR (270 MHz, $CDCl_3$) δ 7.50 - 7.30 (m, 5H, SPh), 5.43 (dd, 1H, H-7), 4.86 (dd, 1H, H-5), 4,50 (dd, 1H, $J_{6,7}$ = 2.3 Hz, $J_{5,6}$ = 10.2 Hz, H-6), 4.21 (ddd, 1H, $J_{4,5}$ = 9.2 Hz, H-4), 4.01 (ddd, 1H, $J_{7,8}$ = 4.0 Hz, H-8), 3.82 (dd, 1H, $J_{8,9'}$ = 6.9 Hz, H-9'), 3.60 (s, 3H, COOMe), 3.58 (dd, 1H, $J_{9,9'}$ = 9.2 Hz, $J_{8,9}$ = 6.9 Hz, H-9), 2.59 (dd, 1H, $J_{3ax,3eq}$ = 14.2 Hz, $J_{3eq,4}$ = 4.6 Hz, H-3eq), 2.08 (dd, 1H, $J_{3ax,4}$ = 11.2 Hz, H-3ax), 2.05, 2.06 (each s, each 3H, 2 x OAc), 1.30, 1.31 (each s, each 3H, $C(CH_3)_2$), 0.85 (s, 9H, Si*t*Bu), 0.07, 0,09 (each s, each 3H, $Si(CH_3)_2$).

Anal. Calcd for $C_{29}H_{44}O_{10}SSi$ (612.81): C, 56.84; H, 7.24. Found: C, 57.05; H, 6.88.

Methyl (Phenyl 5,7-di-*O*-acetyl-3-deoxy-8,9-*O*-isopropylidene-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (6). To a solution of silyl derivative **5** (100 mg, 0.16 mmol) in THF (4.0 mL) was added *n*-Bu4NF (57 mL, 0.20 mmol), and the mixture was stirred at room temperatre. After 3 h, the mixture was diluted with CH_2Cl_2 and washed with aq NH_4Cl solution and then H_2O. After drying with $MgSO_4$, the organic phase was concentrated *in vacuo*. Purification of this residue on a column of silica gel with $CHCl_3$/Acetone (12:1 v/v) afforded **6** (57 mg, 70 %) and methyl (phenyl 4,7-di-*O*-acetyl-3-deoxy-8,9-*O*-isopropylidene-2-thio-β-D-*glycero*-D-*galacto*-2-

nonulopyranosid)onate (23 mg, 28 %). **6**: $[\alpha]_D^{26}$ - 142.8 ° (*c* 1.14, $CHCl_3$); IR (cm^{-1}): 3472, 2974, 1740, 1440, 1374, 1242, 1125; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49 - 7.32 (m, 5H, SPh), 5.47 (dd, 1H, $J_{6,7}$ = 1.8 Hz, H-7), 4.60 (dd, 1H, $J_{4,5}$ = 8.9 Hz, H-5), 4.55 (dd, 1H, $J_{5,6}$ = 10.1 Hz, H-6), 4.22 (m, 1H, H-4), 4.04 (ddd, 1H, $J_{7,8}$ = 4.3 Hz, H-8), 3.81 (dd, 1H, $J_{8,9'}$ = 6.7 Hz, H-9'), 3.60 (s, 3H, COOMe), 3.60 (dd, 1H, $J_{9,9'}$ = 9.2 Hz, $J_{8,9}$ = 6.4 Hz, H-9), 2.78 (dd, 1H, $J_{3eq,4}$ = 4.9 Hz, H-3eq), 2.70 (d, 1H, $J_{4,OH}$ = 5.5 Hz, 4-OH), 2.07, 2.14 (each s, each 3H, 2 x OAc), 2.03 (dd, 1H, $J_{3ax,3eq}$ = 14.0 Hz, $J_{3ax,4}$ = 11.9 Hz, H-3ax), 1.32, 1.33 (each s, each 3H, $C(CH_3)_2$).

Anal. Calcd for $C_{23}H_{30}O_{10}S$ (498.55): C, 55.41; H, 6.07. Found: C, 55.64; H, 6.17.

Methyl (Phenyl 4,7-di-*O*-acetyl-3-deoxy-8,9-*O*-isopropylidene-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate: $[\alpha]_D^{26}$ - 86.4 ° (*c* 0.54 $CHCl_3$); IR (cm^{-1}): 3502, 2944, 1737, 1440, 1374, 1242, 1140; ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 - 7.32 (m, 5H, SPh), 5.41 (dd, 1H, $J_{6,7}$ = 1.8 Hz, $J_{7,8}$ = 4.6 Hz, H-7), 5.38 (dd, 1H, H-4), 4.40 (dd, 1H, $J_{5,6}$ = 9.8 Hz, H-6), 4.08 (ddd, 1H, H-8), 3.83 (dd, 1H, $J_{8,9'}$ = 6.4 Hz, H-9'), 3.63 (dd, 1H, $J_{9,9'}$ = 9.2 Hz, $J_{8,9}$ = 6.7 Hz, H-9), 3.61 (s, 3H, COOMe), 3.43 (bs, 1H, 5-OH), 3.28 (bdd, 1H, $J_{4,5}$ = 9.2 Hz, H-5), 2.75 (dd, 1H, $J_{3eq,4}$ = 4.9 Hz, H-3eq), 2.16, 2.10 (each s, each 3H, 2 x OAc), 1.95 (dd, 1H, $J_{3ax,3eq}$ = 14.0 Hz, $J_{3ax,4}$ = 11.6 Hz, H-3ax), 1.36, 1.33 (each s, each 3H, $C(CH_3)_2$).

