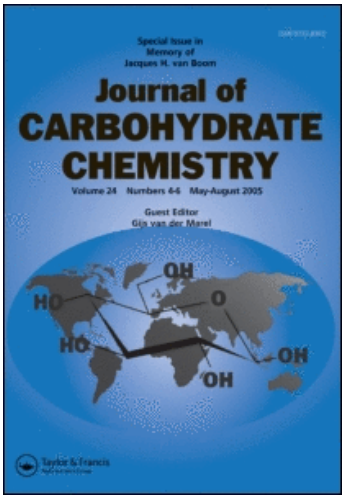


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Eike Kirchner[a]; Frauke Thiem[b]; Rudolt Dernick[b]; Jochen Heukeshoven[b]; Joachim Thieina[a]
[a] Organisch Chemisches institue der Westfalischen Wilheims-Universitat Munster, Munster, Fed. Rep. Germany [b] Hernrich-Pette-Institut Fur Experimentelle Virologie und Immunologie an der Universitat, Hamburg 20, Fed. Rep. Germany

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# STUDIES ON THE GLYCOSYLATION OF *N*-ACETYLNEURAMINIC ACID

Elke Kirchner,[a] Frauke Thiem,[b] Rudolf Dernick,[b]
Jochen Heukeshoven,[b] and Joachim Thiem[a]*

Organisch-Chemisches Institut der Westfälischen
Wilhelms-Universität Münster,[a] Orléans-Ring 23,
D-4400 Münster, Fed. Rep. Germany
and
Heinrich-Pette-Institut für Experimentelle Virologie
und Immunologie an der Universität Hamburg,[b]
Martinistraße 52, D-2000 Hamburg 20, Fed. Rep. Germany

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## ABSTRACT

Glycal derivatives of *N*-acetylneuraminic acid were prepared and their *N*-iodosuccinimide-mediated glycosylation shown to proceed only with most reactive alcohols. Their reduced enol ether reactivity is attributed to the $\alpha,\beta$-unsaturated ester feature. Thus several reduced glycal derivatives were synthesized. These could be glycosylated with simple alcohols as well as other saccharides as aglycones in average to modest yields with the trans-diaxial addition compounds prevailing. A number of selective and specific preparations led to both the anomeric phenylthioglycosides of *N*-acetylneuraminic acid. These could be used in phenylmercuric triflate-promoted glycosylations to afford several disaccharide derivatives.

## INTRODUCTION

Sialic acids represent a number of complex higher saccharides most of which are terminally bound to glycoproteins and glycolipids of various tissues in many, predominantly animal species.[1-3] *N*-Acetylneuraminic acid (**1**), the most prominent sialic acid, occurs mainly $\alpha,2\rightarrow3$- or $\alpha,2\rightarrow6$-glycosidically linked to the preterminal sugars such as

galactose, *N*-acetylgalactosamine, glucose or *N*-acetylglucosamine, at the non-reducing end of the glycoprotein chain.

Earlier glycosylations with *N*-acetylneuraminic acid derivatives allowed the preparation of simple glycosides.[4,5] Later more advanced Koenigs-Knorr variations made disaccharides available,[6-8] and subsequently also even larger entities[9-14] could be prepared. Another approach, which involves a Lewis acid-mediated glycosylation of glycosyl fluorides of **1**, has had approximately similar success to the previous methods.[15]

Usually the yields in glycosylations of this most complex sugar are modest, certainly considerably below the general standard. As frequently discussed, some of the unusually high yields given for the preparation of highly complex glycoprotein sugar portions could not be attained by others in corresponding, much simpler cases. Perhaps these discrepancies are due both to specific "know-how" as well as minor structural deviations. Furthermore, stereoselectivity in glycosylations represents another problem. The lack of a neighboring group adjacent to the anomeric center causes anomeric mixtures to form. Recent use of chemoenzymic approaches to *N*-acetylneuraminic acid glycosides[16,17] provides a new approach to the problems of yields and stereospecificity.

The research described in the present communication was commenced originally to study the *N*-iodosuccinimide mediated glycosylation of glycals[18] in the sialic acid series. This reaction has had considerable impact on the preparation of axially glycosylated 2-deoxy sugars (e.g., lit.[19]). Also, there was evidence that the conformational influence of certain substituents could be used effectively for an approach to equatorial anomers.[20] Thus, it was of particular interest to study the influence of carboxy groups adjacent to the anomeric center.

## RESULTS AND DISCUSSION

*N*-Acetylneuraminic acid (**1**) was obtained from oriental swallow nests[21] which contained approximately 5% of **1** as determined by Aminoff's test.[22] The hydrolysis and work-up

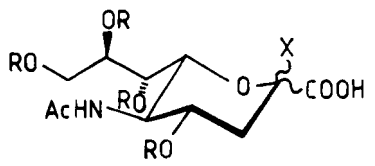
according to reference 23 gave **1** in approximately 4% yield. The preparation of the glycals of *N*-acetylneuraminic acid followed essentially the previously described procedure.[24] After peracetylation to give an anomeric mixture of **2**, the glycosyl chloride **3** was obtained conventionally using hydrogen chloride in acetic acid. Further treatment with triethylamine in dioxane gave the glycal **8**, which was saponified to give the unblocked derivative **10** (63% overall yield based on **3**).

In the acetylation step, **1** gave 52% of the peracetate **2** and ca. 8% of a crystalline side product, identified as the tetra-O-acetate of the 1,7-lactone **7** which adopted a $^5C_2$ conformation. This structural assignment depends upon the unusually small coupling constants throughout ($J_{3a,4}$ = 3.8, $J_{3b,4}$ = 3.2, $J_{4,5}$ = 2.2, $J_{5,6}$ = 2.0 Hz), which is in accord with all equatorial hydrogen atoms. The δ-lactone structure evidently is thermodynamically favored and probably formed via the $^5C_2$ conformation of the β-anomer of **1** by internal esterification.

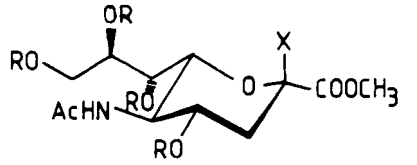
Another deviation from the previous studies[24] occurred in the alkaline hydrolysis step (**8** → **10**). In addition to the crystalline glycal derivative **10**, the $^1$H NMR spectrum of which in $D_2O$ can be fully assigned, another compound (**9**) was obtained in 22% yield (based on **3**). Except for the downfield chemical shift of H-4 (δ 5.67), not much difference between the spectra of **9** and **10** was observed. Obviously, compound **9** is the 4-O-monoacetate. Hydrolysis of the 4-O-acetyl group occurs with difficulty and thus **9** is a useful intermediate for regioselective transformations.

In contrast to the previous esterification of **10** with diazomethane, acid catalysed methylation to give the crystalline compound **11** was easier and preferred. Peracetylation led to the crystalline peracetate **12**, and its $^1$H NMR spectrum gave unequivocal evidence for the structure and the conformation as a $^6H_5$ half chair or half boat ($J_{5,6}$ = 10.0 Hz).

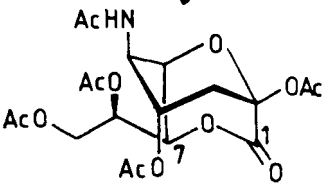
By an alternative route **1** was transformed into the methyl ester **4**[4] and peracetylated to give the β-anomer **5**.[5] Compound **5** reacted with titanium tetrachloride[10] to give



| | R | X |
|---|---|---|
| 1 | H | OH |
| 2 | Ac | OAc |
| 3 | Ac | Cl |



| | R | X |
|---|---|---|
| 4 | H | OH |
| 5 | Ac | OAc |
| 6 | Ac | Cl |



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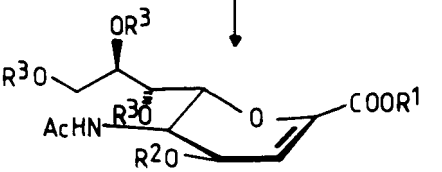
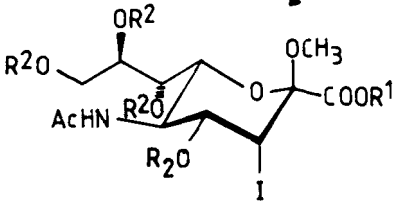
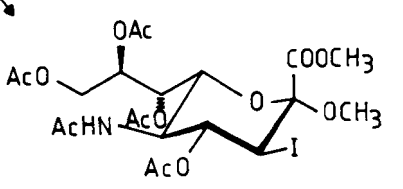


| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| 8 | H | Ac | Ac |
| 9 | H | Ac | H |
| 10 | H | H | H |
| 11 | $CH_3$ | H | H |
| 12 | $CH_3$ | Ac | Ac |
| 13 | $Bu_4N^{\oplus}$ | H | H |
| 14 | $Bu_4N^{\oplus}$ | Ac | Ac |





18

| | $R^1$ | $R^2$ |
|---|---|---|
| 15 | H | H |
| 16 | $CH_3$ | Ac |
| 17 | $Bu_4N^{\oplus}$ | Ac |

the β-chloro derivative **6** which, on treatment with triethylamine, afforded the peracetylated crystalline ester **12**. As further proof of the glycal structure, the crystalline tetrabutyl ammonium salt **13** was prepared from **10**, and acetyled to afford the salt **14**, a compound easily soluble in organic solvents.

Initial *N*-iodosuccinimide glycosylation experiments were performed with the unblocked glycal **10** and methanol at room temperature. Indeed, after several days the crystalline adduct **15** could be obtained in 50% yield. The exclusive trans-diaxial arrangement of iodine and the methoxy group following addition across the enol ether bond was demonstrated by the upfield shift of H-3 (δ 4.58) carrying the iodine. A small coupling constant $J_{3,4}$ = 4.0 Hz supported this assignment of an axially positioned iodine at C-3 and thus the singular formation of the β-glycoside **15**.

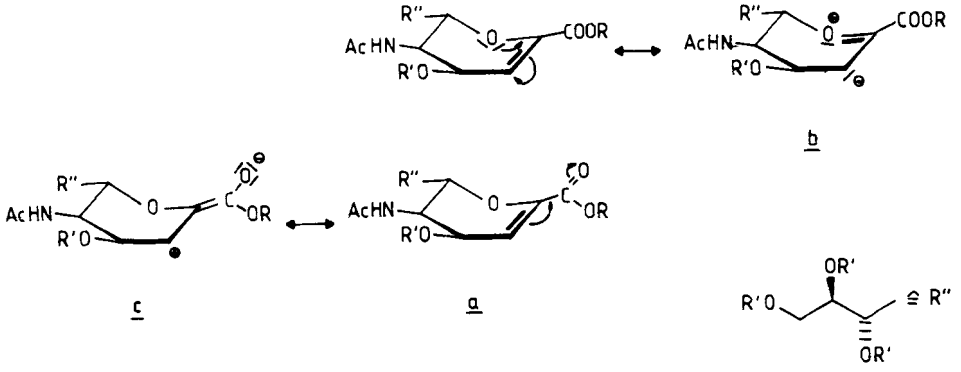
A similar reaction of the peracetylated ester **12** with methanol/*N*-iodosuccinimide gave a mixture of isomers **16** and **18** in approximately 70% yield and in a ratio 70:30. Compounds **16** and **18** were separated by preparative layer chromatography to give pure crystalline materials. The structural assignments were based on the different $J_{3,4}$ coupling constants which, in the case of the α-anomer **18**, showed the trans diaxial arrangement with a value of 11.2 Hz. In contrast, the β-anomer **16** had a $J_{3,4}$ coupling constant of 4.0 Hz. Furthermore, in both adducts an additional methoxy group was observed. Interestingly, the uniform trihydroxypropyl side chain at C-6 adopted a different conformation in **16** than in **18**, as deduced from the quite different coupling constants $J_{7,8}$ = 4.6 in **16** and 8.6 Hz in **18**. This difference in conformation may be a result of an interaction with the anomeric substituents or the steric interaction with the large iodine substituent at C-3. A corresponding glycosylation could be effected using the tetra-n-butylammonium salt **14**, which gave exclusively the β-methyl glycoside **17** (62%) by the *N*-iodosuccinimide procedure.

