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Studies on the Synthesis of Tunicamycin. The Preparation of 7-deoxy-2-deamino-6-Hydroxy Tunicamine and Related Products.

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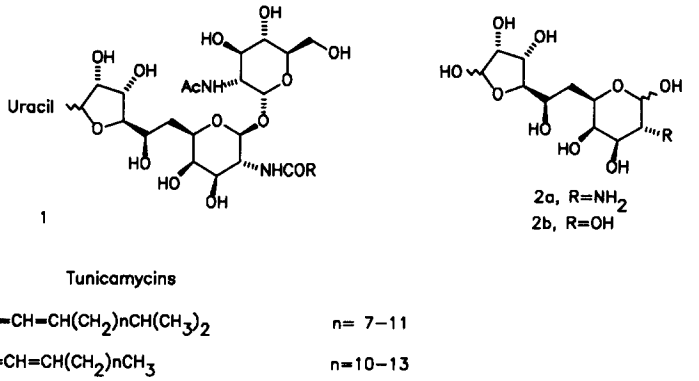
Abstract: The condensation of methyl 5-deoxy-5-diazo-2,3-O-isopropylidene-β-D-ribofuranoside with 1,2:3,4-di-O-isopropylidene-D-galactohexonodialdo-1,5-pyranoside gave the ketone C-disaccharide **11** as the sole product. This ketone was transformed into different derivatives. Thus, its reduction led stereoselectively to the corresponding alcohols. Similar transformations led to the corresponding alkane and amino derivatives, of potential biological interest as inhibitors for glycosidases.These results can be useful for the synthesis of tunicamine and its analogues.

INTRODUCTION

Tunicamycins (**1**) are a family of nucleosides isolated from *Streptomyces lysosuperficus*, fermentation broth that exhibit antibiotic and antiviral activity.[1] Their biological action relies on their dramatic inhibitory effects on the biosynthesis of certain polysaccharides, glycolipids and glycoproteins; this makes them potential antibiotics, antiviral agents and even antitumour agents for leukemia cells.[2] Biochemical studies have revealed that tunicamycins inhibit the transferase enzymes involved in processing UDP glucose and UDP galactose derivatives. Tunicamycins comprise at least 16 homologues that vary in the fatty acid of the galactose residue. Structurally, these complex carbohydrates contain the undecose fragment tunicamine **2a**, together with α,β-trehalose. Many antibiotics closely related to tunicamycin such as those in the streptovirudin[3] and corynetoxin[4] families contain this undecose component, and others such as Hikizimycin[5] include an eleven-carbon amino-sugar unit in a open chain (Figure 1). The synthesis of **1** is interesting and attractive not only on account of their biological properties, but also of the ability to build the C-disaccharide **2a**.[6] In fact, many research groups[7] have undertaken the synthesis of C-disaccharides, prompted by their potential inhibitory activity against glycosidases[8] or from conformational studies.[9]

We previously[10] accomplished the synthesis of the deaminotunicamine **2b** by using the well-known condensation reaction between a diazo compound and an aldehyde, which, to our knowledge, had not yet been used to prepare these products. We found the reaction of 6-deoxy-6-diazo-1,2:3,4-di-O-isopropylidene-D-galactose with methyl 2,3-O-isopropylidene-β-D-ribo-pentonodialdo-1,4-furanoside to give a 1:1 mixture of the ketone and a single epoxide in a 82% yield. The transformation of these products into deamino tunicamine was succesfully accomplished by reduction. In continuance of our research programme aimed at the total synthesis of tunicamycin, in this work we assayed the condensation between the diazo derivative of D-ribose and the aldehyde of D-galactose in order to derive conclusions on the influence of the starting reactants on the ratio of the condensation products with a view of applying the results to the synthesis of **2a**. Our synthetic method also allows one to prepare analogues of the deaminotunicamine **2b**, which is of biological interest. The results and conclusions obtained from these studies on deaminotunicamine will be greatly useful for the synthesis of tunicamine **2a**.

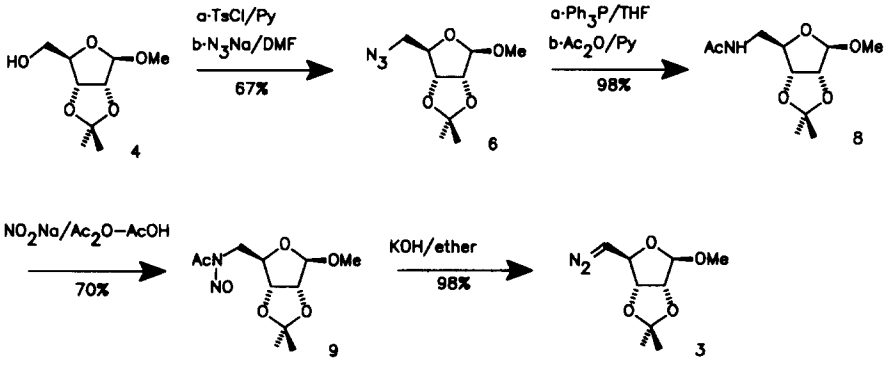
Figure 1



RESULTS AND DISCUSSION

The diazo derivative of methyl β-D-ribofuranoside, **3**, was sucessfully prepared from the methyl 2:3-O-isopropylidene-β-D-ribofuranose **4**[11] according to Scheme I (the same procedure used for the galactose derivative). Thus, tosylation of **4** and conversion into the azido derivative **6** was achieved in a 90% overall yield. Reduction of **6** to the amino **7** was performed using two different procedures (triphenyl phosphine and aluminium lithium hydride treatments), with quantitative yields in both cases.[12] Acetylation of **7** followed by N-nitrosation yielded the N-nitroso derivative **9**, alkaline treatment of which furnished the diazo derivative **3** in a 70% overall yield from **4**. The structure of the 5-deoxy-5-diazo derivative **3** was quite clear from its NMR and IR spectra, the later of which exhibited a strong absortion band at 2080 cm^{-1}.

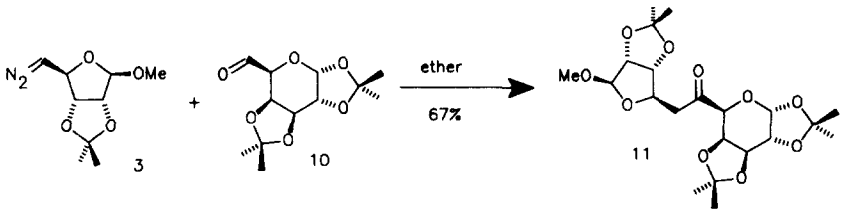
Scheme I



Condensation of the diazo compound **3** with the aldehyde **10**, synthesized from 1,2:3,4-di-O-Isopropylidene-D-galactopyranose by oxidation with nicotiniun dichromate,[13] was carried out in diethyl ether at r.t. in the absence of catalyst. After 6 hours, the reaction was complete and gave ketone **11** as the sole product in a 67% yield after purification by column chromatograhy on silica gel (no epoxide were detected). The influence of the solvent polarity on the product ratio was studied. Thus, the condensation was performed in various solvents of variable polarity (MeOH, DMF, chloroform, hexane and benzene); in all cases, the ketone was the sole product obtained. This result is completely different from that obtained in the condensation between the diazo derivative of D-galactose and the

aldehyde ribose, where the solvent polarity had a marked effect on the product ratio. Despite the rules established for this type of condensations,[14] predicting the condensation products ratio when a non-stabilized diazo compound is involved remains difficult.[15]

Scheme II



We subsequently explored various transformations of the ketone **11**. First, **11** was reduced to the corresponding alcohols with different hydrides at a variable temperature. Thus, with sodium borohydride at 25°C, the result was a mixture of the alcohols **12**:**13** in a quantitative 73:27 ratio. In order to boost the stereoselectivity of the reduction, ketone **11** was treated with Super-hydride and K-Selectride at -78°C and 25°C, respectively. In both cases, the alcohol **12** was obtained in quantitative yield and with complete stereoselectivity (table 1). On the other hand, the alcohol **13** was obtained quantitatively and fully stereoselectively by reduction with zinc borohydride at -78°C.[16] This stereochemical result is justified by the complexation effect of the zinc cation on the ketone group. The stereochemistry of both alcohols was accurately established from the well-known epoxide **14**. The absolute stereochemistry of this epoxide, synthesized by condensation of the diazo derivative of D-galactose and the aldehyde of D-ribose, was clearly elucidated by opening the oxirane ring with Super-hydride. This reaction gave the alcohols **15** and **12** in a 5:1 ratio. The former was compared with the di-O-Isopropylidene derivative of deamino tunicamine.[17] The second was undoubtedly the alcohol **13**. A comparison of its physical and spectral properties with those of the product obtained in the reduction of ketone **11** afforded the establishment of the absolute configurations **12** and **13**. Product **16**, the acetyl derivative of **12**, was prepared to confirm the structure of this alcohol.