Anal. Calcd for $C_{23}H_{30}O_{10}S$ (498.55): C, 55.41; H, 6.07. Found: C, 55.84; H, 6.45.

Methyl (Phenyl 7-*O*-benzoyl-4-*O*-*t*-butyldimethylsilyl-3-deoxy-8,9-*O*-isopropylidene-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (7). To a solution of silyl derivative **4** (*100* mg, *0.18* mmol) in CH_2Cl_2 (*5.0* mL) were added benzoyl chloride (109 mL, 0.90 mmol) and pyridine (152 mL), and the mixture was stirred at - 40 °C. After 6 h, the mixture was diluted with EtOAc and washed with aq $NaHCO_3$ solution and water. After drying with $MgSO_4$, the organic phase was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:3 - 1:2 v/v) afforded **7** (112 mg, 93 %): $[\alpha]_D^{26}$ - 24.0 ° (*c* 0.80, $CHCl_3$); IR (cm^{-1}): 3508, 2950, 1731, 1452, 1440, 1374, 1266; ^1H NMR (270 MHz, $CDCl_3$) δ 8.06 - 7.30 (m, 10H, SPh and COPh), 5.71 (dd, 1H, $J_{7,8}$ = 4.0 Hz, H-7), 4.40 (dd, 1H, $J_{6,7}$ = 1.7 Hz, $J_{5,6}$ = 9.6 Hz, H-6), 4.18 (2 x ddd, 2H, H-4 and H-8), 4.06 (dd, 1H, $J_{8,9'}$ = 6.1 Hz, H-9'), 3.66 (dd, 1H, $J_{9,9'}$ = 8.9 Hz, $J_{8,9}$ = 6.6 Hz, H-9), 3.63 (s, 3H, COOMe), 3.32 (d, 1H, $J_{5,OH}$ = 3.6 Hz, 5-OH), 3.17 (ddd, 1H, $J_{4,5}$ = 9.2 Hz, H-5), 2.54 (dd, 1H, $J_{3eq,4}$ = 5.0 Hz, H-3eq), 1.90 (dd, 1H, $J_{3ax,3eq}$ = 14.2 Hz, $J_{3ax,4}$ = 11.6 Hz, H-3ax), 1.26, 1.31 (each s, each 3H, $C(CH_3)_2$), 0.88 (s, 9H, Si*t*Bu), 0.13 (s, 6H, $Si(CH_3)_2$).

Anal. Calcd for $C_{32}H_{44}O_9SSi$ (632.85): C, 60.73; H, 7.01. Found: C, 61.15; H, 6.76.

Methyl (Phenyl 7-*O*-benzoyl-4-*O*-*t*-butyldimethylsilyl-3-deoxy-8,9-*O*-isopropylidene-5-*O*-methoxymethyl-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (8). To a solution of the 5-hydroxyl derivative **7** (130 mg, 0.21 mmol) and Molecular Sieves 4A (100 mg) in CH_2Cl_2 (2.0 mL) were added dimethoxymethane (1.0 mL) and a catalytic amount of P_2O_5, and the mixture was stirred at 0 °C. After 3 h, the mixture was diluted with CH_2Cl_2 and washed with aq $NaHCO_3$ solution and water. After drying with $MgSO_4$, the organic phase was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:3 - 1:2 v/v) afforded **8** (88 mg, 63 %): $[\alpha]_D^{26}$ - 77.5 ° (*c* 1.06, $CHCl_3$); IR (cm^{-1}): 2950, 1728, 1452, 1383, 1260, 1200; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 - 7.31 (m, 10H, SPh and COPh), 5.77 (dd, 1H, $J_{7,8}$ = 4.9 Hz, H-7), 4.75, 4.72 (each d, 2H, $J_{A,B}$ = 5.5 Hz, OCH_2OCH_3), 4.49 (dd, 1H, $J_{6,7}$ = 1.2 Hz, H-6), 4.26 (ddd, 1H, H-4), 4.25 (ddd, 1H, H-8), 4.02 (dd, 1H, $J_{8,9'}$ = 6.7 Hz, H-9'), 3.68 (dd, 1H, $J_{9,9'}$ = 9.2 Hz, $J_{8,9}$ = 6.1 Hz, H-9), 3.59 (s, 3H, COOMe), 3.45 (s, 3H, OCH_3), 3.27 (dd, 1H, $J_{4,5}$ = 7.9 Hz, $J_{5,6}$ = 9.8 Hz, H-5), 2.53 (dd, 1H, $J_{3eq,4}$ = 4.3 Hz, H-3eq), 2.01 (dd, 1H, $J_{3ax,3eq}$ = 14.0 Hz, $J_{3ax,4}$ = 11.0 Hz, H-3ax), 1.28, 1.35 (each s, each 3H, $C(CH_3)_2$), 0.85 (s, 9H, Si*t*Bu), 0.11, 0.12 (each s, each 3H, $Si(CH_3)_2$).