All attempts to use a more complex nucleophile (e.g., 1,2;3,4-di-O-benzylidene-α-D-galactopyranose[25]) as an aglyconic sugar in the *N*-iodosuccinimide glycosylation of

the glycal derivatives **12** or **14** under broadly varied conditions did not meet with success. A simple survey reveals that glycals like those generalized as **a** display the expected cyclic vinyl ether character as depicted by the mesomeric structure **b**. This situation should allow the *N*-iodosuccinimide glycosylation to operate as demonstrated previously;[18-20] however, structure **a** also has an $\alpha,\beta$-unsaturated carbonyl functionality and thus the mesomeric structure of the enolate **c** may be expected to contribute to the resonance hybrid. The latter effect results in a considerably reduced electron density at position 3.

These systems definitely do not exhibit the typical electron rich vinyl ether character but rather that of a normal or slightly deactivated cyclic olefin. Whereas the glycal **10** with the free acid group and the more soluble tetraalkylammonium salt **14** react smoothly with lower alcohols, the esterified glycal **12** is not sufficiently reactive for *N*-iodosuccinimide glycosylations.

At this stage it was decided to overcome the unfavourable carbonyl activity by an intermediate reduction to a primary alcohol with the option of a subsequent reoxidation. Previously, ketosides have been reduced to the corresponding alcohols using sodium borohydride in water at low temperature.[26] By applying this procedure to the glycal **11**, an



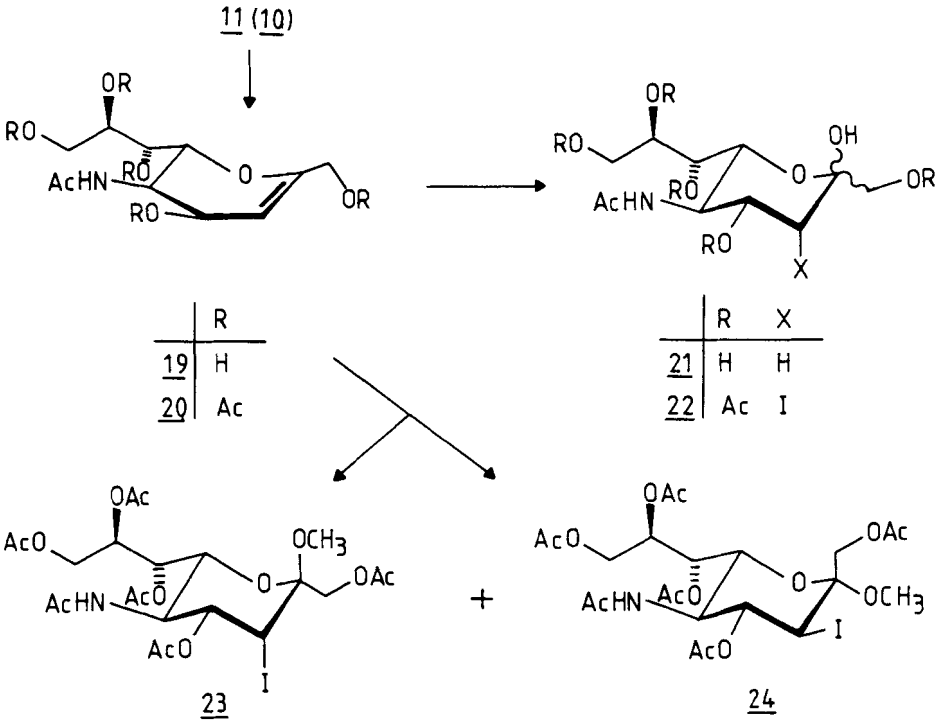
optimized yield of 25% of the crystalline alcohol **19** could be obtained. The reaction was hampered by concomitant saponification of the ester group, and furthermore the product **19** showed a high vinylic activity and added water under slightly acid conditions to give the ketose **21**. In fact, treatment of **19** in 0.01 N aqueous hydrochloric acid gave a fast and complete conversion to **21**.

An alternative approach was studied using sodium bis(2-methoxy-ethoxy)aluminium dihydride (vitride)[27] which was shown to selectively reduce even unsaturated carboxyl compounds to alcohols.[28,29] The reaction with the free carboxylic acid containing glycal **10** in toluene/tetrahydrofuran suspension proceeded but the overall yield of **19** did not exceed 20%.

The $^1$H NMR spectrum of **19** shows H-1a and H-1b at δ 3.84 and 3.91, respectively, and owing to the alcohol function at C-1, H-3 is shifted upfield (δ 4.79). Furthermore, allylic coupling constants between the protons H-1a, H-1b and H-3 are observed. The other coupling constants are similar to those of the adduct from which corresponding conformations may be deduced. In the hydrated derivative **21** similar coupling constants to those in *N*-acetylneuraminic acid (**1**)[30,31] were observed. H-3a and 3e resonate at δ 1.56 and 1.98 and demonstrate that **21** is saturated.

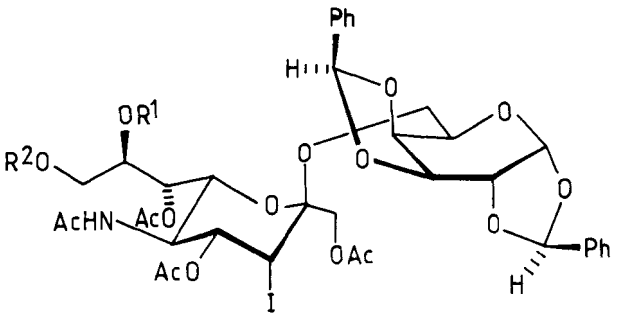
After acetylation of **19** to give the solid hexaacetate **20**, *N*-iodosuccinimide glycosylation with methanol rapidly produced the anomers **23** and **24** in 70% yield and in a ratio of 5:1. The $^1$H NMR spectrum of **23** again revealed a small $J_{3,4}$ = 3.8 Hz coupling constant, which is in accord with the prevailing diaxial addition which lead to the β-compound.

The corresponding reaction of **20** and 1,2:3,4-di-*O*-benzylidene-α-D-galactopyranose[25] similarly gave, after separation, the crystalline disaccharide derivative **25** in 22% yield as the only product. This compound was assigned a β-glycoside structure based on the $J_{3,4}$ coupling constant of 3.9 Hz. The other NMR data are nicely in accord with this structure. As a side product the 3-deoxy-3-iodo ketose **22** was obtained in approximately 30% yield. Evidently its formation must be assigned to the competition of water with the




| | R |
|---|---|
| 19 | H |
| 20 | Ac |

| | R | X |
|---|---|---|
| 21 | H | H |
| 22 | Ac | I |

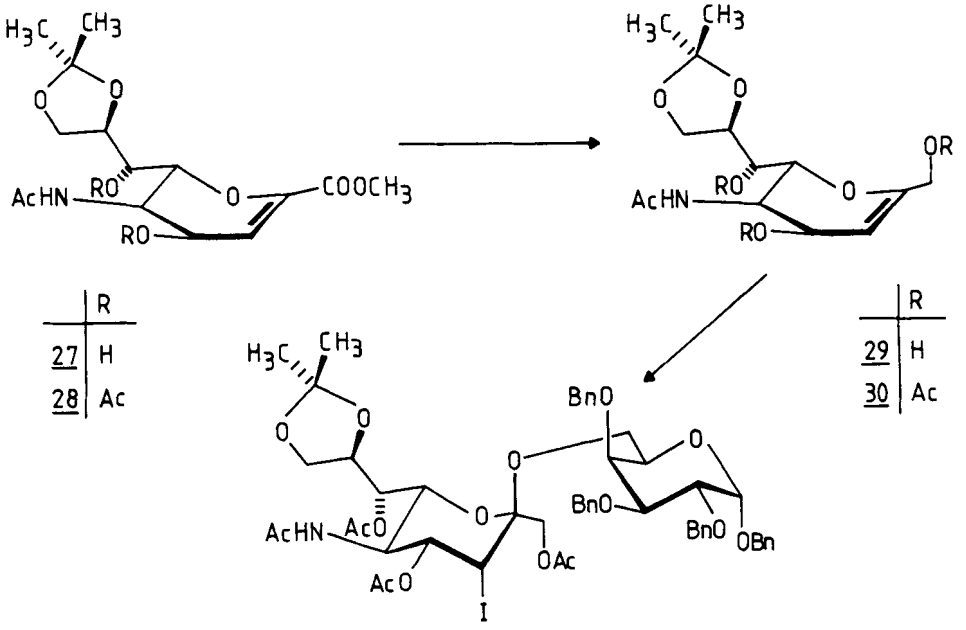



| | $R^1$ | $R^2$ |
|---|---|---|
| 25 | Ac | Ac |
| 26 | $H_3C-\overset{I}{C}-CH_3$ | |

6-hydroxy group of the sugar as the nucleophile reacting with the enol ether 20. Obviously in these modified *N*-acetylneuraminic acid derivatives the yields are modest in contrast to other *N*-iodosuccinimide glycosylations.[19] The predominant or exclusive formation of the trans-diaxial addition product, however, is in accord with previous findings.

Further studies were conducted to improve both the reduction process and the glycosylation. Solubility problems associated with the former reaction were overcome by employing selectively blocked precursors. Thus the methyl-ester 11 was isopropylidenated at the positions 8 and 9 to give the crystalline derivative 27. The regiochemical selectivity in this reaction becomes evident upon acetylation. In the triacetate 28 the $^1$H NMR spectrum shows H-7 ($\delta$ 5.37) downfield and not much change at H-8 and H-9, in contrast to compound 27.

In contrast to expectation, diisobutyl aluminum hydride in tetrahydrofuran caused concommitant degradations of 27. The best reduction was performed with sodium borohydride in methanol at 0°C which afforded the vinylic alcohol 29 in ca. 70% yield. The proton H-3 no longer shows conjugation to the




| | R |
|---|---|
| 27 | H |
| 28 | Ac |

| | R |
|---|---|
| 29 | H |
| 30 | Ac |

31

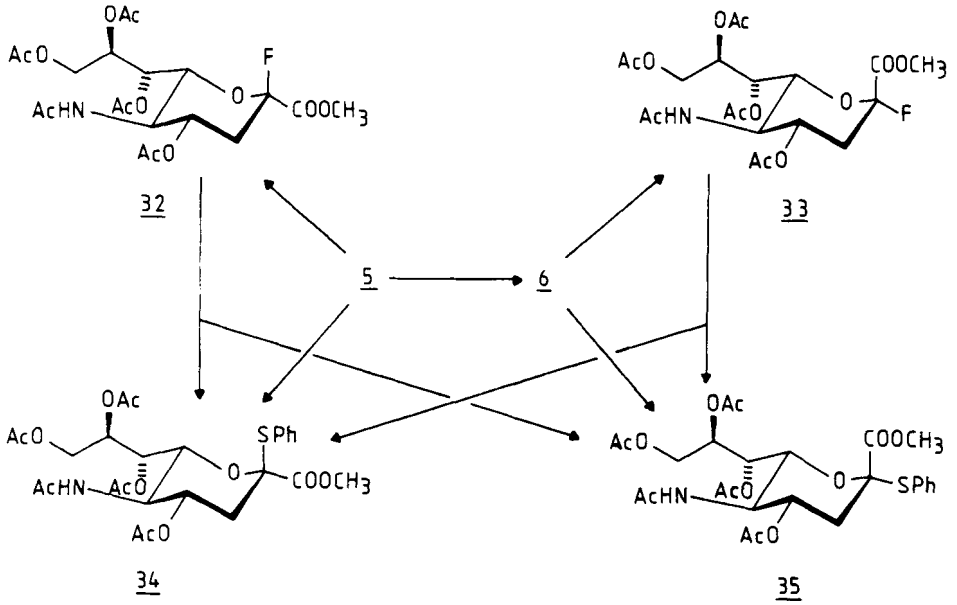
ester function as in 27 and thus undergoes a characteristic upfield shift (27: δ 5.91, 29: δ 4.40). Following acetylation to compound 30 the *N*-iodosuccinimide glycosylation with the same 1,2:3,4-di-O-benzylidene-α-D-galactopyranose[25] was performed. After separation, the disaccharide 26, which exhibited the $^1$H NMR data similar to 25, was obtained in approximately 20% yield.