Scheme III

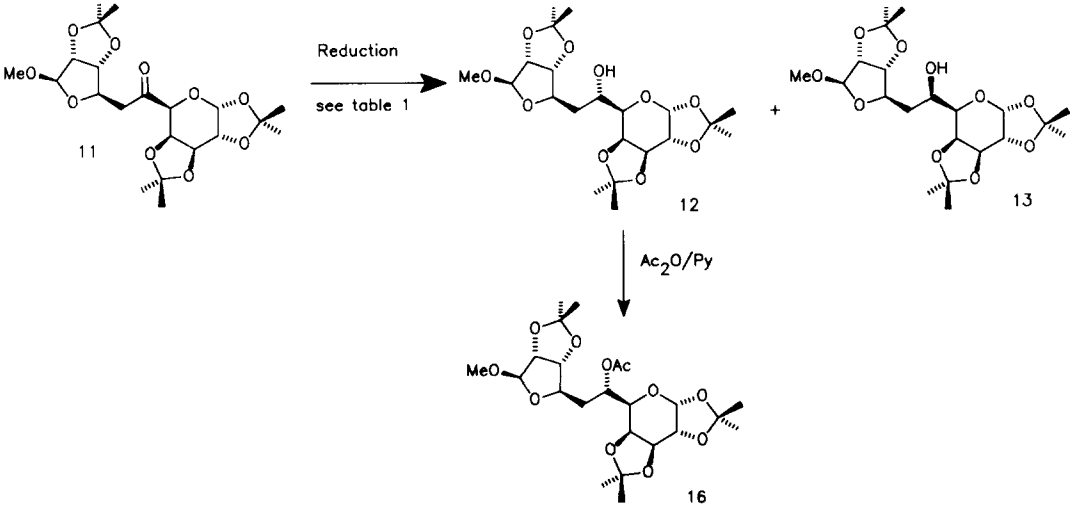
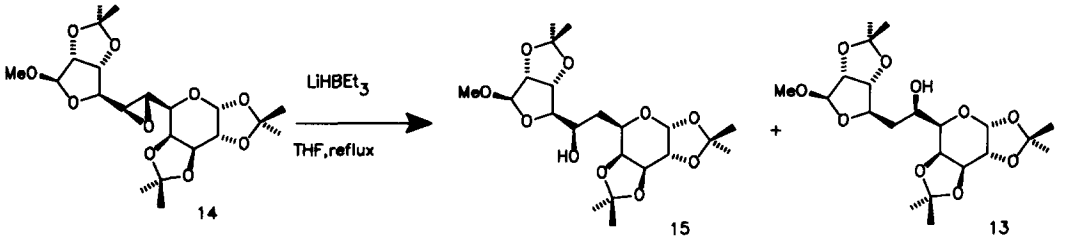


Table 1

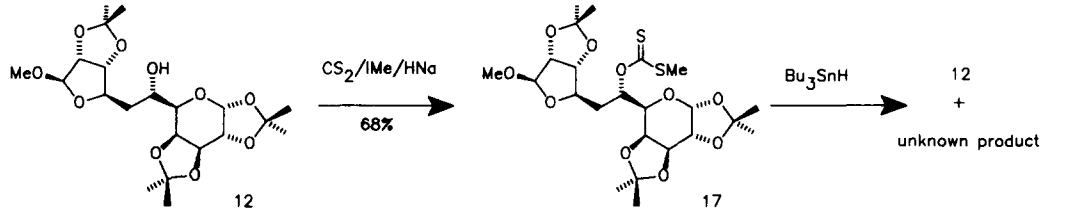
Reagent	Temperature (ºC)	Reaction time (min)	Ratio 12/13
BH4Na	25	5	73:27
BH4Na	-78	5	83:17
Zn(BH4)2	25	24	1:1
Zn(BH4)2	-78	24	0:100
Super-hydride	25	5	84:16
Super-hydride	-78	5	100:0
K-selectride	25	5	100:0
K-selectride	-78	5	100:0

Scheme IV



We thought it of interest to prepare other derivatives of these C-disaccharides with a view to the synthesis of new tunicamine analogues. For this purpose, the deoxy and amine derivatives were seemingly the most promising. In fact, C-amine glycosides are potent inhibitors for glycosidases.[18] With regard to the deoxy analogue, we first attempted the deoxygenation of **12** by reaction of its corresponding xanthogenate **17** with tributyltin hydride in toluene.[19] However, the attempt proved unsuccessful and the starting alcohol **12**, together with an unknown product,[20] were obtained. Other approaches such as reduction of the tosylated derivative of **12** with lithium aluminium hydride in anhydrous THF or direct treatment of alcohol **12** with trimethylsilyl chloride and sodium iodide were similarly unsuccessful.[21] Likewise, the Wolff-Kishner reduction[22] of the hydrazone of **11** also failed.

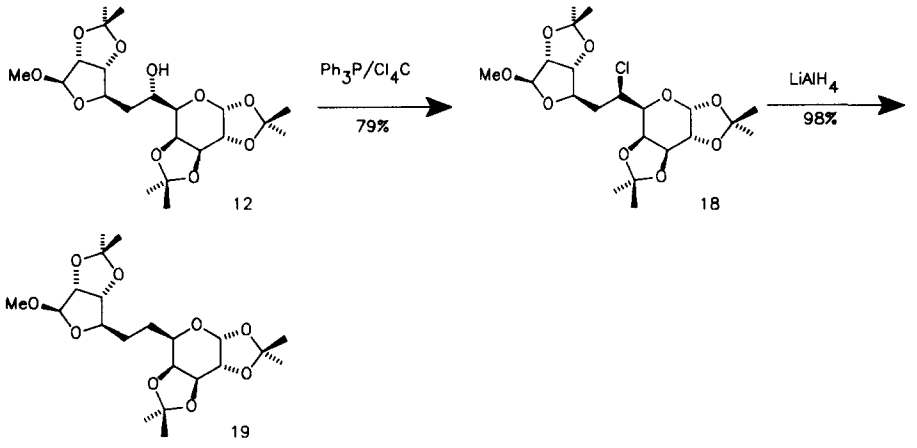
Scheme V



We thus decided to prepare halo-derivatives that could be reduced to the corresponding alkanes. Initially, we assayed direct bromination with N-bromo succinimide and triphenyl phosphine; however, the reaction did not work

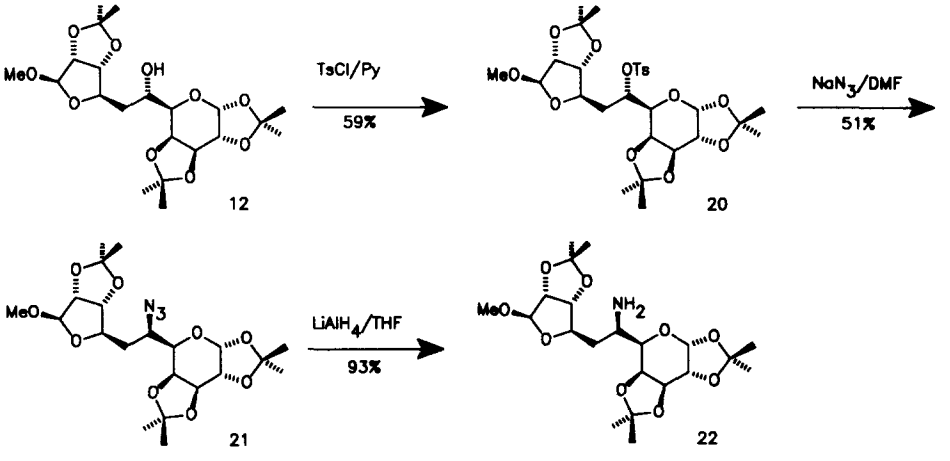
and the starting alcohol was recovered. Finally, chloration with triphenyl phosphine in carbon tetrachloride provided the chloro derivative **18** in good yield. Treatment of **18** with lithium aluminium hydride in anhydrous THF under reflux gave the alkane **19** quantitatively.

Scheme VI



The amine derivative was prepared from the tosyl derivative **20**. This was reacted with sodium azide in DMF under reflux to obtain the azido C-disaccharide **21** in a moderate yield.[23] Finally, hydride reduction of **21** with lithium aluminium yielded the amino analogue **22** quantitatively.