Anal. Calcd for $C_{34}H_{48}O_{10}SSi$ (676.90): C, 60.33; H, 7.15. Found: C, 60.19; H, 7.16.

Methyl (Phenyl 4-*O*-*t*-butyldimethylsilyl-3-deoxy-8,9-*O*-isopropylidene-5-*O*-methoxymethyl-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (9). To a solution of **8** (91 mg, 0.14 mmol) in MeOH (4.0 mL) was added NaOMe (22 mg, 0.41 mmol), and the mixture was stirred at room temperature. After 12 h, the mixture was neutralized with Dowex 50W-X8 (H^+ form) and filtered. The filtrate was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:2 v/v) afforded **9** (78 mg, 95 %): $[\alpha]_D^{26}$ - 185.3 ° (*c* 0.99, $CHCl_3$); IR (cm^{-1}): 3448, 2950, 1737, 1440, 1383, 1257, 1209, 1131; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 - 7.27 (m, 5H, SPh), 4.93, 4.71 (each d, 2H, $J_{A,B}$ = 6.1 Hz, OCH_2OCH_3), 4.39 (dd, 1H, $J_{5,6}$ = 9.8 Hz, $J_{6,7}$ = 1.2 Hz, H-6), 4.21 (ddd, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 4.11 (ddd, 1H, $J_{7,8}$ = 6.4 Hz, $J_{8,9}$ = 5.8 Hz, H-8), 4.03 (dd, 1H, $J_{8,9'}$ = 6.4 Hz, H-9'), 3.98 (ddd, 1H, $J_{7,OH}$ = 8.24 Hz, H-7), 3.96 (dd, 1H, $J_{9,9'}$ = 8.9 Hz, H-9), 3.56 (dd, 1H, H-5), 3.48 (s, 3H, COOMe), 3.45 (s, 3H, OCH_3), 2.84 (d, 1H, 7-OH), 2.57 (dd, 1H, $J_{3eq,4}$ = 4.9 Hz, $J_{3ax,3eq}$ = 14.0 Hz, H-3eq), 2.01 (dd, 1H, $J_{3ax,4}$ = 11.3 Hz, H-3ax), 1.45, 1.42 (each s, each 3H, $C(CH_3)_2$), 0.90 (s, 9H, Si*t*Bu), 0.14, 0.13 (each s, each 3H, $Si(CH_3)_2$).

Anal. Calcd for $C_{27}H_{44}O_9SSi$ (572.79): C, 56.62; H, 7.74. Found: C, 56.86; H, 7.77.

Methyl (Phenyl 4,5,7-tri-*O*-acetyl-8,9-*O*-isopropylidene-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (10). To a solution of acetonide **3** (552 mg, 1.33 mmol) in pyridine (3.0 mL) was added acetic anhydride (5.0 mL), and the mixture was stirred at room temperature. After 3 h, the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane(1:1 v/v) afforded **10** (677 mg, 94 %): $[\alpha]_D^{26}$ - 125.3 ° (*c* 1.02, $CHCl_3$); IR (cm^{-1}): 2986, 1743, 1440, 1371, 1233; ^1H NMR (270 MHz, $CDCl_3$) δ 7.53 - 7.28 (m, 5H, SPh), 5.46 (dd, 1H, $J_{6,7}$ = 2.3 Hz, H-7), 5.45 (ddd, 1H, $J_{4,5}$ = 9.6 Hz, H-4), 4.90 (dd, 1H, H-5), 4.62 (dd, 1H, $J_{5,6}$ = 9.9 Hz, H-6), 3.99 (ddd, 1H, $J_{7,8}$ = 4.0 Hz, H-8), 3.81 (dd, 1H, $J_{8,9'}$ = 6.9 Hz, H-9'), 3.62 (s, 3H, COOMe), 3.60 (dd, 1H, $J_{9,9'}$ = 8.9 Hz, $J_{8,9}$ = 6.6 Hz, H-9), 2.77 (dd, 1H, $J_{3eq,4}$ = 5.0 Hz, $J_{3ax,3eq}$ = 13.9 Hz, H-3eq), 2.11 (dd, 1H, $J_{3ax,3eq}$ = 11.6 Hz, H-3ax), 2.02, 2.04, 2.07 (each s, each 3H, 3 x OAc), 1.31, 1.32 (each s , each 3H, $C(CH_3)_2$).

Anal. Calcd for $C_{25}H_{32}O_{11}S$ (540.59): C, 55.55; H, 5.97. Found: C, 55.52; H, 5.93.