The same reaction was also performed using the mixture of 2,4,4,6-tetrabromocyclohexadienone (TBCO) and iodine, which is supposed to give the iodonium 2,3,6-tribromophenolate in situ and thus may be employed instead of *N*-iodosuccinimide.[33] However, the yields of 26 were below 10%, which renders this variation less effective. As another aglycone, benzyl 2,3,4-tri-O-benzyl-α-D-galactopyranoside[34] was employed and again only the β-glycosidically linked disaccharide 31 resulted in approximately 20% yield.

These results clearly demonstrate the limits of the *N*-iodosuccinimide glycosylation procedure for the formation of sialic acid glycosides. The carboxy functional group causes a drastic decrease in the enol ether electron density and thus the introduction of less nucleophilic aglycones is hampered. Having overcome this drawback by carboxy reduction, the method proved useful again but gave exclusively the trans diaxial addition product, in accord with previous findings, and thus gave the undesired anomer. The modest yields may be attributed to severe steric interactions which have caused problems in other sialic acid derivative glycosylations.

Next we turned our interest to glycosylations employing thioglycosides which were to be activated by thiophilic catalysts. The formation of thiophenyl glycosides seemed to be more attractive than thioalkyl derivatives because in the glycosylation the C-S cleavage step would be favored by the stabilized thiophenolate leaving group.

Standard preparations for thioglycosides involve acid catalyzed thiolyses of peracetylated carbohydrates.[35] Thus several *N*-acetylneuraminic acid derivatives like the β-acetate 5, the β-chloride 6, and the β-fluoride 32, as well as the α-glycoside 33, all of which were prepared from 5 or




6, respectively,[36] were treated with thiophenol in the presence of various Lewis acids.[37-39] As compiled in Table 1, almost regardless of the leaving group in the starting material all entries show the predominant or exclusive formation of the $\beta$-thiophenyl glycoside **34** with $\beta:\alpha$ ratios varying from 1:0 to 4:3.

In contrast to previous findings in glycosylations using titanium tetrafluoride,[40] neither the $\beta$- nor the $\alpha$-fluoride **32** and **33** reacted with thiophenol in the presence $TiCl_4$. Finally potassium methoxide (cf. lit.[41]) proved to be the best catalyst in promoting the exclusive formation of the $\alpha$-thioglycoside, giving **35** after reacetylation.

The structural assignment by $^1H$ NMR is in accord with the general feature that H-3e is further downfield in the $\alpha$- than the $\beta$-glycoides, and H-4 is shifted in the other direction.[42,43] Thus H-3e in the $\alpha$-derivative **35** occurs at $\delta$ 2.83 and in the $\beta$-anomer **34** at $\delta$ 2.62; in **35** H-4 resonates at higher field ($\delta$ 4.84) than in **34** ($\delta$ 5.35).

Systematic studies employing mercuric salts for glycosylations of thioglycosides, according to the Pearson conception of soft acid-soft base pairs, were performed

TABLE 1. Preparation of Thiophenyl Glycosides 34 and 35 of *N*-Acetylneuraminic Acid.[a]

| Entry | Starting material | | Catalyst | Yield (%) | Ratio 34(β):35(α) |
|---|---|---|---|---|---|
| 1 | β-acetate | 5 | $ZrCl_4$ | 76 | 5:2 |
| 2 | β-chloride | 6 | $ZnCl_2$ | 73 | 2:1 |
| 3 | β-fluoride | 32 | $BF_3 \cdot Et_2O$ | 80 | 4:3 |
| 4 | α-fluoride | 33 | $BF_3 \cdot Et_2O$ | 29 | 3:2 |
| 5 | β-acetate | 5 | $BF_3 \cdot Et_2O$ | 66 | 1:0 |
| 6 | β-chloride | 6 | $KOCH_3$ | 60 | 0:1 |

a. in chloroform at room temperature



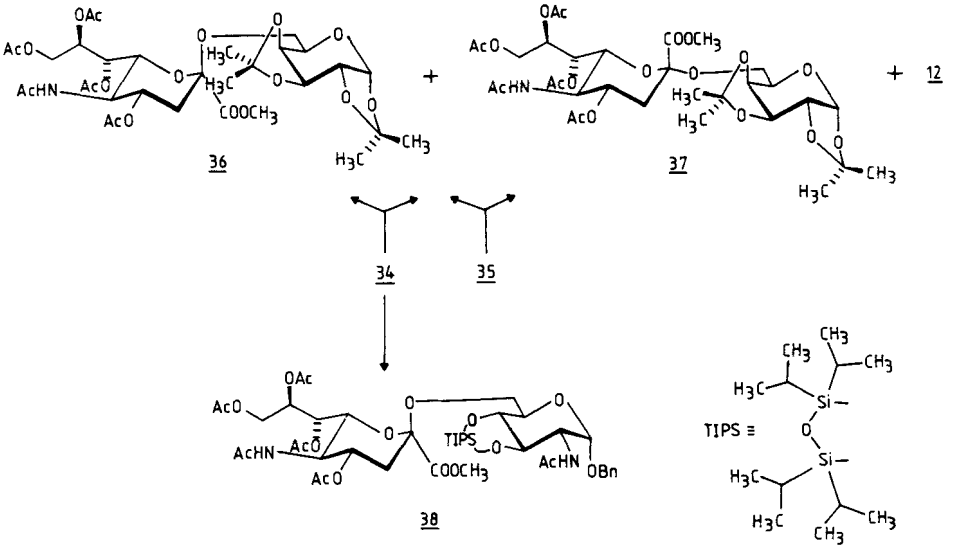
previously by Ferrier et al.[44] and later by others.[45-47] Phenylmercuric triflate[47,48] seemed to be of particular interest and its application was tested in various solvent systems using the galactose derivative as aglycon component. As compiled in Table 2, the anomeric selectivity could be directed by the solvent polarity. In the more polar mixture [acetonitrile/toluene (1:1)] a predominant formation of the α,2→6-glycosidically linked disaccharide 37 was observed. In dichloromethane/toluene (1:1) the β,2→6-disaccharide 36 clearly prevailed. Interestingly these ratios are obtained more or less regardless of the stereochemistry of the starting material and, therefore, β/α-mixtures could be employed.

In all cases the yields were somewhat reduced with the α-thioglycoside as the stating material. By rough comparison in all these entries the elimination byproduct, the enol ether 12, remained in the range of 10-20%, which corresponds to other glycosylations in sialic acids.[15]

As another thiophilic agent, bromonium ions from *N*-bromosuccinimide previously have been shown to promote glycosylations of thioglycosides with alcohols. Attractive yields contrasted with poor stereoselectivities.[46,49] Treatment of the β-thioglycoside 34 with the galacto derivative in the presence of *N*-bromosuccinimide in nitromethane/toluene (1:1) gave both the disaccharides 36 and 37 in 28% yield and a ratio of 1:1.

**TABLE 2.** Disaccharide Formation by Glycosylation of Thiophenyl Glycosides

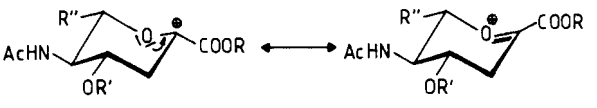
| Entry | Starting material | Solvent | Yield (%) | Ratio 36(β):37(α) | Bypro-duct 12 (%) |
|---|---|---|---|---|---|
| 1 | β-thiophenyl glycoside **34** | acetonitrile/ toluene, 1:1 | 30 | 1:4 | 16 |
| 2 | α-thiophenyl glycoside **35** | acetonitrile/ toluene, 1:1 | 24 | 1:5 | 13 |
| 3 | β/α-thiophenyl glycosides **34/35** | acetonitrile/ toluene, 1:1 | 25 | 2:3 | 5 |
| 4 | β-thiophenyl glycoside **34** | dichloromethane/ toluene, 1:1 | 35 | 5:2 | 21 |
| 5 | α-thiophenyl glycoside **35** | dichloromethane/ toluene, 1:1 | 13 | 1:1 | 7 |
| 6 | β/α-thiophenyl glycosides **34/35** | dichloromethane/ toluene, 1:1 | 22 | 2:1 | 8 |



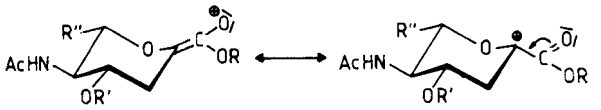
Finally, **34** was reacted with benzyl 2-acetamido-2-deoxy-3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-D-glucopyranoside[50] and phenylmercuric triflate. In a very modest yield (approximately 10%) exclusively the β,2→6-disaccharide **38** resulted. This differed considerably from previous Koenigs-Knorr reactions in which a precursor to **38** and its α,2→6-anomer were obtained in approximately 50% yield and a β:α ratio of 4:1.[50]

The structural assignments to the disaccharides **36** and **37**, previously described without experimental details,[7] or incomplete analytical data,[10,15] are straightforward when $^1$H NMR spectroscopy is employed. Again H-3e' in the β-anomer **36** resonates at higher field (δ 2.49) than in the α-glycoside **37** (δ 2.62) and the opposite applies to their H-4' signals. Remarkably, the $J_{7',8'}$ coupling constant in the β-glycoside **36** is much smaller (4.4 Hz) than in the α-anomer **37** (7.9 Hz) which points to a conformational deviation in the side chain dependent on the anomeric configuration.

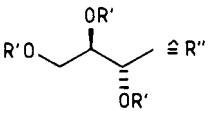
Mechanistically the thioglycoside glycosylations promoted by thiophilic agents are understood to proceed by an $S_N1$ type process. The intermediate oxocarbenium ion **d** should be more stable than in the normal sugar series because stabilization is expected by participation of the lone pairs of electrons on the ring oxygen atom (mesomeric form **e**) as well as the α-carboxyalkyl function (mesomeric form **f**). Thus, in this case further studies are required which involve nucleophiles with enhanced nucleophilicity in order




**e**




**f** **d**



to increase the overall yields. Attack of nucleophilic species from the axial direction at C-2 is expected and goes along with the anomeric effect. In the case of non-polar solvents, the sugar nucleophile is supposed to follow this path directly and give axial substitution, that is, the $\beta$-glycoside. Polar solvents, however, may themselves be involved in the formation of an intimate ion pair predominantly at the axial face. Consequently the incoming sugar nucleophile will be directed preferrably to attack from the backside. This gives rise to a prevailing $\alpha$-glycoside formation.

## EXPERIMENTAL

**General Procedures.** Reactions were followed by TLC on silica gel foils $GF_{254}$ (Merck). Detection was done by UV absorption and/or spraying with concd sulfuric acid or 10% ethanolic sulfuric acid and subsequent heating. Preparative LC was on silica gel plates 60 $F_{254}$ 0.25, 0.5, and 2.0 mm (Merck). Column chromatography was on silica gel 60 (Merck). HPLC was conducted with a Waters pump 1145, LC spectrophotometer Lambda-Max model 481 (Waters), differential refractometer type 98.00 (Knauer), and integrator CR-3 A (Shimadzu); columns 8 × 250 mm, LiChrosorb Si 60, LiChrosorb RP-8, 5 $\mu$m (Merck). Melting points were determined with a Leitz- and a Reichert heating microscope (Mettler-FP 61) and are uncorrected. Optical rotations were taken on Perkin-Elmer polarimeters (241 and 243) in 1 dm cuvettes at 20°C and 589 nm (Na D-line). $^1$H NMR spectra were recorded with the Bruker instruments WH 270 (270 MHz), WM 300 (300 MHz), and WM 400 (400 MHz) and TMS as the internal standard. In most cases assignments were supported by double resonance experiments. For specific problems 2D-COSY measurements were performed using the Bruker software 1985 and an Aspekt-3000 computer.