Scheme VII



In conclusion, we have demonstrated the usefulness of our method for preparing C-disaccharides. These reactions have been used in the synthesis of deamino tunicamine and its analogues. We trust these results can be translated to tunicamine synthesis and are currently conducting research to ascertain it.

EXPERIMENTAL PART

Melting points are given uncorrected. IR spectra were recorded on a Beckamn Aculab IV spectrophotometer; (wavenumbers are expressed in cm^{-1}). ^{1}H-NMR spectra were obtained at 200 MHz on a Bruker WP 200SY using $CDCl_3$ as solvent. Chemical shifts (δ) are expressed in ppm, with the signal for $CHCl_3$ as internal reference. Notations indicate signal multiplicity (s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet). Coupling constants are expressed as J values, in Hertz units. Mass spectra were recorded on a Hewlett-Packard 5988A instrument. Microanalyses were performed by the "Servicio de Microanálisis de la Universidad de Málaga". Specific rotations were measured with a Perkin-Elmer 241 polarimeter. Silica gel for column chromatography was Merck silica-gel 60 No. 7736. Analytical thin-layer chromatography was perfomed on Merck silica-gel 60 No.7747.

Methyl 2,3-O-isopropylidene-5-O-tosyl-β-D-ribofuranoside (5): To a cold solution containing 20 g of the alcohol **4** in 50 mL of anhydrous pyridine 27.6 g of tosyl chloride was added in small portions. After 3 h, the reaction was complete and the crude mixture was poured into ice-water with vigorous stirring. The tosyl derivative precipitated as a white solid, and the suspension was filtered. The solid was then washed with cold water twice and dried under high vacuum. An amount of 35 g of the tosyl derivative **5** was obtained as a white solid (100%). m.p. 78.5-79.5°C. $[\alpha]_D^{20}$ = -50.0° (c 1.68, $CHCl_3$). IR: 2952, 1596, 1451, 1383 cm^{-1}. ^{1}H-NMR (δ): 7.78 (d, 2H, J=8.4 Hz, aromatic H); 7.33 (d, 1H, J= 8.4 Hz, aromatic H); 4.90 (s, 1H, H-1); 4.57 (dd, 1H, $J_{3,4}$= 0.8 Hz, $J_{3,2}$= 6.1 Hz, H-3); 4.50 (d, 1H, $J_{2,3}$= 6.1 Hz, H-2); 4.28 (dt, 1H, $J_{4,3}$=0.8 Hz, $J_{4,5}$= $J_{4,5'}$=7.0 Hz, H-4); 3.98 (d, 2H, $J_{4,5}$= 7.0 Hz, H-5, H-5'); 3.21 (s, 3H, -OMe); 2.43 (s, 3H, Ar-Me); 1.42 and 1.26 (2s, 6H, C<u>Me</u>$_2$). Elemental analysis: Calcd for $C_{16}H_{22}O_7$ S 53.63% C; 6.14% H. Found 53.40% C; 6.14% H.

Methyl 5-deoxy-5-azido-2,3-O-isopropylidene-β-D-ribofuranoside (6): A mixture of 4.7 g of the tosyl derivative **5** and 6.6 g of sodium azide in 20 mL of DMF was refluxed for 2 h. After this time, the reaction was complete and the heterogeneous brown mixture was cooled, diluted with water (50 mL) and extracted with chloroform (3x40 mL). The organic layer was washed with water and dried over anhydrous sodium sulphate. The solvent was removed by rotary evaporation to give 3 g of the azido derivative **5**. This compound was reducedto the amino derivative **7**,without further purification. However, purification by column chromatography on silica gel (eluent 10:1 hexane:AcOEt) provided 2 g of the pure azido **5** derivative (67%). $[\alpha]_D^{20}$ = -50.9° (c 2.75, $CHCl_3$). IR: 2946, 2108, 1451, 1380, 1273 cm^{-1}. ^{1}H-NMR (δ): 4.97 (s, 1H, H-1); 4.57 (s, 2H, H-2, H-3); 4.26 (t, 1H, $J_{4,5}$= $J_{4,5'}$= 7.1 Hz, H-4); 3.42 (dd, 1H, $J_{5,4}$= 7.1, $J_{5,5'}$=12.6 Hz, H-5); 3.34 (s, 3H, -OMe); 3.23 (dd, 1H, $J_{5',4}$= 7.1 Hz, $J_{5,5'}$=12.6 Hz, H-5'); 1.45 and 1.29 (2s, 6H, C<u>Me</u>$_2$). ^{13}C-NMR (δ): 112.5 (<u>C</u>Me$_2$); 109.7 (C-1); 85.3, 85.0, 81.9 (C-2, C-3, C-4); 55.1 (OMe); 53.6 (C-5); 26.30 and 24.8 (C<u>Me</u>$_2$). MS (m/z): 214 (M^+-15, 35); 173 (100); 141 (8); 115 (48); 113 (61); 85 (58); 59 (79). Elemental analysis: Calcd for $C_9H_{15}O_4N_3$ 47.16% C; 6.55% H; 18.34% N. Found 47.43% C; 6.51% H; 18.43% N.

Methyl 5-deoxy-5-amino-2,3-O-isopropylidene-β-D-ribofuranoside (7). Procedure A: To a solution containing 1.1 g of the azido derivative **6** in 10 mL of anhydrous THF 1 g of lithium aluminium hydride was added in small portions. The suspension was stirred at r.t. in a nitrogen atmosphere for 8 hours. After this time, 10 mL of a 10% aqueous solution of KOH was added dropwise to destroy excess hydride and the crude mixture was extracted with dichloromethane (3x1, 10 mL). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated in vacuo to obtain 0.9 g of the pure amino compound **7** (93%). **Procedure B**: 14 g of triphenyl phophine was added to 50 mL of a THF solution containing 10 g of the azido derivative **6**. The solution was stirred at r.t. overnight. After this time, the reaction was complete; 50 mL of water was added and the mixture stirred vigorously for 5 h. The crude mixture was extracted with dichloromethane (3x1, 20 mL). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The amino compound **7** was obtained in virtually quantitative yield and subjected to the following step without further purification. $[\alpha]_D^{20}$ = -78.3° (c 0.60, $CHCl_3$). IR: 3386, 3320, 2996, 1457, 1373, 1272 cm^{-1}. ^{1}H-NMR (δ): 4.91 (d, 1H, $J_{1,2}$= 1.0 Hz, H-1); 4.53 (m, 2H, H-2, H-3); 4.11 (t, 1H, $J_{4,5}$= $J_{4,5'}$= 6.8 Hz, H-4); 3.31 (s, 3H, -OMe); 2.74 (d, 2H, $J_{5,4}$= $J_{4,5'}$=6.8 Hz, H-5, H-5'); 1.44 and 1.27 (2s, 6H, C<u>Me</u>$_2$). ^{13}C-NMR (δ): 111.8 (<u>C</u>Me$_2$); 109.2 (C-1); 88.6, 85.1, 81.8 (C-2, C-3, C-

4); 54.6 (OMe); 45.2 (C-5); 26.1 and 24.5 ($C\underline{Me}_2$). MS (m/z): 188 (M^+-15, 12); 172 (19); 156 (16); 145 (25); 115 (66); 114 (100); 113 (46); 99 (34); 87 (93); 85 (87); 56 (74). Elemental analysis: Calcd for $C_9H_{17}O_4N$ 53.20% C; 8.37% H; 6.89% N. Found 52.74% C; 8.18% H; 7.22% N.

Methyl 5-deoxy-5-acetamido-2,3-O-isopropylidene-β-D-ribofuranoside (8): To a solution containing 8 g of the amino derivative **7** in 30 mL of anhydrous pyridine 10 mL of acetic anhydride was added. The reaction mixture was allowed to stand at r.t. overnight. After this time, ice water was poured into the crude mixture, which was extracted with chloroform three times (30 mL). The combined organic layers were washed successivelly with diluted ClH, saturated sodium hydrogen carbonate solution, and water, dried over anhydrous sodium sulphate, filtered and concentrated in vacuo to obtain 9.5 g of the pure acetamido compound **8** (98.4%) as a white solid. m. p. 76-78°C. $[\alpha]_D^{20}$ = -79.4° (c 0.70, $CHCl_3$). IR: 3330, 2990, 1642, 1439, 1382, 1276 cm^{-1}. ^{1}H-NMR (δ): 6.45 (m, 1H, MeCONH-); 4.89 (s, 1H, H-1); 4.53 (d, 1H, $J_{2,3}$= 6.2 Hz, H-2); 4.48 (d, 1H, $J_{2,3}$= 6.2 Hz, H-3); 4.25 (t, 1H, $J_{4,5}$= $J_{4,5'}$= 5.8 Hz, H-4); 3.35 (m, 2H, H-5, H-5'); 3.31 (s, 3H, -OMe); 1.93 (s, 3H, -COMe); 1.39 and 1.22 (2s, 6H, $C\underline{Me}_2$). ^{13}C-NMR (δ): 170.5 (-COMe); 112.3 ($\underline{C}Me_2$); 109.8 (C-1); 85.7, 85.3, 81.9 (C-2, C-3, C-4); 55.1 (OMe); 42.2 (C-5); 26.2 and 24.7 ($C\underline{Me}_2$); 23.0 (-COMe). MS (m/z): 230 (M^+-15, 26); 173 (31); 127 (62); 98 (50); 85 (100). Elemental analysis: Calcd for $C_{11}H_{19}O_5N$ 53.87% C; 7.75% H; 5.71% N. Found 53.81% C; 7.58% H; 5.62% N.