Methyl (Phenyl 4,5,7-tri-*O*-acetyl-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (11). A solution of acetonide **10** (350 mg, 0.65 mmol) in 70 % acetic acid (5.0 mL) was stirred at 60 °C. After 2 h, the mixture was diluted with EtOAc and washed with aq $NaHCO_3$ solution and water. After drying with $MgSO_4$, the organic phase was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:1 - 2:1 v/v) afforded **11** (307 mg, 95 %): $[\alpha]_D^{26}$ - 126.0 ° (*c* 1.10, $CHCl_3$); IR (cm^{-1}): 3490, 2950, 1737, 1440, 1371, 1245; ^1H NMR (270 MHz, $CDCl_3$) δ 7.63 - 7.30 (m, 5H, SPh), 5.03 (dd, 1H, $J_{5,6}$ = 9.9 Hz, $J_{4,5}$ = 9.6 Hz, H-5), 4.89 (d, 2H, H-6 and H-7), 4.45 (m, 1H, H-4), 3.88 (m, 1H, H-8), 3.66 (m, 1H, H-9'), 3.55 (s, 3H, COOMe), 3.48 (dd, 1H, $J_{9,9'}$ = 12.5, $J_{8,9}$ = 3.0 Hz, H-9), 2.83 (dd, 1H, $J_{3ax,3eq}$ = 13.9 Hz, $J_{3eq,4}$ = 5.0 Hz, H-3eq), 2.43 - 2.68 (m, 2H, 8-OH and 9-OH), 2.10 (m, 1H, H-3ax), 2.03, 2.06, 2.15 (each s, each 3H, 3 x OAc).

Anal. Calcd for $C_{22}H_{28}O_{11}S$ (500.52): C, 52.79; H, 5.64. Found: C, 52.62; H, 5.89.

Methyl (Phenyl 4,5,7-tri-*O*-acetyl-9-*O*-*t*-butyldimethylsilyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (12). To a solution of **11** (320 mg, 0.64 mmol) in pyridine (10.0 mL) was added *t*-butyldimethylsilyl chloride (145 mg, 0.96 mmol), and the mixture was stirred at room temperature. After 12 h, to this mixture was added MeOH (2.0 mL), and then the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (3:1 - 2:1 v/v) afforded **12** (358 mg, 91 %): $[\alpha]_D^{26}$ - 77.4 ° (*c* 1.04, $CHCl_3$); IR (cm^{-1}): 3514, 2944, 1737, 1470, 1368, 1242; ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 - 7.17 (m, 5H, SPh), 5.43

(ddd, 1H, $J_{4,5}$ = 10.1 Hz, $J_{5,6}$ = 9.8 Hz, H-4), 5.22 (dd, 1H, $J_{6,7}$ = 1.5 Hz, $J_{7,8}$ = 7.3 Hz, H-7), 4.92 (dd, 1H, H-5), 4.89 (dd, 1H, H-6), 3.94 (bddd, 1H, H-8), 3.65 (dd, 1H, $J_{9,9'}$ = 10.4 Hz, $J_{8,9}$ = 4.5 Hz, H-9), 3.55 (dd, 1H, $J_{8,9'}$ = 6.1 Hz, H-9'), 3.55 (s, 3H, COOMe), 2.82 (bs, 1H, 8-OH), 2.77 (dd, 1H, $J_{3ax,3eq}$ = 13.8 Hz, $J_{3eq,4}$ = 4.9 Hz, H-3eq), 2.11 (dd, 1H, $J_{3ax,4}$ = 11.6 Hz, H-3ax), 2.09, 2.04, 2.01 (each s, each 3H, 3 x OAc), 0.92 (s, 9H, Si*t*Bu), 0.67, 0.60 (each s, each 3H, $Si(CH_3)_2$).

Anal. Calcd for $C_{28}H_{42}O_{11}SSi$ (614.79): C, 54.70; H, 6.89. Found: C, 54.99; H, 6.83.

Methyl (Phenyl 4,5,7,9-tetra-*O*-acetyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (13). Method I (from 11): To a solution of acetyl derivative **11** (720 mg, 1.44 mmol) in CH_2Cl_2 was added a solution of AcCl (0.2 mL, 2.82 mmol) in pyridine (0.46 mL), and the mixture was stirred - 40 °C. After 10 min, to this solution was added MeOH (5.0 mL), and the mixture was stirred at room temperature. After 1 h, the mixture was diluted with EtOAc and washed with aq $NaHCO_3$ solutiuon and water. After drying with $MgSO_4$, the organic phase was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:1 - 2:1 v/v) afforded **13** (728 mg, 93 %). **Method II (from 15)**: A solution of acetonide **15** (125 mg, 0.19 mmol) in 80 % acetic acid (3.0 mL) was stirred at room temperature. After 24 h, the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:1 v/v) afforded **13** (83 mg, 82 %) and **16** (14 mg, 12%), respectively. **13**: $[\alpha]_D^{26}$ - 105.4 ° (*c* 0.83, $CHCl_3$); IR (cm^{-1}): 3472, 2956, 1743, 1431, 1371, 1233; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 - 7.33 (m, 5H, SPh), 5.46 (ddd, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.15 (dd, 1H, $J_{7,8}$ = 6.7 Hz, H-7), 4.96 (dd, 1H, H-5), 4.78 (dd, 1H, $J_{5,6}$ = 10.4 Hz, $J_{6,7}$ = 2.1 Hz, H-6), 4.15 (dd, 1H, $J_{8,9'}$ = 3.1 Hz, H-9'), 4.08 (dd, 1H, $J_{8,9}$ = 5.8 Hz, $J_{9,9'}$ = 11.6 Hz, H-9), 4.03 (dddd, 1H, H-8), 3.62 (s, 3H, COOMe), 2.76 (dd, 1H, $J_{3ax,3eq}$ = 14.0 Hz, $J_{3eq,4}$ = 4.9 Hz, H-3eq), 2.56 (d, 1H, $J_{8,OH}$ = 7.0 Hz, 8-OH), 2.11 (dd, 1H, $J_{3ax,4}$ = 11.6 Hz, H-3ax), 2.02, 2.05, 2.08, 2.09 (each s, each 3H, 4 x OAc).