**5-Acetamido-2,4,8,9-tetra-O-acetyl-$\beta$-D-glycero-D-galacto-2-nonulopyranosonic acid-1,7-lactone (7).** Following peracetylation of *N*-acetylneuraminic acid dihydrate (1, 4.9 g, 14.2 mmol) with acetic anhydride (10 mL) in anhyd pyridine (50 mL) plus a catalytic amount of 4-dimethylaminopyridine for 90 min at 60°C, the clear, yellow solution was concen-

trated and then freeze-dried. The residue, taken up in aq sodium hydrogencarbonate, was extracted with ethyl acetate to give after evaporation 500 mg (7.7%), of **7**, mp 204-205°C, $[\alpha]_D^{20}$ +82.1° (c 0.58, acetone). $^1$H NMR ($CDCl_3$) δ 2.15 (dd, H-3a), 2.38 (dd, H-3e), 5.10 (ddd, H-4), 4.24 (ddd, H-5), 4.19 (d≈s, H-6), 4.65 (d, H-7), 5.47 (ddd, H-8), 4.75 (dd, H-9a), 4.29 (dd, H-9b), 6.09 (d, NH), 2.06, 2.07, 2.10, 2.11, 2.12 (each s, each 3H, NAc and OAc); $J_{3a,3e}$ = 14.8, $J_{3a,4}$ = 3.8, $J_{3b,4}$ = 3.2, $J_{4,5}$ = 2.2, $J_{5,6}$ ≈ 2.0, $J_{5,NH}$ = 8.2, $J_{6,7}$ ≈ 0, $J_{7,8}$ = 8.4, $J_{8,9a}$ = 2.4, $J_{8,9b}$ = 4.4, $J_{9a,9b}$ = 12.6 Hz.

The remaining aqueous phase was further treated (cf. lit.[24]) and gave compound **2** 4.55 g (62%), further processed as described.

Compound **2** (4.55 g, 8.8 mmol) was treated following the literature procedure[24] to give the crystalline **5-acetamido-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonic acid (10).** The yield was 1.35 g (63% based on **3** in a three-step-one-pot process) mp 139-141°C decomp, $[\alpha]_D^{20}$ +41.4° (c 0.66, water) [lit.[29]: 137-140°C decomp, $[\alpha]_D^{20}$ +41.6° (c 0.25, water)]. $^1$H NMR ($D_2O$) δ 5.90 (d, H-3), 4.38 (dd, H-4), 3.95 (dd, H-5), 4.19 (dd, H-6), 3.50 (dd, H-7), 3.78 (ddd, H-8), 3.74 (dd, H-9a), 3.51 (dd, H-9b), 1.93 (s, 3H, NAc); $J_{3,4}$ = 2.5, $J_{4,5}$ = 9.0, $J_{5,6}$ = 10.9, $J_{6,7}$ = 1.0, $J_{7,8}$ = 9.4, $J_{8,9a}$ = 2.6, $J_{8,9b}$ = 6.2, $J_{9a,9b}$ = 11.8 Hz.

In course of the HPLC separation (Merck RP 8, 0.1% acetic acid) of **10**, as a faster moving fraction **5-acetamido-4-O-acetyl-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonic acid (9)** could be isolated and crystallized from methanol to give 550 mg (22% based on **3**), amorphous solid, $[\alpha]_D^{20}$ + 22.8°C (c 0.5, methanol). $^1$H NMR ($CD_3OD+D_2O$) δ 5.88 (d, H-3), 5.67 (dd, H-4), 4.27 (dd, H-5), 4.40 (dd, H-6), 3.63 (dd, H-7), 3.90 (ddd, H-8), 3.84 (dd, H-9a), 3.66 (dd, H-9b), 1.99 (s, 3H, NAc), 2.09 (s, 3H, OAc); $J_{3,4}$ = 2.4, $J_{4,5}$ = 8.4, $J_{5,6}$ = 11.2, $J_{6,7}$ = 1.0, $J_{7,8}$ = 8.2, $J_{8,9a}$ = 2.8, $J_{8,9b}$ = 5.4, $J_{9a,9b}$ = 11.0 Hz.

**Methyl 5-Acetamido-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonate (11).**

a) Compound **10** (5.34, 18.0 mmol) and an ion exchange resin

(Lewatite SP 1080 $H^+$, 1.0 g) in methanol (250 mL) were refluxed for 1 h. The cold mixture was eluted through an ion exchange column (Lewatite MP 5080, $OH^-$) with methanol (300 mL). After evaporation, the residue was recrystallized from methanol to give 3.9 g (72%) of **11**. Further elution with acetic acid (20%, 300 mL) gave **10** (1.1 g, 20%).

b) Compound **12** (3.1 g, 6.4 mmol), dissolved in anhyd methanol (10 mL), is treated with a sodium methylate solution in methanol (1%) at room temperature. After deacetylation, the mixture was treated with a acidic ion exchange resin (Dowex 50 $H^+$) and evaporated to give 1.06 g (54%), mp 223°C decomp, $[\alpha]_D^{20}$ +38.6° (c 0.36, water) [lit.[24]: mp 225-227°C decomp, $[\alpha]_D^{25}$ +42.3° (c 5.5, water)]. $^1H$ NMR ($D_2O$) δ 5.93 (d, H-3), 4.40 (dd, H-4), 3.97 (dd, H-5), 4.17 (dd, H-6), 3.53 (dd, H-7), 3.80 (ddd, H-8), 3.76 (dd, H-9a), 3.54 (dd, H-9b), 3.69 (s, 3H, $CO_2CH_3$), 1.93 (s, 3H, NAc); pyridine-$d_5$) δ 6.20 (H-3), 5.09 (dd, H-4), 4.90 (ddd, H-5), 5.06 (dd, H-6), 4.51 (dd, H-7), 4.82 (ddd, H-8), 4.51 (dd, H-9a), 4.38 (dd, H-9b), 9.46 (d, NH), 3.56 (s, 3H, $COOCH_3$), 2.00 (s, 3H, NAc); [coupling constants: in $D_2O$ (in pyridine-$d_5$)] $J_{3,4}$ = 2.5 (2.4), $J_{4,5}$ = 8.8 (8.4), $J_{5,6}$ = 11.0 (10.0), $J_{5,NH}$ = (8.0), $J_{6,7}$ = 1.0 (1.0), $J_{7,8}$ = 9.3 (9.4), $J_{8,9a}$ = 2.8 (2.8), $J_{8,9b}$ = 6.1 (5.4, $J_{9a,9b}$ = 11.8 (11.0) Hz.

**Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonate (12).**

a) Compound **11** (3.0 g, 10.0 mmol) dissolved in anhyd pyridine (30 mL) was treated with acetic anhydride (6 mL) and a catalytic amount of 4-dimethylaminopyridine for 1 h at room temperature and 30 min at 60°C. After addition of methanol (10 mL) the mixture was evaporated, taken up in ethyl acetate, washed with dil sulfuric acid, water, dried ($Na_2SO_4$), concentrated and the residue recrystallized from ethanol/n-hexane to give 3.3 g (71%).

b) The β-chloride **6** (4.5 g, 8.8 mmol) is dissolved in anhyd dioxane (30 mL) and treated with anhyd triethylamine (3.8 mL) for 30 min at room temperature. After freeze-drying of the mixture, the residue was separated and purified by HPLC (toluene/ethanol, 5:1). Yield: 3.16 g (74%). mp 130.7°C, $[\alpha]_D^{20}$ 80.0° (c 0.95, chloroform). $^1H$ NMR ($CDCl_3$) δ 5.99 (d,

H-3), 5.51 (dd, H-4), 4.41 (m, 2H, H-5,-6), 5.52 (dd, H-7), 5.35 (ddd, H-8), 4.66 (dd, H-9a), 4.20 (dd, H-9b), 6.13 (d, NH), 3.79 (s, 3H, $COOCH_3$), 1.90, 2.03 (2), 2.06, 2.10 (each s, each 3H, NAc and OAc); ($C_6D_6$) δ 6.07 (d, H-3), 5.53 (dd, H-4), 4.71 (ddd, H-5), 4.31 (dd, H-6), 5.73 (dd, H-7), 5.78 (ddd, H-8), 5.12 (dd, H-9a), 4.42 (dd, H-9b), 5.73 (d, NA), 3.43 (s, 3H, 3H, $COOCH_3$), 1.69, 1.75, 1.76, 1.84, 1.94 (each s, each 3H, NAc and OAc); [coupling constants: in $CDCl_3$ (in $C_6D_6$)] $J_{3,4}$ = 3.1 (2.7), $J_{4,5}$ = 7,8 (8.4), $J_{5,6}$ = ~(10.0), $J_{5,NH}$ = 9.0 (10.0), $J_{6,7}$ = 2.8 (2.8), $J_{7,8}$ = 4.2 (4.0), $J_{8,9a}$ = 3.1 (2.8), $J_{8,9b}$ = 7.4 (7.8), $J_{9a,9b}$ = 12.4 (12.4) Hz.

**5-Acetamido-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonic Acid Tetra-n-butylammonium Salt (13).** The acid (**10**, 1.08 g, 3.72 mmol), dissolved in water (2 mL), was neutralized with an aq tetra-n-butylammonium hydroxide solution, evaporated and dried to give 1.96 g (99%), colourless crystalls, mp 97-102°C, $[\alpha]_D^{20}$ +15.95° (c 0.79, water). $^1H$ NMR ($D_2O$) δ 5.56 (d, H-3), 4.34 (dd, H-4), 3.93 (dd, H-5), 4.09 (dd, H-6), 3.47 (dd, H-7), 3.82 (ddd, H-8), 3.74 (dd, H-9a), 3.52 (dd, H-9b), 1.95 (s, 3H, NAc), 0.82 (t, 9H, $CH_2$-$CH_2$-$CH_2$-$\underline{CH_3}$), 1.23 (tq, 6H, $CH_2$-$CH_2$-$\underline{CH_2}$-$CH_3$), 1.52 (m, 6H, $CH_2$-$\underline{CH_2}$-$CH_2$-$CH_3$), 3.07 (m, 6H, $\underline{CH_2}$-$CH_2$-$CH_2$-$CH_3$); $J_{3,4}$ = 2.4, $J_{4,5}$ = 9.0, $J_{5,6}$ = 11.0, $J_{6,7}$ ≈ 1.0, $J_{7,8}$ ≈ 9.0, $J_{8,9a}$ = 9.2, $J_{8,9b}$ = 6.0, $J_{9a,9b}$ = 11.7, $J_{H,H}$(butyl) = 7.2 and 7.5 Hz.

**5-Acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonic Acid Tetra-n-butylammonium Salt (14).** Compound **13** (560 mg, 1.1 mmol) dissolved in anhyd pyridine (2 mL) was treated with acetic anhydride (1.2 mL) for 12 h at room temperature. After repeated coevaporation with toluene, the residue was dried in high vacuo to give 772 mg (98%), syrup, $[\alpha]_D^{20}$ +36.0° (c 0.86, chloroform). $^1H$ NMR ($CDCl_3$) δ 5.85 (d, H-3), 5.31 (dd, H-4), 4.43 (ddd, H-5), 4.34 (ddat, H-6), 5.56 (dd, H-7), 5.46 (ddd, H-8), 4.52 (dd, H-9a), 4.26 (dd, H-9b), 6.38 (d, NH), 1.94 (s, 3H, NAc), 2.03, 2.04, 2.05, 2.06 (each s, each 3H, OAc), 1.00 (t, 9H, $CH_2$-$CH_2$-$CH_2$-$\underline{CH_3}$), 1.42 (tq, $CH_2$-$CH_2$-$\underline{CH_2}$-$CH_3$), 1.64 (mc, $CH_2$-$\underline{CH_2}$-$CH_2$-$CH_3$), 3.24 (mc, $\underline{CH_2}$-$CH_2$-$CH_2$-$CH_3$); $J_{3,4}$ = 3.7, $J_{4,5}$ = 5.4, $J_{5,6}$ = 6.2, $J_{5,NH}$ = 9.0, $J_{6,7}$

≈ 5.8, $J_{7,8}$ = 4.2, $J_{8,9a}$ = 3.6, $J_{8,9b}$ = 7.0, $J_{9a,9b}$ = 12.0, $J_{HH}$(butyl) = 7.2 and 7.1 Hz.