Methyl 5-(N-nitroso)-acetamido-5-deoxy-2,3-O-isopropylidene-β-D-ribofuranoside (9): A solution containing 9 g of **8** in 44 mL of glacial acetic acid and 220 mL of acetic anhydride was cooled at -10°C. Under vigorous stirring, 65 g of sodium nitrite was slowly added over 1 h. Then, the reaction mixture was stirred for 8 h and subsequently poured over ice-water and extracted with diethyl ether (200 mL, 4x1). The organic phase was washed with 5% sodium hydrogen carbonate several times until all acetic acid was removed. Finally, washing with water, drying over sodium sulphate, filtering and concentration, afforded a crude mixture. Column chromatography on silica gel (10:1 Hexane:EtOAc) provided 7 g of product **9** (70%) as a yellow liquid. $[\alpha]_D^{20}$ = -48.1° (c 1.60, $CHCl_3$). IR: 2997, 1735, 1516, 1424, 1378 cm^{-1}. ^{1}H-NMR (δ): 4.89 (s, 1H, H-1); 4.59 (d, 1H, $J_{2,3}$=5.9 Hz, H-2); 4.43 (d, 1H, $J_{3,2}$= 5.9 Hz, H-3); 4.06 (dd, 1H, $J_{4,5}$= 6.1 Hz, $J_{4,5'}$= 7.5 Hz, H-4); 3.93 (dd, 1H, $J_{5,5'}$=12.5 Hz, $J_{5',4}$= 7.5 Hz, H-5'); 3.87 (dd, 1H, $J_{5,5'}$=12.5 Hz, $J_{5,4}$= 6.1 Hz, H-5); 3.31 (s, 3H, -OMe); 2.77 (s, 3H, -N(NO)CO$\underline{Me}$); 1.39 and 1.24 (2s, 6H, $C\underline{Me}_2$). ^{13}C-NMR (δ): 174.5 (-NCOMe); 111.3 ($\underline{C}Me_2$); 109.6 (C-1); 85.1, 82.5, 82.1 (C-2, C-3, C-4); 55.2 (OMe); 41.0 (C-5); 26.2 and 24.8 ($C\underline{Me}_2$); 22.4 (-COMe).

Methyl 5-deoxy-5-diazo-2,3-O-isopropylidene-β-D-ribofuranoside (3): A solution containing 2.36 g of **9** in 20 mL of tert-butyl methyl ether and 3.5 mL of methanol was treated with 10.6 mL of 40% KOH at 0°C, under a nitrogen atmosphere in the dark, with stirring. After 5 min., the crude mixture was diluted with water, the organic layer separated and the aq. layer extracted with ether twice. The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated in vacuo at 25° C to obtain 1.80 g of the pure product **3** as a yellow syrup (98%). (CAUTION: Unstabilized diazo compounds are potentially explosive. They are normaly used in solution. However, we observed no decomposition during manipulation of this compound or isolation by solvent removal). IR: 2947, 2080, 1457, 1382, 1104 cm^{-1}. ^{1}H-NMR (δ): 4.93 (s, 1H, H-1); 4.88 (d, $J_{4,5}$=7.3 Hz, H-4); 4.61 (d, $J_{2,3}$= 6.1 Hz, H-2); 4.53 (d, $J_{3,2}$= 6.1 Hz, H-3); 3.74 (d, $J_{5,4}$=7.3 Hz, H-5); 3.33 (s, 3H, -OMe); 1.44 and 1.27 (s, 6H, CMe_2). ^{13}C-NMR (δ): 112.6 ($\underline{C}Me_2$); 108.5 (C-1); 85.1, 84.6, 83.7 (C-2, C-3, C-4); 54.6 (OMe); 26.7 and 24.9 ($C\underline{Me}_2$).

Methyl 5-C-(6-keto-1,2:3,4-di-O-isopropylidene-D-galactopyranos-6-yl)-5-deoxy-2,3-O-isopropylidene-β-D-ribofuranoside (11): To a solution containing 1.7 g of **3** in 10 mL of diethyl ether, a solution containing 2.0 g of **10** in 10 mL of ether was added dropwise at 0°C. After 3 h of stirring, the reaction was complete. Column chromatography on silica gel (10:1 hexane:EtOAc) of the crude mixture provided 2.3 g of the ketone **11** as a white solid (67%). m.p. 102 °C. $[\alpha]_D^{20}$ = -132.3° (c 0.63, $CHCl_3$). IR: 2996, 1719, 1382, 1254 cm^{-1}. ^{1}H-NMR (δ): 5.59 (d, 1H, $J_{1,2}$=4.9 Hz, H-1); 4.89 (s, 1H, H-11); 4.66 (dd, 1H, $J_{8,7}$= 7.8 Hz, $J_{8,7'}$= 7.1 Hz, H-8); 4.58 (dd, 1H, $J_{3,4}$= 7.9 Hz, $J_{3,2}$= 2.2 Hz, H-3); 4.54 (s, 2H, H-9, H-10); 4.51(dd, 1H, $J_{4,5}$= 1.9 Hz, $J_{4,3}$= 7.9 Hz, H-4); 4.30 (dd, 1H, $J_{2,1}$=4.9 Hz, $J_{2,3}$= 2.2 Hz, H-2); 4.15 (d, 1H, $J_{5,4}$=1.9 Hz, H-5); 3.28 (s, 3H, -OMe); 2.93 (dd, 1H, $J_{7,8}$= 7.8 Hz, $J_{7,7'}$= 12.5 Hz, H-7); 2.90 (dd, 1H, $J_{7',8}$= 7.1 Hz, $J_{7,7'}$= 12.5 Hz, H-7'); 1.46, 1.44, 1.39, 1.29, 1.26 and 1.22 (6s, 18H, 3 $C\underline{Me}_2$).

^{13}C-NMR (δ): 196.0 (C-6); 112.2, 109.5 and 108.8 (3 $\underline{C}Me_2$); 109.6 (C-11); 96.3 (C-1); 85.2, 84.1 and 81.9 (C-8, C-9, C-10); 73.5, 72.2, 70.4 and 70.3 (C-2, C-3, C-4, C-5), 54.7 (OMe); 44.9 (C-7); 26.4, 25.8, 25.7, 24.9, 24.7 and 24.0 (3 $C\underline{Me_2}$). MS (m/z): 429 (M^+-15, 3); 337 (2); 279 (5); 229 (18); 171 (37); 141 (21); 97 (25); 85 (28); 71 (100). Elemental analysis: Calcd for $C_{21}H_{32}O_{10}$ 56.75% C; 7.21% H. Found 57.30% C; 7.20% H.