Anal. Calcd for $C_{24}H_{30}O_{12}S$ (542.56): C, 53.13; H, 5.57. Found: C, 53.26; H, 5,62.

Methyl (Phenyl 9-*O*-*t*-butyldimethylsilyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (14). To a solution of **2** (300 mg, 0.80 mmol) in pyridine (10.0 mL) was added *t*-butyldimethylsilyl chloride (181 mg, 1.20 mmol), and the mixture was stirred at room temperature. After 12 h, to this solution was added MeOH (1.20 mL), and then the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (3:1 - 2:1 v/v) afforded **14** (361 mg, 92 %): mp 148 - 147 °C (EtOH - hexane); $[\alpha]_D^{26}$ - 154.9 ° (*c* 1.04, MeOH); IR (cm^{-1}): 3424, 2926,

1728, 1461, 1362, 1296, 1254, 1113; ^{1}H NMR (270 MHz, CD_3OD) δ 7.55 - 7.26 (m, 5H, SPh), 4.43 (dd, 1H, $J_{5,6}$ = 9.9 Hz, $J_{6,7}$ = 1.0, H-6), 3.92 (ddd, 1H, H-4), 3.89 (dd, 1H, $J_{8,9'}$ = 2.3 Hz, H-9'), 3.86 (dd, 1H, H-7), 3.74 (dd, 1H, $J_{8,9}$ = 5.3 Hz, $J_{9,9'}$ = 10.2 Hz, H-9), 3.67 (ddd, 1H, $J_{7,8}$ = 9.2 Hz, H-8), 3.49 (s, 3H, COOMe), 3.44 (ddd, 1H, $J_{4,5}$ = 9.2 Hz, H-5), 2.56 (dd, 1H, $J_{3eq,4}$ = 5.0 Hz, H-3eq), 1.85 (dd, 1H, $J_{3ax,3eq}$ = 13.9 Hz, $J_{3ax,4}$ = 11.9 Hz, H-3ax), 0.90 (s, 9H, Si*t*Bu), 0.07 (s, 6H, $Si(CH_3)_2$).

Anal. Calcd for $C_{22}H_{36}O_8SSi$ (488.68): C, 54.07; H, 7.43. Found: C, 54.25; H, 7.37.

Methyl (Phenyl 4,5,7,8-tetra-*O*-acetyl-9-*O*-*t*-butyldimethylsilyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (15). To a solution of silyl derivative **14** (225 mg, 0.46 mmol) in pyridine (3.0 mL) was added acetic anhydride (2.0 mL) at room temperature. After 5 h, the mixture was diluted with EtOAc and washed with aq $NaHCO_3$ solution and water. After drying with $MgSO_4$, the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:3 - 1:1 v/v) afforded **15** (291 mg, 96 %): $[\alpha]_D^{26}$ - 58.8 ° (*c* 0.69, $CHCl_3$); IR (cm^{-1}): 2932, 1740, 1437, 1368, 1236; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.51 - 7.31 (m, 5H, SPh), 5.50 (dd, 1H, H-7), 5.42 (ddd, 1H, $J_{3ax,4}$ = 11.5 Hz, $J_{4,5}$ = 9.6 Hz, H-4), 5.05 (ddd, 1H, $J_{8,9}$ = 6.6 Hz, $J_{7,8}$ = 4.6 Hz, H-8), 4.89 (dd, 1H, H-5), 4.76 (dd, 1H, $J_{5,6}$ = 10.2 Hz, $J_{6,7}$ = 2.3 Hz, H-6), 3.98 (dd, 1H, $J_{8,9'}$ = 3.3 Hz, $J_{9,9'}$ = 11.6 Hz, H-9'), 3.58 (dd, 1H, H-9), 3.58 (s, 3H, COOMe), 2.70 (dd, 1H, $J_{3ax,3eq}$ = 13.9 Hz, $J_{3eq,4}$ = 4.9 Hz, H-3eq), 2.07 (m, 1H, H-3ax), 2.01, 2.05, 2.06, 2.08 (each s, each 3H, 4 x OAc), 0.87 (s, 9H, Si*t*Bu), 0.00, 0.01 (each s, each 3H, $Si(CH_3)_2$).

Anal. Calcd for $C_{30}H_{44}O_{12}SSi$ (656.82): C, 54.86; H, 6.75. Found: C, 54.89; H, 6.68.