**(Methyl-5-acetamido-3,5-dideoxy-3-iodo-β-D-erythro-L-manno-2-nonulopyranosid)onic Acid (15).** A mixture of compound **10** (29.1 mg, 0.1 mmol) and *N*-iodosuccinimide (22.5 mg, 0.1 mmol) in anhyd acetonitrile (3 mL) and anhyd methanol (1 mL) was stirred at 60°C for 90 min and then another portion of *N*-iodosuccinimide (11.3 mg, 0.05 mmol) was added. After 3 days the product crystallized from the mixture and was recrystallized from methanol to give 22.5 mg (50%), colourless needles, mp 173°C, $[\alpha]_D^{20}$ -16.4° (c 0.56 methanol). $^1$H NMR ($CD_3OD$) δ 4.58 (d, H-3), 3.44 (dd, H-4), 4.26 (dd≈t, H-5), 3.95 (dd, H-6), 3.46 (dd, H-7), 3.77-3.85 (m, 2H, H-8, H-9a), 3.65 (dd, H-9b), 1.99 (s, 3H, NAc); $J_{3,4}$ = 4.0, $J_{4,5}$ = 10.0, $J_{5,6}$ = 10.5, $J_{6,7}$ = 1.0, $J_{7,8}$ = 9.2, $J_{8,9b}$ = 6.0, $J_{9a,9b}$ = 12.0 Hz.

**Methyl (Methyl-5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-3-iodo-β-D-erythro-L-manno- and α-D-erythro-L-gluco-2-nonulopyranosid)onate (16 and 18).** Compound 12 (46.1 mg, 0.1 mmol) and *N*-iodosuccinimide (NIS, 113 mg, 0.5 mmol) were dissolved in anhyd acetonitrile (5 mL) and anhyd methanol (100 μL, 0.25 mmol) and heated with stirring to 80°C. After several further additions of NIS and methanol, work-up after 3 days was done by evaporation and extraction of the residue with dichloromethane. The solution was washed with aq sodium thiosulfate solution, water, dried ($Na_2SO_4$) and concentrated. The remaining 55.4 mg (90%) of slightly yellow syrup was separated by preparative LC (toluene/i-propanol, 5:1, threefold development) to give together 41.3 mg (67%) of the separated crystalline anomers **16** and **18**.

*β*-Anomer **16**: 29.6 mg (48%), mp 202°C, $[\alpha]_D^{20}$ +32.9° (c 0.35, chloroform). $^1$H NMR ($CDCl_3$) δ 4.70 (d, H-3), 4.84 (dd, H-4), 4.29 (ddd≈dd, H-5), 4.09 (dd, H-6), 5.34 (dd, H-7), 5.29 (ddd, H-8), 4.85 (dd, H-9a), 4.20 (dd, H-9b), 5.40 (d, NH), 1.93 (s, 3H, NAc), 2.04, 2.09 (2), 2.21 (each s, each 3H, OAc), 3.30 (s, 3H, $OCH_3$), 3.84 (s, 3H, $COOCH_3$); $J_{3,4}$ = 4.0, $J_{4,5}$ = 10.4, $J_{5,NH}$ = 9.3, $J_{5,6}$ = 10.5, $J_{6,7}$ = 1.7, $J_{7,8}$ = 4.6, $J_{8,9a}$ = 2.4, $J_{8,9b}$ = 7.0, $J_{9a,9b}$ = 12.5 Hz.

*α*-Anomer **18**: 11.7 mg (19%), mp 153°C, $[\alpha]_D^{20}$ -117.1° (c 0.14, chloroform). $^1$H NMR ($CDCl_3$) δ 4.06 (d, H-3), 5.44 (dd,

H-4), 4.22 (ddd≈dq, H-5), 4.59 (dd, H-6), 5.26 (dd, H-7), 5.34 (ddd, H-8), 4.24 (dd, H-9a), 4.05 (dd, H-9b), 5.37 (d, NH), 1.90 (s, 3H, NAc), 2.03, 2.07, 2.09, 2.14 (each s, each 3H, OAc), 3.52 (s, 3H, $OCH_3$), 3.85 (s, 3H, $COOCH_3$); $J_{3,4}$ = 11.2, $J_{4,5}$ = 10.1, $J_{5,NH}$ = 10.0, $J_{5,6}$ = 10.8, $J_{6,7}$ = 2.0, $J_{7,8}$ = 8.6, $J_{8,9a}$ = 2.6, $J_{8,9b}$ = 6.0, $J_{9a,9b}$ = 12.4 Hz.

**(Methyl-5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-3-iodo-β-D-erythro-L-manno-2-nonulopyranosid)onic Acid Tetra-n-butylammonium Salt (17).** Compound **14** (28.1 mg, 0.04 mmol) and *N*-iodosuccinimide (33.8 mg, 0.15 mmol) dissolved in anhyd acetonitrile (5 mL) and anhyd methanol (100 μL, 0.25 mmol) were reacted for 3 days and work-up was done as described in the previous preparation. The raw material was purified by preparative TLC (n-propanol/acetic acid/water, 9:5:5, twofold development). The yield was 21.3 mg (62%), syrup, $[\alpha]_D^{20}$ +5.4° (c 0.98, chloroform). $^1H$ NMR ($CDCl_3$) δ 4.76 (d, H-3), 4.85 (dd, H-4), 4.33 (dd, H-5), 3.96 (dd, H-6), 5.31 (m, H-7), 5.41 (ddd, H-8), 3.96 (dd, H-6), 5.31 (m, H-7), 5.41 (ddd, H-8), 4.73 (dd, H-9a), 4.17 (dd, H-9b), 5.04 (d, NH), 1.92 (s, 3H, NAc), 2.03 (2), 2.07, 2.21 (each s, each 3H, OAc), 3.22 (s, 3H, $OCH_3$), 1.00 (t, 9H, $CH_2$-$CH_2$-$CH_2$-$C\underline{H}_3$), 1.42 (tq, 6H, $CH_2$-$CH_2$-$C\underline{H}_2$-$CH_3$), 1.65 (mc, 6H, $CH_2$-$C\underline{H}_2$-$CH_2$-$CH_3$), 3.25 (mc, 6H, $C\underline{H}_2$-$CH_2$-$CH_2$-$CH_3$); $J_{3,4}$ = 3.8, $J_{4,5}$ = 10.0, $J_{5,NH}$ = 9.4, $J_{5,6}$ ≈ 9.6, $J_{6,7}$ ≈ 1.0, $J_{7,8}$ = 5.3, $J_{8,9a}$ = 3.4, $J_{8,9b}$ = 6.3, $J_{9a,9b}$ = 12.3, $J_{H,H}$(butyl) = 7.2 and 7.4 Hz.

**5-Acetamido-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enitol (19).**

a) An aq solution of compound **11** (915 mg, 3.0 mmol, 30 mL) was added dropwise at 0°C to an aq solution of sodium borohydride (1.0 g, 26.5 mmol, 30 mL) and stirred for 90 min. After another 4 h at room temperature, the mixture was concentrated to dryness and taken up in methanol. The solution was eluted on ion exchange resin Lewatite SP 1080 $H^+$ and subsequently Lewatite MP 5080 $OH^-$, then evaporated and recrystallized from methanol. The yield was 206 mg (25%).

b) Sodium-bis(2-methoxy-ethoxy)-aluminium-dihydride (Vitride, 60% solution in benzene, 0.5 mL, ca. 1.0 mmol) in anhyd tetrahydrofuran (5 mL) was heated under reflux and

treated with a solution of **10** (29.1 mg, 0.1 mmol) in anhyd toluene/tetrahydrofuran (1:2, 5 mL) for 30 min. After another 3 h at room temperature, the mixture was neutralized with acetic acid under cooling and coevaporated with methanol several times. The residue taken up in methanol, was treated as in a) and crystallized to give 5.6 mg (20%), colorless needles, mp 170°C, $[\alpha]_D^{20}$ +42.5° (c 0.2, methanol). $^1$H NMR ($D_2O$) δ 3.84 and 3.91 (AB system x d, 2H, H-1a, H-1b), 4.79 (d, H-3), 4.25 (ddt, H-4), 3.88 (dd, H-5), 4.02 (dd, H-6), 3.46 (dd, H-7), 3.72 (ddd, H-8), 3.72 (dd, H-9a), 3.49 (dd, H-9b), 1.93 (s, 3H, NAc); $J_{A,B}$ = 13.2, $J_{1a,4}$ = $J_{1b,4}$ = 1.0, $J_{3,4}$ = 2.0, $J_{4,5}$ = 8.5, $J_{5,6}$ = 11.0, $J_{6,7}$ = 1.2, $J_{7,8}$ = 9.2, $J_{8,9a}$ = 2.7, $J_{8,9b}$ = 6.8, $J_{9a,9b}$ = 12.4 Hz.

Anal. Calcd for $C_{11}H_{19}NO_7$ (277.3): C, 47,65; H, 6.91; N, 5.05. Found: C, 47,18; H, 6.96; N, 4.79.

**5-Acetamido-1,4,7,8,9-penta-O-acetyl-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enitol (20).** Compound **19** (138.5 mg, 0.5 mmol) was dissolved in anhyd pyridine (1.5 mL) and treated with acetic anhydride (0.8 mL) in the presence of catalytic amounts of 4-dimethylaminopyridine for 45 min at room temperature and for 45 min at 60°C. Following coevaporation with methanol, the residue was dissolved in ethyl acetate, washed with dil hydrochloric acid, aq sodium hydrogencarbonate solution, and water, dried ($Na_2SO_4$) and the solvent evaporated. From dioxane the syrup was obtained as a white powder after freeze-drying. The yield was 178 mg (73%), softening interval 48-52°C, $[\alpha]_D^{20}$ +27.6° (c 0.72, chloroform). $^1$H-NMR ($CDCl_3$) δ 4.38 and 4.55 (each m, 2H, H-1a and H-1b), 4.97 (dt, H-3), 5.38 (m, 43H, H-4, H-5, H-6), 4.28 (dd, H-6), 5.47 (dd, H-7), 5.38 (ddd≈dt, H-8), 4.41 (dd, H-9a), 4.14 (dd, H-9b), 5.47 (d, NH), 1.95 (s, 3H, NAc), 2.05, 2.06, 2.07, 2.10, 2.13 (each s, each 3H, OAc); ($C_6D_6$) δ 4.26 and 4.50 (each m, 2H, H-1a and H-1b), 4.85 (dt, H-3), 5.37 (ddd, H-4), 4.58 (ddd≈dt, H-5), 4.16 (dd, H-6), 5.54 (dd, H-7), 5.54 (ddd, H-8), 4.66 (dd, H-9a), 4.21 (dd, H-9b), 5.65 (d, NH), 1.69 (s, 3H, NAc), 1.74, 1.76, 1.79, 1.83, 1.92 (each s, each 3H, OAc); [coupling constants: in $CDCl_3$ (in $C_6D_6$)] $J_{1a,1b}$ = 13.6 (13.4), $J_{1a,4}$ = ./.(1.0), $J_{1b,4}$ = ./.(0.6), $J_{3,4}$ = 3.0 (2.6), $J_{4,5}$ = ./.(8.9), $J_{5,6}$ =

8.4 (10.0), $J_{5,NH}$ = 9.0 (9.9), $J_{6,7}$ = 3.9 (2.6), $J_{7,8}$ = 6.0 (4.4), $J_{8,9a}$ = 3.2 (2.6), $J_{8,9b}$ = 6.4 (6.6), $J_{9a,9b}$ = 12.4 (12.4) Hz.