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-7-deoxy-L-*glycero*-L-*allo*-α-D-*galacto*-undecodialdo-1,5-pyranoside)-11,8-β-furanoside (12): A volume of 10 mL of 1 M Super-hydride in THF was added, under a nitrogen atmosphere at -78°C, to a solution containing 1.7 g of the ketone **11** in 15 mL of THF. After 30 min, the reduction was complete. Then, 20 mL of water was added to the crude mixture. The organic layer was separated and the aq. layer extracted with THF (3x1). The combined organic layers were dried over sodium sulphate, filtered and concentrated in vacuo. The crude obtained, 1.7 g, was the pure alcohol **12** (100%). Further purification by column chromatography on silica gel (4:1 hexane:EtOAc) provided the pure alcohol as a white solid. m. p. 95°C. $[\alpha]_D^{20}$= -67.1° (c 3.50, $CHCl_3$). IR: 3521, 2940, 1457, 1382, 1256 cm^{-1}. ^{1}H-NMR (δ): 5.57 (d, 1H, $J_{1,2}$=5.1 Hz, H-1); 4.91 (s, 1H, H-11); 4.58 (m, 3H, H-3, H-9, H-10); 4.43 (t, 1H, $J_{8,7}$= $J_{8,7'}$= 7.1 Hz, H-8); 4.31 (dd, 1H, $J_{2,1}$=5.1 Hz, $J_{2,3}$= 2.2 Hz, H-2); 4.28 (dd, 1H, $J_{4,5}$=1.8 Hz, $J_{4,3}$= 7.9 Hz, H-4); 4.03 (ddd, 1H, $J_{6,5}$= 4.9 Hz, $J_{6,7'}$= $J_{6,7}$= 7.3 Hz, H-6); 3.65 (dd, 1H, $J_{5,6}$=4.9 Hz, $J_{5,4}$= 1.8 Hz, H-5); 3.32 (s, 3H, -OMe); 1.85 (dd, 2H, $J_{7,8}$= 7.1 Hz, $J_{7,6}$= 7.3 Hz, H-7, H-7'); 1.49, 1.43, 1.30, 1.29 and 1.27 (5s, 18H, 3 $C\underline{Me_2}$). ^{13}C-NMR (δ): 112.2, 109.5, 108.6 (3 $\underline{C}Me_2$); 109.7 (C-11); 96.5 (C-1), 85.4, 84.1 and 83.9 (C-8, C-9, C-10); 72.4, 70.9, 70.4, 68.7 and 68.4 (C-2, C-3, C-4, C-5, C-6); 55.0 (OMe); 36.8 (C-7); 26.4, 25.8, 25.7, 24.9, 24.8 and 24.1 (3 $C\underline{Me_2}$). MS (m/z): 431 (M^+-15, 2); 399 (13); 341(4); 259 (26); 201 (33); 185 (22); 143 (36); 100 (92); 85 (70); 59 (100). Elemental analysis: Calcd for $C_{21}H_{34}O_{10}$ 56.50% C; 7.62% H. Found 56.53 % C; 7.81 % H

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-7-deoxy-L-*glycero*-L-*manno*-α-D-*galacto*-undecodialdo-1,5-pyranoside)-11,8-β-furanoside (13): A volume of 1 mL of 1 M zinc borohydride in THF was added, under a nitrogen atmosphere at -78°C, to a solution containing 0.1 g of the ketone **11** in 1 mL of THF. After 24 h the reduction was complete (8 h using hydride in excess). Then, 5 mL of water was added to the crude mixture. The organic layer was separated and the aq. layer extracted with THF (3x1). The combined organic layers were dried over sodium sulphate, filtered and concentrated in vacuo to obtain 0.1 g of the pure alcohol **13** (100%). $[\alpha]_D^{20}$= -12.0° (c 0.20, $CHCl_3$). IR: 3467, 2992, 1457, 1384, 1070 cm^{-1}. ^{1}H-NMR (δ): 5.50 (d, 1H, $J_{1,2}$=4.9 Hz, H-1); 4.92 (s, 1H, H-11); 4.61 (m, 3H, H-3, H-9, H-10); 4.47 (t, 1H, $J_{8,7}$= $J_{8,7'}$= 2.4 Hz, H-8); 4.33 (dd, 1H, $J_{2,1}$=4.9 Hz, $J_{2,3}$= 2.1 Hz, H-2); 4.19 (dd, 1H, $J_{4,5}$=1.8 Hz, $J_{4,3}$= 7.8 Hz, H-4); 4.05 (ddd, 1H, $J_{6,5}$= 7.0 Hz, $J_{6,7'}$= 7.5 Hz, $J_{6,7}$= 10.3 Hz, H-6); 3.55 (dd, 1H, $J_{5,6}$=7.0 Hz, $J_{5,4}$= 1.8 Hz, H-5); 3.30 (s, 3H, -OMe); 2.10 (ddd, 1H, $J_{7,8}$= 2.4 Hz, $J_{7,6}$= 10.3 Hz, $J_{7,7'}$= 14.5 Hz, H-7); 1.63 (ddd, 1H, $J_{7',8}$= 2.4 Hz, $J_{7',6}$= 7.5 Hz, $J_{7,7'}$= 14.5 Hz, H-7'); 1.50, 1.45, 1.42, 1.30 and 1.27 (5s, 18H, 3 $C\underline{Me_2}$). ^{13}C-NMR (δ): 112.5, 109.7, 108.5 (3 $\underline{C}Me_2$); 109.8 (C-11); 96.5 (C-1), 85.5, 84.6 and 84.1 (C-8, C-9, C-10); 71.0, 70.8, 70.4, 69.5 and 67.9 (C-2, C-3, C-4, C-5, C-6); 55.1 (OMe); 38.1 (C-7); 26.5, 26.0, 25.9, 25.1, 24.9 and 24.6 (3 $C\underline{Me_2}$). MS (m/z): 431 (M^+-15, 4); 399 (7); 341(10); 299 (8); 259 (13); 201 (18); 185 (26); 143 (31); 113 (60); 100 (100); 97 (36); 85 (68); 59 (90). Exact mass calcd for $C_{21}H_{34}O_{10}$: 446.2152. Found: 446.2183.

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-6-deoxy-L-*allo*-α-D-*galacto*-undecodialdo-1,5-pyranoside) -11,8-β-furanoside (15): A volume of 1 mL of 1 M Super-hydride in THF was added, under a nitrogen atmosphere, to a solution containing 0.1 g of the epoxide **14**[10] in 5 mL of anhydrous THF. The reaction mixture was then refluxed for 5 h, after which the crude mixture was concentrated and purified by column chromatography on silica-gel (5:1 hexane:EtOAc) to obtain 83 mg of product **15** (83%) and 10 mg of the alcohol **13** (10%). Product **15**: Colourless liquid. $[\alpha]_D^{20}$= -11.2° (c 2.24, $CHCl_3$). IR: 3467, 2992, 1384, 1070 cm^{-1}. ^{1}H-NMR (δ): 5.52 (d, 1H, $J_{1,2}$=5.0 Hz, H-1); 4.95 (s, 1H, H-11); 4.83 (d, 1H, $J_{9,10}$= 5.9 Hz, H-9); 4.61 (dd, 1H, $J_{3,4}$= 7.8 Hz, $J_{3,2}$= 2.4 Hz, H-3); 4.55 (d, 1H, $J_{10,9}$= 5.9 Hz, H-10); 4.30 (dd, 1H, $J_{2,1}$=5.0 Hz, $J_{2,3}$= 2.4 Hz, H-2); 4.23 (d, 1H, $J_{8,7}$= 3.4 Hz, H-8); 4.15-4.12 (m, 2H, H-4, H-5); 3.90 (dc, 1H, $J_{6,7}$= $J_{6',7}$= $J_{7,OH}$= 2.4 Hz, $J_{7,8}$= 3.4 Hz, H-7); 3.49 (w s, 1H, OH); 3.42 (s, 3H, -OMe); 1.95 (ddd, 1H, $J_{6,6'}$= 14.5 Hz, $J_{5,6}$= 10.5 Hz, $J_{6,7}$= 2.4 Hz, H-6); 1.59 (ddd, 1H, $J_{6,6'}$= 14.5 Hz, $J_{5,6'}$= 4.3 Hz, $J_{6',7}$= 2.4 Hz, H-6'); 1.55, 1.46, 1.45, 1.34, 1.33 and 1.30 (6s, 18H, 3 $C\underline{Me_2}$). ^{13}C-NMR (δ): 112.01, 109.16, 108.74 (3 $\underline{C}Me_2$); 110.26 (C-11); 96.46 (C-1), 91.36 (C-8); 85.87 (C-10); 80.44 (C-9); 73.60 (C-4); 70.99 (C-3); 70.59 (C-2); 68.55

(C-7); 64.28 (C-5); 55.85 (OMe); 33.52 (C-6); 26.39, 26.02, 25.97, 25.11, 24.70 and 24.41 (3 $C\underline{Me}_2$). MS (FAB) (m/z): 447 (M^+); 431 (43.8); 415 (81); 339 (25); 356 (10); 223 (19); 157 (23.7); 139 (24); 129 (35.6); 115 (35.6); 113 (49.4); 111 (32.8); 101 (26); 100 (37); 85 (72); 59 (100). Exact mass calcd for $C_{21}H_{34}O_{10}$ -15: 431.1917. Found: 431.1918.