Methyl (Phenyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (16). A solution of compound **15** (200 mg, 0.30 mmol) in AcOH/THF/H_2O (3:1:1 v/v/v, 10 mL) was stirred at room temperture. After 20 h, the mixture was diluted with EtOAc, and washed with aq $NaHCO_3$ solution and water, thoroughly. After drying with $MgSO_4$, the organic phase was concentrated *in vacuo*. Purification of this residue on a short column of silica gel with EtOAc/hexane (1:1 v/v) afforded **16** (126 mg, 76 %): $[\alpha]_D^{27}$ -108.2 ° (*c* 0.73, $CHCl_3$); IR (cm^{-1}): 3523, 1748; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 - 7.29 (m, 5H, SPh), 5.45 (ddd, 1H, $J_{3eq,4}$ = 4.9 Hz , $J_{3ax,4}$ = 11.6 Hz, H-4), 5.39 (dd, 1H, $J_{6,7}$ = 2.4 Hz, H-7), 4.99 (dd, 1H, $J_{4,5}$ = $J_{5,6}$ = 10.1 Hz, H-5), 4.85 (ddd, 1H, $J_{7,8}$ = 4.9 Hz, $J_{8,9}$ = 4.6 Hz, H-8), 4.75 (dd, 1H, H-6), 3.92 (ddd, 1H, H-9), 3.67 (s, 3H, COOMe), 3.45 (ddd, 1H, $J_{8,9'}$ = 3.4 Hz, $J_{9,9'}$ = 11.3 Hz, H-9'), 2.72 (dd, 1H, $J_{3ax,3eq}$ = 14.0 Hz, H-3eq), 2.28 (dd, 1H,

$J_{9,OH}$ = $J_{9',OH}$ = 7.0 Hz, 9-OH), 2.06 (dd, 1H, H-3ax), 2.11, 2.06, 2.04, 2.01 (each s, each 3H, 4 x OAc).

Anal. Calcd for $C_{24}H_{30}O_{12}S$ (542.55): C, 53.13; H, 5.57. Found: C, 52.94; H, 5.69.

Methyl (Phenyl 9-*O*-triphenylmethyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (17). To a solution of **2** (84 mg, 0.22 mmol) in pyridine (1.0 mL) was added triphenylmethyl chloride (141 mg, 0.51 mmol), and the mixture was stirred at room temperature. After 17 h, to this solution was added MeOH (1.0 mL), and then the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (2:1 - 3:1 v/v) afforded **17** (134 mg, 97 %): mp 173.5 - 174.5 °C (EtOH - hexane); $[\alpha]_D^{27}$ - 134.4 ° (*c* 0.92, $CHCl_3$); IR (cm^{-1}): 3414, 1735; ^1H NMR (500 MHz, $CDCl_3$) δ 7.46 - 7.16 (m, 20H, SPh and CPh_3), 4.35 (d, 1H, H-6), 4.27 (bs, 1H, 5-OH), 4.01 (ddd, 1H, $J_{4,5}$ = 9.2 Hz, H-4), 3.95 (d, 1H, $J_{7,8}$ = 7.9 Hz, H-7), 3.86 (m, 1H, H-8), 3.79 (bs, 1H, 7-OH), 3.53 (dd, 1H, $J_{5,6}$ = 9.5 Hz, H-5) 3.45 (s, 3H, COOMe), 3.40 (bs, 1H, 4-OH), 3.40 (m, 1H, $J_{8,9'}$ = 5.8 Hz, H-9'), 3.34 (dd, 1H, $J_{8,9}$ = 6.1 Hz, $J_{9,9'}$ = 9.5 Hz, H-9), 2.92 (m, 1H, 8-OH), 2.58 (dd, 1H, $J_{3eq,4}$ = 4.6 Hz, $J_{3ax,3eq}$ = 13.7 Hz, H-3eq), 2.41 (bs, 1H, 9-OH), 2.18 (dd, 1H, $J_{3ax,4}$ = 12.2 Hz, H-3ax).

Anal. Calcd for $C_{35}H_{36}O_8S$ (616.72): C, 68.16; H, 5.88. Found: C, 68.20; H, 5.81.