Anal. Calcd for $C_{21}H_{29}NO_{12}$ (487.5): C, 51.74; H, 6.00; N, 2.87. Found: C, 51.48, H, 5.97; N, 2.85.

**5-Acetamido-3,5-dideoxy-α/β-D-glycero-D-galacto-2-nonulopyranose (21).** A solution of compound 19 (22.7 mg, 0.1 mmol) was kept in 0.01 N hydrochloric acid (1 mL) for 45 min at 50°C. After cooling and neutralizing with an ion exchange resin ($OH^-$), the product was obtained as a syrup. The yield was 29.0 mg (98%). $^1H$ NMR ($D_2O$) δ 3.38 (mc, 2H, H-1a, -1b), 1.56 (dd, H-3a), 1.98 (dd, H-3e), 3.90 (ddd, H-4), 3.68 (dd, H-5), 3.83 (dd, H-6), 3.38 (dd, H-7), 3.61 (ddd, H-8), 3.69 (dd, H-9a), 3.46 (dd, H-9b), 1.90 (s, 3H, NAc); $J_{3a,3e}$ = 13.0, $J_{3a,4}$ = 11.5, $J_{3e,4}$ = 5.0, $J_{4,5}$ = 9.8, $J_{5,6}$ = 10.6, $J_{6,7}$ = 1.2, $J_{7,8}$ = 8.8, $J_{8,9a}$ = 2.7, $J_{8,9b}$ = 6.5, $J_{9a,9b}$ = 11.5 Hz.

**Methyl 5-Acetamido-1,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-iodo-β-D-erythro-L-manno (23) and α-D-erythro-L-gluco-2-nonulopyranoside (24).** A solution of the glycal 20 (48.7 mg, 0.1 mmol) in anhyd acetonitrile (2 mL) was treated with *N*-iodosuccinimide (56.3 mg, 0.25 mmol) and anhyd methanol (0.5 mL) and left for 12 h at room temperature. After evaporation the residue was dissolved in dichloromethane, successively washed with aq sodium thiosulfate and water, dried ($Na_2SO_4$) and concentrated. The crude yield was 45.3 mg (70%). Further preparative LC (toluene/ethanol, 5:1) gave a purified anomeric mixture of 23:24 = 5:1. $^1H$ NMR ($CDCl_3$) of 23: δ 4.15 (m, 2H, H-1a, H-1b), 4.53 (d, H-3), 4.75 (dd, H-4), 4.30 (ddd≈dd, H-5), 4.21 (dd, H-6), 5.28 (dd, H-7), 5.21 (ddd≈dt, H-8), 4.48 (dd, H-9a), 4.14 (dd, H-9b), 5.42 (d, NH), 3.29 (s, 3H, $OCH_3$), 1.56, 1.94, 2.04, 2.08, 2.09, 2.19 (each s, each 3H, NAc and OAc); $J_{3,4}$ = 3.8, $J_{4,5}$ = 10.0, $J_{5,6}$ = 10.2, $J_{5,NH}$ = 9.0, $J_{6,7}$ = 1.5, $J_{7,8}$ = 6.2, $J_{8,9a}$ = 2.4, $J_{8,9b}$ = 6.2, $J_{9a,9b}$ = 12.4 Hz.

**1,2;3,4-Di-O-benzylidene-6-O-(5-acetamido-1,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-iodo-β-erythro-L-manno-2-nonulopyranosyl)-α-D-galactopyranose (25):** The glycal 20 (97.4 mg, 0.2 mmol), dissolved in anhyd acetonitrile (5 mL), was treated with 1,2;3,4-di-O-benzylidene-α-D-galactopyra-

nose[25] (71.2 mg, 0.2 mmol) and *N*-iodosuccinimide (67.5 mg, 0.3 mmol). After 2 h more NIS (22.5 mg, 0.1 mmol) was added and the mixture heated to 60°C for 2 h and then left for 25 h at room temperature. Following work-up as described in the previous experiment, the residue was dissolved in methanol and separated by HPLC on a reversed phase column (RP-8, Merck) by elution with 75% aq methanol. The product fractions were pooled and recrystallized from methanol to give 41.9 mg (22%), colourless crystals, mp 192°C, $[\alpha]_D^{20}$ -35.0° (c 0.52, chloroform). $^1$H NMR ($CDCl_3$) δ 5.83 (d, H-1), 4.42 (dd, H-2), 4.76 (dd, H-3), 4.32 (dd, H-4), 4.20 (m, H-5), 3.73 (mc, H-6a), 3.48 (mc, H-6b), 4.11 and 4.20 (AB, 2H, H-1a', H-1b'), 4.48 (d, H-3', 4.70 (dd, H-4'), 4.37 (dddapdd, H-5'), 4.11 (dd, H-6'), 5.23 (m, 2H, H-7, H-8), 4.45 (dd, H-9a'), 4.12 (dd, H-9b'), 5.34 (d, NH), 5.78 and 5.85 (each s, PhCH), 1.90, 1.91, 2.03, 2.07, 2.17 (each s, each 3H, NAc and OAc), 7.42 and 7.54 (each mc, 10H, Aryl-H); $J_{1,2}$ = 5.2, $J_{2,3}$ = 2.4, $J_{3,4}$ = 8.2, $J_{4,5}$ = 1.8, $J_{1a',1b'}$ = 9.5, $J_{3',4'}$ = 3.9, $J_{4',5'}$ = 10.3, $J_{5',6'}$ = 10.2, $J_{5',NH}$ = 9.8, $J_{6',7'}$ = 1.5, $J_{8',9a'}$ = 2.4, $J_{8',9b'}$ = 6.2, $J_{9a',9b'}$ = 12.4 Hz.

Anal. Calcd for $C_{41}H_{48}INO_{18}$ (965.7): C, 50.78; H, 4.99; N, 1.44. Found: C, 50.76; H, 5.03; N, 1.47

As a side product of this reaction **5-Acetamido-1,4,7,8,9-penta-O-acetyl-3,5-dideoxy-3-iodo-α/β-D-erythro-L-manno-2-nonulopyranose (22)** was obtained and isolated as one fraction, 34.5 mg (28%). $^1$H NMR showed a ratio α:β = 1:4. $^1$H NMR ($CDCl_3$) δ 4.52 (d, H-3), 4.82 (dd, H-4), 5.26 (m, 2H, H-7, H-8), 5.85 (d, NH), 1.94, 2.05, 2.09, 2.10, 2.14, 2.19 (each s, each 3H, NAc and OAc); $J_{3,4}$ = 4.0, $J_{4,5}$ = 10.0, $J_{5,NH}$ ≈ 8.4 Hz. The minor component was the α-anomer, as is evident from resonances at 1.89, 2.05, 2.09, 2.13, 2.14, 2.15 (each s, each 3H, NHc and OAc).

**Methyl 5-Acetamido-2,6-anhydro-8,9-O-isopropylidene-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonate (27).** A solution of compound **11** (1.0 g, 3.3 mmol) in anhyd acetone (40 mL) was treated with 2,2-dimethoxypropane and dry ion exchange resin (Dowex-50 $H^+$) at room temperature for 30 min. Following filtration and evaporation, column chromotography (toluene/ethanol, 5:1) gave colorless crystals, 610

mg (54%), mp 178°C, $[\alpha]_D^{20}$ +29.8° (c 1.32, methanol). $^1$H NMR (pyridine-$d_5$) δ 6.41 (d, H-3), 5.07 (dd, H-4), 4.82 (m, H-5), 4.29 (dd, H-6), 4.65 (dd, H-7), 4.82 (m, H-8), 4.48 (dd, H-9a), 4.38 (dd, H-9b), 3.61 (s, 3H, $OCH_3$), 2.04 (s, 3H, NAc), 1.39, 1.52 (each s, each 3H, $C(CH_3)_2$); $J_{3,4}$ = 2.5, $J_{4,5}$ = 8.6, $J_{5,6}$ = 10.4, $J_{6,7}$ = 1.2, $J_{7,8}$ = 7.7, $J_{8,9a}$ = 5.6, $J_{8,9b}$ = 6.4, $J_{9a,9b}$ = 8.6 Hz.

Anal. Calcd for $C_{15}H_{23}NO_8$ (345.4): C, 52.12; H, 6.71; N, 4.06. Found: C, 52,10; H, 6.74; N, 4.13.

**Methyl 5-Acetamido-4,7-di-O-acetyl-2,6-anhydro-8,9-O-isopropylidene-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonate (28).** Compound 27 (10 mg, 0.03 mmol) was dissolved in anhyd pyridine (0.5 mL), treated with acetic anhydride (0.1 mL) and left for 12 h at room temperature. After coevaporation with toluene, 9.6 mg (75%) was obtained, a syrup, $[\alpha]_D^{20}$ +9.7° (c 0.25, dichloromethane). $^1$H-NMR ($CDCl_3$) δ 5.91 (d, H-3), 5.64 (dd, H-4), 4.22 (ddd, H-5), 4.39 (dd, H-6), 5.37 (dd, H-7), 4.36 (ddd, H-8), 4.12 (dd, H-9a), 3.95 (dd, H-9b), 5.50 (d, NH), 2.08, 2.12, 2.16 (each s, each 3H, NAc and OAc), 3.79 (s, 3H, $OCH_3$), 1.35, 1.37 (each s, each 3H, $C(CH_3)_2$); $J_{3,4}$ = 2.5, $J_{4,5}$ = 8.3, $J_{5,NH}$ = 9.0, $J_{5,6}$ = 10.6, $J_{6,7}$ = 2.3, $J_{7,8}$ = 5.5, $J_{8,9a}$ = 6.2, $J_{8,9b}$ = 6.6, $J_{9a,9b}$ = 8.9 Hz.

Anal. Calcd for $C_{19}H_{27}NO_{10}$ (429.4): C, 53.10; H, 6.34; N, 3.26. Found: C, 52.99; H, 6.41; N, 3.27.

**5-Acetamido-2,6-anhydro-8,9-O-isopropylidene-3,5-dideoxy-D-glycero-D-galacto-non-2-enitol (29).** Compound 27 (550 mg, 1.6 mmol) was dissolved in anhyd methanol (30 mL) and treated at 0°C successively with sodium borohydride (900 mg). After complete addition, the mixture was stirred for 1 h at room temperature, then neutralized with an ion exchange resin (Dowex-50, $H^+$), filtered and the resin washed with methanol. The combined filtrates were evaporated and coevaporated with anhyd methanol to remove methyl borate to give 344 mg (68%), syrup, $[\alpha]_D^{20}$ -27.0° (c 1.39, methanol). $^1$H NMR (pyridine-$d_5$) δ 5.10 (mc, 2H, H-1a, -1b), 4.40 (d, H-3), 5.02 (dd, H-4), 4.85 (ddd, H-5), 4.55 (dd, H-6), 4.22 (dd, H-7), 4.75 (ddd, H-8), 4.42 (dd, H-9a), 4.32 (dd, H-9b), 2.08 (s, 3H, NAc), 1.41, 1.51 (each s, each 3H, $C(CH_3)_2$);

$J_{3,4}$ = 2.0, $J_{4,5}$ = 9.0, $J_{5,6}$ = 10.6, $J_{6,7}$ = 1.7, $J_{7,8}$ = 7.6, $J_{8,9a}$ = 5.4, $J_{8,9b}$ = 6.3, $J_{9a,9b}$ = 8.4 Hz.

Anal. Calcd for $C_{14}H_{23}NO_7$ (317.3): C, 52.98; H, 7.30; N, 4.41. Found: C, 52.81; H, 7.29; N, 4.46.