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-6-O-acetyl-7-deoxy-L-*glycero*-L-*allo*-α-D-*galacto*-undecodialdo-1,5-pyranoside)-11,8-β-furanoside (16): A solution containing 0.5 g of **12** in 5 mL of pyridine was treated with 1 mL of acetic anhydride. After 4 h, the crude mixture was diluted with chloroform (10 mL) and poured over ice-water. The organic phase was separated and the aq. layer extracted with more chloroform (10 mL, 2x1). The combined organic layers were washed with 1 M ClH, saturated sodium hydrogen carbonate, and brine. Finally, the solution was dried over anhydrous magnesium sulphate, filtered and concentrated. The crude obtained (0.5 g) was the pure O-acetyl derivative **16** as a colourless liquid (91%). $[\alpha]_D^{20}$= -65.3° (c 3.75, $CHCl_3$). IR: 2992, 2936, 1734, 1383 cm^{-1}. ^{1}H-NMR (δ): 5.51 (d, 1H, $J_{1,2}$=5.0 Hz, H-1); 5.30 (dt, 1H, $J_{6,7}$= $J_{6,7'}$= 7.3 Hz, $J_{6,5}$= 5.9 Hz, H-6); 4.88 (s, 1H, H-11); 4.54 (s, 1H, H-9); 4.53 (dd, 1H, $J_{3,4}$= 7.7 Hz, $J_{3,2}$= 1.7 Hz, H-3); 4.31 (dd, 1H, $J_{8,7}$= 6.5 Hz, $J_{8,7'}$= 8.4 Hz, H-8); 4.25 (s, 1H, H-10); 4.21 (dd, 1H, $J_{4,5}$=1.6 Hz, $J_{4,3}$= 7.7 Hz, H-4); 4.17 (dd, 1H, $J_{2,1}$=5.0 Hz, $J_{2,3}$= 1.7 Hz, H-2); 3.86 (dd, 1H, $J_{5,4}$= 1.6 Hz, $J_{5,6}$= 5.9 Hz, H-5); 3.33 (s, 3H, -OMe); 2.03 (s, 3H, -OCOMe); 2.01(ddd, 1H, $J_{7,8}$= 6.5 Hz, $J_{7,6}$= 7.3 Hz, $J_{7,7'}$= 13 Hz, H-7); 1.84 (ddd, 1H, $J_{7',8}$= 8.4 Hz, $J_{7',6}$= 7.3 Hz, $J_{7,7'}$= 13 Hz, H-7'); 1.49, 1.41, 1.28, 1.27, and 1.26 (5s, 18H, 3 $C\underline{Me}_2$). ^{13}C-NMR (δ) : 170.5 (OCOMe); 112.2, 109.4, 108.4 ($\underline{C}Me_2$); 109.9 (C-11); 96.5 (C-1); 85.3, 84.1, 83.4 (C-8, C-9, C-10); 71.3, 71.1, 70.6, 70.0, 67.2 (C -2, C-3, C-4, C-5, C-6); 55.2 (OMe); 35.1 (C-7); 26.4, 25.9, 25.8, 24.9, 24.8, 24.3 (3 $C\underline{Me}_2$); 21.2 (OCOMe). MS (m/z): 473 (M^+-15, 9); 370 (4); 355 (9); 281 (6); 252 (11); 173 (27); 141 (27); 123 (26); 115 (34); 113 (95); 100 (100); 85 (67); 59 (67). Exact mass calcd for $C_{23}H_{35}O_{11}$: 488.2257. Found: 488.2271.

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-6-O-(S-methyldithiocarbonate)-7-deoxy-L-*glycero*-L-*allo*-α-D-*galacto*-undecodialdo-1,5-pyranoside)-11,8-β-furanoside (17): To a solution containing 0.414 g of **13** and 1 mg of imidazol in 5 mL of anhydrous THF, 0.06g of 60% sodium hydride was added under a nitrogen atmosphere at 0°C. After 5 min, 0.2 mL of carbon sulphide was added to the suspension and the crude mixture was stirred vigorously at 0°C for 30 min. Then, 0.1 mL of methyl iodide was added and, after 15 min. the suspension was diluted with 10 mL of ether. The organic phase was filtered and concentrated to obtain the entitled product, virtually pure. Further purification by column chromatography on silica gel (4:1 hexane:EtOAc) provided 0.338 g of the product **17** as a yellow syrup (68%). $[\alpha]_D^{20}$= -70.3° (c 3.00, $CHCl_3$). IR: 2995, 2943, 1381, 1212 cm^{-1}. ^{1}H-NMR (δ): 6.04 (dt, 1H, $J_{6,7'}$= $J_{6,5}$= 6.9 Hz, $J_{6,7}$= 5.0 Hz, H-6); 5.49 (d, 1H, $J_{1,2}$=5.1 Hz, H-1); 4.89 (s, 1H, H-11); 4.55 (dd, 1H, $J_{3,4}$= 7.8 Hz, $J_{3,2}$= 2.5 Hz, H-3); 4.54 (s, 2H, H-9, H-10); 4.32 (m, 2H, H-8, H-4); 4.26 (dd, 1H, $J_{2,1}$=5.1 Hz, $J_{2,3}$= 2.5 Hz, H-2); 4.14 (dd, 1H, $J_{5,4}$= 1.6 Hz, $J_{5,6}$= 6.9 Hz, H-5); 3.33 (s, 3H, -OMe); 2.51 (s, 3H, -OCSS$\underline{Me}$); 2.24 (ddd, 1H, $J_{7,8}$= 6.9 Hz, $J_{7,6}$= 5.0 Hz, $J_{7,7'}$= 14.5 Hz, H-7); 2.08 (ddd, 1H, $J_{7',8}$= 7.2 Hz, $J_{7',6}$= 6.9 Hz, $J_{7,7'}$= 14.5 Hz, H-7'); 1.50, 1.41, 1.28 and 1.26 (4s, 18H, 3 $C\underline{Me}_2$). ^{13}C-NMR (δ) : 187.1 (O$\underline{C}$SSMe); 112.3, 109.6, 108.7 ($\underline{C}Me_2$); 109.9 (C-11); 96.5 (C-1); 85.3, 84.2, 83.2 (C-8, C-9, C-10); 79.8 (C-6); 71.1, 71.0, 70.6, 66.9 (C -2, C-3, C-4, C-5); 55.4 (OMe); 34.5 (C-7); 26.4, 25.9, 25.8, 24.9, 24.5 (3 $C\underline{Me}_2$); 18.6 (OCSS$\underline{Me}$). MS (m/z): 521 (M^+-15, 4); 428 (1); 370 (9); 310 (13); 239 (21); 197 (29); 173 (66); 115 (63); 113 (88); 100 (44); 91 (52); 85 (71); 59 (100). Exact mass calcd for $C_{23}H_{35}O_{10}S_2$: 536.1749. Found: 536.1743.

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-6,7-dideoxy-6-chloro-L-*glycero*-L-*manno*-α-D-*galacto*-undecodialdo-1,5-pyranoside)-11,8-β-furanoside (18): A solution containing 170 mg of the alcohol **12** and 130 mg of triphenyl phosphine in 5 mL of carbon tetrachloride was refluxed for 48 h under a nitrogen atmosphere. After this time, TLC analysis showed the reaction to be complete. The solvent was then removed in vacuo. Further purification of the crude mixture by column chromatography on silica gel (4:1 hexane:EtOAc) provided 0.140 mg of the chloro derivative **18** as a white solid (79%). m. p. 46°C. $[\alpha]_D^{20}$= -23.6° (c 1.40, $CHCl_3$). IR: 2993, 1492, 1381 cm^{-1}. ^{1}H-NMR (δ): 5.47 (d, 1H, $J_{1,2}$=5.0 Hz, H-1); 4.93 (s, 1H, H-11); 4.62 (dd, 1H, $J_{3,4}$= 7.9 Hz, $J_{3,2}$= 2.2 Hz, H-3); 4.57 (s, 2H, H-9, H-10); 4.54 (dd, 1H, $J_{4,5}$= 1.4 Hz, $J_{4,3}$= 7.9 Hz, H-4); 4.50 (ddd, 1H, $J_{6,7}$= 12.1 Hz, $J_{6,5}$= 9.8 Hz, $J_{6,7'}$= 3.0 Hz, H-6); 4.32 (dd, 1H, $J_{8,7'}$= 11.1 Hz, $J_{8,7}$= 2.0 Hz, H-8); 4.26 (dd, 1H, $J_{2,1}$=5.0 Hz, $J_{2,3}$= 2.2 Hz, H-