Methyl (Phenyl 4,7,8-tri-*O*-benzyl-9-*O*-triphenylmethyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (18). To a solution of triphenylmethyl derivative **17** (119 mg, 0.19 mmol), barium oxide (702 mg, 4.58 mmol), and barium hydroxide octahydrate (130 mg, 0.41 mmol), in *N,N*-dimethylformamide (2.0 mL) was added benzyl bromide (0.55 mL, 4.6 mmol) and the mixture was stirred at room temperature. After 28 h, this mixture was concentrated *in vacuo*. The residue was diluted with $CHCl_3$ and washed with aq $NaHCO_3$ solution and water. After drying with $MgSO_4$, the mixture was concentrated *in vacuo*. A solution of the residue in MeOH (2.0 mL) was treated with diazomethane, and stirred at room temperature. After 1 h, to this solution was added acetic acid (0.2 mL), and then the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:10 - 1:4 v/v) afforded **18** (123 mg, 71 %) and tetra-*O*-benzyl derivative **19** (27 mg, 14%), respectively. **18**: $[\alpha]_D^{27}$ - 25.5 ° (*c* 0.83, $CHCl_3$); IR (cm^{-1}): 3491, 1736; ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 - 7.05 (m, 35H, SPh, CPh_3 and -CH_2-*Ph*), 4.76, 4.71 (each d, 2H, $J_{A,B}$ = 10.6 Hz, -CH_2-Ph), 4.56 (dd, 1H, $J_{5,6}$ = 9.8 Hz, $J_{6,7}$ = 2.8 Hz, H-6), 4.55, 4.47 (each d, 2H, $J_{A,B}$ = 11.3 Hz, -CH_2Ph), 4.47, 4.35 (each d, 2H, $J_{A,B}$ = 11.6 Hz, -CH_2-Ph), 4.18 (dd, 1H, $J_{7,8}$ = 7.6 Hz, H-7), 3.99 (ddd, 1H, $J_{8,9'}$ = 3.3 Hz, H-8), 3.88 (ddd, 1H,

$J_{4,5}$ = 8.9 Hz, H-4), 3.68 (dd, 1H, H-5), 3.67 (dd, 1H, H-9'), 3.56 (s, 3H, COOMe), 3.29 (dd, 1H, $J_{8,9}$ = 5.6 Hz, $J_{9,9'}$ = 10.1 Hz, H-9), 2.60 (dd, 1H, $J_{3eq,4}$ = 4.3 Hz, H-3eq), 2.44 (bs, 1H, 5-OH), 1.83 (dd, 1H, $J_{3ax,4}$ = 11.3 Hz, $J_{3ax,3eq}$ = 14.0 Hz, H-3ax).

Anal. Calcd for $C_{56}H_{54}O_8S$ (887.09): C, 75.82; H, 6.14. Found: C, 75.72; H, 6.35.

Methyl (Phenyl 4,5,7,8-tetra-*O*-benzyl-9-*O*-triphenylmethyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (19). Method I (from 18): To a solution of **18** (35 mg, 39 μmol) in *N*,*N*-dimethylformamide (2.0 mL), sodium hydride (55% in oil, 10 mg, 0.23 mmol) was added and stirred at room temperature. After 1 h, to the mixture was added benzyl bromide (20 μL, 0.17 mmol) and stirred at room temperature. After 28 h, this mixture was concentrated *in vacuo*. The residue was diluted with $CHCl_3$ and washed with aq NH_4Cl solution and water. After drying with $MgSO_4$, the mixture was concentrated *in vacuo*. A solution of this residue in MeOH (2.0 mL) was treated with diazomethane, and stirred at room temperature. After 1 h, to this solution was added acetic acid (0.2 mL), and then the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:10 - 1:4 v/v) afforded **19** (36 mg, 93 %). **Method II (from 17)**: To a solution of triphenylmethyl derivative **17** (50 mg, 81 μmol) in *N*,*N*-dimethylformamide (2.0 mL), sodium hydride (55% in oil, 51 mg, 1.17 mmol) was added and stirred at room temperature. After 1 h, to the mixture was added benzyl bromide (0.21 mL, 0.18 mmol) and stirred at room temperature. After 24 h, to the mixture was added MeONa/MeOH (2 mL) and stirred at room temperature. After 1h, this mixture was diluted with $CHCl_3$ and washed with aq NH_4Cl solution and water. After drying with $MgSO_4$, the mixture was concentrated *in vacuo*. A solution of this residue in MeOH (2.0 mL) was treated with diazomethane, and stirred at room temperature. After 1 h, to this solution was added acetic acid (0.2 mL), and then the mixture was concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:10 - 1:4 v/v) afforded **19** (36 mg, 45 %) and by-product **20** (23 mg, 33 %), respectively. **19**: $[\alpha]_D^{27}$ - 35.1 ° (*c* 0.53, $CHCl_3$); IR (cm^{-1}): 3414, 1734; ^1H NMR (270 MHz, $CDCl_3$) δ 7.53 - 6.95 (m, 40H, SPh, CPh_3 and -CH_2-*Ph*)), 4.93, 4.34 (each d, 2H, $J_{A,B}$ = 11.2 Hz, -CH_2-Ph), 4.76, 4.71 (each d, 2H, $J_{A,B}$ = 12.2 Hz, -CH_2-Ph), 4.62 (1H, dd, $J_{5,6}$ = 9.6 Hz, $J_{6,7}$ = 2.0 Hz, H-6), 4.48, 4.40 (each d, 2 x 2H, $J_{A,B}$ = 11.2 Hz, 2 x -CH_2-Ph), 4.35 (dd, 1H, $J_{7,8}$ = 7.2 Hz, H-7), 4.12 (ddd, 1H, $J_{4,5}$ = 9.9 Hz, H-4), 3.99 (ddd, 1H, H-8), 3.71 (dd, 1H, $J_{8,9'}$ = 4.6 Hz, H-9'), 3.69 (dd, 1H, H-5), 3.53 (s, 3H, COOMe), 3.31 (dd, 1H, $J_{8,9}$ = 1.9 Hz, $J_{9,9'}$ = 10.2 Hz, H-9), 2.61 (dd, 1H, $J_{3eq,4}$ = 4.3 Hz, H-3eq), 2.01 (dd, 1H, $J_{3ax,4}$ = 10.6 Hz, $J_{3ax,3eq}$ = 14.2 Hz, H-3ax).