**5-Acetamido-1,4,7-tri-O-acetyl-2,6-anhydro-8,9-O-isopropylidene-3,5-dideoxy-D-glycero-D-galacto-non-2-enitol (30).** Compound **29** (69.8 mg, 0.22 mmol) was dissolved in anhyd pyridine (4 mL), treated with acetic anhydride (0.33 mL) and a catalytic amount of 4-dimethylaminopyridine. After 12 h at room temperature evaporation and coevaporation with toluene gave a residue which was chromatographed (dichloromethane/methanol, 20:1) to give 75 mg of a colorless syrup (77%), $[\alpha]_D^{20}$ +18.6° (c 0.3, dichloromethane). $^1H$ NMR ($CDCl_3$) δ 4.30 and 4.53 ((AB)d, 2H, H-1a, -1b), 4.88 (d, H-3), 5.49 (ddt, H-4), 4.73 (ddd, H-5), 4.20 (dd, H-6), 5.47 (dd, H-7), 4.43 (ddd, H-8), 4.13 (dd, H-9a), 3.98 (dd, H-9b), 5.19 (d, NH), 1.67, 1.71, 1.97, 2.17 (each s, each 3H, NAc and OAc), 1.37, 1.45 (each s, each 3H, $C(CH_3)_2$); $J_{1a,1b}$ = 13.4, $J_{1a,3}$ = 2.2, $J_{1a,4}$ = 1.0, $J_{1b,3}/J_{1b,4}$ = 1.0, $J_{3,4}$ = 2.4, $J_{4,5}$ = 8.6, $J_{5,NH}$ = 10.1, $J_{5,6}$ = 10.6, $J_{6,7}$ = 2.4, $J_{7,8}$ = 6.8, $J_{8,9a}$ = 6.6, $J_{8,9b}$ = 6.3, $J_{9a,9b}$ = 8.8 Hz.

Anal. Calcd for $C_{20}H_{29}NO_{10}$ (443.4): C, 54.13; H, 6.59; N, 3.16. Found: C, 54.55; H, 6.50; N, 3.19.

**1,2;3,4-Di-O-benzylidene-6-O-(5-acetamido-1,4,7-tri-O-acetyl-3,5-dideoxy-3-iodo-8,9-O-isopropylidene-β-D-erythro-L-manno-2-nonulopyranosyl)-α-D-galactopyranose (26).**

a) The glycal derivative **30** (48 mg, 0.11 mmol) and 1,2;3,4-di-O-benzylidene-α-D-galactopyranose[25] (77 mg, 0.22 mmol) were dissolved in anhyd acetonitrile (3 mL) and stirred for 30 min with molecular sieves 3 Å and 4 Å. *N*-Iodosuccinimide (61.8 mg, 0.27 mmol) was added and the mixture left at room temperature for 1 day. After filtration and evaporation, the residue was dissolved in dichloromethane, successively washed with aq sodium thiosulfate and water, dried ($Na_2SO_4$) and concentrated *in vacuo*. Following gel filtration, separation was effected by HPLC (toluene/ethanol, 5:1) to give 18.2 mg (17%) of **26**.

b) Similarly, **30** (87 mg, 0.20 mmol) and the galactose derivative (105 mg, 0.34 mmol) were dissolved in anhyd dichlo-

romethane (10 mL) and stirred with molecular sieves 3 Å for 30 min. The mixture was treated with 2,4,4,6-tetrabromocyclohexadienone (TBCO, 78 mg, 0.19 mmol) and iodine (96 mg, 0.76 mmol) and stirred for 24 h at room temperature. After evaporation, the residue was dissolved in dichloromethane, washed with aq sodium thiosulfate, 0.1 N sodium hydroxide (to remove the resulting tribromophenol) and water, dried ($Na_2SO_4$) and purified as described in a) to give 12.4 mg (7%), colorless syrup, $[\alpha]_D^{20}$ -19.3° (c 0.9, chloroform). $^1H$ NMR ($CDCl_3$) δ 5.80 (d, H-1), 4.41 (dd, H-2), 4.75 (dd, H-3), 4.32 (dd, H-4), 4.13 (ddd, H-5), 3.69 (dd, H-6a), 3.82 (dd, H-6b), 4.12 (s, H-1a'), 4.07 (s, H-1b'), 4.39 (d, H-3'), 4.67 (dd, H-4'), 4.18 (ddd, H-5'), 4.07 (dd, H-6'), 5.05 (dd, H-7'), 4.20 (ddd, H-8'), 3.88 (dd, H-9a'), 3.95 (dd, H-9b'), 5.21 (d, NH), 1.61, 1.88, 1.97, 2.15 (each s, each 3H, OAc, NAc), 1.28, 1.34 (each s, each 3H, $C(CH_3)_2$), 5.77 and 5.83 (each s, PhCH), 7.40 (m, 10H, Aryl-H); $J_{1,2}$ = 5.1, $J_{2,3}$ = 2.1, $J_{3,4}$ = 8.2, $J_{4,5}$ = 1.4, $J_{5,6a}$ = 4.8, $J_{5,6b}$ = 6.2, $J_{6a,6b}$ = 9.2, $J_{3',4'}$ = 3.9, $J_{4',5'}$ = 10.4, $J_{5',NH}$ = 9.8, $J_{5',6'}$ = 10.0, $J_{6',7'}$ = 1.8, $J_{7',8'}$ = 7.4, $J_{8',9a'}$ = 6.0, $J_{8',9b'}$ = 7.0, $J_{9a',9b'}$ = 8.8 Hz.

Anal. Calc for $C_{42}H_{52}INO_{16}$ (953.4): C, 52.87; H, 5.50; N, 1.47. Found: C, 53.72; H, 5.29; N, 1.47.

**1,2,3,4-Tetra-O-benzyl-6-O-(5-acetamido-1,4,7-tri-O-acetyl-3,5-dideoxy-3-iodo-8,9-O-isopropylidene-β-D-erythro-L-manno-2-nonulopyranosyl)-α-D-galactopyranose (31).** The glycal **30** (48 mg, 0.11 mmol) and benzyl 2,3,4-tri-O-benzyl-α-D-galactopyranoside[34] (97 mg (0.22 mmol), dissolved in anhyd acetonitrile (3 mL), were stirred for 30 min with molecular sieves 3 Å; then, NIS (42 mg, 0.18 mmol) was added and stirring continued at room temperature for 24 h. The work-up and purification were done as in the previous preparation to give 19 mg (16%), colourless syrup, $[\alpha]_D^{20}$ -21.2° (c 0.95, chloroform. $^1H$ NMR ($CDCl_3$) δ 4.84 (d, H-1), 3.90 (mc, 2H, H-3), 3.96 (mc, H-4), 3.87 (ddd, H-5), 3.42 (dd, H-6a), 3.38 (dd, H-6b), 4.08 (s, H-1a'), 4.17 (s, H-1b'), 4.34 (d, H-3'), 4.64 (dd, H-4'), 4.30 (ddd, H-6'), 4.15 (dd, H-6'), 5.00 (dd, H-7'), 4.18 (ddd, H-8'), 3.91 (dd, H-9a'), 3.86 (dd, H-9b'), 1.52, 1.85, 1.98, 2.11 (each s, each 3H,

OAc, NAc), 1.23, 1.30 (each s, each 3H, $C(CH_3)_2$), 5.18 (d, NH, 7.40 (mc, 20H, Aryl-H), 4.99, 5.28, 5.77, 5.83 (4 AB, each 2H, Aryl-$C\underline{H}_2$); $J_{1,2}$ = 3.4, $J_{4,5}$ = 1.6, $J_{5,6a}$ = 5.4, $J_{5,6b}$ = 6.4, $J_{6a,6b}$ = 8.9, $J_{3',4'}$ = 4.0, $J_{4',5'}$ = 10.2, $J_{5',6'}$ = 10.6, $J_{5',NH}$ = 9.8, $J_{6',7'}$ = 2.2, $J_{7',8'}$ = 7.6, $J_{8',9a'}$ = 6.0, $J_{8',9b'}$ = 6.5, $J_{9a',9b'}$ = 9.0 Hz.

Anal. Calcd for $C_{54}H_{64}INO_{16}$ (1110.0): C, 58.43; H, 5.81; N, 1.26. Found: C, 58.41, H, 6.12; N, 1.30.

**Methyl (Phenyl-5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-β-(34) and α-D-glycero-D-galacto-2-nonulopyranosid)onate (35).**

a) The β-acetate 5 (103 mg, 0.19 mmol), dissolved in anhyd chloroform, (5 mL) was treated with thiophenol (0.03 mL, 0.29 mmol) and portionwise with zirconium tetrachloride (66 mg, 0.28 mmol) at room temperature. After 12 h the mixture was diluted with dichloromethane, washed with aq sodium hydrogencarbonate and water, dried ($Na_2SO_4$) and concentrated to give 86 mg (76%) of a mixture of **34** and **35** [**34**:**35** = 5:2 ($^1$H NMR)].

b) The β-chloride **6** (106.7 mg, 0.2 mmol) in anhyd chloroform (5 mL) was treated with thiophenol (0.3 mL, 2.92 mmol). At 5-10°C anhyd zinc chloride (44 mg, 3.2 mmol) was added portionwise, and the mixture further stirred for 12 h at room temperature. Work-up as in a) gave 86 mg (73%) of product [**34**:**35** = 2:1 ($^1$H NMR)].

c) The β-fluoride **32** (60 mg, 0.12 mmol) in anhyd chloroform (5 mL), thiophenol (0.02 mL, 0.19 mmol) and boron trifluoride etherate (0.4 mL) were kept at room temperature for 24 h. Work-up as previously described gave 56.1 mg (80%) of product [**34**:**35** = 4:3 ($^1$H NMR)].

d) The α-fluoride **33** (60 mg, 0.12 mmol) was reacted and worked up as in c) to give 21 mg (29%) of product [**34**:**35** = 3:2 ($^1$H NMR)].

e) The β-acetate 5 (700 mg, 1.2 mmol) dissolved in anhyd chloroform (100 mL), was treated with thiophenol (0.25 mL, 2.4 mmol) and boron trifluoride etherate (8 mL, 48.8 mmol) at room temprature for 12 h. Work-up as in a) and a subsequent column chromatography (toluene/ethanol, 5:1) gave 505 mg (66%), colorless crystalls, mp 84-87°C, $[\alpha]_D^{20}$ -99.6° (c 0.29, chloroform). $^1$H NMR ($C_6D_6$) δ 2.03 (dd, H-3a), 2.81