2); **3.65** (dd, 1H, $J_{5,4}$= 1.4 Hz, $J_{5,6}$= 9.8 Hz, H-5); 3.45 (s, 3H, -OMe); 2.51 (ddd, 1H, $J_{7,8}$= 2.0 Hz, $J_{7,6}$= 12.1 Hz, $J_{7,7'}$= 14.5 Hz, H-7); 1.57 (ddd, 1H, $J_{7',8}$= 11.1 Hz, $J_{7',6}$= 3.0 Hz, $J_{7,7'}$= 14.5 Hz, H-7'); 1.49, 1.46, 1.36, 1.33, 1.29 and 1.28 (6s, 18H, 3 C<u>Me</u>$_2$). ^{13}C-NMR (δ) : 112.2, 109.3, 108.7 (<u>C</u>Me$_2$); 109.7 (C-11); 96.8 (C-1); 85.6, 84.3, 83.3 (C-8, C-9, C-10); 70.9, 70.7, 70.4 (C -2, C-3, C-4, C-5); 56.0 (C-6); 54.9 (OMe); 39.4 (C-7); 26.4, 25.9, 25.8, 24.9, 24.8, 24.5 (3 C<u>Me</u>$_2$). MS (m/z): 449 (M^+-15, 8); 451(M^++2 -15 , 3); 391 (9); 331 (38); 277 (11); 177 (14); 149 (10); 115 (34); 113 (54); 100 (55); 85 (56); 59 (100). Elemental analysis: Calcd for $C_{21}H_{33}O_9Cl$ 54.25% C; 7.15% H. Found 54.65 % C; 7.44 % H.

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-6,7-dideoxy-L-*ribo*-α-D-*galacto*-undecodialdo-1,5-pyranoside)-11,8-β-furanoside (19): To a solution containing 110 mg of the chloro derivative **18** in 5 mL of anhydrous THF, excess lithium aluminium hydride was added in one portion. The mixture was heated under a nitrogen atmosphere for 4 h. TLC analysis revealed depletion of the starting material after this time. Then, the suspension was cooled at 0°C and a 10% NaOH solution (5 mL) was added dropwise to destroy excess hydride. During the addition, a white solid was formed that was dissolved by adding of 15 mL of water. The aqueous phase was extracted with chloroform (10 mL, 3x1) and the combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated in vacuo to obtain 100 mg of the alkane derivative **19** as a white solid, that required no further purification (98%).m. p. 93°C. $[\alpha]_D^{20}$= -52.5 (c 1.6, $CHCl_3$). IR: 2995, 2945, 1380, 1211 cm^{-1}. ^{1}H-NMR (δ): 5.48 (d, 1H, $J_{1,2}$=5.1 Hz, H-1); 4.89 (s, 1H, H-11); 4.55 (dd, 1H, $J_{3,4}$= 7.9 Hz, $J_{3,2}$= 2.2 Hz, H-3); 4.51 (m, 2H, H-9, H-10); 4.25 (dd, 1H, $J_{2,1}$=5.1 Hz, $J_{2,3}$= 2.2 Hz, H-2); 4.17 (m, 1H, H-8); 4.08 (dd, 1H, $J_{4,5}$= 1.9 Hz, $J_{4,3}$= 7.9 Hz, H-4); 3.74 (m, 1H, H-5); 3.31 (s, 3H, -OMe); 1.85-1.51 (m, 4H, H-6, H-6', H-7, H-7'); 1.48, 1.43, 1.41, 1.31, 1.29 and 1.27 (6s, 18H, 3 C<u>Me</u>$_2$). ^{13}C-NMR (δ) : 112.5, 109.1, 108.3 (<u>C</u>Me$_2$); 109.5 (C-11); 96.6 (C-1); 86.4, 85.5, 84.2 (C-8, C-9, C-10); 72.8, 70.9, 70.5 (C-2, C-3, C-4); 66.3 (C-5); 56.0 (C-6); 55.0 (OMe); 30.5, 26.4 (C-6, C-7); 26.5, 26.0, 25.9, 25.0, 24.9, 24.5 (3 C<u>Me</u>$_2$). MS (m/z): 415 (M^+-15, 2); 357 (2); 297 (6); 254 (3); 229 (5); 171 (13); 141 (15); 113 (89); 100 (100); 85 (50); 59 (49). Elemental analysis: Calcd for $C_{21}H_{34}O_9$ 58.59% C; 7.91% H. Found 58.42 % C; 7.74 % H.

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-6-O-tosyl-7-deoxy-L-*glycero*-L-*allo*-α-D-*galacto*-undecodialdo-1,5-pyranoside)-11,8-β-furanoside (20): A solution containing 0.49 g of **12** in 5 mL of pyridine was treated with 0.5 g of p-toluensulphonyl chloride. After 48 h, the crude mixture was diluted with chloroform (10 mL) and poured over ice-water. The organic phase was separated and the aq. layer extracted with more chloroform (10 mL, 2x1). The combined organic layers were washed with 1 M ClH, saturated sodium hydrogen carbonate, and brine. Finally, the solution was dried over anhydrous magnesium sulphate, filtered and concentrated. The crude obtained (0.6 g) was purified by column chromatography on silica gel (5:1 hexane: EtOAc), which afforded 0.39 g of the pure O-tosyl derivative **20** as a white solid (59%). m. p. 61°C. $[\alpha]_D^{20}$= -63.4° (c 0.71, $CHCl_3$). IR: 2937, 2345, 1599, 1457, 1212 cm^{-1}. ^{1}H-NMR (δ): 7.78 (d, 2H, J= 8.2 Hz, H aromatic); 7.25 (d, 2H, H aromatic); 5.22 (d, 1H, $J_{1,2}$=5.0 Hz, H-1); 4.85 (s, 1H, H-11); 4.69 (ddd, 1H, $J_{6,7}$= 4.4 Hz, $J_{6,7'}$= 6.8 Hz, $J_{6,5}$= 7.5 Hz, H-6); 4.53 (dd, 1H, $J_{3,4}$= 7.9 Hz, $J_{3,2}$= 2.3 Hz, H-3); 4.49 (s, 2H, H-9, H-10); 4.32 (dd, 1H, $J_{4,5}$=1.7 Hz, $J_{4,3}$= 7.9 Hz, H-4); 4.22 (dd, 1H, $J_{8,7}$= 7.8 Hz, $J_{8,7'}$= 6.8 Hz, H-8); 4.19 (dd, 1H, $J_{2,1}$=5.0 Hz, $J_{2,3}$= 2.3 Hz, H-2); 4.02 (dd, 1H, $J_{5,4}$= 1.7 Hz, $J_{5,6}$= 7.5 Hz, H-5); 3.26 (s, 3H, -OMe); 2.38 (s, 3H, pMeAr); 2.17 (ddd, 1H, $J_{7,8}$= 7.8 Hz, $J_{7,6}$= 4.4 Hz, $J_{7,7'}$= 15.1 Hz, H-7); 2.02 (dt, 1H, $J_{7',8}$= $J_{7',6}$= 6.8 Hz, $J_{7,7'}$= 15.1 Hz, H-7'); 1.47, 1.39, 1.29 and 1.25 (4s, 18H, 3 C<u>Me</u>$_2$). ^{13}C-NMR (δ) : 144.1, 133.7 (C-1', C-4', Ar); 129.2, 128.1 (C-2', C-3', C-5', C-6', Ar); 112.2, 109.4, 108.7 (<u>C</u>Me$_2$); 109.7 (C-11); 96.1 (C-1); 85.2, 83.8, 82.6 (C-8, C-9, C-10); 79.1 (C-6); 70.8, 70.4, 70.3, 66.9 (C -2, C-3, C-4, C-5); 55.1 (OMe); 35.3 (C-7); 26.4, 25.72, 25.70, 24.9, 24.8, 24.4 (3 C<u>Me</u>$_2$); 21.5 (Me, Ar). MS (m/z): 585 (M^+-15, 4); 467 (6); 396 (2); 310 (4); 295 (9); 252 (6); 213 (6); 173 (22); 169 (14); 155 (52); 141 (30); 123 (21); 113 (67); 100 (87); 91 (86); 85 (78); 59 (100). Elemental analysis: Calcd for $C_{28}H_{40}O_{12}S$ 56.00% C; 6.66% H. Found 56.36 % C; 6.66 % H.