Anal. Calcd for $C_{63}H_{60}O_8S$ (977.21): C,77.43; H, 6.91. Found: C, 77.32; H, 6.34.

20: $[\alpha]_D^{27}$ 20.6 ° (*c* 0.65, $CHCl_3$); IR (cm^{-1}): 1491, 1449; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 - 7.04 (m, 20H, SPh), 4.70, 4.59 (each d, 2H, $J_{A,B}$ = 11.6 Hz, -C*H*$_2$-Ph), 4.66, 4.33 (each d, 2H, $J_{A,B}$ = 11.3 Hz, -C*H*$_2$-Ph), 4.62, 4.43 (each d, 2H, $J_{A,B}$ = 11.3 Hz, -C*H*$_2$-Ph), 4.45 (1H, dd, H-4), 4.38 (bs, 1H, H-6), 3.87 (d, 1H, $J_{7,8}$ = 9.2 Hz, H-7), 3.54 (d, 1H, $J_{4,5}$ = 4.9 Hz, H-5), 3.30 (dd, 1H, $J_{8,9'}$ = 1.8 Hz, $J_{9,9'}$ = 10.1 Hz, H-9'), 3.26 (ddd, 1H, $J_{8,9}$ = 4.0 Hz, H-8), 2.92 (dd, 1H, H-9), 2.52 (d, 1H, $J_{3eq,4}$ = 4.6 Hz, H-3eq), 2.04 (dd, 1H, $J_{3ax,4}$ = 5.8 Hz, $J_{3ax,3eq}$ = 11.9 Hz, H-3ax); ^{13}C NMR (127 MHz, $CDCl_3$) δ 91.9 (C1), 86.2 (C2), 77.4 (C8), 77.4 (C5), 74.0 (C4), 72.4 (-*C*H$_2$-Ph), 72.4 (C7), 71.8 (C6), 71.4 (-*C*H$_2$-Ph), 64.7 (-*C*H$_2$-Ph), 61.8 (C9), 36.2 (C3).

HRFABMS: Calcd for $C_{55}H_{50}O_7SNa$, 877.31753 $(M + Na)^+$; Found 877.31797.

Anal. Calcd for $C_{55}H_{50}O_7S$ (855.05): C, 77.26; H, 5.89. Found: C, 77.29; H, 5.84.

Methyl (Phenyl 4,5,7,8-tetra-*O*-benzyl-3-deoxy-2-thio-β-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (21). A solution of compound **19** (60 mg, 60 μmol) in MeOH/$CHCl_3$ (10:1 v/v, 5.5 mL) was refluxed with Dowex 50W-X8 (H^+ form) ion exchange resin (250 mg). After 12 h, the mixture was filtered and concentrated *in vacuo*. Purification of this residue on a column of silica gel with EtOAc/hexane (1:4 - 1:2 v/v) afforded **20** (41 mg, 91 %): $[\alpha]_D^{27}$ - 95.0 ° (*c* 0.56, $CHCl_3$); IR (cm^{-1}): 3525, 1738; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 - 7.21 (m, 25H, SPh and -CH_2-*Ph*)), 4.91, 4.36 (each d, 2H, $J_{A,B}$ = 11.3 Hz, -C*H*$_2$-Ph), 4.85, 4.50 (each d, 2H, $J_{A,B}$ = 11.6 Hz, -C*H*$_2$-Ph), 4.65 (s, 2H, -C*H*$_2$-Ph), 4.52, 4.61 (each d, 2H, $J_{A,B}$ = 11.3 Hz, -C*H*$_2$-Ph), 4.33 (dd, 1H, $J_{5,6}$ = 9.5 Hz, $J_{6,7}$ = 2.5 Hz, H-6), 4.28 (dd, 1H, $J_{7,8}$ = 2.5 Hz, H-7), 4.14 (ddd, 1H, $J_{4,5}$ = 8.6 Hz, H-4), 4.05 (ddd, 1H, $J_{8,9'}$ = 4.6 Hz, H-9'), 3.77 (dd, 1H, H-5), 3.70 (ddd, 1H, $J_{8,9}$ = 4.6 Hz, $J_{9,9'}$ = 12.2 Hz, H-9), 3.59 (ddd, 1H, H-8), 3.57 (s, 3H, COOMe), 2.76 (dd, 1H, $J_{3eq,4}$ = 4.3 Hz, H-3eq), 2.43 (dd, 1H, $J_{9,OH}$ = 6.8 Hz, $J_{9',OH}$ = 6.7 Hz, 9-OH), 2.03 (dd, 1H, $J_{3ax,4}$ = 11.3 Hz, $J_{3ax,3eq}$ = 14.0 Hz, H-3ax).

Anal. Calcd for $C_{44}H_{46}O_8S$ (734.90): C, 71.91; H, 6.31. Found: C, 71.83; H, 6.51.

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