(dd, H-3e), 5.29 (ddd, H-4), 4.50 (dd, H-5), 4.67 (dd, H-6), 5.75 (dd, H-7), 5.43 (ddd, H-8), 5.00 (dd, H-9a), 4.38 (dd, H-9b), 4.86 (d, NH), 3.26 (s, 3H, $COOCH_3$), 1.64, 1.68 (2), 1.89, 1.95 (each s, each 3H, OAc, NAc), 7.60, 7.06 (m, 10H, Aryl-H); $J_{3a,3e}$ = 14.0, $J_{3a,4}$ = 12.0, $J_{3e,4}$ = 4.8, $J_{4,5}$ = 11.1, $J_{5,NH}$ = 10.4, $J_{5,6}$ = 10.6, $J_{6,7}$ = 1.7, $J_{7,8}$ = 4.0, $J_{8,9a}$ ◘ 2.1, $J_{8,9b}$ = 8.8, $J_{9a,9b}$ = 12.4 Hz. $^1H$ NMR ($CDCl_3$) δ 2.00 (dd, H-3a), 2.62 (dd, H-3e), 5.35 (ddd, H-4), 4.10 (ddd, H-5), 4.55 (dd, H-6), 5.40 (dd, H-7), 5.49 (ddd, H-8), 3.93 (dd, H-9a), 4.43 (dd, H-9b), 5.45 (d, NH), xx (s, 3H, $COOCH_3$), 1.85, 1.90, 1.96, 2.04, 2.08 (each s, each 3H, OAc, NAc), 7.35 (mc, 10H, Aryl-H), $J_{3a,3e}$ = 13.9, $J_{3a,4}$ = 11.4, $J_{3e,4}$ = 4.8, $J_{4,5}$ = 10.8, $J_{5,HH}$ = 10.2, $J_{5,4}$ = 10.6, $J_{6,7}$ = 2.5, $J_{7,8}$ = 1.8, $J_{8,9a}$ = 2.1, $J_{8,9b}$ = 8.3, $J_{9a,9b}$ = 12.4 Hz. f) The β-chloride 6 (175 mg, 0.34 mmol) dissolved in anhyd chloroform (5 mL), was treated with thiophenol (0.04 mL, 0.34 mmol) and methanolic potassium hydroxide (0.5 M, 1.0 mL) at room temperature. After another 24 h the mixture was filtered, washed with methanol/chloroform, dried ($Na_2SO_4$) and the solvent evaporated. The residue was dissolved in anhyd pyridine (3 mL) and treated with acetic anhydride (1 mL) for 12 h at room temperature. The mixture was evaporated and coevaporated with toluene to give 120 mg (60%), colorless crystalls, mp 97-102°C, $[\alpha]_D^{20}$ +10.1° (c 4.43, chloroform). $^1H$ NMR ($C_6D_6$) δ 2.00 (mc, H-3a), 2.98 (dd, H-3e), 4.81 (ddd, H-4), 4.33 (ddd, H-5), 4.31 (dd, H-6), 5.52 (dd, H-7), 5.64 (ddd, H-8), 4.76 (dd, H-9a), 4.45 (dd, H-9b), 3.23 (s, 3H, $COOCH_3$), 1.59, 1.60, 1.79, 1.93, 1.94 (each s, each 3H, OAc, NAc), 7.64 (mc, 10H, Aryl-H); $J_{3a,3e}$ = 12.5, $J_{3a,4}$ = 10.0, $J_{3e,4}$ = 4.5, $J_{4,5}$ = 8.5, $J_{5,HH}$ = 10.0, $J_{5,6}$ = 9.0, $J_{6,7}$ = 2.0, $J_{7,8}$ = 7.0, $J_{8,9a}$ = 2.5, $J_{8,9b}$ = 6.5, $J_{9a,9b}$ = 12.5 Hz. $^1H$ NMR ($CDCl_3$) δ 2.00 (dd, H-3a), 2.83 (dd, H-3e), 4.84 (dd, H-4), 3.98 (ddd, H-5), 4.21 (dd, H-6), 5.29 (dd, H-7), 5.29 (ddd, H-8), 4.40 (dd, h-9a), 3.92 (dd, H-9b), 5.27 (d, NH), 3.57 (s, 3H, $COOCH_3$), 1.87, 2.02, 2.05, 2.14, 2.15 (each s, each 3H, OAc, NAc), 7.48 (mc, 10H, Aryl-H); $J_{3a,3e}$ = 12.5, $J_{3a,4}$ = 10.5, $J_{3a,4}$ = 4.5, $J_{4,5}$ = 9.5, $J_{5,HH}$ = 10.5, $J_{5,6}$ = 11.5, $J_{6,7}$ = 5.0, $J_{8,9a}$ = 2.0, $J_{8,9b}$ = 8.5, $J_{9a,9}$ = 12.5 Hz.

Anal. Calcd for $C_{26}H_{33}NO_{12}S$ (583.6): C, 53,50; H, 5.69; N, 2.39. Found for **34**: C, 53.36; H, 5.61; N, 2.37. Found for 35: C, 53.12; H, 5.53; N, 2.31.

**1,2;3,4-Di-O-isopropylidene-6-O-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-(36) and α-D-glycero-D-galacto-2-nonulopyranosonate)-α-D-galactopyranose (37).**
a) The β-thiophenyl glycoside **34** (99.2 mg, 0.17 mmol) and 1,2;3,4-di-O-isopropylidene-α-D-galactopyranose (65 mg, 0.25 ml) dissolved in anhyd acetonitrile/toluene (1:1, 4 mL), were treated with phenylmercuric triflate (85 mg, 0.20 mmol) for 24 h at room temperature. After addition of a few drops of pyridine, dichloromethane was added and the solution washed successively with aq ethylenediamine tetraacetate (EDTA, 5%), saturated aq sodium hydrogencarbonate and water, then dried ($Na_2SO_4$) and concentrated. The residue was separated by HPLC (toluene/ethanol, 5:1) to give 17.2 mg unreacted galactose derivate , 7 mg (6%) **36**, 10 mg **34**, 28 mg (24%) **37**, and 4 mg (5%) **12** (cf. entry 1, Table 2). Reactions in entries 2 and 3 (Table 2) were performed in a corresponding manner.
b) A mixture of the galactose derivative (71 mg, 0.27 mmol), phenylmeruric triflate (105.2 mg, 0.25 mmol) and some molecular sieves 3 and 4 Å were dried in high vacuo. Following nitrogen at room temperature, a solution of **34** (125.6 mg, 0.21 mmol) in the same solvent (1 mL) was added dropwise and then the reaction mixture was left for 12 h. The work-up and separation followed a) and afforded unreacted galactose derivative 12.3 mg, 38.4 mg (25%) **36**, 15.1 mg (10%) **37**, and 21.4 mg (21%) **12**. (cf. entry 4, Table 2) Reactions in entries 5 and 6 (Tables 2) were done in a similar manner.
c) Compound **34** (50 mg, 0.09 mmol) and the galactose derivative (34 mg, 0.13 mmol) were coevaporated several times with anhyd toluene, then dissolved in anhyd nitromethane/toluene, 1:1 and stirred for 30 min with molecular sieves (ca. 100 mg 3 Å and 4 Å). After addition of *N*-bromosuccinimide (17 mg, 0.1 mmol) the reaction was left at room temperature for 24 h. For work-up it was diluted with ether and filtered, then washed with aq sodium hydrogensulfite (10%), water, and aq sodium hydrogencarbonate, dried ($Na_2SO_4$), concentrated and

purified chromatographically (toluene/ethyl acetate, 1:3) to give 17.5 mg (28%) of product [36:37 = 1:1 ($^1$H NMR)].
Compound **36**: colourless solid, softening mp 90°C, $[\alpha]_D^{20}$ -47.0° (c 1.92, dichloromethane). $^1$H NMR ($CDCl_3$) δ 5.50 (d, H-1), 4.34 (dd, H-2), 4.67 (dd, H-3), 4.20 (mc, H-4), 3.97 (ddd, H-5), 3.45 (dd, H-6a), 3.99 (dd, H-6b), 2.10 (mc, H-3a'), 2.49 (dd, H-3e'), 5.28 (ddd, H-4'), 4.10 (ddd, H-5'), 4.37 (dd, H-6'), 5.45 (dd, H-7'), 5.20 (ddd, H-8'), 4.84 (dd, H-9a'), 4.20 (dd, H-9b'), 5.26 (d, NH), 3.84 (s, 3H, $COOCH_3$), 1.97, 2.02, 2.03, 2.06, 2.15 (each s, each 3H, OAc, NAc); 1.34, 1.43, 1.48, 1.57 (each s, each 3H, $C(CH_3)_2$); $J_{1,2}$ = 5.1, $J_{2,3}$ = 2.4, $J_{3,4}$ = 8.0, $J_{4,5}$ = 1.6, $J_{5,6a}$ = 5.3, $J_{5,6b}$ = 8.6, $J_{6a,6b}$ = 9.5, $J_{3a',3e'}$ = 13.0, $J_{3a',4'}$ = 12.0, $J_{3e',4'}$ = 5.4, $J_{4',5'}$ = 10.2, $J_{5',HH}$ = 10.0, $J_{5',6'}$ = 8.0, $J_{6',7'}$ = 2.0, $J_{7',8'}$ = 4.2, $J_{8',9a'}$ = 2.4, $J_{8',9b'}$ = 8.0, $J_{9a',9b'}$ = 12.5 Hz.
Compound **37**: colourless syrup, $[\alpha]_D^{20}$ -40.0° (c 0.87, dichloromethane. $^1$H NMR ($CDCl_3$) δ 5.51 (d, H-1), 4.27 (dd, H-2), 4.60 (dd, H-3), 4.24 (dd, H-4), 3.81 (ddd, H-5), 3.59 (dd, H-6a), 3.90 (mc, H-6b), 2.10 (dd, H-3a'), 2.62 (dd, H-3e'), 4.88 (ddd, H-4'), 4.09 (ddd, H-5'), 4.10 (dd, H-6'), 5.32 (dd, H-7'), 5.41 (ddd, H-8'), 4.29 (dd, H-9a'), 4.17 (dd, H-9b'), 5.15 (d, NH), 3.78 (s, 3H, $COOCH_3$), 1.88, 2.02, 2.04, 2.13 (2), (each s, each 3H, OAc, NAc), 1.32, 1.33, 1.42, 1.54 (each s, each 3H, $C(CH_3)_2$); $J_{1,2}$ = 5.0, $J_{2,3}$ = 2.4, $J_{3,4}$ = 7.6, $J_{4,5}$ = 2.0, $J_{5,6a}$ = 5.5, $J_{5,6b}$ = 7.4, $J_{6a,6b}$ = 8.4, $J_{3a',3e'}$ = 12.0, $J_{3a',4'}$ = 11.4, $J_{3e',4'}$ = 4.5, $J_{4',5'}$ = 8.6, $J_{5',NH}$ = 9.9, $J_{5',6'}$ = 9.6, $J_{6',7'}$ = 2.0, $J_{7',7a'}$ = 7.9, $J_{8',9a'}$ = 2.8, $J_{8',9b'}$ = 5.4, $J_{9a',9b'}$ = 11.4 Hz.

Anal. Calcd for $C_{32}H_{47}NO_{18}$ (733.7): C, 52.38; H, 6.46; N, 1.91. Found for **36**: C, 52.41; H, 6.41; N, 1.85. Found for **37**: C, 52.53, H, 6.51; N, 1.87.

**Benzyl 2-Acetamido-2-deoxy-3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-6-O-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosonate)-α-D-glucopyranoside (38).** A *mixture of phenylmercuric* triflate (95 mg, 0.22 mmol) and benzyl 2-acetamido-2-deoxy-3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-

D-glucopyranoside[50] (45 mg, 0.1 mmol) dissolved in anhyd toluene/acetonitrile (1:1, 3 mL), was stirred with molecular sieves (3 Å and 4 Å) for 30 min under nitrogen. The mixture was treated dropwise with a solution of **34** (111 mg, 0.19 mmol) in anhyd toluene/acetonitril (1:1, 2 mL), kept at room temperature for 24 h and worked up as before, and the mixture separated by HPLC (toluene/ethanol, 5:1). Obtained were the aglycone sugar component 4.7 mg, 36.2 mg (32%) **34**, 21 mg (22%) **12**, and 13.6 mg (8%) of product as a colorless syrup, $[\alpha]_D^{20}$ +60.4° (c 0.24, dichloromethane). $^1$H NMR ($CDCl_3$) δ 4.83, (dd, H-1), 3.93 (dd, H-6a), 3.88 (dd, H-6b), 6.51 (d, NH), 1.05 (mc, 28H, i-$C_3H_7$), 2.04 (dd, H-2a'), 2.47 (dd, H-3e'), 5.01 (mc, H-4'), 4.18 (ddd, H-5'), 4.48 (dd, H-6'), 5.35 (dd, H-7'), 5.45 (mc, H-8'), 5.27 (dd, H-9a'), 5.45 (mc, NH), 3.76 (s, 3H, $COOCH_3$), 1.81, 1.82, 1.87, 1.90, 2.01 (each s, each 3H, OAc, NAc), 4.48 and 4.76 (AB, 2H, $PhCH_2$), 7.36 (m, 5H, Aryl-H); $J_{1,2}$ = 3.6, $J_{2,NH}$ = 10.8, $J_{5,6a}$ = 2.7, $J_{5,6b}$ = 2.1, $J_{6a,6b}$ = 11.0, $J_{3a',3e'}$ = 13.5, $J_{3a',4'}$ = 11.1, $J_{3e',4'}$ = 5.4, $J_{4',5'}$ = 9.0, $J_{5',6'}$ = 10.0, $J_{5',NH}$ = 10.8, $J_{6',7'}$ = 2.4, $J_{7',8'}$ = 9.0, $J_{8',9a'}$ = 2.4 Hz.

Anal. Calcd for $C_{47}H_{74}N_2O_{19}Si_2$ (1027.3) C, 54.95; H, 7.26; N, 2.73. Found: C, 54.99; H, 7.38; N, 2.52.



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