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-6-azido-6,7-dideoxy-L-*glycero*-L-*manno*-α-D-*galacto*-undecodialdo-1,5-pyranoside)-11,8-β-furanoside (21): A solution containing 0.2 g of the tosyl derivative **20** in 5 mL of DMF was treated with 0.2 g of sodium azide and refluxed for 16 h. After this time, TLC analysis

revealed depletion of the starting C-disaccharide. The crude mixture was then cooled and diluted with chloroform (20 mL). The organic phase was washed with water three times and the aq. layer extracted with more chloroform (10 mL, 2x1). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated. Purification by column chromatography on silica gel (4:1 hexane: EtOAc) provided 80 mg of the pure azido derivative **21** as a colourless liquid (51%). $[\alpha]_D^{20}$ = -40.5° (c 1.85, $CHCl_3$). IR: 2997, 2118, 1456, 1381, 1252 cm^{-1}. ^{1}H-NMR (δ): 5.47 (d, 1H, $J_{1,2}$=5.0 Hz, H-1); 4.94 (s, 1H, H-11); 4.62 (dd, 1H, $J_{3,4}$= 7.9 Hz, $J_{3,2}$= 2.4 Hz, H-3); 4.57, 4.56 (2s, 2H, H-9, H-10); 4.42 (dd, 1H, $J_{8,7}$= 12.1 Hz, $J_{8,7'}$= 3.4 Hz, H-8); 4.36 (dd, 1H, $J_{4,5}$=1.7 Hz, $J_{4,3}$= 7.9 Hz, H-4); 4.28 (dd, 1H, $J_{2,1}$=5.0 Hz, $J_{2,3}$= 2.4 Hz, H-2); 3.86 (ddd, 1H, $J_{6,7}$= 2.3 Hz, $J_{6,7'}$= 11.5 Hz, $J_{6,5}$= 9.7 Hz, H-6); 3.46 (dd, 1H, $J_{5,4}$= 1.7 Hz, $J_{5,6}$= 9.7 Hz, H-5); 3.30 (s, 3H, -OMe); 2.17 (ddd, 1H, $J_{7,8}$= 12.1 Hz, $J_{7,6}$= 2.3 Hz, $J_{7,7'}$= 14.4 Hz, H-7); 1.57 (ddd, 1H, $J_{7',8}$= 3.4 Hz, $J_{7',6}$= 11.5 Hz, $J_{7,7'}$= 14.4 Hz, H-7'); 1.46, 1.38, 1.34 and 1.28 (4s, 18H, 3 $C\underline{Me}_2$). ^{13}C-NMR (δ) : 112.2, 109.4, 108.6 ($\underline{C}Me_2$); 109.8 (C-11); 96.5 (C-1); 85.5, 84.4, 83.4 (C-8, C-9, C-10); 70.85, 70.82, 70.4, 69.3 (C-2, C-3, C-4, C-5); 58.6 (C-6); 55.1 (OMe); 36.6 (C-7); 26.4, 25.9, 25.8, 24.9, 24.8, 24.5 (3 $C\underline{Me}_2$). MS (m/z): 456 (M^+-15, 6); 428 (5); 396 (5); 354 (11);279 (40); 278 (76); 236 (37); 171 (45); 113 (43); 100 (65); 85 (51); 71 (100); 59 (64). Exact mass calcd for $C_{21}H_{33}O_9N_3$ -15: 456.1982. Found: 456.1974.

Methyl (1,2:3,4:9,10-tri-O-isopropylidene-6-amino-6,7-dideoxy-L-*glycero*-L-*manno*-α-D-*galacto*-undecodialdo-1,5-pyranoside)-11,8-β-furanoside (22): To a solution containing 80 mg of the azido derivative **21** in 3 mL of anhydrous THF, 0.1 g of lithium aluminium hydride was added in small portions. The suspension was stirred under a nitrogen atmosphere at r.t. for 5 hours. After this time, 5 mL of a 10% aqueous solution of KOH was added dropwise to destroy excess hydride and the crude mixture was extracted with dichloromethane (3x1, 5 mL). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated in vacuo to obtain 70 mg of the pure amino compound **22** as a brown solid that required no further purification (93%). m. p. 78°C. $[\alpha]_D^{20}$ = -76.0° (c 0.50, $CHCl_3$). IR: 3398, 2997, 1455, 1381, 1255 cm^{-1}. ^{1}H-NMR (δ): 5.49 (d, 1H, $J_{1,2}$=5.1 Hz, H-1); 4.91 (s, 1H, H-11); 4.58 (dd, 1H, $J_{3,4}$= 7.9 Hz, $J_{3,2}$= 2.4 Hz, H-3); 4.57 (s, 2H, H-9, H-10); 4.45 (dd, 1H, $J_{8,7}$= 11.5 Hz, $J_{8,7'}$= 3.6 Hz, H-8); 4.39 (dd, 1H, $J_{4,5}$=1.9 Hz, $J_{4,3}$= 7.9 Hz, H-4); 4.27 (dd, 1H, $J_{2,1}$=5.1 Hz, $J_{2,3}$= 2.4 Hz, H-2); 3.36 (dd, 1H, $J_{5,4}$= 1.9 Hz, $J_{5,6}$= 8.2 Hz, H-5); 3.30 (s, 3H, -OMe); 3.19 (ddd, 1H, $J_{6,7}$= 2.0 Hz, $J_{6,7'}$= 11.0 Hz, $J_{6,5}$= 8.2 Hz, H-6); 2.05 (ddd, 1H, $J_{7,8}$= 11.5 Hz, $J_{7,6}$= 2.0 Hz, $J_{7,7'}$= 14.0 Hz, H-7); 1.60 (w s, 2H, -NH_2); 1.38 (ddd, 1H, $J_{7',8}$= 3.6 Hz, $J_{7',6}$= 11.0 Hz, $J_{7,7'}$= 14.0 Hz, H-7'); 1.47, 1.45, 1.39, 1.32 and 1.28 (5s, 18H, 3 $C\underline{Me}_2$). ^{13}C-NMR (δ) : 112.1, 109.2, 108.4 ($\underline{C}Me_2$); 109.6 (C-11); 96.6 (C-1); 85.6, 84.8, 83.9 (C-8, C-9, C-10); 71.2, 70.9, 70.8, 70.4 (C -2, C-3, C-4, C-5); 55.0 (OMe); 48.4 (C-6); 38.9 (C-7); 26.5, 26.0, 25.9, 25.0, 24.9, 24.6 (3 $C\underline{Me}_2$). MS (m/z): 430 (M^+-15, 3); 356 (3); 258 (4); 216 (36); 185 (10); 184 (100); 126 (8); 100 (14); 86 (26); 85 (23); 71 (14); 59 (23). Elemental analysis: Calcd for $C_{21}H_{35}O_9N$ 56.63% C; 7.86% H; 3.14% N. Found 56.86% C; 8.02% H; 2.89% N.

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20. The unknown product had the following ^{1}H and ^{13}C-NMR spectra (δ): 5.51 (d, 1H, $J_{1,2}$=5.1 Hz, H-1); 5.38 (dt, 1H, $J_{6,7'}$= $J_{6,5}$= 6.9 Hz, $J_{6,7}$= 5.0 Hz, H-6); 4.89 (s, 1H, H-11); 4.55 (dd, 1H, $J_{3,4}$= 7.8 Hz, $J_{3,2}$= 2.5 Hz, H-3); 4.54 (s, 1H, H-10); 4.35-4.25 (m, 3H, H-8, H-9, H-4); 4.29 (dd, 1H, $J_{2,1}$=5.1 Hz, $J_{2,3}$= 2.5 Hz, H-2); 3.90 (dd, 1H, $J_{5,4}$= 1.6 Hz, $J_{5,6}$= 6.9 Hz, H-5); 3.35 (s, 3H, -OMe); 2.31 (s, 3H, SMe); 2.21-1.80 (m, 2H, H-7, H-7'); 1.50, 1.41, 1.28 and 1.26 (4s, 18H, 3 CMe_2). 172; 112.5, 109.6, 108.7 (CMe_2); 110.1 (C-11); 96.5 (C-1); 85.3, 84.5, 83.1 (C-8, C-9, C-10); 74.2, 71.5, 70.5, 68.6, 66.9 (C-2, C-3, C-4, C-5, C-6); 55.4 (OMe); 34.5 (C-7); 26.4, 25.9, 25.8, 24.9, 24.5 (3 CMe_2); 18.6 (SMe). Alkaline hydrolysis of this product yielded the starting alcohol **12**.
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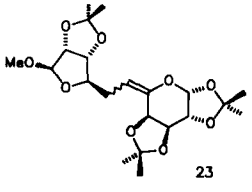
23. The moderate yield of the azido derivative **21** from the tosylated product **20** was a result of the formation of the corresponding elimination products **23** and **24**. The structure of the alkene **24** was demonstrated by comparison with data reported by J. A. Secrist III and S. R. Wu (*J. Org. Chem.*, **1979**, *44*, 1434).



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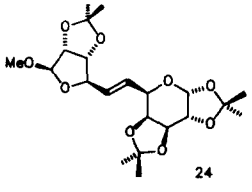

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